Published in final edited form as:

Mayo Clin Proc. 2016 August ; 91(8): 1045–1055. doi:10.1016/j.mayocp.2016.05.010.

Prophylactic Plasma Transfusion Prior to Interventional Radiology Procedures Is Not Associated with Reduced Bleeding Complications

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Abstract

Objective—To determine the association between prophylactic plasma transfusion and periprocedural RBC transfusion rates in patients with elevated INR values undergoing interventional radiology procedures.

Patients and Methods—In this retrospective cohort study, adult patients undergoing interventional radiology procedures with a preprocedural INR available within 30 days of the procedure during a study period of Jan 1st, 2009 to Dec 31st, 2013 were eligible for inclusion. Baseline characteristics, coagulation parameters, transfusion requirements, and procedural details were extracted. Univariate and multivariable propensity-matched analyses were used to assess the relationships between prophylactic plasma transfusion and the outcomes of interest, with a primary outcome assessed *a priori* of RBC transfusion occurring during the procedure or within the first 24 hours post-procedurally.

Results—A total of 18,204 study participants met inclusion criteria for this study, and 1,803 (9.9%) had an INR ≥ 1.5 prior to their procedure. Among these, 196 patients (10.9%) received

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Declaration of Interests:

The authors declare that they have no conflicts of interest.

prophylactic plasma transfusion with a median (interquartile range) time between plasma initiation and procedural start of 1.9 (1.1 – 3.2) hours. In multivariable propensity-matched analysis, plasma administration was associated with increased periprocedural RBC transfusions [OR (95% CI) = 2.20 (1.38 – 3.50); $P < .001$] and postprocedural ICU admission rates [OR (95% CI) = 2.11 (1.41 – 3.14); $P < .001$] compared to those who were not transfused preprocedurally. Similar relationships were seen at higher INR thresholds for plasma transfusion.

Conclusion—In patients undergoing interventional radiology procedures, preprocedural plasma transfusions given in the setting of elevated INR values were associated with increased periprocedural RBC transfusions. Additional research is needed to clarify this potential association between preprocedural plasma and periprocedural RBC transfusion.

Introduction

Prophylactic plasma transfusion is commonly performed before interventional radiology procedures despite increased attention on the deleterious effects and high costs of blood product utilization.¹ Nearly 4 million units of plasma are transfused each year in the United States alone,² and it has been estimated that approximately 50% of plasma transfusions occur outside of published guidelines.³⁻⁵ In fact, the most commonly cited reason for plasma transfusion is correction of abnormal coagulation tests prior to an invasive procedure,^{6,7} though prior studies have failed to show a correlation between mild-to-moderate coagulation abnormalities (i.e. INR ≥ 2) and bleeding complications in patients undergoing invasive percutaneous procedures.⁸ In addition, plasma transfusion does not reliably normalize mild-to-moderate elevations in the International Normalized Ratio (INR),⁹⁻¹² and in the absence of active bleeding is not recommended for the correction of a mild coagulopathy. Furthermore, as studies have failed to demonstrate a clear relationship between mild-to-moderate elevations in INR and increased procedural bleeding risk, the utility of decreasing an elevated INR for the prevention of bleeding complications remains theoretical at best.^{8,13-15} Nonetheless, consensus guidelines released by the Society of Interventional Radiology Standards of Practice Committee identify an INR < 1.5 as the goal for patients undergoing procedures with moderate or high bleeding risk.¹

The purpose of this investigation was to determine the association between prophylactic plasma transfusion and periprocedural outcomes in patients with abnormal coagulation tests undergoing percutaneous image-guided interventions, with a primary outcome of periprocedural RBC transfusions. We hypothesized that prophylactic plasma administration would not be associated with decreased periprocedural RBC transfusion rates.

