Coagulation Abnormalities in Pediatric and Adult Patients After Sclerotherapy or Embolization of Vascular Anomalies

Keira P. Mason[1,2]
Ellis J. Neufeld[3]
Victoria E. Karian[2]
David Zurakowski[4]
Babu V. Koka[1]
Patricia E. Burrows[2]

OBJECTIVE. The purpose of our study was to examine the coagulation status in patients with vascular anomalies who had undergone sclerotherapy or embolization.

SUBJECTS AND METHODS. Ours was a prospective pilot study of 29 patients who had undergone sclerotherapy or embolization of large vascular anomalies. Fibrinogen, platelet, and d-dimer levels and prothrombin time were obtained before, immediately after, and on the day after the procedure.

RESULTS. Five patients with venous malformations had positive d-dimer levels before the procedure. A subgroup analysis revealed a relationship between the type of agent used and the change in coagulation status. Specifically, a positive relationship was found between the use of dehydrated alcohol or sodium tetradecyl sulfate and a disruption in coagulation profiles as evidenced by a decrease in platelets and fibrinogen, an increase in prothrombin time, and a conversion from negative to positive d-dimers. In contrast, sclerotherapy or embolization with cyanoacrylic, polyvinyl alcohol foam particles, or platinum microcoils was not associated with coagulation disturbances.

CONCLUSION. The coagulation disturbances that occur in response to dehydrated alcohol or sodium tetradecyl sulfate sclerotherapy or embolization could compromise the patient's clotting ability. Patients who receive dehydrated alcohol or sodium tetradecyl sulfate during a preoperative sclerotherapy or embolization may experience coagulation disturbances that could increase the risk of bleeding, thrombosis, or hematoma. This patient population may benefit from the use of glue, foam, or coils as a substitute for dehydrated alcohol or sodium tetradecyl sulfate.

Vascular tumors and anomalies exhibit a range of coagulopathies. Kaposiform hemangioendothelioma and tufted angioma may manifest thrombocytopenia and coagulopathy known as Kasabach-Merritt syndrome [1–3]. Vascular anomalies, including Klippel-Trenaunay and Parkes-Weber syndromes, have been reported to manifest both chronic consumption coagulopathies and acute changes in response to surgical procedures, such as fracture reduction or surgery related to childbirth [4, 5].

Although extensive limb venous malformations [6] and some hemangiomas [7] may manifest coagulation disturbances, to our knowledge, no studies in the literature detail the coagulation profiles of patients with vascular anomalies both at baseline and 24 hr after sclerotherapy or embolization. Our study was designed to study specific coagulation parameters in patients with arteriovenous malformation, venous malformation, lymphatic malformation, lymphaticovenous malformation, and hemangioma to determine whether these patients have prolonged disruption of their coagulation status after sclerotherapy or embolization. Treatments consisted of either single-agent or combination therapy that included dehydrated alcohol (Ethanol; American Regent Laboratories, Shirley, NY), sodium tetradecyl sulfate injection (Sotradecol; Elkins-Sinn, Cherry Hill, NJ), n-butyl-2-cyanoacrylate liquid emboli (Trufill; Cordis, Miami, FL), tungsten powder (Cordis), polyvinyl alcohol foam particles (Boston Scientific, Natick, MA), or platinum microcoils (Target Therapeutics, Fremont, CA). Changes in the coagulation status of the patients were monitored both immediately after the procedure and 24 hr later.

Received February 13, 2001; accepted after revision June 28, 2001.

[1]Department of Anesthesia, Children's Hospital, 300 Longwood Ave., Boston, MA 02115-5737. Address correspondence to K. P. Mason.

[2]Department of Radiology, Children's Hospital, Boston, MA 02115-5737.

[3]Department of Hematology–Oncology, Children's Hospital, Boston, MA 02115-5737.

[4]Department of Biostatistics, Children's Hospital, Boston, MA 02115-5737.

