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CLINICAL GUIDELINE

Platelet Transfusion: A Clinical Practice Guideline From the AABB

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Background: Platelet transfusions are administered to prevent or treat bleeding in patients with quantitative or qualitative platelet disorders. The AABB (formerly, the American Association of Blood Banks) developed this guideline on appropriate use of platelet transfusion in adult patients.

Methods: These guidelines are based on a systematic review of randomized, clinical trials and observational studies that reported clinical outcomes on patients receiving prophylactic or therapeutic platelet transfusions. A literature search from 1900 to September 2014 with no language restrictions was done. Examined outcomes included all-cause mortality, bleeding-related mortality, bleeding, and number of platelet units transfused. An expert panel reviewed the data and developed recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

Recommendation 1: The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia. The AABB recommends transfusing hospitalized adult patients with a platelet count of 10×10^9 cells/L or less to reduce the risk for spontaneous bleeding. The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective (Grade: strong recommendation; moderate-quality evidence).

Recommendation 2: The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count less than 20×10^9 cells/L (Grade: weak recommendation; low-quality evidence).

Recommendation 3: The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than 50×10^9 cells/L (Grade: weak recommendation; very low-quality evidence).

Recommendation 4: The AABB suggests prophylactic platelet transfusion for patients having major elective nonneuraxial surgery with a platelet count less than 50×10^9 cells/L (Grade: weak recommendation; very low-quality evidence).

Recommendation 5: The AABB recommends against routine prophylactic platelet transfusion for patients who are nonthrombocytopenic and have cardiac surgery with cardiopulmonary bypass (CPB). The AABB suggests platelet transfusion for patients having CPB who exhibit perioperative bleeding with thrombocytopenia and/or evidence of platelet dysfunction (Grade: weak recommendation; very low-quality evidence).

Recommendation 6: The AABB cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous) (Grade: uncertain recommendation; very low-quality evidence).

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Approximately 2.2 million platelet doses are transfused annually in the United States (1). A high proportion of these platelet units are transfused prophylactically to reduce the risk for spontaneous bleeding in patients who are thrombocytopenic after chemotherapy or hematopoietic progenitor cell transplantation (HPCT) (1–3). Unlike other blood components, platelets must be stored at room temperature, limiting the shelf life of platelet units to only 5 days because of the risk for bacterial growth during storage. Therefore, maintaining hospital platelet inventories is logistically difficult and highly resource-intensive (4, 5). Platelet transfusion is associated with several risks to the recipient (Table 1), including allergic reactions and febrile nonhemolytic reactions. Sepsis from a bacterially contaminated platelet unit represents the most frequent infectious complication from any blood product today (8). In any situation where platelet transfusion is being considered, these risks must be balanced against the potential clinical benefits.

Guideline Focus

These guidelines were designed to provide pragmatic recommendations, on the basis of the best available published evidence, about when platelet transfusion may be appropriate in adult patients. For several common clinical situations, we attempted to identify a platelet count threshold below which platelet transfusion may improve hemostasis and above which platelet transfusion is unlikely to benefit the patient. We did not attempt to address all clinical situations in which platelets may be transfused, and these guidelines are not intended to serve as standards. Clinical judgment, and not a specific platelet count threshold, is paramount in deciding whether to transfuse platelets.

Target Population

These guidelines provide advice for adult patients who are candidates for platelet transfusion.

Table 1. Approximate Per-Unit Risks for Platelet Transfusion in the United States

Adverse Event	Approximate Risk per Platelet Transfusion	Reference
Febrile reaction	1/14	6
Allergic reaction	1/50	7
Bacterial sepsis	1/75 000	8
TRALI*	1/138 000	9
HBV infection	1/2 652 580	Personal communication†
HCV infection	1/3 315 729	Personal communication†
HIV infection	0 (95% CI, 0 to 1/1 461 888)	Personal communication†

HBV = hepatitis B virus; HCV = hepatitis C virus; TRALI = transfusion-related acute lung injury.
* The overall risk for TRALI from all plasma-containing blood products is currently estimated to be approximately 1/10 000 (10).
† Notari E, Dodd R, Stramer S. Personal communication.

GUIDELINE DEVELOPMENT PROCESS

The AABB commissioned and funded the development of these guidelines.

Panel Composition

A panel of 21 experts was convened. Fifteen participants were members of the Clinical Transfusion Medicine Committee of the AABB, all of whom were hematologists or pathologists with expertise in transfusion medicine. Five additional panel members included a neurosurgeon, a cardiac surgeon, a critical care specialist, an anesthesiologist, and a hematologist, representing the American Association of Neurological Surgeons, the Society of Thoracic Surgeons, the Society of Critical Care Medicine, the American Society of Anesthesiologists, and the American Society of Hematology, respectively. The final panel member was a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist. Committee members had no substantial conflicts of interest as defined by the AABB conflict of interest policy. Pursuant to the policy, individual members were required to disclose actual and apparent financial, professional, or personal conflicts (Appendix Table 1, available at www.annals.org).

Systematic Review of the Evidence

The guidelines were developed on the basis of a recent systematic review of the literature on platelet transfusions, published separately (11). The search strategy is provided in Appendix Table 2 (available at www.annals.org). We searched PubMed from 1946 to the first week of April 2013, and the Cochrane Central Register of Controlled Trials and Web of Science from 1900 to the first week of April 2013 (1024 studies identified). An updated search of these databases was done from the first week of April 2013 to the first week of September 2014. Randomized, controlled trials (RCTs) and observational studies (prospective or retrospective cohort studies, case–control studies, and those with no control group) were eligible for inclusion. Outcomes of interest included all-cause mortality, bleeding-related mortality, bleeding, and number of platelet units transfused. Although all observational studies meeting the inclusion criteria were reviewed, data from observational studies were not used when more than 2 RCTs addressed a particular question. There were no language restrictions. After exclusions, 17 RCTs and 53 observational studies were included in the final systematic review. Only 1 relevant observational study (12) from the updated search was identified, and evidence from this study did not change our GRADE judgments of evidence quality or recommendation strength.

Grading of Evidence

The GRADE method was used to assess the quality of the evidence and determine the strength of recommendations (13, 14). The recommendations were developed by consensus at an in-person panel meeting. Panel member judgments on 4 GRADE factors (quality of evidence, balance between the intervention's benefits and harms, resource use, patient values, and preferences) and ratings of the strength of recommendations were validated using an online survey tool 1 week after the meeting.

Definitions

In this guideline, a platelet unit refers to 1 apheresis platelet unit or a pool of 4 to 6 whole blood-derived platelet concentrates, typically containing 3 to 4 × 10^{11} platelets. Thrombocytopenia refers to a platelet count below the lower limit of the normal range used by the laboratory performing the count. Seven platelet trials included in the systematic review (15–21) used a variation of the World Health Organization scale (22) to assess patient bleeding outcomes (23). A summary of the modified World Health Organization scale is provided in Table 2.

CLINICAL RECOMMENDATIONS

Clinical Setting 1: Hospitalized Adult Patients With Therapy-Induced Hypoproliferative Thrombocytopenia

Recommendations

Recommendation 1: The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in adult patients with therapy-induced hypoproliferative thrombocytopenia.

The AABB recommends transfusing hospitalized adult patients with a platelet count of 10 × 10^9 cells/L or less to reduce the risk for spontaneous bleeding.

The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective.

Quality of evidence: moderate; strength of recommendation: strong.