Materials and Methods

This is a retrospective observational cohort study conducted under the approval of the Mayo Clinic (Rochester, Minnesota) Institutional Review Board. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used in the design and conduct of this study, as well as in the reporting of results.¹⁶

Study Population

Inclusion criteria for this investigation were age $\geq$ 18 years of age and completion of a percutaneous invasive image-guided intervention (i.e. inpatient or outpatient procedures performed by the Division of Vascular/Interventional Radiology) at a single tertiary care center in Rochester, Minnesota between January 1st 2009 and December 31st 2013. Interventional procedures performed by other medical providers (e.g. cardiologists) were not included. An additional inclusion criterion was the presence of an INR in the 30-day interval preceding the procedure. Exclusion criteria included lack of valid research authorization and prior inclusion in the study (no patient was included twice). For patients with multiple interventional procedures, only the first procedure with a valid INR was included.

Outcome variables

The primary outcome for this study was the presence of a periprocedural RBC transfusion. To qualify, the RBC transfusion initiation time was required to occur during the procedural encounter or within 24 hours following discharge from the procedural environment. RBC transfusions initiated prior to entering the procedure suite were not included in the outcome evaluation. Additional secondary outcomes included unanticipated return to the procedural suite or transfer to an operating room within 24 hours of the index procedure; postprocedural ICU admission; postprocedural mechanical ventilation; ICU length of stay; hospital length of stay; and hospital mortality.

Predictor variables

The primary predictor variable for this investigation was the presence or absence of a preprocedural prophylactic plasma transfusion. For patients with multiple preprocedural INR values, the value closest to the time of the procedure was utilized. The presence and timing of all periprocedural transfusion episodes were extracted from the electronic health record. Prophylactic plasma transfusions were defined as plasma administered after the qualifying INR value and within 24 hours of the procedure. Plasma transfusions preceding measurement of the qualifying INR were not included. Moreover, intraoperative and postprocedural plasma transfusions were not considered in the analyses as our aim was to specifically investigate the impact of preprocedural plasma administration. Additionally, this exclusion of plasma administration after the start of the procedure avoids the potential for cause-effect inversion with the outcomes of interest. To further ensure against cause-effect inversion, the timing of plasma transfusion was defined as the actual transfusion initiation time as documented in the electronic health record rather than the time of issue from the blood bank. Patient demographics, baseline clinical characteristics, and procedural and anesthesia-related details were also extracted from the electronic medical record. Procedures were classified based upon bleeding risk as identified by the Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-guided Interventions into low, moderate, or high risk categories (Table 1).¹

Data Sources

Screening for potential study participants was performed using the Perioperative Data Mart, an institutional resource that captures clinical and procedural data for all patients who are

admitted to an acute care environment including procedural suites, operating rooms, intensive care units, and progressive care units at the study's participating institution.¹⁷ This robust data warehouse also contains information on baseline demographics and clinical characteristics, fluid and transfusion therapies, periprocedural medications and laboratory values, postprocedural outcomes, and lengths of stay. Additional pertinent baseline characteristics were obtained from a second validated database, the Mayo Clinic Life Sciences System (MCLSS).¹⁸ Both databases have undergone extensive validation with accuracy superior to manual data collection alone.¹⁹

Sample size Calculation

Assuming a periprocedural RBC transfusion event rate of 15% in the target study population (pre-procedural INR ≥ 1.5 , based on historical data from the participating institution) and a prophylactic plasma transfusion rate of 10% in those with a preprocedural INR ≥ 1.5 , the sample size required to identify an odds ratio of 0.5 in those who receive a prophylactic plasma transfusion compared to those who do not was estimated to be 1998 total study participants (two-sided alpha of 0.05, beta = 0.20). Furthermore, assuming that 80% of patients would have a qualifying preprocedural INR and approximately 10% of qualifying INR values would be ≥ 1.5 , we estimated the need to evaluate approximately 24,000 unique participants having undergone the procedures of interest.

Statistical Analysis

Baseline demographics, clinical characteristics and procedure-related information were summarized and presented as median (25% – 75% interquartile range) for continuous data elements and frequencies (%) for categorical data, respectively. An INR ≥ 1.5 was used as a threshold for coagulopathy in this study for two reasons: 1) an INR < 1.5 has been identified by the 2011 Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-guided Interventions as the goal for patients undergoing procedures with moderate or high bleeding risk,¹ and 2) the decision to transfuse plasma prior to invasive procedures is commonly based on threshold values, with INR ≥ 1.5 a commonly used trigger in local practice. Recognizing that transfusion strategies may vary significantly by practice location,²⁰ sensitivity analyses using INRs ≥ 1.75 and ≥ 2.0 were planned a priori.