AJR 2001;177:1359–1363

0361–803X/01/1776–1359

This study was designed to ascertain whether a relationship exists between coagulation responses and such factors as the type of agent used, procedure performed, or patient demographics (age, body weight, or type or location of lesion). The ability to predict postprocedure coagulation disturbances may have substantial implications. Identifying those patients who are at high risk of coagulopathies may affect the management of these patients who receive sclerotherapy or embolization as a precursor to a surgical resection. Furthermore, this population may benefit from frequent monitoring of coagulation status and replacement therapy, if clinically warranted.

Subjects and Methods

After receiving approval from our institutional review board, we enrolled 29 children and adults with extensive vascular anomalies requiring sclerotherapy or embolization between December 1999 and July 2000. We obtained fibrinogen (mg/dL), prothrombin (sec), platelet ($\times 10^3/\mu L$), and d-dimer levels. All procedures were performed by the same interventional radiologist. Informed consent was obtained for the interventional procedure and necessary blood tests. Partial thromboplastin time was not studied because some patients were placed on IV heparin after the procedures. Inclusion criteria required that these patients enroll only once, agree to an overnight admission after the procedure, and sign an informed consent form (parents were asked to sign for patients younger than 18 years old). One hundred eleven patients were excluded from the study because they had undergone the same procedure within the past month, had already been enrolled once in the study, had small anomalies (requiring < 5 mL of dehydrated alcohol), or were on anticoagulants. Blood samples were drawn from a fresh venipuncture before (within 24 hr), immediately after (within 30 min), and the day after (24 hr later) the procedure. The initial blood samples were drawn to establish the patient's baseline coagulation profile. Two specific changes were examined: change occurring immediately after the procedure versus the baseline and change occurring 24 hr after the procedure versus the baseline.

Embolization of vascular anomalies involved cannulation of the femoral or axillary artery and selective catheterization of supplying arteries with a guiding catheter. After angiography was completed, the patient's feeding arteries were catheterized supraselectively (third-order or greater arterial branches), as close to the arteriovenous shunt as possible, with a microcatheter. Dehydrated alcohol, 1% or 3% sodium tetradecyl sulfate, n-butyl-2-cyanoacrylate mixed with ethiodized oil (Ethiodol; Savage Laboratories, Melville, NY) and tungsten powder, polyvinyl alcohol foam particles, or platinum microcoils were injected or placed into appropriate vessels, using inflow occlusion (proximal balloon catheter or tourniquet) when appropriate. After approximately 5 min, contrast material injection was repeated, and more dehydrated alcohol was injected if necessary.

Sclerotherapy was performed by direct percutaneous cannulation of the anomalous veins of the venous malformations, cystic portions of the lymphatic malformations and arteriovenous shunt, or draining veins of the arteriovenous malformations. Contrast material injection was recorded using the digital subtraction technique. Appropriate outflow occlusion was applied (tourniquet, blood pressure cuff, or manual compression), and contrast material injection was repeated until no undesirable outflow into normal vessels occurred. Dehydrated alcohol was then injected under visual (for superficial lesions) or fluoroscopic guidance. For the latter, dehydrated alcohol was opacified by mixing it with metrizamide powder and 15–320 mL of Amipaque (Winthrop, New York, NY) or oily contrast medium (8–2 mL of Ethiodol). When tourniquet or blood pressure cuff was used, outflow occlusion was maintained for 10–30 min after the injection. In some patients, a pedal IV cannula was placed for infusion of heparinized saline into the leg veins. These patients received an initial bolus of heparin (50 U/kg) and were kept heparinized (20 U/kg per hour) overnight to prevent deep venous thrombosis caused by prolonged tourniquet occlusion (>30 min) during sclerotherapy of diffuse venous malformations.

All procedures were performed with the patient under general endotracheal anesthesia with neuromuscular blockade and controlled positive pressure ventilation. To facilitate supraselective arterial embolization, we manipulated controlled ventilation to create hypercarbia. One week after the procedure, patients were contacted by telephone for follow-up of complications and recovery.

