# Appropriateness of Plasma Transfusion

## A College of American Pathologists Q-Probes Study of Guidelines, Waste, and Serious Adverse Events

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• ***Context.***—**Plasma transfusion guidelines support patient care and safety, management of product wastage, and compliance; yet, there is little information across multiple institutions about use of and adherence to plasma transfusion guidelines.**

***Objective.***—**To survey multiple institutions regarding their plasma transfusion guidelines and compliance, plasma wastage rates, and incidence of transfusion reactions associated with plasma transfusion.**

***Design.***—**The College of American Pathologists Q-Probes model was used to collect data from 89 participating institutions. Each site was asked to provide data relevant to its most recent 40 adult patient plasma transfusion episodes, and complete a questionnaire regarding plasma transfusion guidelines, utilization and wastage of plasma, and transfusion reactions related to plasma transfusion.**

***Results.***—**The participating institutions reported a total of 3383 evaluable plasma transfusion episodes with transfusion of 9060 units of plasma. Compliance with institution-specific guidelines was seen in 3018 events (89%). Pretransfusion and posttransfusion coagulation testing was done in 3281 (97%) and 3043 (90%) of these episodes, respectively. Inappropriate criteria were noted for more than 100 transfusion episodes. Thirty-two plasma transfusion episodes (1%) were associated with a transfusion reaction. Serious and fatal reactions were reported. Median plasma wastage rate for the year preceding the study was 4.5%.**

***Conclusions.***—**Most participating institutions are compliant with plasma transfusion guidelines based on published references, supported by appropriate testing. With transfusions for indications that lack evidence of efficacy and incidence of transfusion reactions, there is an ongoing role for transfusion service leaders to continue to update and monitor plasma transfusion practices.**

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Evaluation of transfusion practices serves multiple roles, primary among them patient safety and compliance in support of patient safety. Transfusion is a lifesaving medical therapy, albeit one that is dependent on a volunteer-based supply and that carries significant risk, ranging from transmission of infectious disease to transfusion reaction. With ongoing developments in transfusion medicine, there are potential gaps in knowledge base and/or practice patterns for many medical providers. Transfusion guidelines based on known and expected clinical benefits of transfusion as well as analysis of risks associated with transfusion are especially important in this setting.

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Transfusion guidelines have been available for decades, and both laboratory[1] and hospital accreditation standards[2–4] require or recommend monitoring of transfusion practice according to the institution's defined transfusion criteria. Since guidelines for transfusion have been available, there has been continual effort to move transfusion practice gradually closer to existing guidelines, while guidelines have also become more refined.

Well-accepted plasma transfusion guidelines come from multiple sources, including the College of American Pathologists (CAP) and AABB (formerly American Association of Blood Banks).[5,6] They share a basis on results of coagulation test results; need for replacement of multiple clotting factors; clinical scenarios in which plasma transfusion is highly likely, such as reversal of warfarin effect and liver disease; and therapy for thrombotic thrombocytopenic purpura and other disorders, often as replacement fluid in plasma exchange therapy.

The CAP Q-Probes program is available to laboratories as a quality monitor that also provides benchmarking against other laboratories. The CAP Quality Practices Committee conducted the Q-Probes study "Appropriateness of Plasma Transfusion" to assess the conformance of plasma transfusion practices with institutional guidelines. As a marker of compliance, rates of pretransfusion and posttransfusion coagulation testing were reviewed. Additional data regard-

| Table 1. Definition of Terms | |
|---|---|
| Plasma transfusion | Transfusion of all forms of plasma (fresh frozen plasma [FFP], frozen extended plasma [FEP], plasma frozen within 24 hours [FP24], 5-day plasma/thawed plasma) for treatment of coagulopathy. |
| Appropriate | Meeting institution-specific transfusion criteria for plasma transfusion. |
| Transfusion event | A single request for release of plasma product (any number of units) for a single transfusion episode. |
| Product wastage | Products requested and prepared but not actually transfused. |
| Massive transfusion protocol | Defined transfusion plan used in the setting of massive hemorrhage, usually with a particular ratio of plasma units transfused in relation to the amount of red blood cells transfused. |

ing plasma wastage and incidence of serious transfusion reactions following plasma transfusion were evaluated.