The relationships between prophylactic preprocedural plasma transfusion and bleeding complications were explored with both univariate and multivariable analyses. Recognizing that observational studies risk unequal distributions of key confounding variables due to the lack of subject randomization, propensity-matched analyses were performed. Logistic regression was used to calculate propensity scores utilizing all hypothesized confounding variables (variables included in the propensity score estimation are included in Supplemental Figure). Using an optimal matching algorithm, a maximum of 2 subjects who did not receive prophylactic plasma transfusion were assigned to each subject who did receive plasma transfusion. Subjects were matched exactly on procedure bleeding risk and on propensity score within 0.5 times the standard deviation of the propensity score.²¹ Standardized mean differences after propensity score adjustment as well as p-values from conditional logistic regression analysis using matched sets as strata were obtained for each covariate to assess

the effectiveness of the propensity score to control for confounding of the observed variables. Conditional logistic regression was then used to estimate the odds of receiving periprocedural RBC transfusion for patients with preprocedural exposure to prophylactic plasma transfusion. Similar procedures were carried out for the secondary outcomes as well.

To further assess the robustness of the study findings, multiple additional sensitivity analyses were planned *a priori*. These pre-specified analyses included: 1) restriction to study participants undergoing low, moderate, or high-risk procedures, respectively; 2) restriction to patients undergoing emergency procedures; and 3) restriction to patients with an INR 1.75 and 2.0, respectively. In addition, recognizing that some preprocedural plasma transfusions may occur in the setting of resuscitation from active bleeding, analyses were also performed with the exclusion of patients having received RBC transfusion in the 24 hour period before procedure initiation. As a post-hoc analysis, we also excluded patients receiving plasma transfusion in the 24 hours before measurement of the qualifying INR. Additionally, to assess the impact of vitamin K administration on periprocedural RBC transfusion rates, we included vitamin K administration as a covariate in the propensity-matched cohort. All statistical analyses were performed using JMP statistical software base version 9.0.1 and SAS 9.3 (SAS Institute Inc., Cary, NC).

Results

A total of 42,952 invasive image-guided interventions were performed over the study period on 24,626 unique patients, with 18,204 having a valid INR within 30 days of the procedure (Figure 1). Among these, 1,803 (9.9%) had a preprocedural INR 1.5, of whom 196 (10.9%) received a prophylactic plasma transfusion prior to entry into the procedural suite. The median (interquartile range) time between INR measurement and procedure onset was 7.5 (3.3 – 21.4) hours for those with INR 1.5 and 5.9 (3.6 – 9.8) hours for those with INR 1.5 receiving preprocedural plasma, with all measurements occurring within 24 hours of the procedural start time. In those who received preprocedural plasma as defined by the study protocol, the median time from initiation of the last qualifying plasma component to the onset of the procedure was 1.9 (1.1 – 3.2) hours with a median (range) plasma transfusion volume of 2 (1 – 6) units. There was no association between plasma volume and preprocedural INR ($P=.49$) or subsequent RBC transfusion rates ($P=.74$). Comparison of baseline clinical, demographic, and procedural characteristics for those with an INR 1.5 are shown in Table 2. Key differences in the full cohort prior to propensity-matching included a higher rate of liver disease, more severe coagulation abnormalities, and an increased incidence of emergency and high-bleeding risk procedures in those receiving prophylactic plasma.

Results of unadjusted analyses evaluating the associations between prophylactic preprocedural plasma transfusions with periprocedural bleeding complications and other patient-important outcomes are shown in Table 3. The frequency of periprocedural RBC transfusion among those who received preprocedural plasma transfusion versus those who did not was 29.6% versus 10.9% ($P<.001$). In patients receiving RBC transfusion, the median (interquartile range) RBC transfusion volume was similar in those who received preoperative plasma and those who did not [2 (1 – 2) units versus 2 (1 – 2) units, $P=.31$]. In

addition, patients receiving prophylactic plasma had higher rates of ICU admission (51.0% versus 27.3%, $P<.001$). There were no significant between group differences in hospital mortality, postoperative mechanical ventilation rates, or ICU or hospital lengths of stay.