Data Analysis

A power analysis (nQuery Advisor, version 4.0; Statistical Solutions, Boston, MA) based on paired

TABLE 1 Data on Demographics, Vascular Anomalies, and Interventional Procedures in 29 Patients Who Received Sclerotherapy, Embolotherapy, or Both

Data Variable	Numeric Value
Age, range (mean ± SD)	6 days–28 yr (11.4 ± 7.4 yr)
Weight, range (mean ± SD)	4.1–82.0 kg (39.5 ± 21.4 kg)
Sex, no. of patients (%)	
Male	10 (35)
Female	19 (65)
Type of vascular anomaly, no. of patients (%)	
Venous	15 (52)
Arteriovenous	11 (38)
Lymphatic	1 (3)
Lymphaticovenous	1 (3)
Hemangioma	1 (3)
Location of vascular anomaly, no. of patients (%)	
Head and neck	13 (45)
Lower extremity	9 (31)
Upper extremity	1 (3)
Thorax	3 (10)
Pelvis and groin	3 (10)
Interventional procedure, no. of patients (%)	
Sclerotherapy	14 (48)
Embolization	9 (31)
Both sclerotherapy and embolization	6 (21)
Therapeutic agent administered, no. of patients (%)	
Dehydrated alcohol	11 (38)
Dehydrated alcohol and 1% sodium tetradecyl sulfate combined	2 (7)
Dehydrated alcohol and 3% sodium tetradecyl sulfate combined	7 (24)
3% sodium tetradecyl sulfate only	2 (7)
Other (powder, glue, coils)	7 (24)
Duration of procedure, range (mean ± SD)	2.0–8.9 hr (4.0 ± 1.7 hr)
Amount of therapeutic agent administered, range (mean ± SD)[a]	0.21 –1.02 mL/kg (0.64 ± 0.28 mL/kg)

Note.—Percentages may not total 100% because of rounding.

[a]Data based on 20 patients who received dehydrated alcohol as agent.

Student's *t* tests with a two-tailed alpha level of 0.05 indicated that a minimum sample size of 25 patients would provide 90% statistical power for detecting a change of one standard deviation (effect size = 1.0) and 75% power for detecting a smaller change (effect size = 0.5) between pretreatment and posttreatment measurements of each of the continuous coagulation variables.

We assessed the continuous coagulation variables, including fibrinogen, platelets, and prothrombin time, for normal distribution using the Kolmogorov-Smirnov goodness-of-fit test and found no significant departures from a normal distribution [8]. Therefore, paired Student's *t* tests were used to assess changes in fibrinogen, platelet count, and prothrombin time between pretreatment and posttreatment measurements. To evaluate whether the size of the patient had an impact on coagulopathic changes, we tested body weight as a covariate using a repeated-measures analysis of variance [9]. Changes in d-dimers were evaluated by the nonparametric Wilcoxon's signed rank test [10]. The association between the amount of dehydrated alcohol administered adjusted for body weight and the changes in each coagulation variable was evaluated by correlation and linear regression. The Spearman rho correlation coefficient was used to assess the relationship between amount of dehydrated alcohol or sodium tetradecyl sulfate administered and changes in d-dimers. Two-tailed *p* values of less than 0.05 were considered statistically significant for all comparisons. Data analysis was performed using the SAS software package (version 6.12; SAS Institute, Cary, NC).

Results

Patient demographics and procedure data are presented in Table 1. Most patients were children: younger than 5 years old, $n = 7$; 5–9 years old, $n = 7$; and 10–18 years old, $n = 10$. Five patients were older than 18 years old. All 29 patients had baseline prothrombin, platelet, and fibrinogen values in the normal range. Five patients with venous malformation, without clinical signs or symptoms of coagulopathy, had positive d-dimer levels at preprocedure evaluation.