Evidence Summary

Three RCTs (n = 1047) compared bleeding outcomes in hospitalized patients with radiation and/or chemotherapy-induced hypoproliferative thrombocytopenia assigned to receive or not receive prophylactic platelet transfusions (Appendix Table 3, available at

Table 2. Summary of the Modified WHO Bleeding Scale*

WHO Bleeding Grade	Examples
Grade 1	Oropharyngeal bleeding ≤30 min in 24 h Epistaxis ≤30 min in previous 24 h Petechiae of oral mucosa or skin Purpura ≤1 inch in diameter Spontaneous hematoma in soft tissue or muscle Positive stool occult blood test Microscopic hematuria or hemoglobinuria Abnormal vaginal bleeding (spotting)
Grade 2	Epistaxis >30 min in 24 h Purpura >1 inch in diameter Joint bleeding Melanotic stool Hematemesis Gross/visible hematuria Abnormal vaginal bleeding (more than spotting) Hemoptysis Visible blood in body cavity fluid Retinal bleeding without visual impairment Bleeding at invasive sites
Grade 3	Bleeding requiring red blood cell transfusion over routine transfusion needs Bleeding associated with moderate hemodynamic instability
Grade 4	Bleeding associated with severe hemodynamic instability Fatal bleeding CNS bleeding on imaging study with or without dysfunction

CNS = central nervous system; WHO = World Health Organization.
* From references 18 and 22.

www.annals.org) (19, 21, 24, 25). All patients had hematologic malignancy treated with chemotherapy or HPCT. Prophylactic platelet transfusions were found to significantly reduce the risk for spontaneous grade 2 or greater bleeding (odds ratio [OR], 0.53 [95% CI, 0.32 to 0.87]). Most bleeding events were classified as grade 2. In the 2 largest trials (19, 21), grade 2 or greater bleeding in patients assigned to the group that did not receive prophylaxis occurred more frequently among patients receiving chemotherapy for acute leukemia compared with autologous HPCT recipients (58% vs. 47% [19, 25]; 51% vs. 28% [21]).

The threshold platelet count at which platelets should be transfused prophylactically to reduce the bleeding risk in hospitalized patients with therapy-induced hypoproliferative thrombocytopenia was examined in 4 RCTs (n = 658) (**Appendix Table 4**, available at www.annals.org). Patients were assigned to receive prophylactic platelet transfusion for a morning platelet count less than 10×10^9 versus 20×10^9 cells/L (26–28) or 30×10^9 cells/L (15). A greater platelet count threshold (20×10^9 or 30×10^9 cells/L) was not associated with a significantly lower incidence of grade 2 or greater bleeding (OR, 0.74 [CI, 0.41 to 1.35]) or bleeding-related mortality (OR, 0.37 [CI, 0.02 to 9.22]). The total number of days with bleeding was greater in the 10×10^9 cells/L threshold group. The 10×10^9 cells/L threshold was associated with lower platelet usage and fewer transfusion reactions.

Four RCTs (n = 1132) (**Appendix Table 5**, available at www.annals.org) examined whether prophylactic transfusion of low-dose platelets (defined as approximately one half of the standard dose of 3 to 4×10^{11} platelets) would provide hemostasis equal to that of standard-dose platelets in patients with therapy-induced hypoproliferative thrombocytopenia (16, 18, 20, 29). There was no difference in grade 2 or greater bleeding in recipients of standard-dose versus low-dose platelets (OR, 0.91 [CI, 0.70 to 1.19]). High-dose platelets (approximately double the standard dose) were compared with standard-dose platelets in 2 RCTs (n = 951) (**Appendix Table 6**, available at www.annals.org) (17, 18). Prophylactic transfusion of high-dose platelets did not reduce the risk for bleeding compared with standard-dose platelets (OR, 1.05 [CI, 0.79 to 1.40]).

Rationale for Recommendations

Before routine platelet prophylaxis was introduced, severe hemorrhage was a common cause of death among patients receiving high-dose chemotherapy (30, 31). Today, severe hemorrhage is rarely encountered in this setting. The original studies of platelet prophylaxis were done decades ago, and both chemotherapy and supportive care for patients with cancer have changed dramatically over time. Therefore, the randomized trials reported by Wandt (21) and Stanworth (19) and their colleagues were designed to answer the question of whether a prophylactic as compared with a therapeutic platelet transfusion strategy provides benefit in contemporary cancer care. In the study by Wandt and colleagues (21), grade 2 or greater bleeding was seen in 42% of patients assigned to receive therapeutic platelet transfusions only, compared with 19% of patients assigned to receive prophylactic platelet transfusion for a platelet count of 10×10^9 cells/L or less ($P < 0.001$). In the subset of patients with acute myelogenous leukemia, intracerebral bleeding (grade 4) occurred significantly more often in the therapeutic platelet group compared with the prophylactic platelet group (7% vs. 2%; $P = 0.010$). In 11 of 13 cases, intracerebral bleeding was detectable on CT scan, but there were no apparent clinical sequelae. Computed tomography scans to investigate new headache or other cerebral symptoms were required only for patients in the therapeutic platelet group, so subclinical intracerebral hemorrhage in the prophylactic platelet group may have been underdiagnosed. In the Trial of Prophylactic Platelets (19), subtler differences in bleeding outcomes were seen between the study groups. Grade 2 or greater bleeding occurred in 50% of patients assigned to the group that did not receive prophylaxis, compared with 43% of patients receiving prophylactic platelet transfusions ($P = 0.06$ for noninferiority). In patients receiving chemotherapy (not HPCT), there was a significant increase in grade 2 or greater bleeding in the group that did not receive prophylaxis (risk difference, 20% [90% CI, 7.9% to 32.2%]). There was also a nonsignificant trend toward increased grade 3 and 4 bleeding for all patients in the group that did not receive prophylaxis. Thus, both the Wandt trial and the

Trial of Prophylactic Platelets support the continued use of prophylactic platelet transfusions in patients with therapy-induced hypoproliferative thrombocytopenia. In this population, we recommend prophylactic platelet transfusion for a morning platelet count of 10×10^9 cells/L or less. Some data suggest that the risk for spontaneous bleeding does not increase until the platelet count decreases to less than approximately 6×10^9 cells/L (18, 32), but the 10×10^9 cells/L platelet count threshold seems to provide a good balance of safety and practicality, and the accuracy of extremely low platelet count measurements is questionable (33, 34). The recommendation for prophylactic platelet transfusion based on a 10×10^9 cells/L platelet count threshold applies to hospitalized patients only. Prophylactic platelet transfusion based on a more liberal (greater) platelet count threshold may be appropriate when treating outpatients, for reasons of practicality (fewer clinic visits).

The Platelet Dose study (18) established that patients receiving low-dose prophylactic platelet transfusions for a morning platelet count of 10×10^9 cells/L or less had the same bleeding risk as patients receiving standard- or high-dose platelets. However, low-dose platelets did need to be transfused more often because they provided a lower increment. It is safe to provide low-dose platelet prophylaxis to patients with therapy-induced hypoproliferative thrombocytopenia, either routinely or as a temporary maneuver in times of platelet shortage. High-dose prophylactic platelet transfusions have not been shown to provide additional benefit, so they are not recommended as routine therapy for inpatients.

Clinical Setting 2: Adult Patients Having Minor Invasive Procedures

Recommendations

Recommendation 2: The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count less than 20×10^9 cells/L.

Quality of evidence: low; strength of recommendation: weak.

Recommendation 3: The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than 50×10^9 cells/L.

Quality of evidence: very low; strength of recommendation: weak.

Evidence Summary

Eight observational studies of central venous catheter (CVC) placement in the setting of thrombocytopenia were identified (n = 1311 cannulations) (**Appendix Table 7**, available at www.annals.org) (12, 35–41). Many patients had acute leukemia or were having HPCT; however, patients with renal failure, critically ill patients, and others were included. Overall bleeding complication rates were low, ranging from 0% to 9% of catheter placements. The largest series of nontunneled CVC placements included 604 cannulations in 193 consecutive patients (41). In multivariate analysis, only patients with preprocedure platelet counts less than 20×10^9 cells/L (n = 93) were at increased risk for bleeding compared with patients with platelet counts greater than 100×10^9 cells/L. Ninety-six percent of bleeding events were grade 1, and the remaining 4% of bleeding events were grade 2, requiring only local compression. In another single-center study, bleeding outcomes were reported on 3170 tunneled CVCs placed under ultrasonography guidance in 2512 patients (38). No bleeding complications occurred in the 344 CVC placements performed with a preprocedure platelet count less than 50×10^9 cells/L, including 42 cases with a platelet count less than 25×10^9 cells/L.

Data from 7 observational studies of children or adults who were thrombocytopenic and had diagnostic or therapeutic lumbar puncture (LP) were evaluated (**Appendix Table 8**, available at www.annals.org) (42–49). The largest was a single-center observational study of 5223 LPs in 956 pediatric patients with acute lymphoblastic leukemia (45). A total of 199 LPs were performed with platelet counts of 20×10^9 cells/L or less, and 742 LPs were performed with platelet counts between 21×10^9 cells/L and 50×10^9 cells/L. No bleeding complications were seen, regardless of platelet count. The upper 95% CI for serious complications was 1.75% for patients with platelet counts of 20×10^9 cells/L or less and 0.37% for patients with platelet counts of 50×10^9 cells/L or less. Traumatic LP (>500 red blood cells per high power field) occurred in 10.5% of procedures but was not associated with adverse clinical outcomes. The largest reported series in adults included 195 diagnostic or therapeutic LPs in 66 adult patients with acute leukemia and thrombocytopenia (49). Patients were prophylactically transfused with platelets for a preprocedure platelet count less than 20×10^9 cells/L. Thirty-five LPs were performed in patients with platelet counts of 20×10^9 to 30×10^9 cells/L, and 40 were done with platelet counts of 31×10^9 to 50×10^9 cells/L. No bleeding complications were seen.