## METHODS

Eighty-nine institutions voluntarily enrolled in the 2011 Q-Probes study "Appropriateness of Plasma Transfusion" received study materials that included a description of the study objectives, background, and references, in addition to data collection forms and instructions for their completion. Instructions included descriptions of cases for inclusion in and exclusion from the data collection, and operational definitions.

Institutions were asked to provide retrospective data related to the first plasma transfusion episode for 40 adult patients: the number of plasma units prepared for the patient, the number of plasma units transfused, the indication(s) for transfusion (chosen from a list), pretransfusion and posttransfusion coagulation test results (prothrombin time [PT], international normalized ratio [INR], activated partial thromboplastin time [aPTT]), and occurrence and type of transfusion reaction. They were asked if the coagulation tests were completed within 24 hours before transfusion and how long after transfusion those tests were repeated, if additional transfusion was requested before completion of posttransfusion coagulation tests, and whether transfusion met the institution's transfusion guidelines. Five laboratory-specific performance indicators were calculated from the study results, specifically: (1) rate of plasma transfusions that met institutional guidelines; (2) rate of pretransfusion coagulation testing; (3) rate of posttransfusion coagulation testing; (4) plasma utilization rate; and (5) rate of reported transfusion reactions.

Plasma transfused as part of trauma resuscitation, massive transfusion protocol, or "keep ahead" orders (orders placed for the possibility of ongoing transfusion needs) were excluded from the study. Plasma used for treatment of thrombotic thrombocytopenic purpura or in therapeutic apheresis was also excluded from the study.

Participating institutions were asked to complete a questionnaire with 14 additional questions related to plasma transfusion guidelines, compliance monitoring and reporting, number of plasma units transfused in the previous year, plasma wastage rate, massive transfusion protocols, and serious plasma-related transfusion reactions.

Each institution was asked to provide demographic information, including institution type (eg, voluntary nonprofit, veterans, proprietary hospital), geographic setting (eg, urban, suburban, rural), and occupied bed size (by increments of 150 beds up to 600 beds, then "over 600 beds").

Terms were defined as described in Table 1.

Responses were analyzed by the CAP to determine demographic profile of responding institutions and rates for each of the parameters being evaluated in the Q-Probes study and associated questionnaire.

All responses were summarized by using SAS 9.2 (SAS Institute, Cary, North Carolina).

## RESULTS

Participants from 89 institutions monitored a total of 3387 plasma transfusion episodes during this study.

Sixty-eight of 81 institutions (83.9%) had an occupied bed size of 450 or fewer beds. Of 84 institutions, 66 (78.6%) were in urban or suburban settings, 15 (17.9%) were in rural settings, and 2 (2.4%) were at federal installations. Twenty of 84 (23.8%) had governmental affiliation. Fifty-two of 84 institutions (61.9%) were voluntary, nonprofit hospitals; 7 of 84 (8.3%) were proprietary hospitals; 6 of 84 (7.1%) were veterans hospitals; and there were fewer in each category of other hospital types (Table 2).

Five primary performance indicators were analyzed (Table 3). There were incomplete data for 4 transfusion episodes, and these were excluded from the analysis. The median rate at which plasma transfusions met institutional criteria was 95%, with 3018 of 3383 transfusions (89%) meeting institution-specific criteria for plasma transfusion. Pretransfusion coagulation testing was performed in 3098 transfusion episodes (97%). Most institutions (76, 89.4%) did not have policies that required posttransfusion coagulation testing before transfusion of additional plasma, though PT and aPTT results were obtained before additional plasma transfusions in 2916 of the 3235 reported cases (90%). Of 9695 plasma units prepared for transfusion, 9060 (93%)