A total of 1,682 of the study subjects were assigned a propensity score; 121 (7%) were not assigned a score as a result of missing hemoglobin values, including 3 (2%) plasma-transfused patients. From those with available propensity scores, 184 study subjects receiving prophylactic plasma transfusion were propensity matched to 359 study subjects who did not. Nine subjects who received plasma were matched to a single non-transfused subject and 175 subjects were matched to 2 non-transfused subjects. A total of 9 subjects who had received a prophylactic plasma transfusion were removed from the propensity matched analyses due the lack of a suitable non-transfused propensity matched study subject. Importantly, propensity matching was effective in addressing the baseline covariate imbalances between the plasma exposure groups (Table 2, Supplemental Figure).

Among this propensity matched cohort, 51 (28%) of the plasma transfused subjects received a periprocedural RBC transfusion compared with 56 (16%) of those who did not receive preprocedural plasma. Conditional logistic regression analysis on these propensity matched subjects identified a statistically significant increase in the risk of periprocedural RBC transfusion in those who received preprocedural prophylactic plasma compared with those that did not [OR (95% CI) = 2.20 (1.38 – 3.50); $P<.001$]. The results of secondary outcome analyses are shown in Table 4, including an increased rate of ICU admission within 24 hours of the procedure [OR (95% CI) = 2.11 (1.41 – 3.14); $P<.001$]. There were no significant differences in postoperative mechanical ventilation rates or hospital mortality.

The results of sensitivity analyses assigned *a priori* are displayed in Supplemental Table. Periprocedural RBC transfusion rates remained higher in plasma transfused patients even at INR transfusion thresholds greater than or equal to 1.75 and 2.0. In addition, prophylactic plasma transfusions for non-emergent procedures and procedures of moderate bleeding risk were associated with increased RBC transfusions. There were no differences in RBC transfusion rates between plasma transfused and non-transfused patients for procedures of low or high bleeding risk. After exclusion of patients receiving RBC transfusion in the 24 hours before the procedure, plasma transfusion remained associated with increased periprocedural RBC transfusion rates [OR (95% CI) = 1.99 (1.20 – 3.30); $P=.008$].

As a post-hoc analysis, 257 patients that received plasma transfusion in the 24 hour period prior to measurement of the qualifying preprocedural INR were excluded, including 180 that received no additional plasma therapy and 77 that received additional preprocedural plasma. Preprocedural plasma remained associated with periprocedural RBC transfusions after exclusion of these patients (Supplemental Table). In addition, a significant difference was noted in vitamin K administration between non-plasma transfused (11.3%) and plasma-transfused (33.7%) groups ($P<.001$). When including vitamin K as a covariate in propensity-matched analysis on the primary outcome, plasma transfusion remained associated with an increased risk of RBC transfusion [OR (95% CI) = 2.08 (1.30 – 3.33); $P=.002$] with no statistically significant association found for vitamin K [OR (95% CI) = 1.76 (0.89 – 3.47); $P=.10$].

Discussion

In this investigation, we aimed to assess the association between prophylactic plasma transfusion and periprocedural bleeding complications in patients with abnormal preprocedural coagulation tests undergoing invasive image-guided interventions, finding no evidence for decreased RBC transfusion rates when plasma was administered before the procedure. Conversely, patients receiving prophylactic plasma actually received more RBCs in the periprocedural period in propensity-matched analysis, a finding which remained significant in multiple sensitivity analyses including at higher INR thresholds for plasma transfusion.

Plasma transfusion for attempted normalization of an elevated preprocedural INR is exceedingly common, accounting for one third of all plasma transfusions.⁶ Unfortunately, there is a lack of data supporting the utility of such practice. A systematic review of 57 randomized controlled trials investigating the ability of prophylactic plasma transfusion to prevent bleeding complications in a variety of clinical settings found insufficient evidence to either support or refute the efficacy of the intervention.⁹ It should be noted that no trials of percutaneous image-guided interventions were identified for inclusion. Remarkably, prior to this investigation, no study had evaluated the utility of plasma transfusion for the prevention of hemorrhagic complications in patients undergoing interventional radiology procedures despite the widespread use of plasma for this indication. Müller and colleagues recently performed a randomized controlled trial of plasma transfusion in critically ill patients with mild-to-moderate elevations in INR (1.5 – 3.0) prior to invasive ICU procedures including central venous catheter or chest tube placement, thoracentesis, percutaneous tracheostomy, and abscess drainage.¹² While the study was stopped before reaching predefined target enrollment due to slow enrollment and was therefore likely not sufficiently powered to detect the primary endpoint, there was no difference in bleeding complications between plasma-transfused or non-plasma transfused groups in the 81 randomized patients.