Rationale for Recommendations

Serious bleeding complications after CVC placement are rare, and when they occur, they are often unrelated to the platelet count (such as accidental arterial puncture). In aggregate, the existing data support the use of a 20×10^9 cells/L platelet count threshold for CVC placement. The reported studies included patients with a wide range of primary diagnoses; this recommendation is intended to be broadly applicable to adult patients with hypoproliferative thrombocytopenia.

Bleeding complications are rare with LPs, but hemorrhage anywhere in the central nervous system has the potential to cause devastating neurologic sequelae. In the absence of better published data supporting the safety of a lower threshold in adult patients, a fairly liberal platelet count threshold for LPs (that is, 50×10^9 cells/L) seems prudent. The 50×10^9 cells/L threshold is intended for simple diagnostic or therapeutic LPs

only. Despite a lack of supportive data, a greater platelet count is often recommended for other procedures, such as epidural anesthesia (50, 51).

Clinical Setting 3: Adult Patients Having Major Elective Nonneuraxial Surgery

Recommendations

Recommendation 4: The AABB suggests prophylactic platelet transfusion for patients having major elective nonneuraxial surgery with a platelet count less than 50×10^9 cells/L.

Quality of evidence: very low; strength of recommendation: weak.

Recommendation 5: The AABB recommends against routine prophylactic platelet transfusion for patients who are nonthrombocytopenic and have cardiac surgery with cardiopulmonary bypass (CPB). The AABB suggests platelet transfusion for patients having CPB who exhibit perioperative bleeding with thrombocytopenia and/or with evidence of platelet dysfunction.

Quality of evidence: very low; strength of recommendation: weak.

Evidence Summary

In 1 series (Appendix Table 9, available at www.annals.org) (52), 95 patients with acute leukemia and thrombocytopenia had 167 invasive procedures, including 29 major surgeries (such as thoracotomy) and 24 moderately invasive procedures (such as arteriovenous fistula construction). Platelet prophylaxis was given before the 130 procedures in which the preoperative platelet count was less than 50×10^9 cells/L. The median postoperative platelet count in these cases was 56×10^9 cells/L. Intraoperative blood loss greater than 500 mL occurred in only 7% of all operations, and there were no deaths due to bleeding. Preoperative platelet count was not significantly associated with intraoperative or postoperative bleeding.

In a meta-analysis of 6 RCTs and a single pilot study conducted during the licensure of aprotinin, adverse outcome data were compared between cardiac surgical patients who received (n = 284) or did not receive (n = 1436) perioperative platelet transfusions (Appendix Table 10, available at www.annals.org) (53). Platelet transfusion was identified as an independent predictor of adverse outcomes, including mortality (OR, 4.76 [CI, 1.65 to 13.73]). It is possible that platelet transfusion served at least in part as a surrogate marker of sicker patients in this analysis, rather than as a direct cause of adverse outcomes (that is, confounding by indication).

Rationale for Recommendations

The consensus opinion of the panel is that platelet counts of 50×10^9 cells/L and greater are safe for major nonneuraxial surgery. There is no evidence of increased perioperative bleeding risk in thrombocytopenic patients with platelet counts greater than 50×10^9 cells/L. We recommend that platelet transfusion be withheld in nonbleeding surgical patients when the platelet count is greater than 50×10^9 cells/L and there is no evidence of coagulopathy. In contrast, we suggest that platelet transfusion should be considered in cardiac surgical patients with perioperative bleeding and thrombocytopenia (see the Definitions section) and/or suspected qualitative platelet abnormalities, which often result from exposure of platelets to the CPB circuit (54). Platelet transfusions are often administered to nonbleeding cardiac surgical patients (55). There are no data supporting this practice, and it should be discouraged.

Clinical Setting 4: Adult Patients Receiving Antiplatelet Therapy Who Have Intracranial Hemorrhage (Traumatic or Spontaneous)

Recommendations

Recommendation 6: The AABB cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous).

Quality of evidence: very low; strength of recommendation: uncertain.

Evidence Summary

Five observational studies (n = 635) examined clinical outcomes among patients receiving antiplatelet agents who present with traumatic brain injury (Appendix Table 11, available at www.annals.org) (56). One study reported a greater mortality rate for patients who received transfusions with platelets (relative risk, 2.4 [CI, 1.2 to 4.9]) (57), and a second study reported a lower mortality rate for patients receiving platelets (relative risk, 0.21 [CI, 0.05 to 0.95]) (58). Three studies showed no significant effect on mortality rates when patients received transfusions with platelets (59–61). One additional observational study (n = 88) reported that patients with traumatic brain injury and moderate thrombocytopenia (50×10^9 to 107×10^9 cells/L) who were transfused with platelets had poorer survival than those who were not transfused with platelets (62). In all of these studies, it was not possible to establish a causal relationship between platelet transfusion and clinical outcomes, and confounding by indication was possible.

Rationale for Recommendations

In patients with intracerebral hemorrhage who are receiving antiplatelet agents, the decision to transfuse platelets requires an individual clinical decision based on various clinical factors, including the size of the bleeding and the patient's level of consciousness. For surgeries involving the central nervous system, platelets are conventionally transfused prophylactically for a preprocedure platelet count less than 80×10^9 to 100×10^9 cells/L, although only low-quality data supporting this threshold are available.

DISCUSSION

A large proportion of platelet transfusions are administered prophylactically to reduce the risk for spon-

taneous hemorrhage in patients receiving chemotherapy or HPCT (1–3). With data available from several RCTs (15–21, 24–29, 63), there is now a solid understanding of the role of platelet transfusions in this specific setting. Platelet prophylaxis, as compared with a therapeutic platelet transfusion strategy, reduces but does not eliminate the risk for bleeding in hospitalized patients with therapy-induced hypoproliferative thrombocytopenia. We recommend that these patients receive prophylactic platelet transfusions for a morning platelet count of 10×10^9 cells/L or less. Clinicians can be assured that prophylaxis with low-dose platelets provides hemostasis that is equal to standard- or high-dose platelets in patients with therapy-induced hypoproliferative thrombocytopenia. However, low-dose platelets must be transfused more often because they provide a lower platelet increment (18).

Only limited data are available to support transfusing platelets for indications other than prophylaxis against spontaneous bleeding in patients with therapy-induced hypoproliferative thrombocytopenia. Our panel took the position that it is appropriate for the AABB to address common and important clinical scenarios, such as the role of platelet transfusions in patients having invasive procedures, even as we await better data. Therefore, we decided to review observational data as a basis for platelet transfusion recommendations. The lower quality of data is reflected in the weak strength of recommendations outside of the hypoproliferative thrombocytopenia setting. In the specific case of CVC placement, our consensus opinion is that recent observational data (38, 41) support a platelet count transfusion threshold of 20×10^9 cells/L. This threshold seems to be reasonable even for the placement of large-bore catheters for apheresis in thrombocytopenic patients (12). Observational data were also used to inform the platelet transfusion recommendation for LP, for which we suggest a threshold platelet count of 50×10^9 cells/L. Most of the published data about the safety of performing diagnostic LP in the setting of thrombocytopenia comes from a single center's experience with pediatric patients (45); it is unclear how generalizable these data are to adult patients. Of 21 case reports of LP-associated spinal hematomas in adults, 17 (81%) occurred at a platelet count less than 50×10^9 cells/L. However, in all but 1 patient, other risk factors for bleeding were identified (50). We believe that clinical judgment should be used about the need for platelet transfusion in patients requiring LP with platelet counts in the range of 20×10^9 cells/L to 50×10^9 cells/L.