| Table 2. Demographics of Participating Institutions | | |
|---|---|---|
| | No. | Percentage |
| Occupied bed size (n = 81) | | |
| 0–150 | 21 | 25.9 |
| 151–300 | 30 | 37.0 |
| 301–450 | 17 | 21.0 |
| 451–600 | 5 | 6.2 |
| >600 | 8 | 9.9 |
| Institution location (n = 84) | | |
| City | 45 | 53.6 |
| Suburban | 21 | 25.0 |
| Rural | 15 | 17.9 |
| Federal installation | 2 | 2.4 |
| Other | 1 | 1.2 |
| Government affiliation (n = 84) | | |
| Nongovernmental | 64 | 76.2 |
| Governmental, nonfederal | 11 | 13.1 |
| Governmental, federal | 9 | 10.7 |
| Institution type (n = 84) | | |
| Voluntary, nonprofit hospital | 52 | 61.9 |
| Proprietary hospital | 7 | 8.3 |
| Veterans hospital | 6 | 7.1 |
| Nongovernmental, university hospital | 4 | 4.8 |
| County hospital | 4 | 4.8 |
| Other, governmental, nonfederal | 3 | 3.6 |
| Department of Defense | 3 | 3.6 |
| State acute hospital | 2 | 2.4 |
| System/integrated delivery network | 1 | 1.2 |
| City hospital | 1 | 1.2 |
| Governmental, nonfederal university hospital | 1 | 1.2 |

| Table 3. Performance Indicators | | | | | | |
|---|---|---|---|---|---|---|
| | | All Institutions Percentiles | | | | |
| Performance Indicators | N | 10th | 25th | Median | 75th | 90th |
| Rate of plasma transfusions that met institutional guidelines | 89 | 72.5 | 87.5 | 95.0 | 100.0 | 100.0 |
| Rate of pretransfusion coagulation testing | 89 | 90.0 | 95.0 | 97.5 | 100.0 | 100.0 |
| Rate of posttransfusion coagulation testing | 89 | 75.0 | 87.0 | 92.5 | 95.0 | 100.0 |
| Plasma transfusion rate | 89 | 81.5 | 91.8 | 96.8 | 99.0 | 100.0 |
| Rate of reported transfusion reactions | 89 | 0.0 | 0.0 | 0.0 | 2.5 | 4.0 |

Abbreviation: N, number.

were transfused. Participants reported a median plasma wastage rate of 4.5% for the preceding year (2010).

Several associations were found between the performance indicators and demographics of the participating institutions (data not shown). Lower rates of plasma transfusions meeting institutional guidelines were associated with institutions that used plasma with extended storage (1–5 days after thawing), and lower rates of plasma utilization tended to occur in larger institutions. Higher rates of pretransfusion coagulation testing tended to occur in institutions that used AABB as a source for developing transfusion guidelines, and lower rates of posttransfusion coagulation testing tended to occur in institutions with the following characteristics: (1) rural location; or (2) where the blood bank supervisor or manager was involved in the development of transfusion guidelines.

Thirty-two transfusions (1%) resulted in a reported transfusion reaction. In the year prior to the study (2010), 4 (4.7%) of the participating institutions had a serious, nonfatal plasma-related transfusion reaction reported, and 5 (5.9%) had a fatal plasma-related transfusion reaction within the 5-year period before the study.

Participants were asked about plasma transfusion guidelines at their institutions. Several individuals in key transfusion leadership roles were involved in development of institution-specific guidelines. At 70 sites (81.4%) the blood bank medical director was involved, at 54 sites (62.8%) the Transfusion/Blood Utilization Committee was involved, at 48 sites (55.8%) the blood bank supervisor/manager was involved, and at 35 sites (40.7%) another medical staff or Executive Committee was involved. The most commonly used reference sources cited in development of institutional plasma transfusion guidelines were AABB (64, 76.2%), CAP (29, 34.5%), and "other published guideline" (41, 48.8%). With 84 responses and 174 sources with "yes" responses, each site used an average of 2.1 sources to guide its own plasma transfusion guidelines.