With regards to the relationship between abnormal coagulation tests and periprocedural bleeding complications in percutaneous interventional radiology procedures, the vast majority of studies to date have failed to show increased bleeding in the setting of abnormal preoperative coagulation parameters, including investigations of patients undergoing angiography,¹³ liver biopsy,¹⁴ central venous catheter placement,^{15,22-24} central venous catheter removal,²⁵ and nephrostomy tube placement.^{26,27} Despite this, Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-Guided Interventions recommend correction of INR to less than 1.5 prior to procedures with moderate to high risk of bleeding. In addition, they recommend an INR of 2.0 as the threshold for treatment in those undergoing procedures of low bleeding risk. While transfusing plasma to a patient with a coagulation test outside of the normal range may make intuitive sense, there is no evidence to support this practice in the absence of active bleeding.^{7,8} If decreasing INR is deemed to be essential prior to the procedure in patients (taking vitamin K antagonists), other options are available including vitamin K administration, the use of prothrombin complex concentrates (PCCs), and procedural delay. While the current investigation was not designed to assess the utility of these interventions, there are potential risks and benefits associated with each. In the absence of active bleeding

or need for emergent procedure, vitamin K is a preferred therapy for reversal (of vitamin K antagonists) though it may make reestablishment of therapeutic anticoagulation difficult.⁷ When emergent reversal (of vitamin K antagonist therapy) is needed, PCCs provide a more (rapid) normalization of coagulation parameters compared to plasma therapy and have an increased safety profile, though there may be a heightened risk for thrombotic events especially with repeat dosing.²⁸

In this investigation, RBC transfusion rates during the procedure or in the first 24 post-procedural hours were higher in patients receiving prophylactic plasma compared with those who did not. While the observational design of this investigation does not allow for precise determination of the circumstances surrounding periprocedural transfusion decisions, there are several plausible explanations for increased RBC transfusion rates in those treated with plasma. First, this finding may be a reflection of heterogeneous provider transfusion practices, with some providers more inclined to transfuse blood products preprocedurally and thereafter. Second, the associated volume expansion that accompanies plasma administration may cause sufficient hemodilution to decrease hemoglobin concentrations below clinical thresholds for RBC transfusion. Furthermore, in some patients the volume expansion inherent in plasma transfusion may lead to increased intravascular pressures and the potential disruption of recently developed hemostatic plugs. This model of intravascular volume-associated increases in clinical bleeding has been similarly postulated in both major trauma²⁹ and acute gastrointestinal hemorrhage,³⁰ lending support to permissive hypotension in the former and restrictive RBC transfusion strategies in the latter. It should also be mentioned that while the INR, which represents only a part of the coagulation cascade, is sensitive to changes in procoagulant factor activity, it is insensitive to anticoagulant and fibrinolytic activity. The administration of plasma, which contains both procoagulant and anticoagulant factors, may result in significant increases in anticoagulant proteins (e.g. antithrombin) with effects that may be magnified in certain clinical settings (e.g. heparin therapy).³¹ Hence, it is possible that in some patients this may paradoxically tip the hemostatic balance point towards a more anticoagulated state. Finally, there remains the very likely possibility of residual confounding despite careful statistical adjustments with plasma transfusion serving as a surrogate for a sicker patient.