Changes in Coagulation Variables

Results from coagulation studies of all the patients are presented in Table 2. Paired Student's *t* tests indicated significant declines in fibrinogen and platelet levels as well as an increase in prothrombin time ($p < 0.001$) immediately after the procedure (post 1) compared with the measurements of these factors obtained before treatment. The nonparametric Wilcoxon's signed rank test revealed a significant conversion from negative to positive d-dimers ($p < 0.01$). At the measurement obtained 24 hr after the procedure (post 2), fibrinogen levels were not significantly lower than at pretreatment ($p = 0.53$), although platelet levels remained significantly lower and prothrombin time higher (both $p < 0.001$) than at pretreatment. The conversion from negative to positive d-dimers was still observed ($p < 0.01$).

For the patients overall, the results of repeated-measures analysis of variance using body weight as a covariate indicated no significant effects of body weight on changes in levels of fibrinogen, platelets, or d-dimers or in prothrombin time between pretreatment and either post 1 or post 2 measurements; neither were significant effects found when the patients were considered separately as the subgroups receiving either dehydrated alcohol or sodium tetradecyl sulfate (all, $p > 0.10$).

Analysis of variance was used to compare the change in fibrinogen and platelet levels and in prothrombin time between patients undergoing sclerotherapy and those undergoing embolization procedures and among patients with different types of vascular anomalies. Neither the interventional procedure performed nor the type of vascular anomaly had an impact on these coagulation variables at post 1 or post 2 ($p > 0.10$ for each).

Although the type of vascular anomaly did not predict a change in coagulation parameters in response to treatment, it did correlate with the presence of a pretreatment (baseline) coagulopathy. Specifically, all five patients who presented with positive d-dimer levels had venous malformations. We found a statistically significant higher proportion of positive d-dimers at presentation among patients with venous malformations (5/15 or 33%) than among those with other vascular anomalies (0/14). A logistic regression model indicated that the odds of a positive d-dimer level at pretreatment were five times higher for patients with venous malformations (odds ratio = 5.0, $p = 0.04$).

TABLE 2 Coagulation Profiles of Patients Receiving Dehydrated Alcohol or Sodium Tetradecyl Sulfate as Sclerotherapy or Embolotherapy Agent

Variables in Coagulation Factors Associated with Agent Used in Procedure	Values of Coagulation Factors Expressed as Mean ± SD or No. (%)						
	Pre	Post 1	Pre vs Post 1	*p*	Post 2	Pre vs Post 2	*p*
All patients ($n = 29$)							
Fibrinogen, mg/dL	252 ± 78	222 ± 75	–30 ± 26	<0.001	241 ± 86	–11 ± 60	0.53
Platelets, $\times 10^3/\mu L$	309 ± 90	269 ± 81	–40 ± 42	<0.001	285 ± 92	–24 ± 40	<0.001
Prothrombin time, sec	11.2 ± 1.0	12.0 ± 0.8	0.8 ± 0.9	<0.001	11.9 ± 0.8	0.7 ± 0.9	<0.001
d-dimers, no. of pts. (%)				<0.01			<0.01
Negative <0.2	24 (83)	19 (65)			17 (59)		
Positive <0.8	4 (14)	8 (28)			7 (24)		
Positive >0.8	1 (3)	2 (7)			5 (17)		
Dehydrated alcohol ($n = 20$)							
Fibrinogen, mg/dL	248 ± 78	213 ± 80	–35 ± 25	<0.001	230 ± 81	–18 ± 58	0.30
Platelets, $\times 10^3/\mu L$	320 ± 100	270 ± 88	–50 ± 40	<0.001	297 ± 98	–23 ± 42	0.02
Prothrombin time, sec	11.1 ± 1.0	11.8 ± 0.8	0.7 ± 0.6	<0.001	11.9 ± 0.7	0.8 ± 0.9	<0.01
d-dimers, no. of pts. (%)				<0.01			<0.01
Negative <0.2	16 (80)	11 (55)			9 (45)		
Positive <0.8	3 (15)	7 (35)			7 (35)		
Positive >0.8	1 (5)	2 (10)			4 (20)		
Sodium tetradecyl sulfate ($n = 11$)							
Fibrinogen, mg/dL	213 ± 83	176 ± 68	–37 ± 68	<0.01	207 ± 73	–6 ± 32	0.61
Platelets, $\times 10^3/\mu L$	316 ± 109	258 ± 77	–58 ± 48	<0.01	276 ± 86	–40 ± 35	<0.01
Prothrombin time, sec	11.2 ± 1.1	12.0 ± 0.9	0.8 ± 0.7	<0.01	11.9 ± 1.0	0.7 ± 0.8	0.04
d-dimers, no. of pts. (%)				0.03			0.02
Negative <0.2	6 (55)	3 (27)			3 (27)		
Positive <0.8	4 (36)	6 (55)			4 (36)		
Positive >0.8	1 (9)	2 (18)			4 (36)		