An elevated PT was the most commonly cited indication (2076, 61.7% of 3366 responses) for transfusion. Other common indications included correction of coagulopathy for bleeding (939, 27.9%), correction of coagulopathy due to warfarin (842, 25%), and as prophylaxis for an invasive procedure (840, 25%) (Table 4). As based on 3359 responses, patients received a median of 2 units of plasma per episode, with the 90th percentile providing 4 units. Most laboratories (70 of 85 responses, 82.4%) supplied the ordered number of plasma units, rather than requiring a standardized dosing algorithm. Correction of pretransfusion coagulation test results was directly correlated with the degree of abnormality of the result (Table 5). Minimally elevated test results were not normalized by transfusion regardless of the indication for transfusion (Figures 1 through 3).

Compliance with institutional plasma transfusion guidelines was monitored in all but 9 (10.6%) of the institutions, and 15 (17.6%) did not report the results of their monitoring to any quality or utilization committee. Forty-eight sites (56.5%) performed only retrospective review, 22 (25.9%) used both retrospective and prospective review, and 6 (7.1%) used only prospective review. Eighteen (21.7%) never contacted the ordering provider to request justification of plasma transfusions that were deemed to be out of compliance. In the most recent year, 39 institutions (60.9%) made up to 10 retrospective contacts regarding plasma transfusions that were considered out of compliance; 9 (14.1%) made 11 to 20, and 5 (7.8%) made more than 20 such communications.

## DISCUSSION

In this Q-Probes study, 89 institutions monitored a total of 3387 plasma transfusion episodes. Use of coagulation test results, development and compliance with plasma transfusion guidelines, and review of plasma transfusion practices were evaluated, as were plasma wastage and history of recent severe plasma-related transfusion reactions.

| Table 4. Indications for Plasma Transfusion[a] | | |
|---|---|---|
| Clinical Indication (N = 3366) | No. | Percentage |
| Elevated PT | 2076 | 61.7 |
| Coagulopathy and bleeding episode | 939 | 27.9 |
| Correct coagulopathy due to warfarin therapy | 842 | 25.0 |
| Coagulopathy and need for invasive medical procedure | 840 | 25.0 |
| Elevated aPTT | 814 | 24.2 |
| Correct coagulopathy due to heparin therapy | 127 | 3.8 |
| Multiple clotting factor deficiencies (eg, liver disease, DIC) | 127 | 3.8 |
| Correct coagulopathy due to other anticoagulant therapy | 103 | 3.1 |
| None | 69 | 2.0 |
| Single clotting factor deficiency (eg, factor V deficiency) | 29 | 0.9 |
| Other | 487 | 14.5 |

Abbreviations: aPTT, activated partial thromboplastin time; DIC, disseminated intravascular coagulation; N, number; PT, prothrombin time.

[a] More than 1 indication could be selected per transfusion event.

| Table 5. Coagulation Test Result Correction Post Transfusion | | | | | | |
|---|---|---|---|---|---|---|
| | | Change Post Transfusion | | | | |
| Test | N | 10th Percentile | 25th Percentile | Median | 75th Percentile | 90th Percentile |
| PT, s | 2416 | +0.5 | −1.0 | −2.0 | −6.0 | −16.0 |
| INR | 2546 | 0 | 0 | 0 | −1.0 | −1.9 |
| aPTT, s | 1237 | +2.0 | 0 | −2.0 | −5.0 | −11.0 |

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; N, number; PT, prothrombin time.

Most of the participating institutions used widely published and well-accepted guidelines as the basis of plasma transfusion guidelines at their individual sites.

Almost all of the plasma transfusion episodes were accompanied by both pretransfusion and posttransfusion coagulation testing; and nearly all the prepared plasma units were transfused.

Compliance with institutional plasma transfusion guidelines was monitored in almost 90% (3018) of the institutions, with a variety of mechanisms, not all of which included contact with the ordering provider or reporting to any quality or utilization committee.

Despite the high rate of close monitoring, there were some plasma transfusion episodes for inappropriate indications, such as treatment to correct the therapeutic effect of heparin (Table 4). It is not uncommon for patients to have multiple indications for plasma transfusion, such as patients who are having warfarin effect reversed in order to undergo an invasive procedure, as is reflected by these data.