This study has several important limitations. Despite the large sample size and sophisticated electronic data extraction techniques and statistical analyses, this is a retrospective investigation with inherent concern for residual confounding and bias. While propensity-matching was successful in addressing baseline imbalances in measured variables, the potential for confounding in unmeasured variables persists, which is a recognized limitation of propensity-adjusted analyses. For example, two variables not captured in the dataset which may influence outcome include a personal or family history of bleeding and the presence or absence of clinical bleeding (e.g. bruising, minor hemorrhage) prior to the interventional procedure. In addition, the non-plasma transfused group may have been sicker despite close propensity-matching, and higher rates of ICU admission and RBC transfusion may simply be a reflection of a sicker group of patients. Moreover, the observational nature of this study makes it difficult to determine the precise clinical circumstances affecting the decision to transfuse or withhold transfusion in the periprocedural period. Periprocedural RBC transfusion was used as a surrogate for bleeding complications; however it is possible

that some patients received RBCs in the absence of clinical bleeding. In addition, some patients may have received preprocedural plasma for indications other than bleeding prophylaxis (e.g. plasmapheresis, antithrombin deficiency, ongoing resuscitation in response to active bleeding). To further address the concern of preprocedural plasma therapy being administered for the treatment of active bleeding, we performed a sensitivity analysis excluding all patients that had received RBC transfusion in the 24 hours before the procedure initiation time. The results of this sensitivity analysis were similar to those performed in the full cohort. On the other hand, the predefined exclusion of plasma transfusions occurring after entry into the procedural suite may have excluded some prophylactic plasma transfusions from analysis. However, this was performed in an attempt to minimize the probability for cause-effect inversion with the primary outcome, as plasma transfusions in the procedural arena are often triggered by ongoing blood loss rather than for the prevention of bleeding complications. It should also be noted that the observed relationships between preprocedural plasma transfusion and the outcomes of interest represent associations, and direct causality cannot be inferred. Moreover, as qualifying plasma transfusions were administered after INR measurement and before entry into the procedural suite, post-transfusion preprocedural INR values were not available to assess the response of INR to plasma transfusion. Therefore, the relationship between degree of post-transfusion INR normalization and bleeding complications remains unknown. Finally, the results of this investigation are derived from a single tertiary care medical center and will ultimately require external validation, ideally in a multicenter prospective investigation or randomized clinical trial.

Conclusion

While coagulation abnormalities are common prior to interventional radiology procedures, prophylactic administration of plasma was not associated with decreased RBC transfusion rates or improved patient outcomes. Further study is necessary to better define these relationships and establish causality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Support

This study was made possible by funding from the Mayo Clinic Department of Anesthesiology and the Critical Care Integrated Multidisciplinary Practice, Rochester, Minnesota. In addition, this study was supported by an NIH R01 grant (HL121232) to Dr. Kor.

Abbreviations

ICU	Intensive Care Unit
INR	International Normalized Ratio
RBC	Red Blood Cell

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Figure 1.
Study population flow diagram.

Table 1Procedural bleeding risk categories for patients with an INR ≥ 1.5 at time of needle placement^a

Low (n=869)	Moderate (n=875)	High (n=59)
<u>Vascular</u> Adrenal vein sampling (n=1) Brachytherapy positioning (n=4) Central line removal (n=23) Central venous catheter (n=105) Dialysis access (n=35) IVC filter placement (n=162) IVC filter removal (n=70) Lytic recheck (n=13) PICC placement (n=89) Venography (n=124)	<u>Vascular</u> Angiography (n=223) Angioplasty (n=12) Arterial embolization, coiling (n=67) Transjugular liver biopsy (n=1) Tunneled venous catheter (n=173) Subcutaneous port (n=20) Chemoembolization (n=2)	<u>Vascular</u> TIPS (n=51)
<u>Nonvascular</u> Drainage catheter exchange (n=39) Loopogram (n=4) Lymphangiogram (n=6) Paracentesis (n=9) Sinogram (n=45) Superficial abscess drainage (n=1) Superficial biopsy (n=138) Thoracentesis (n=1)	<u>Nonvascular</u> Intraabdominal or retroperitoneal abscess drainage (n=234) Transabdominal liver biopsy (n=3) Percutaneous cholecystostomy (n=71) Percutaneous cholangiogram (n=57) Radiofrequency ablation (n=3) Spine procedures (n=7) Cryoablation (n=2)	<u>Nonvascular</u> Renal biopsy (n=5) Biliary interventions (n=3)