Note.—Pre = pretreatment (i.e., within 24 hr of procedure), Post 1 = within 30 min after procedure, Post 2 = within 24 hr after procedure, pts. = patients. In evaluations of changes in coagulation factors, the values of *p* were based on paired Student's *t* tests for fibrinogen, platelets, and prothrombin times and on nonparametric Wilcoxon's signed rank test for d-dimers.

Coagulation Variables in Response to Dehydrated Alcohol

A subgroup analysis of the 20 patients who received dehydrated alcohol was performed; these results are provided in Table 2. A comparison of pretreatment and post 1 values showed that for patients who received dehydrated alcohol, fibrinogen and platelet levels were significantly lower and prothrombin time was significantly higher at post 1 ($p < 0.001$). On average, these patients showed a decrease of 35 mg/dL in fibrinogen and 50 $\times 10^3/\mu L$ in platelets and an increase of 0.7 sec in prothrombin time. Furthermore, there was a conversion from 20% positive (4/20 patients) to 45% positive (9/20 patients) d-dimer levels ($p < 0.01$). Further comparison of pretreatment values with post 2 values revealed an average decrease of 23 $\times 10^3/\mu L$ in platelets ($p = 0.02$), an increase of 0.8 sec in prothrombin time ($p < 0.01$), and no differences in fibrinogen ($p = 0.30$). At post 2, there was a 55% (11/20 patients) conversion to positive d-dimer levels ($p < 0.01$).

A significant correlation was found between the milliliters of dehydrated alcohol administered per kilogram and the decrease in platelet values from pretreatment to post 1 ($r = –0.41$, $p = 0.02$). This negative correlation indicates that an increase in dehydrated alcohol dosage is associated with a decrease in platelet count. Linear regression revealed that the drop in platelet count can be estimated by the following equation: $y = 20 + 41 \times$ dehydrated alcohol dose (mL/kg). For example, administration of 1.0 mL/kg of dehydrated alcohol is associated with a predicted reduction of 61 $\times 10^3/\mu L$ at post 1. The dosage of dehydrated alcohol was not associated with any other changes in the levels of fibrinogen or platelets or in prothrombin time at post 1 or post 2 (all, $p > 0.25$).

Coagulation Variables in Response to Sodium Tetradecyl Sulfate

A separate subgroup analysis of the 11 patients who received sodium tetradecyl sulfate was performed; the results are shown in Table 2. In comparing pretreatment and post 1 values, we found that patients who received sodium tetradecyl sulfate had significantly lower levels of fibrinogen and platelets and had significantly longer prothrombin time at post 1 ($p < 0.01$). On average, these patients showed a decrease of 37 mg/dL in fibrinogen, a decrease of 58 $\times 10^3/\mu L$ in platelets, and an increase of 0.8 sec in prothrombin time. Furthermore, there was a conversion from 45% positive (5/11 patients) to 73% positive (8 /11) d-dimer levels ($p = 0.03$). Comparison of pretreatment and post 2 values revealed an average decrease of 40 $\times 10^3/\mu L$ in platelet count ($p < 0.01$) and an average increase of 0.7 sec in prothrombin time ($p = 0.04$). At post 2, the 73% (8/11patients) conversion to positive d-dimers persisted ($p = 0.02$).