Comparison With Other Published Guidelines

Our recommendation to provide prophylactic platelet transfusion at a platelet count of 10×10^9 cells/L or less for patients with therapy-induced hypoproliferative thrombocytopenia is consistent with the current standard of practice as reflected in other published transfusion guidelines (64–70). The recommendation of using a 50×10^9 cells/L or greater platelet count as a safe level to perform LP in adults falls within the spectrum of other published guidelines, which have typically recommended platelet thresholds ranging from 20×10^9 to 50×10^9 cells/L (50, 65, 66). The recommendation of a 50×10^9 cells/L platelet transfusion threshold for major nonneuraxial procedures is also consistent with other guidelines (64–70). The suggestion to transfuse platelets to patients having CPB with perioperative bleeding and thrombocytopenia or suspected platelet dysfunction is concordant with the guideline from the Society of Thoracic Surgeons (71), which states, "It is reasonable to transfuse non-red cell hemostatic blood components based on clinical evidence of bleeding and preferably guided by specific point-of-care tests." We consider coronary artery bypass graft to serve as a model for all surgeries requiring CPB. Our recommendation to use a platelet count threshold of 20×10^9 cells/L for CVC placement represents the most substantial break from other published guidelines (64–70, 72, 73). The 2012 Society of Interventional Radiology guideline, for example, recommends a minimum platelet count of 50×10^9 cells/L for CVC placement (73). We believe that existing observational data (38, 41) are sufficiently compelling to support using a lower platelet threshold. Adherence to this lower threshold should reduce transfusion risks while conserving resources.

Recommendations for Future Research

Grade 2 bleeding remains very common among patients receiving marrow-suppressive therapy, even with routine platelet prophylaxis (18, 19, 21). Other means of preventing bleeding in this setting should be explored, such as using antifibrinolytic therapy. Serious or life-threatening bleeding (grade 3 or 4) is fortunately rare. When severe bleeding occurs in patients with therapy-induced hypoproliferative thrombocytopenia, it is often at a platelet count greater than the 10×10^9 cells/L threshold typically used for prophylaxis (25). Future studies should explore the role of platelet prophylaxis in patient subgroups that may have specific risk factors for bleeding.

Data addressing the question of a minimum safe platelet count for performing invasive procedures are limited and observational in nature. Randomized trials of prophylactic platelet transfusion for procedures would be valuable but would present logistic and ethical challenges. However, it would be straightforward to establish registries to document the outcomes of consecutive patients having specific procedures. We believe that this should be a high research priority.

Platelet count is the main laboratory measurement used to guide platelet transfusion; however, it provides no qualitative information about platelet hemostatic function. The clinical utility of in vitro platelet hemostasis testing, particularly at the point of care, remains a key area of exploration.

The ideal approach to platelet transfusion would be to administer sufficient platelets to optimize patient outcomes while avoiding unnecessary transfusions with their attendant risks and costs. The recommendations in this guideline reflect the AABB's current thinking on

how platelet transfusions should be used in various clinical settings. These recommendations are not meant to be interpreted as strict standards but should provide a useful adjunct to providers' clinical judgment as individualized transfusion decisions are being made. We anticipate that these guidelines will be refined and improved over time, using new data from well-designed prospective trials.

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References

1. **Whitaker BI.** The 2011 National Blood Collection and Utilization Survey Report. Washington, DC: U.S. Department of Health and Human Services; 2013. Accessed at www.hhs.gov/ash/bloodsafety/2011-nbcus.pdf on 25 September 2014.
2. **Greeno E, McCullough J, Weisdorf D.** Platelet utilization and the transfusion trigger: a prospective analysis. Transfusion. 2007;47:201-5. [PMID: 17302764]
3. **Estcourt L, Stanworth S, Doree C, Hopewell S, Murphy MF, Tinmouth A, et al.** Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation. Cochrane Database Syst Rev. 2012;5:CD004269. [PMID: 22592695] doi:10.1002/14651858.CD004269.pub3
4. **Fuller AK, Uglik KM, Braine HG, King KE.** A comprehensive program to minimize platelet outdating. Transfusion. 2011;51:1469-76. [PMID: 21303370] doi:10.1111/j.1537-2995.2010.03039.x
5. **Riley W, Smalley B, Pulkrabek S, Clay ME, McCullough J.** Using lean techniques to define the platelet (PLT) transfusion process and cost-effectiveness to evaluate PLT dose transfusion strategies. Transfusion. 2012;52:1957-67. [PMID: 22320153] doi:10.1111/j.1537-2995.2011.03539.x
6. **Heddle NM, Blajchman MA, Meyer RM, Lipton JH, Walker IR, Sher GD, et al.** A randomized controlled trial comparing the frequency of acute reactions to plasma-removed platelets and prestorage WBC-reduced platelets. Transfusion. 2002;42:556-66. [PMID: 12084163]
7. **Heddle NM, Klama L, Meyer R, Walker I, Boshkov L, Roberts R, et al.** A randomized controlled trial comparing plasma removal with white cell reduction to prevent reactions to platelets. Transfusion. 1999;39:231-8. [PMID: 10204584]
8. **Stramer SL.** Current risks of transfusion-transmitted agents: a review. Arch Pathol Lab Med. 2007;131:702-7. [PMID: 17488155]
9. **Eder AF, Dy BA, Perez JM, Rambaud M, Benjamin RJ.** The residual risk of transfusion-related acute lung injury at the American Red Cross (2008-2011): limitations of a predominantly male-donor plasma mitigation strategy. Transfusion. 2013;53:1442-9. [PMID: 23113676] doi:10.1111/j.1537-2995.2012.03935.x
10. **Toy P, Gajic O, Bacchetti P, Looney MR, Gropper MA, Hubmayr R, et al; TRALI Study Group.** Transfusion-related acute lung injury: incidence and risk factors. Blood. 2012;119:1757-67. [PMID: 22117051] doi:10.1182/blood-2011-08-370932
11. **Kumar AMR, Grossman BJ, Kaufman RM, Tobian AAR, Kleinman S, Gernsheimer T, et al.** Platelet transfusion – a systematic review of the clinical evidence. Transfusion. 2014. [Forthcoming]
12. **Duffy SM, Coyle TE.** Platelet transfusions and bleeding complications associated with plasma exchange catheter placement in patients with presumed thrombotic thrombocytopenic purpura. J Clin Apher. 2013;28:356-8. [PMID: 23720092] doi:10.1002/jca.21279
13. **Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al; GRADE Working Group.** GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336:924-6. [PMID: 18436948] doi:10.1136/bmj.39489.470347.AD
14. **Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al; GRADE Working Group.** Going from evidence to recommendations. BMJ. 2008;336:1049-51. [PMID: 18467413] doi:10.1136/bmj.39493.646875.AE
15. **Diedrich B, Remberger M, Shanwell A, Svahn BM, Ringdén O.** A prospective randomized trial of a prophylactic platelet transfusion trigger of 10 × 10(9) per L versus 30 × 10(9) per L in allogeneic hematopoietic progenitor cell transplant recipients. Transfusion. 2005;45:1064-72. [PMID: 15987349]
16. **Heddle NM, Cook RJ, Tinmouth A, Kouroukis CT, Hervig T, Klapper E, et al; SToP Study Investigators of the BEST Collaborative.** A randomized controlled trial comparing standard- and low-dose strategies for transfusion of platelets (SToP) to patients with thrombocytopenia. Blood. 2009;113:1564-73. [PMID: 19109560] doi:10.1182/blood-2008-09-178236
17. **Sensebé L, Giraudeau B, Bardiaux L, Deconinck E, Schmidt A, Bidet ML, et al.** The efficiency of transfusing high doses of platelets in hematologic patients with thrombocytopenia: results of a prospective, randomized, open, blinded end point (PROBE) study. Blood. 2005;105:862-4. [PMID: 15367427]
18. **Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, Strauss RG, et al.** Dose of prophylactic platelet transfusions and prevention of hemorrhage. N Engl J Med. 2010;362:600-13. [PMID: 20164484] doi:10.1056/NEJMoa0904084
19. **Stanworth SJ, Estcourt LJ, Powter G, Kahan BC, Dyer C, Choo L, et al; TOPPS Investigators.** A no-prophylaxis platelet-transfusion strategy for hematologic cancers. N Engl J Med. 2013;368:1771-80. [PMID: 23656642] doi:10.1056/NEJMoa1212772
20. **Tinmouth A, Tannock IF, Crump M, Tomlinson G, Brandwein J, Minden M, et al.** Low-dose prophylactic platelet transfusions in recipients of an autologous peripheral blood progenitor cell transplant and patients with acute leukemia: a randomized controlled trial with a sequential Bayesian design. Transfusion. 2004;44:1711-9. [PMID: 15584985]