IVC – inferior vena cava, PICC – peripherally inserted central catheter, TIPS – transjugular intrahepatic portosystemic shunt

^aAdapted from Consensus Guidelines for Periprocedural Management of Coagulation Status and Hemostasis Risk in Percutaneous Image-guided Interventions.¹

Table 2

Demographic and clinical characteristics of patients with INR 1.5

	No plasma therapy (N=1607)		Plasma therapy (N=196)		Unadjusted <i>P</i> -value	Stratified <i>P</i> -value ^c
<u>Demographics</u>						
Age (y)	61.2	(16.2)	60.6	(17.2)	.66	.75
Gender					.06	.97
Female	646	(40%)	65	(33%)		
Male	961	(60%)	131	(67%)		
BMI§	29.0	(24.8, 33.8)	28.4	(24.9, 32.3)	.18	.33
<u>Comorbidities</u>						
Cancer	258	(16%)	31	(16%)	.93	.78
Metastatic cancer	93	(6%)	7	(4%)	.20	.77
Cerebrovascular disease	209	(13%)	28	(14%)	.62	.83
CHF	340	(21%)	43	(22%)	.80	.91
Diabetes	292	(18%)	35	(18%)	.91	.64
Diabetes w/ organ damage	73	(5%)	6	(3%)	.34	.25
Dementia	20	(1%)	2	(1%)	.79	.79
Leukemia	35	(2%)	1	(1%)	.12	.99
Lymphoma	87	(5%)	11	(6%)	.91	.56
MI	220	(14%)	26	(13%)	.87	.75
COPD	191	(12%)	30	(15%)	.17	.90
Asthma	131	(8%)	18	(9%)	.62	.67
ILD	51	(3%)	4	(2%)	.38	.83
Pulmonary disease	329	(20%)	41	(21%)	.88	.91
Peripheral vascular disease	129	(8%)	8	(4%)	.05	.88
CT disease	57	(4%)	11	(6%)	.15	.67
Chronic renal failure	500	(31%)	66	(34%)	.47	.69
Hemiplegia	18	(1%)	4	(2%)	.27	1.00
Liver disease					.04	.81
None	1394	(87%)	157	(80%)		
Mild	93	(6%)	16	(8%)		
Moderate to severe	120	(7%)	23	(12%)		
Peptic ulcer	133	(8%)	17	(9%)	.85	.96
Charlson score	2	(0, 5)	2	(1, 5)	.52	.86
<u>Perioperative medications</u>						
Aspirin	351	(22%)	34	(17%)	.15	.77
Clopidogrel	57	(4%)	5	(3%)	.47	.73
NSAIDS	94	(6%)	16	(8%)	.20	.77
Thrombin inhibitor	48	(3%)	1	(1%)	.04	1.00

	No plasma therapy (N=1607)		Plasma therapy (N=196)		Unadjusted <i>P</i> -value	Stratified <i>P</i> -value ^c
LMW heparin (within 24 hours)	118	(7%)	16	(8%)	.68	.74
Therapeutic heparin (within 24 hours)	190	(12%)	13	(7%)	.03	.62
Warfarin	505	(31%)	48	(24%)	.05	.86
Baseline laboratory values						
Platelet count ^b	191.0	(116.5, 289.0)	163.0	(82.5, 271.5)	.002	.48
INR	1.7	(1.5, 2.0)	1.9	(1.7, 2.3)	<.001	.60
Creatinine ^b	1.1	(0.8, 1.8)	1.2	(0.8, 2.2)	.04	.55
Albumin ^b	3.2	(2.8, 3.8)	3.1	(2.5, 3.6)	.02	.32
Hemoglobin ^b	10.0	(9.0, 11.9)	9.5	(8.5, 10.8)	<.001	.80
aPTT ^b	37.0	(32.0, 51.0)	39.0	(33.0, 49.0)	.33	.17
Procedural characteristics						
ASA PS ^{a,b}					.04	.45
1-2	207	(36%)	22	(23%)		
3-4	355	(63%)	70	(74%)		
5+	6	(1%)	2	(2%)		
Procedure bleed risk					<.001	-
Low	805	(50%)	64	(33%)		
Moderate	753	(47%)	122	(62%)		
High	49	(3%)	10	(5%)		
Emergency procedure	49	(3%)	20	(10%)	<.001	.80
Anesthesia type					<.001	.96
General	163	(10%)	42	(21%)		
Monitored anesthesia care	132	(8%)	20	(10%)		
RN sedation	1312	(82%)	134	(68%)		
Procedure duration (m)	24	(14, 44)	29	(15, 61)	.01	.85

P-values for continuous variables are from rank sum tests. P-values for categorical variables are from Chi-Square tests.