Coagulation Variables in Response to the Combination of Dehydrated Alcohol and Sodium Tetradecyl Sulfate

A significant correlation between the total milliliters of combined dehydrated alcohol and sodium tetradecyl sulfate administered per kilogram and the decrease in platelets was seen in pretreatment and post 1 values ($r = –0.47$, $p = 0.01$). This negative correlation indicates that an increase in total dosage (mL/kg) is associated with a greater decline in platelets. The total dose was not correlated with any other changes in fibrinogen, platelets, or prothrombin time at post 1 or post 2 (all $p > 0.25$). A significant correlation was found between a greater amount of dehydrated alcohol and sodium tetradecyl sulfate (mL/kg) administered and the conversion from negative to positive d-dimer levels at pretreatment and at both post 1 (Spearman rho = 0.41, $p = 0.04$) and post 2 (Spearman rho = 0.43, $p = 0.03$).

Coagulation Variables in Response to Coils, Powder, or Glue

No significant changes were detected between pretreatment and post 1 values in fibrinogen, platelets, prothrombin time, or d-dimer conversion in response to coils, powder, or glue ($p > 0.10$ for each). In addition, no significant changes in the coagulation variables were found between pretreatment and post 2 values ($p > 0.25$ for each).

Discussion

A consumptive coagulopathic state has been described for patients with Klippel-Trenaunay and Parkes-Weber syndromes [11, 12], some of whom have had severe hemorrhage from rectosigmoid varices and bleeding after routine procedures such as electrosurgical excision of the cervix [5, 13]. Disseminated intravascular coagulation has also been associated with the syndrome [4]. To our knowledge, ours is the first report of the coagulation response of vascular anomalies to sclerotherapy or embolization procedures.

Although all patients' baseline prothrombin, platelet, and fibrinogen values were in the normal range, the five patients who presented with positive d-dimer values had venous malformations. Comparatively, the odds of presenting with positive d-dimer levels were five times higher for patients with a venous malformation than for patients with other malformations. Although these patients did not manifest clinical signs or symptoms of coagulopathy, their positive d-dimer levels presumably represent a chronic mild form of consumptive coagulopathy, despite their having expected values for platelets, fibrinogen, and prothrombin time. D-dimers arise from degradation of crosslinked fibrin, which in turn depends on thrombin-cleavage of fibrinogen. Thus, d-dimers serve as a surrogate marker for thrombin activation, which presumably takes place in abnormal venous endothelium. Further coagulation studies are needed to elucidate the mechanisms behind thrombin generation.

A chronic coagulopathy could have serious implications for a patient's ability to respond to sclerotherapy or embolization. Severe deficiency of normal clotting factors or platelets may prevent a successful response to treatment. Occasionally, to facilitate successful thrombosis, we administered cryoprecipitate, platelets, or fresh frozen plasma to patients with chronic coagulopathy (such as low platelets, low fibrinogen, or positive d-dimers) before performing sclerotherapy or embolization. Most patients, however, had venous and arteriovenous malformations.