21. **Wandt H, Schaefer-Eckart K, Wendelin K, Pilz B, Wilhelm M, Thalheimer M, et al; Study Alliance Leukemia.** Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study. Lancet. 2012;380:1309-16. [PMID: 22877506] doi:10.1016/S0140-6736(12)60689-8
22. **Miller AB, Hoogstraten B, Staquet M, Winkler A.** Reporting results of cancer treatment. Cancer. 1981;47:207-14. [PMID: 7459811]
23. **Estcourt LJ, Heddle N, Kaufman R, McCullough J, Murphy MF, Slichter S, et al; Biomedical Excellence for Safer Transfusion Collaborative.** The challenges of measuring bleeding outcomes in clinical trials of platelet transfusions. Transfusion. 2013;53:1531-43. [PMID: 23305609] doi:10.1111/trf.12058
24. **Murphy S, Litwin S, Herring LM, Koch P, Remischovsky J, Donaldson MH, et al.** Indications for platelet transfusion in children with acute leukemia. Am J Hematol. 1982;12:347-56. [PMID: 6981349]
25. **Stanworth SJ, Estcourt LJ, Llewelyn CA, Murphy MF, Wood EM; TOPPS Study Investigators.** Impact of prophylactic platelet transfusions on bleeding events in patients with hematologic malignancies: a subgroup analysis of a randomized trial (CME). Transfusion. 2014; 54:2385-93. [PMID: 24724863] doi:10.1111/trf.12646
26. **Heckman KD, Weiner GJ, Davis CS, Strauss RG, Jones MP, Burns CP.** Randomized study of prophylactic platelet transfusion threshold during induction therapy for adult acute leukemia: 10,000/microL versus 20,000/microL. J Clin Oncol. 1997;15:1143-9. [PMID: 9060557]
27. **Zumberg MS, del Rosario ML, Nejame CF, Pollock BH, Garzarella L, Kao KJ, et al.** A prospective randomized trial of prophylactic platelet transfusion and bleeding incidence in hematopoietic stem cell transplant recipients: 10,000/L versus 20,000/microL trigger. Biol Blood Marrow Transplant. 2002;8:569-76. [PMID: 12434952]
28. **Rebulla P, Finazzi G, Marangoni F, Avvisati G, Gugliotta L, Tognoni G, et al.** The threshold for prophylactic platelet transfusions in adults with acute myeloid leukemia. Gruppo Italiano Malattie Ematologiche Maligne dell'Adulto. N Engl J Med. 1997;337:1870-5. [PMID: 9407153]
29. **Roy AJ, Jaffe N, Djerassi I.** Prophylactic platelet transfusions in children with acute leukemia: a dose response study. Transfusion. 1973;13:283-90. [PMID: 4750180]
30. **Fritz RD, Forkner CE Jr, Freireich EJ, Frei E 3rd, Thomas LB.** The association of fatal intracranial hemorrhage and blastic crisis in patients with acute leukemia. N Engl J Med. 1959;261:59-64. [PMID: 13666978]
31. **Han T, Stutzman L, Cohen E, Kim U.** Effect of platelet transfusion on hemorrhage in patients with acute leukemia. An autopsy study. Cancer. 1966;19:1937-42. [PMID: 5224775]
32. **Slichter SJ, Harker LA.** Thrombocytopenia: mechanisms and management of defects in platelet production. Clin Haematol. 1978; 7:523-39. [PMID: 363326]
33. **Lozano M, Mahon A, van der Meer PF, Stanworth S, Cid J, Devine D, et al; Biomedical Excellence for Safer Transfusion (BEST) Collaborative.** Counting platelets at transfusion threshold levels: impact on the decision to transfuse. A BEST Collaborative - UK NEQAS(H) International Exercise. Vox Sang. 2014;106:330-6. [PMID: 24330101] doi:10.1111/vox.12110
34. **Segal HC, Briggs C, Kunka S, Casbard A, Harrison P, Machin SJ, et al.** Accuracy of platelet counting haematology analysers in severe thrombocytopenia and potential impact on platelet transfusion. Br J Haematol. 2005;128:520-5. [PMID: 15686462]
35. **Barrera R, Mina B, Huang Y, Groeger JS.** Acute complications of central line placement in profoundly thrombocytopenic cancer patients. Cancer. 1996;78:2025-30. [PMID: 8964028]
36. **Doerfler ME, Kaufman B, Goldenberg AS.** Central venous catheter placement in patients with disorders of hemostasis. Chest. 1996; 110:185-8. [PMID: 8681626]
37. **Fisher NC, Mutimer DJ.** Central venous cannulation in patients with liver disease and coagulopathy–a prospective audit. Intensive Care Med. 1999;25:481-5. [PMID: 10401942]
38. **Haas B, Chittams JL, Trerotola SO.** Large-bore tunneled central venous catheter insertion in patients with coagulopathy. J Vasc Interv Radiol. 2010;21:212-7. [PMID: 20123206] doi:10.1016/j.jvir.2009.10.032
39. **Mumtaz H, Williams V, Hauer-Jensen M, Rowe M, Henry-Tillman RS, Heaton K, et al.** Central venous catheter placement in patients with disorders of hemostasis. Am J Surg. 2000;180:503-5. [PMID: 11182407]
40. **Ray CE Jr, Shenoy SS.** Patients with thrombocytopenia: outcome of radiologic placement of central venous access devices. Radiology. 1997;204:97-9. [PMID: 9205228]
41. **Zeidler K, Arn K, Senn O, Schanz U, Stussi G.** Optimal preprocedural platelet transfusion threshold for central venous catheter insertions in patients with thrombocytopenia. Transfusion. 2011;51:2269-76. [PMID: 21517892] doi:10.1111/j.1537-2995.2011.03147.x
42. **Breuer AC, Tyler HR, Marzewski DJ, Rosenthal DS.** Radicular vessels are the most probable source of needle-induced blood in lumbar puncture: significance for the thrombocytopenic cancer patient. Cancer. 1982;49:2168-72. [PMID: 7074532]
43. **Creutzfeldt CJ, Weinstein JR, Longstreth WT Jr, Becker KJ, McPharlin TO, Tirschwell DL.** Prior antiplatelet therapy, platelet infusion therapy, and outcome after intracerebral hemorrhage. J Stroke Cerebrovasc Dis. 2009;18:221-8. [PMID: 19426894] doi:10.1016/j.jstrokecerebrovasdis.2008.10.007
44. **Feusner J.** Platelet transfusion "trigger" for lumbar puncture [Letter]. Pediatr Blood Cancer. 2004;43:793. [PMID: 15368544]
45. **Howard SC, Gajjar A, Ribeiro RC, Rivera GK, Rubnitz JE, Sandlund JT, et al.** Safety of lumbar puncture for children with acute lymphoblastic leukemia and thrombocytopenia. JAMA. 2000;284: 2222-4. [PMID: 11056594]
46. **Kitanovski L, Trampus-Bakija A, Benedik-Dolnicar M.** Prophylactic platelet transfusions before lumbal puncture. Zdravniski Vestnik-Slovenian Medical Journal. 2008;77:I111-I5.
47. **Ruell J, Karuvattil R, Wynn R, Will A.** Platelet count has no influence on traumatic and bloody lumbar puncture in children undergoing intrathecal chemotherapy [Letter]. Br J Haematol. 2007;136: 347-8. [PMID: 17156399]
48. **Veen JJ, Vora AJ, Welch JC.** Lumbar puncture in thrombocytopenic children [Letter]. Br J Haematol. 2004;127:233-4. [PMID: 15461636]
49. **Vavricka SR, Walter RB, Irani S, Halter J, Schanz U.** Safety of lumbar puncture for adults with acute leukemia and restrictive prophylactic platelet transfusion. Ann Hematol. 2003;82:570-3. [PMID: 12904898]
50. **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;148:15-25. [PMID: 19775301] doi:10.1111/j.1365-2141.2009.07899.x
51. **Choi S, Brull R.** Neuraxial techniques in obstetric and non-obstetric patients with common bleeding diatheses. Anesth Analg. 2009;109:648-60. [PMID: 19608843] doi:10.1213/ane.0b013e3181ac13d1
52. **Bishop JF, Schiffer CA, Aisner J, Matthews JP, Wiernik PH.** Surgery in acute leukemia: a review of 167 operations in thrombocytopenic patients. Am J Hematol. 1987;26:147-55. [PMID: 3661547]
53. **Spiess BD, Royston D, Levy JH, Fitch J, Dietrich W, Body S, et al.** Platelet transfusions during coronary artery bypass graft surgery are associated with serious adverse outcomes. Transfusion. 2004;44: 1143-8. [PMID: 15265117]
54. **Whitlock R, Crowther MA, Ng HJ.** Bleeding in cardiac surgery: its prevention and treatment–an evidence-based review. Crit Care Clin. 2005;21:589-610. [PMID: 15992674]
55. **Qureshi H, Lowe D, Dobson P, Grant-Casey J, Parris E, Dalton D, et al; National Blood Service/Royal College of Physicians National Comparative Audit of Blood Transfusion programme.** National comparative audit of the use of platelet transfusions in the U.K. Transfus Clin Biol. 2007;14:509-13. [PMID: 18359658] doi:10.1016/j.tracli.2008.01.002
56. **Nishijima DK, Zehtabchi S, Berrong J, Legome E.** Utility of platelet transfusion in adult patients with traumatic intracranial hemorrhage and preinjury antiplatelet use: a systematic review. J Trauma