In this study, the median pretransfusion INR for all results was 2.1. In the 2011 National Blood Collection and Utilization Survey,[7] it was 2.5, and in a more recent study by Triulzi et al[8] it was 1.9. Although INR is widely used to guide plasma transfusion therapy, there is literature suggesting that low elevations of INR do not correlate well with bleeding risk[9] and do not decrease significantly in response to standard doses of plasma (Figures 1 through 3; Table 5).[10]

In the case of correction of warfarin therapy, plasma is frequently transfused for elevations in the INR that would be considered subtherapeutic for preventing thrombosis. This reflects the relationship between the INR and the PT, in which an INR up to approximately 1.6 correlates with PT results that are within the normal range and adequate hemostatic coagulation factor levels.[11]

The setting of compensated cirrhosis further complicates test result interpretation relative to transfusion decisions because when patients have elevated PT results they actually have a balanced abnormality in clotting and anticoagulant factors. In most cases they are not at risk for bleeding secondary to an invasive procedure.[12]

Despite this knowledge base, there are also practice guidelines in place for which INR of 1.5 or less is recommended for radiologically guided or surgical procedures.[13] In addition to gaps between understanding of INR and clinical scenarios for guiding plasma transfusion, there are also gaps in plasma-dosing orders.[8]

In this study, the median plasma dose was 2 units, as was seen in a 2013 report on plasma transfusion in Ontario, Canada.[14] Dosing recommendations of approximately 15 mL/kg[16] for a "typical" 70-kg patient would lead to a dose of approximately 1050 mL or 4 to 5 units of plasma. Underdosing may result in a small change in test results and may account for some of the results observed in this study. Clinically, the outcome of such underdosing would likely be additional plasma transfusion, with the main risk being one of delay between the first and second doses. Despite underdosing for many transfusions, effects may be seen in the PT and INR results when there are very high pretransfusion results. This study did not evaluate individual cases' test results with plasma transfusion doses, nor did it inquire about use of other concurrent therapies such as vitamin K. With the range of indications for ordering plasma transfusion and anecdotal experiences with a range of outcomes in complex clinical scenarios, an ordering provider may remain unaware of the specific linkage between plasma transfusion dose and expected effect on test results. In this