We identified a relationship between the type of agent administered and the disruption in coagulation profiles. This relationship was not influenced by the type of procedure performed, specifically sclerotherapy or embolization. Sclerotherapy or embolization with n-butyl-2-cyanoacrylate mixed with Ethiodol and tungsten powder, polyvinyl alcohol foam particles, or platinum microcoils did not affect the coagulation status in these patients, either immediately or the day after the procedure. In contrast, those patients who received either dehydrated alcohol or sodium tetradecyl sulfate did manifest a coagulopathic response to interventional therapy. Immediately after the procedure, they had a statistically significant conversion in d-dimer levels, decreases in levels of platelets and fibrinogen, and prolongation in prothrombin time. Although the drop in fibrinogen was transient and reverted to pretreatment levels within 24 hr, the changes in platelets, d-dimers, and prothrombin time remained. The difference in coagulation responses caused by the various embolizing or sclerosing agents may be attributed to their mode and speed of action; n-butyl-2-cyanoacrylate polymerizes within a few seconds, usually on the arterial side of the arteriovenous malformation, to cause thrombosis. This quick action may reduce the platelet and fibrinogen consumption that occurs with n-butyl-2-cy-

anoacrylate as compared with alcohol. The immediate action of polyvinyl alcohol foam particles and microcoils may also explain the lack of coagulopathic response to these agents.

In general, the amount of dehydrated alcohol or sodium tetradecyl sulfate used reflects both the size of the vascular anomaly and the extent of vascular sclerosis or embolization. In examining the coagulation response to this combination therapy, the total amount of dehydrated alcohol and sodium tetradecyl sulfate administered was evaluated in relation to the change in coagulation parameters. A dose-dependent correlation existed between the total dosage of dehydrated alcohol and sodium tetradecyl sulfate administered and the decrease in platelets found immediately after the procedure. In contrast, those patients who received neither dehydrated alcohol nor sodium tetradecyl sulfate showed no change in coagulation after sclerotherapy or embolization. At our institution, the volume of alcohol and sodium tetradecyl sulfate currently administered is limited to 1 mL/kg and 0.5 mL/kg, respectively. A direct correlation between the decrease in platelets and the total amount of dehydrated alcohol and sodium tetradecyl sulfate used suggests that patients who receive large per-kilogram volumes of dehydrated alcohol and sodium tetradecyl sulfate may be at risk of experiencing a decline in platelets immediately after the procedure. If these patients have undergone embolization, systemic heparinization, and arterial cannulation, they may be at subsequent risk of bleeding from the arteriotomy site. In addition, patients who receive large doses of dehydrated alcohol and sodium tetradecyl sulfate may be unable to effectively thrombose after the sclerotherapy or embolization. Such an event may compromise a successful outcome.

Patients who are scheduled for an operative procedure, such as resection of vascular anomaly, in the days after undergoing a dehydrated alcohol or sodium tetradecyl sulfate sclerotherapy or embolization may be at risk of excessive bleeding. Extensive vascular (especially venous) malformations are known to be associated with a form of consumption coagulopathy [2–4]. In our clinical experience, sclerotherapy in such patients has led to clinically symptomatic coagulopathy, requiring administration of blood products and postponement of planned surgery. Most of these patients were not included in our study because they were receiving anticoagulation or blood products concurrent with their procedures. When possible, in these situations, practitioners may choose to avoid the use of dehydrated alcohol or sodium tetradecyl sulfate and, instead, use n-butyl-2-cyanoacrylate, platinum microcoils, or polyvinyl alcohol foam particles when preparing for an operative resection. The use of these agents, which caused no coagulopathic response, may be a safe practice that could reduce the risk of intraoperative or postoperative hemorrhage.

Our data show that although embolization and sclerotherapy affect platelet counts and coagulation factors in a predictable fashion, these effects are minimal in most patients with normal or near normal preprocedure coagulation status, and patients are not at increased risk of bleeding. However, we predict that patients who undergo sclerotherapy or embolization and who have moderate consumption coagulopathy before treatment will find their coagulation status more impaired after the procedure. Such patients would have an increased risk of bleeding, especially during surgery, on the days immediately after sclerotherapy or embolization. They would likely benefit from preprocedure hematologic consultation, possible pretreatment to maximize fibrinogen and platelet levels, and close monitoring of coagulation parameters after sclerotherapy or embolization.