ASA PS = American Society of Anesthesiologist's Physical Classification Score; NSAIDS = Non-steroidal anti-inflammatory drugs; INR = international normalized ratio; aPTT = activated partial thromboplastin time; RN = registered nurse.

^aTo compare ASA PS between treatment groups, patients with values greater than 4 were included in the 3-4 category.

^bSome values are missing for body mass index (n=53), Platelet count (n=79), creatinine (n=92), albumin (n=890), hemoglobin (n=121), aPTT (n=697), and ASA PS (n=1141).

^cStratified p-values correspond to the comparison of the given characteristic for the propensity-matched strata.

Table 3

Univariate analysis of primary and secondary outcomes by the presence of absence of preprocedural plasma transfusion in those with preprocedural INR ≥ 1.5

Outcome	No plasma therapy (n = 1607)	Plasma therapy (n = 196)	OR (95% CI)	P-value ^c
Periprocedural RBC ^a	172 (11%)	58 (30%)	3.51 (2.48-4.95)	<.001
Return to procedure suite within 24 hrs ^a	50 (3%)	10 (5%)	1.67 (0.83-3.36)	.15
ICU admission ^a	433 (27%)	100 (51%)	2.82 (2.09-3.81)	<.001
ICU length of stay (days, n=533) ^b	3.0 (1.2-9.8)	3.7 (1.9-6.9)	--	.44
Postprocedural MV ^a	96 (6%)	18 (9%)	1.59 (0.94-2.70)	.08
Duration of MV (days, n=114) ^b	3.1 (0.3-14.6)	1.4 (0.5-11.2)	--	.39
Hospital LOS (days, n=1425) ^b	11.8 (5.1-25.5)	12.0 (6.1-22.9)	--	.79
Hospital Mortality ^a	158 (10%)	28 (14%)	1.53 (0.99-2.36)	.06

OR = odds ratio; CI = confidence interval; RBC = red blood cell transfusion; ICU = intensive care unit; MV = mechanical ventilation; LOS = length of stay

^a number (%)

^b median (25%-75% interquartile range).

^c p-values are from logistic regression for categorical variables and from rank-sum tests for continuous variables.

Table 4

Conditional logistic regression on the propensity matched cohort.

Outcome	No plasma therapy (n = 359)	Plasma therapy (n = 184)	OR (95% CI)	P-value ^c
Periprocedural RBC ^a	56 (16%)	51 (28%)	2.20 (1.38 – 3.50)	<.001
Return to procedure suite within 24 hrs ^a	10 (3%)	10 (5%)	2.00 (0.83 – 4.81)	.12
ICU admission ^a	117 (33%)	89 (48%)	2.11 (1.41 – 3.14)	<.001
ICU length of stay (days, n=206) ^b	3.9 (1.5 -10.3)	3.7 (1.8-5.9)	--	.68
Postprocedural MV ^a	26 (7%)	15 (8%)	1.13 (0.57 – 2.24)	.73
Duration of MV (days, n=41) ^b	2.8 (0.3-14.5)	2.7 (0.3-13.6)	--	.49
Hospital LOS (days, n=474) ^b	13.1 (5.1-28.0)	12.0 (5.9-22.9)	--	.58
Hospital Mortality ^a	51 (14%)	24 (13%)	0.89 (0.53 – 1.47)	.64

OR = odds ratio; CI = confidence interval; RBC = red blood cell transfusion; EBL = estimated blood loss; ICU = intensive care unit; MV = mechanical ventilation; LOS = length of stay

^a number (%)

^b median (25%-75% interquartile range).

^c p-values are from conditional logistic regression for categorical variables and rank-sum tests for continuous variables.