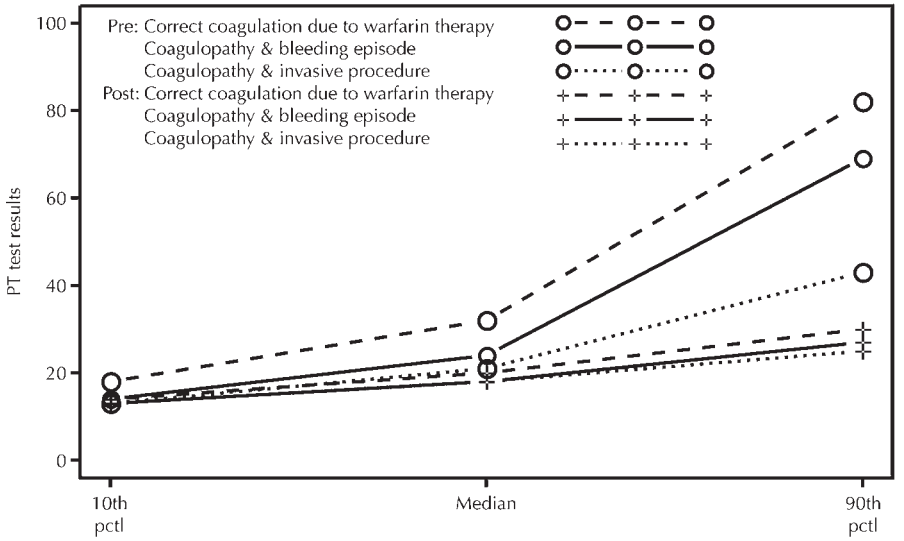


**Figure 1.** *Prothrombin time (PT) test results: pre- and post transfusion. Abbreviation: pctl, percentile.*

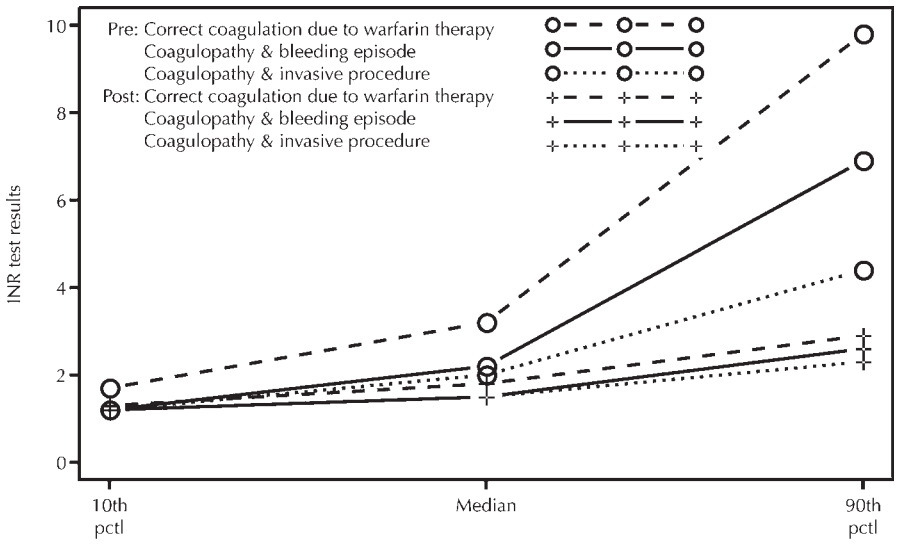


**Figure 2.** *International normalized ratio (INR) test results: pre- and post transfusion. Abbreviation: pctl, percentile.*

regard, plasma transfusion guidelines should include dosing recommendations.

During this study, the rate of transfusion reactions following plasma transfusion was similar to reported data.[7,15] The occurrence of serious and fatal transfusion reactions, even in this small number of sites, serves as a reminder of the risks of plasma transfusion and importance of consistent use of current transfusion guidelines to avoid inappropriate transfusion.

Since most of the transfusion episodes reviewed for this Q-Probes study met institutional transfusion guidelines, the data suggest a need for continued education in the arena of plasma transfusion, continued vigilance in compliance monitoring, and effective feedback about compliance data to ordering providers in the arena of plasma transfusion to optimize expected benefit and avoid serious adverse reactions.

## CONCLUSIONS

This Q-Probes study demonstrated that most participating hospital transfusion services have plasma transfusion guidelines that have been developed from well-accepted, published recommendations from sources representing expertise in transfusion medicine, including AABB and CAP. These institutions also had a high rate of both pretransfusion and posttransfusion coagulation testing, generating results that could guide plasma transfusion practice in a clinically relevant time frame.

Though most plasma transfusions reviewed for this Q-Probes study met institutional guidelines, the use of plasma for indications that lack evidence of clinical efficacy and frequent use of a 2-unit plasma transfusion dose suggest that plasma transfusion practice still has room for improvement, particularly given the documented incidence of recent, rare, but clinically significant adverse reactions that have occurred at participating institutions.

Transfusion service laboratories, their medical directors, and transfusion committees have an ongoing role in updating, maintaining, and monitoring use of appropriate, evidence-based criteria for transfusion. This may include dropping outdated criteria and adding new criteria as they develop, as well as implementation of additional blood management strategies.