Because we only tracked coagulation parameters for 24 hr after the procedure, predicting how long the coagulopathy could persist is difficult. Patients scheduled for nonelective surgery in the days after the procedure should have their coagulation parameters closely monitored. When indicated, practitioners should consider using replacement therapy (fresh frozen plasma, cryoprecipitate, or platelets) for these patients. We have occasionally deferred surgery for patients who manifest considerable consumptive coagulopathy immediately after the preoperative interventional procedure and have advised these patients to avoid elective surgery and other activities that could predispose them to bleeding.

Our study was limited in its consideration of the diverse vascular anomalies; the outcome data were restricted by the limited number of patients with each type of vascular anomaly located at various anatomic sites. Larger scale studies are needed to evaluate the coagulation disturbances specific to each type and site of vascular anomaly. None of our patients manifested a clinical complication from these coagulation disruptions at 1-week follow-up. The consumption of platelets and fibrinogen is not likely to be clinically important in patients with small malformations and normal baseline coagulation status. Further studies are needed to evaluate the specific changes in thrombin activation that occur with sclerotherapy and embolization, especially in those patients with extensive vascular anomalies and baseline consumption coagulopathy. Identification of these coagulation pathways and triggers may enable us to identify those who are at increased risk of a clinically important coagulopathy or an unsuccessful response to sclerotherapy or embolization with dehydrated alcohol or sodium tetradecyl sulfate.

References

1. Mueller BU, Mulliken JB. The infant with a vascular tumor. *Semin Perinatol* **1999**;23:332–340
2. Neubert AG, Golden MA, Rose NC. Kasabach-Merritt coagulopathy complicating Klippel-Trenaunay-Weber syndrome in pregnancy. *Obstet Gynecol* **1995**;85:831–833
3. D'Amico JA, Hoffman GC, Dyment PG. Klippel-Trenaunay syndrome associated with chronic disseminated intravascular coagulation and massive osteolysis. *Cleve Clin Q* **1997**;44:181–188
4. Yamamoto H, Muneta T, Asahina S, Furuya K, Suzuki K. Lower leg fracture with Parkes-Weber syndrome complicated by disseminated intravascular coagulation. *J Orthop Trauma* **1995**;9:449–452
5. Aronoff DM, Roshon M. Severe hemorrhage complicating the Klippel-Trenaunay-Weber syndrome. *South Med J* **1998**;91:1073–1075
6. Enjolras O, Ciabrini D, Mazoyer E, Laurian C, Herbreteau D. Extensive pure venous malformations in the upper or lower limb: a review of 27 cases. *J Am Acad Dermatol* **1997**;36:219–225
7. Dube B, Pillai PN, Singhal GD, Khanna NN. Blood coagulation studies in children with surface hemangiomas. *Int Surg* **1975**;60:524–526
8. Sokal RR, Rohlf FJ. *Biometry*, 3rd ed. New York: Freeman, **1995**:708–714
9. Wallenstein S, Zucker CL, Fleiss JL. Some statistical methods useful in circulation research. *Circ Res* **1980**;47:1–9
10. Armitage P, Berry G. *Statistical methods in medical research*, 3rd ed. Cambridge, MA: Blackwell Science, **1994**:448-452
11. Kasabach HH, Merritt KK. Capillary hemangioma with extensive purpura: report of a case. *Am J Dis Child* **1940**;59:1063–1070
12. Poon MC, Kloiber R, Birdsell DC. Epsilon-aminocaproic acid in the reversal of consumptive coagulopathy with platelet sequestration in vascular malformation of Klippel-Trenaunay syndrome. *Am J Med* **1989**;87:211–213
13. Katsaros D, Grundfest-Broniatowski S. Successful management of visceral Klippel-Trenaunay-Weber syndrome with the antifibrinolytic agent tranexamic acid (cyclocapron): a case report. *Am Surg* **1998**;64:302–304