Acute Care Surg. 2012;72:1658-63. [PMID: 22695437] doi:10.1097/TA.0b013e318256dfc5

57. **Ohm C, Mina A, Howells G, Bair H, Bendick P.** Effects of antiplatelet agents on outcomes for elderly patients with traumatic intracranial hemorrhage. J Trauma. 2005;58:518-22. [PMID: 15761345]

58. **Wong DK, Lurie F, Wong LL.** The effects of clopidogrel on elderly traumatic brain injured patients. J Trauma. 2008;65:1303-8. [PMID: 19077618] doi:10.1097/TA.0b013e318185e234

59. **Downey DM, Monson B, Butler KL, Fortuna GR Jr, Saxe JM, Dolan JP, et al.** Does platelet administration affect mortality in elderly head-injured patients taking antiplatelet medications? Am Surg. 2009;75:1100-3. [PMID: 19927514]

60. **Ivascu FA, Howells GA, Junn FS, Bair HA, Bendick PJ, Janczyk RJ.** Predictors of mortality in trauma patients with intracranial hemorrhage on preinjury aspirin or clopidogrel. J Trauma. 2008;65:785-8. [PMID: 18849791] doi:10.1097/TA.0b013e3181848caa

61. **Washington CW, Schuerer DJ, Grubb RL Jr.** Platelet transfusion: an unnecessary risk for mild traumatic brain injury patients on antiplatelet therapy. J Trauma. 2011;71:358-63. [PMID: 21825939] doi:10.1097/TA.0b013e318220ad7e

62. **Anglin CO, Spence JS, Warner MA, Paliotta C, Harper C, Moore C, et al.** Effects of platelet and plasma transfusion on outcome in traumatic brain injury patients with moderate bleeding diatheses. J Neurosurg. 2013;118:676-86. [PMID: 23259827] doi:10.3171/2012.11.JNS12622

63. **Solomon J, Bofenkamp T, Fahey JL, Chillar RK, Beutel E.** Platelet prophylaxis in acute non-lymphoblastic leukaemia [Letter]. Lancet. 1978;1:267. [PMID: 74683]

64. **British Committee for Standards in Haematology, Blood Transfusion Task Force.** Guidelines for the use of platelet transfusions. Br J Haematol. 2003;122:10-23. [PMID: 12823341]

65. **JPAC – Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee.** Transfusion Handbook: Transfusion in Surgery. 2013. Accessed at www.transfusionguidelines.org.uk/transfusion-handbook/7-effective-transfusion-in-surgery-and-critical-care/7-1-transfusion-in-surgery on 25 September 2014.

66. **Haas FLJM, van Rhenen DJ, de Vries RRP, Overbeeke MAM, Novotny VMJ, Henny CP.** Blood Transfusion Guideline. Utrecht, Netherlands: Institute for Healthcare Improvement; 2011. Accessed at www.sanquin.nl/repository/documenten/en/prod-en-dienst/287294/blood-transfusion-guideline.pdf on 25 September 2014.

67. **Samama CM, Djoudi R, Lecompte T, Nathan N, Schved JF; French Health Products Safety Agency (AFSSAPS) Expert Group.** Perioperative platelet transfusion. Recommendations of the French Health Products Safety Agency (AFSSAPS) 2003. Minerva Anestesiol. 2006;72:447-52. [PMID: 16682914]

68. **Samama CM, Djoudi R, Lecompte T, Nathan-Denizot N, Schved JF; Agence Française de Sécurité Sanitaire des Produits de Santé expert group.** Perioperative platelet transfusion: recommendations of the Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSaPS) 2003. Can J Anaesth. 2005;52:30-7. [PMID: 15625253]

69. **Schiffer CA, Anderson KC, Bennett CL, Bernstein S, Elting LS, Goldsmith M, et al; American Society of Clinical Oncology.** Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol. 2001;19:1519-38. [PMID: 11230498]

70. **Tosetto A, Balduini CL, Cattaneo M, De Candia E, Mariani G, Molinari AC, et al; Italian Society for Haemostasis and Thrombosis.** Management of bleeding and of invasive procedures in patients with platelet disorders and/or thrombocytopenia: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISET). Thromb Res. 2009;124:e13-8. [PMID: 19631969] doi:10.1016/j.thromres.2009.06.009

71. **Ferraris VA, Brown JR, Despotis GJ, Hammon JW, Reece TB, Saha SP, et al; Society of Thoracic Surgeons Blood Conservation Guideline Task Force.** 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg. 2011;91:944-82. [PMID: 21353044] doi:10.1016/j.athoracsur.2010.11.078

72. **Malloy PC, Grassi CJ, Kundu S, Gervais DA, Miller DL, Osnis RB, et al; Standards of Practice Committee with Cardiovascular and Interventional Radiological Society of Europe (CIRSE) Endorsement.** Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol. 2009;20:S240-9. [PMID: 19394868] doi:10.1016/j.jvir.2008.11.027

73. **Patel IJ, Davidson JC, Nikolic B, Salazar GM, Schwartzberg MS, Walker TG, et al; Standards of Practice Committee, with Cardiovascular and Interventional Radiological Society of Europe (CIRSE) Endorsement.** Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. J Vasc Interv Radiol. 2012;23:727-36. [PMID: 22513394] doi:10.1016/j.jvir.2012.02.012

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Appendix Table 1. Panel Member Conflicts of Interest

Panel Member	Conflicts of Interest
Kelley E. Capocelli, MD	None
Mark D. Cipolle, MD, PhD	None
Claudia S. Cohn, MD, PhD	None
Benjamin Djulbegovic, MD, PhD	None
Mark K. Fung, MD, PhD	None
Terry Gernsheimer, MD	None
Brenda J. Grossman, MD, MPH	None
Richard M. Kaufman, MD	None
Steven Kleinman, MD	None
Paul D. Mintz, MD	None
Barbara A. O'Malley, MD	None
Deborah A. Sesok-Pizzini, MD	None
Aryeh Shander, MD	None
Gary E. Stack, MD, PhD	None
Alan T. Tinmouth, MD	None
Aaron A.R. Tobian, MD, PhD	None
Kathryn E. Webert, MD, MSc	None
Robert Weinstein, MD	None
Babu G. Welch, MD	None
Glenn J. Whitman, MD	None
Edward C. Wong, MD	None

Appendix Table 2. Search Strategy Used for Systematic Review of the Literature*

PubMed

1. Search strategy for prophylactic platelet transfusion studies
(blood transfusion OR Blood Transfusion[Mesh] OR "Blood Cells/transplantation"[Mesh] OR transfus* [tiab])
AND
(Platelet Count[Mesh] OR platelet count [tiab]) OR Platelet [tiab] transfusion OR Platelet Transfusion[Mesh] OR platelet* [tiab]
AND
(Prophyla* [tiab] OR bleed* OR transfus*[tiab])
AND
(threshold* OR trigger* OR count OR policy [tiab] OR adminis* OR guideline* OR dose [tiab] OR dosing [tiab] OR dosage [tiab] OR transfus*[tiab] OR practice [tiab] OR transfus*)
2. Search strategy for therapeutic platelet transfusion studies
(blood transfusion OR Blood Transfusion[Mesh] OR "Blood Cells/transplantation"[Mesh] OR transfus* [tiab])
AND
(Platelet Count[Mesh] OR platelet count [tiab]) OR Platelet [tiab] transfusion OR Platelet Transfusion[Mesh] OR platelet* [tiab]
AND
(Therapeutic [tiab] OR therap*[tiab])
AND
(threshold* OR trigger* OR count OR policy [tiab] OR adminis* OR guideline* OR dose OR dosing OR dosage OR practice [tiab] OR transfus* [tiab])