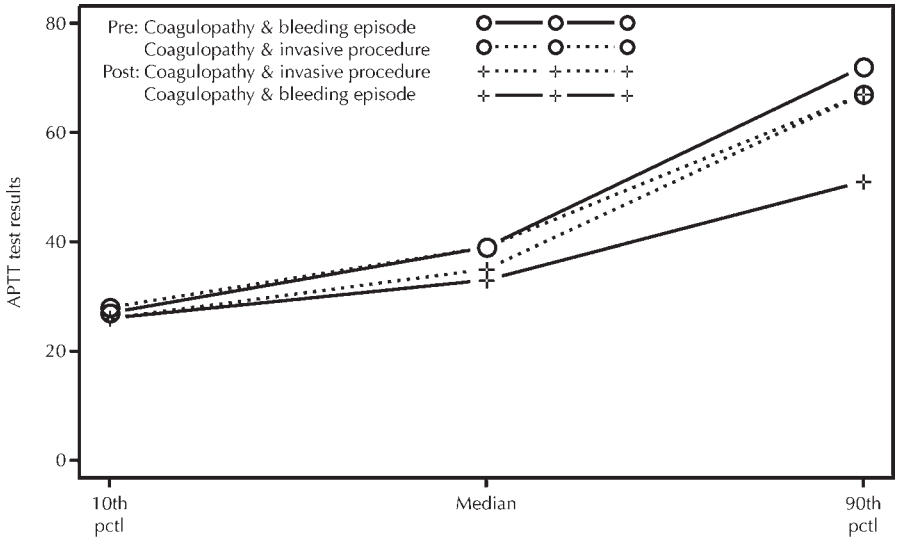


**Figure 3.** *Activated partial thromboplastin time (aPTT) test results: pre- and post transfusion. Abbreviation: pctl, percentile.*

## References


1. Sharkey FE, ed. *Laboratory Accreditation Manual*. Northfield, IL: College of American Pathologists; 2012.

2. Belanger AC. Joint Commission on Accreditation of Healthcare Organizations' expectations for transfusion medicine in health care organizations. *Arch Pathol Lab Med*. 1999;123(6):472–474.

3. Performance improvement (PI).01.01.01: introduction to medical staff ongoing professional practice evaluation (MS).08.01.03. *Comprehensive Accreditation Manual for Hospitals*. Oakbrook Terrace, IL: The Joint Commission; July 2015.

4. QM.7 measurement, monitoring, analysis. *National Integrated Accreditation for Healthcare Organizations (NIAHO) Interpretive Guidelines and Surveyor Guidance*. Version 11. Hovik, Norway: Det Norske Veritas; 2014.

5. Practice parameter for the use of fresh-frozen plasma, cryoprecipitate, and platelets: Fresh-Frozen Plasma, Cryoprecipitate, and Platelets Administration Practice Guidelines Development Task Force of the College of American Pathologists. *JAMA*. 1994;271(10):777–781.

6. Roback JD, Caldwell S, Carson J, et al. Evidence-based practice guidelines for plasma transfusion. *Transfusion*. 2010;50(6):1227–1239.

7. Whitaker B, Hinkins S. *The 2011 National Blood Collection and Utilization Survey Report*. Washington, DC: US Department of Health and Human Services; 2011.

8. Triulzi D, Gottschall J, Murphy E, et al. A multicenter study of plasma use in the United States. *Transfusion*. 2015;55(6):1313–1319.

9. Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. *Transfusion*. 2005;45(9):1413–1425.

10. Abdel-Wahab OI, Healy B, Dzik WH. Effect of fresh-frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. *Transfusion*. 2006;46(8):1279–1285.

11. Matevosyan K, Madden C, Barnett SL, Beshay JE, Rutherford C, Sarode R. Coagulation factor levels in neurosurgical patients with mild prolongation of prothrombin time: effect on plasma transfusion therapy. *J Neurosurg*. 2011; 114(1):3–7.

12. Roberts JR, Bambha K. Balanced coagulopathy in cirrhosis-clinical implications: a teachable moment. *JAMA Intern Med*. 2014;174(11):1723–1724.

13. Patel IJ, Davidson JC, Nikolic B, et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. *J Vasc Interv Radiol*. 2012;23(6): 727–736.

14. Tinmouth A, Thompson T, Arnold DM, et al. Utilization of frozen plasma in Ontario: a provincewide audit reveals a high rate of inappropriate transfusions. *Transfusion*. 2013;53(10):2222–2229.

15. Mazzei CA, Popovsky MA, Kopko PM. Noninfectious complications of blood transfusion. In: Fung MK, ed. *Technical Manual*. Bethesda, MD: American Association of Blood Banks; 2014:665–696.

16. Fung MK, Grossman BJ, Hillyer C, Westhoff CM, eds. *Technical Manual*. 18th ed. Bethesda, MD: AABB; 2014.