Cochrane Central Register of Controlled Trials

3. Search strategy for prophylactic platelet transfusion studies
Prophyla* platelet* transfuse*
4. Search strategy for therapeutic platelet transfusion studies
Therapeutic* platelet* transfuse*

Web of Science

No subject heading-all keywords
5. Search strategy for prophylactic platelet transfusion studies (blood transfusion OR Blood Cells transplantation OR transfus*)
AND
(platelet AND (count OR transfus*)) OR (Prophyla* OR bleed* OR transfus*) (whole phrase in title field)
AND
(threshold* OR trigger* OR count* OR policy OR adminis* OR guideline* OR dose OR dosing OR dosage OR practice OR transfus*)
6. Search strategy for therapeutic platelet transfusion studies (blood transfusion OR Blood Cells transplantation OR transfus*)
AND
(platelet AND (count OR transfus*)) OR (Therapeutic [tiab] OR therap*[tiab]) (whole phrase in title field)
AND
(threshold* OR trigger* OR count OR policy [tiab] OR adminis* OR guideline* OR dose OR dosing OR dosage OR practice [tiab] OR transfus* [tiab])
7. Additional search
The yield on the original search strategy was not optimum for all diseases. Therefore, we also searched the Pubmed clinical queries by using a combination of 2 terms of "platelet transfusion" AND "disease category".
7.1. Platelet transfusion AND idiopathic thrombocytopenic purpura. The resultant search strategy from PubMed Clinical Queries is shown below:
Therapy/Broad[filter] AND (("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields]) AND ("purpura, thrombocytopenic, idiopathic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombocytopenic"[All Fields] AND "idiopathic"[All Fields]) OR "idiopathic thrombocytopenic purpura"[All Fields] OR ("idiopathic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])))
7.2. Platelet transfusion AND Disseminated Intravascular Coagulation
Therapy/Broad[filter] AND (("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields]) AND ("disseminated intravascular coagulation"[MeSH Terms] OR ("disseminated"[All Fields] AND "intravascular"[All Fields] AND "coagulation"[All Fields]) OR "disseminated intravascular coagulation"[All Fields]))
7.3. Platelet transfusion AND Idiopathic Thrombocytopenic Purpura
Therapy/Broad[filter] AND (("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields]) AND ("purpura, thrombocytopenic, idiopathic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombocytopenic"[All Fields] AND "idiopathic"[All Fields]) OR "idiopathic thrombocytopenic purpura"[All Fields] OR ("idiopathic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])))
7.4. Platelet transfusion AND Thrombotic Thrombocytopenic Purpura - Hemolytic Uremic Syndrome
Therapy/Broad[filter] AND (("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields]) AND (("purpura, thrombotic thrombocytopenic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombotic"[All Fields] AND "thrombocytopenic"[All Fields]) OR "thrombotic thrombocytopenic purpura"[All Fields] OR ("thrombotic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])) AND ("haemolytic uraemic syndrome"[All Fields] OR "hemolytic-uremic syndrome"[MeSH Terms] OR ("hemolytic-uremic"[All Fields] AND "syndrome"[All Fields]) OR "hemolytic-uremic syndrome"[All Fields] OR ("hemolytic"[All Fields] AND "uremic"[All Fields] AND "syndrome"[All Fields]) OR "hemolytic uremic syndrome"[All Fields])))
8. Manual search
The search strategy was supplemented by a manual search of references of the obtained full-text articles and existing guidelines in the field. In addition, we also contacted the members of the AABB Guidelines Panel to identify any unpublished articles or studies that were missed in the search.
All obtained citations were entered into an EndNote database. In the first step, all duplicate citations were removed using the remove duplicate feature in the EndNote. Next, the abstract and title of all remaining citations were printed and manually reviewed for inclusion or exclusion by 2 reviewers according to the predetermined criteria. All the included studies were first sorted on the basis of study design and disease category. That is, in the first attempt, all reviewed studies were classified as randomized or observational; then, within the study design, all studies were collated according to the broad category of treatment versus prophylactic followed by various disease categories (e.g., surgery, hematologic malignant tumors, and central venous catheter). All included observational studies within a disease category were classified as prospective observational or retrospective observational. For prospective observational cohort studies, we classified all studies either as cohort studies with comparison or without comparison. For retrospective observational studies, all studies were further classified as retrospective cohort with comparison or single-group or case series or case reports.

* From reference 11.

Appendix Table 3. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion in Therapy-Induced Hypoproliferative Thrombocytopenia

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Prophylactic Platelet Transfusion	No Prophylactic Platelet Transfusion	Odds Ratio (95% CI)	Absolute		
Grade 2 or greater bleeding: 3 (21, 24, 25)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias†	192/528 (36.4)	258/519 (49.7)	0.53 (0.32–0.87)	153 fewer bleeding events per 1000 (from 35 fewer to 257 fewer bleeding events)	Moderate	Critical
Grade 2 or greater bleeding, chemotherapy subgroup: 3 (21, 24, 25)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias†	77/187 (41.2)	115/169 (68.0)	0.34 (0.22–0.52)	260 fewer bleeding events per 1000 (from 155 fewer to 361 fewer bleeding events)	Moderate	Critical
Grade 2 or greater bleeding, auto HPCT subgroup: 2 (21, 25)	Randomized trials	Serious‡	No serious inconsistency	No serious indirectness	No serious imprecision	None	103/308 (33.4)	128/313 (40.9)	0.48 (0.12–1.92)	160 fewer bleeding events per 1000 (from 332 fewer to 162 more bleeding events)	Moderate	Critical
All-cause mortality: 4 (21, 24, 25, 63)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious§‖	Reporting bias¶	13/545 (2.4)	16/531 (3.0)	0.72 (0.30–1.55)	8 fewer deaths per 1000 (from 21 fewer to 16 more deaths)	Low	Critical
Bleeding-related mortality: 4 (21, 24, 25, 63)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious‖	Reporting bias¶	3/544 (0.6)	4/530 (0.8)	0.54 (0.09–3.10)	3 fewer deaths per 1000 (from 7 fewer to 15 more deaths)	Low	Critical

HPCT = hematopoietic progenitor cell transplantation.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Only 3/6 RCTs reported this outcome.
‡ In Wandt et al (21), protocol deviations occurred in 30% of transfusions in the therapeutic group vs. 14% in the prophylactic group.
§ Stanworth et al (19) reported no deaths due to bleeding. We used the continuity correction (0.5 as event) to include this study in pooling the data.
‖ Wide CIs.
¶ Only 4/6 randomized, controlled trials reported this outcome.

Appendix Table 4. Higher Versus Lower Platelet Count Thresholds for Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Transfusion Threshold $<20 \times 10^9$ cells/L or $<30 \times 10^9$ cells/L	Transfusion Threshold $<10 \times 10^9$ cells/L	Odds Ratio (95% CI)	Absolute		
Grade 2 or greater bleeding: 4 (15, 26–28)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	None	58/329 (17.6)	71/329 (21.6)	0.74 (0.41–1.35)	47 fewer bleeding events per 1000 (from 114 fewer to 55 more bleeding events)	Moderate	Critical
All-cause mortality: 3 (26–28)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	None	43/242 (17.8)	51/250 (20.4)	0.7 (0.4–1.22)	52 fewer deaths per 1000 (from 111 fewer to 34 more deaths)	Moderate	Important
Bleeding-related mortality: 4 (15, 26-28)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	None	0/329 (0)	1/329 (0.3)	0.37 (0.02–9.22)	2 fewer deaths per 1000 (from 3 fewer to 24 more deaths)	Moderate	Critical

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Wide CIs.

Appendix Table 5. Standard-Dose Versus Low-Dose Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Standard-Dose Platelets	Low-Dose Platelets	Odds Ratio (95% CI)	Absolute		
Grade 2 or greater bleeding: 4 (16, 18, 20, 29)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	None	330/569 (58.0)	335/563 (59.5)	0.91 (0.70–1.19)	23 fewer bleeding events per 1000 (from 88 fewer to 41 more bleeding events)	Moderate	Critical
All-cause mortality: 3 (16, 18, 20)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	Reporting bias‡	4/539 (0.7)	9/531 (1.7)	0.43 (0.13–1.42)	10 fewer deaths per 1000 (from 15 fewer to 7 more deaths)	Low	Important
Bleeding-related mortality: 3 (14, 18, 20)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	Reporting bias§	0/539 (0)	0/531 (0)	Not pooled	Bleeding-related deaths not pooled	Low	Important

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Wide CIs.
‡ 3/7 trials reported this outcome.
§ 4/7 trials reported this outcome.

Appendix Table 6. High-Dose Versus Standard-Dose Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	High dose platelets	Standard dose platelets	Odds Ratio (95% CI)	Absolute		
Grade 2 or greater bleeding 2 (17,18)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	None	305/480 (63.5)	294/471 (62.4)	1.05 (0.79 to 1.40)	11 more bleeding events per 1000 (from 75 more bleeding events)	Moderate	Critical
All-cause mortality 1 (18)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	Reporting bias‡	7/432 (1.6)	4/423 (0.9)	1.73 (0.5 to 5.94)	7 fewer deaths per 1000 (from 5 fewer to 44 more deaths)	Low	Important
Bleeding-related mortality 2 (17, 18)	Randomized trials	No serious risk	No serious inconsistency	No serious indirectness	Serious†	Reporting bias§	1/480 (0.2)	0/471 (0)	2.94 (0.12 to 72.48)	–	Low	Important

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Wide CIs.
‡ 3/7 trials reported this outcome.
§ 4/7 trials reported this outcome.

Appendix Table 7. Prophylactic Platelet Transfusion for Central Venous Catheter Placement

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Prophylactic Platelet Transfusion	No Prophylactic Platelet Transfusion	Odds Ratio (95% CI)	Absolute		
Bleeding: 1 (40)	Observational study	Serious†	No serious inconsistency	No serious indirectness	Serious‡	Reporting bias§	0/37 (0)	4/68 (5.9)	0.19 (0.01–3.65)	47 fewer bleeding events per 1000 (from 58 fewer to 156 more bleeding events)	Very low	Critical
All-cause mortality: 1 (40)	Observational study	Serious†	No serious inconsistency	No serious indirectness	Serious‡	Reporting bias§	10/37 (27.0)	9/68 (13.2)	2.43 (0.89–6.66)	138 more deaths per 1000 (from 12 fewer to 472 more deaths)	Very low	Critical

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† The authors did not provide details on co-interventions.
‡ Wide CIs.
§ Only 1 study (36) reported a comparison of platelet transfusion vs. no platelet transfusion in patients having central venous catheter placement. Six additional observational studies (969 cannulations) without a comparison group (35, 37–41) were identified in the original literature search to April 2013. One additional observational study without a comparison group (57 apheresis catheter placements in patients with thrombotic thrombocytopenic purpura) (12) was identified in the updated literature search to September 2014. These 7 studies reported overall bleeding rates of 0%–9% in thrombocytopenic patients having central venous catheter placement.

Appendix Table 8. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion for Lumbar Puncture

Studies by Subgroup, *n*	Quality Assessment*						Events/Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Prophylactic Platelet Transfusion†	No Prophylactic Platelet Transfusion	Relative	Absolute		
Spinal hematoma (pediatric patients): 5 (44-48)	Observational study	Serious‡	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/1450 (0)	NA	NA	NA	Very low	Critical
Spinal hematoma (adult patients): 2 (42, 49)	Observational study	Serious§	No serious inconsistency	No serious indirectness	No serious imprecision	None	2/86 (2.3)	NA	NA	NA	Very low	Critical

NA = not applicable.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Some authors did not report the number of lumbar puncture procedures done but report only the total number of patients; therefore, the denominator is number of patients.
‡ Only 2/5 studies reported data from consecutive patients.
§ Neither of the 2 studies reported data from consecutive patients.

Appendix Table 9. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion for Surgery

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Prophylactic Platelet Transfusion	No Prophylactic Platelet Transfusion	Odds Ratio (95% CI)	Absolute		
All-cause mortality: 1 (52)	Observation study	Serious†	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias‡	22/95 (23.2)	NA	NA	NA	Very low	Critical
Bleeding-related mortality: 1 (52)	Observation study	Serious†	No serious inconsistency	No serious indirectness	No serious imprecision	Reporting bias‡	0/95 (0)	NA	NA	NA	Very low	Critical

NA = not applicable.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† The study included 435 consecutive patients with acute leukemia, and 95 patients had 167 operations with a platelet count $<100 \times 10^9$ cells/L and 130 operations with platelet counts $<50 \times 10^9$ cells/L. Only 7% of operations had intraoperative blood loss >500 mL, and 7% required >4 units of red cells transfused in the perioperative period.
‡ Only 2 studies reported data on the effect of platelet transfusion on clinical outcomes in patients having surgical procedures.

Appendix Table 10. Platelet Transfusion Versus No Platelet Transfusion for Coronary Artery Bypass Graft Surgery

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Platelet Transfusion	No Platelet Transfusion	Odds Ratio (95% CI)	Absolute		
Mortality: 1 (53)	6 randomized trials, 1 observational study	Serious†	Serious ‡	No serious indirectness	No serious imprecision	Serious reporting bias§	284	1436	4.76 (1.65–13.73)	NA	Very low	Critical

NA = not applicable.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Individual patient data from 6 randomized, double-blinded, phase III placebo-controlled trials evaluating aprotinin use in coronary artery bypass graft surgery were pooled together in this analysis. Data from 37 patients participating in a pilot study were also included in the analysis. The distribution of the quantity of platelets transfused was highly skewed between 2 groups. The data-recording tool did not always delineate single-donor plateletpheresis units (presumably those with <5–6 units) vs. pooled random donor units (those with ≥5–24 units). The patients receiving platelets were not similar to patients who did not receive platelets (potential confounding by indication). Transfusion was not randomly assigned in this patient population, and there is a concern that multivariate analysis may not adequately control for confounding and bias. To address this issue, authors used propensity score matching for analysis. The risk estimates reported here are derived from the propensity score analysis.
‡ The 6 randomized, controlled trials were originally designed to evaluate aprotinin and not prophylactic use of platelets among patients having coronary artery bypass graft surgery.
§ The study did not report comprehensive bleeding outcomes and may be limited by outcome reporting bias.

Appendix Table 11. Platelet Transfusion Versus No Platelet Transfusion in Patients Who Were Thrombocytopenic and Had a Traumatic Brain Injury

Studies by Subgroup, *n*	Quality Assessment*						Patients, *n/N (%)*		Effect		Quality	Importance
	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Platelet Transfusion	No Platelet Transfusion	Odds Ratio (95% CI)	Absolute		
Mortality (on antiplatelet therapy): 5 (43, 57-60)	Observational studies	Serious†	No serious inconsistency	No serious indirectness	Serious‡	Reduced effect for RR >1 or <1†	67/375 (17.9)	76/384 (19.8)	1.11 (0.51–2.46)	17 more deaths per 1000 (from 86 fewer to 180 more deaths)	Very low	Critical
Mortality (no antiplatelet therapy): 1 (62)	Observational studies	Serious§	No serious inconsistency	No serious indirectness	Serious‡	Reduced effect for RR >1 or <1†	3/35 (8.6)	11/53 (20.8)	0.36 (0.09–1.39)	133 fewer deaths per 1000 (from 189 fewer to 81 more deaths)	Very low	Critical

RR = relative risk.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† All included studies were based on registry data; thus, they experienced limitations inherent to retrospective analysis of a secondary dataset. Most of these studies did not adequately control for confounding factors (e.g., concomitant warfarin use). Even with attempts to adjust for differences in baseline prognostic variables, it is probable that significant bias existed in the decision about whether to transfuse platelets. The included studies provided limited information about the timing of transfusion after injury, which may affect outcomes.
‡ Wide CIs.
§ Experienced from limitations inherent to retrospective analysis of a secondary dataset. Inclusion criteria were brain injuries confirmed by the presence of abnormal neuroimaging or a Glasgow Coma Scale score <13 after resuscitation. Instead of randomization, the study relied on variation in clinical practice to elucidate differences in outcome between patients who did and did not receive a transfusion. Of the 480 patients included in this study, mortality data were available for patients with moderate thrombocytopenia, defined as a platelet count of 50 to 107 × 10^9 cells/L (*n = 88*).