

Comparing the Results of Coagulation Tests on Blood Drawn by Venipuncture and Through Heparinized Tunneled Venous Access Devices in Pediatric Patients With Cancer

Pamela S. Hinds, PhD, Alice Quargnenti, BSN, Jami Gattuso, MSN, Deo Kumar Srivastava, PhD, Xin Tong, MPH, Linda Penn, MT (AMT), Nancy West, RN, Patricia Cathey, RN, Darlene Hawkins, RN, Judith Wilimas, MD, Matthew Starr, BSN, and David Head, MD

Purpose/Objectives: To compare the accuracy of three coagulation tests (prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen (FBG)) performed on blood samples collected through heparinized tunneled venous access devices (TVADs) with those from venipuncture.

Design: Descriptive comparative with patients serving as their own controls.

Setting: Pediatric comprehensive care setting for children and adolescents experiencing catastrophic diseases.

Sample: 53 patients who had TVADs, had not received asparaginase during the previous 14 days, and had coagulation studies ordered. Patients ranged in age from 2-20 years (\bar{X} = 9.2 years, SD = 5). The most common diagnoses were neuroblastoma and acute myelocytic leukemia.

Methods: Blood was collected through TVADs within seconds of collection of the venipuncture sample. The first 3 ml of blood from a TVAD was discarded; the research nurse then drew three sequential samples of 3 ml each. Laboratory personnel were blinded to the source of all four samples until all analyses had been completed.

Main Research Variables: PT, aPTT, and FBG.

Findings: For all patients, results of PT, aPTT, and FBG tests on each of the three blood samples obtained through the TVAD differed significantly from results of the same tests on blood obtained by venipuncture.

Conclusions: These findings indicate that neither a 6 ml, 9 ml, nor 12 ml discard from a heparinized TVAD is sufficient to yield clinically trustworthy PT, aPTT, or FBG values.

Implications for Nursing: Nurses who have been persuaded by patients or parents to withdraw blood samples for coagulation indicators from a TVAD rather than from a venipuncture should have access to this research-based information that the three indicators, particularly aPTT, differ significantly from each other as to make it unreliable and potentially unsafe to sample blood from a TVAD to assess coagulation.

Key Points . . .

- ▶ Although sequential discard volumes (6 ml, 9 ml, and 12 ml) from a tunneled venous access device (TVAD) become closer in value to the coagulation values from a venipuncture, the TVAD values are statistically significantly different at all discard volumes from the coagulation values.
- ▶ Reviews by clinical experts comparing TVAD and venipuncture coagulation values indicated that, of the three coagulation indicators (PT, FBG, aPTT), the aPTT values were more likely to be evaluated as clinically significantly different from each other than were the values of the other two indicators.

Pamela S. Hinds, PhD, is director of nursing research in the Division of Patient Care Services, Alice Quargnenti, BSN, is a staff nurse in the Hematology/Oncology Inpatient Unit, Jami Gattuso, MSN, is a nursing research specialist in the Division of Patient Care Services, Deo Kumar Srivastava, PhD, is an associate member in the Department of Biostatistics, Xin Tong, MPH, is an associate biostatistician in the Department of Biostatistics, Linda Penn, MT (AMT), is a technician in the Department of Pathology, Nancy West, RN, is a lead clinical research associate in the Critical Care Division, Patricia Cathey, RN, is a clinical nurse coordinator, Darlene Hawkins, RN, is a pediatric oncology nurse in the Ambulatory Care Unit, Judith Wilimas, MD, is a member of the International Outreach Program, and Matthew Starr, BSN, is a student in the Professional Oncology Program, all at St. Jude Children's Research Hospital in Memphis, TN. David Head, MD, is interim chair of pathology and medical director of laboratory medicine at Vanderbilt Medical Center in Nashville. This study was funded, in part, by a grant from the Association of Pediatric Oncology Nurses, the Cancer Center Support Grant P30 CA-21765 from the National Cancer Institute, and the American Lebanese Syrian Associated Charities. (Submitted April 2001. Accepted for publication August 23, 2001.) (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Forum or the Oncology Nursing Society.)

Digital Object Identifier: 10.1188/02.ONF.E26-E34

Most children and adolescents receiving treatment for cancer require the insertion of one or more tunneled venous access devices (TVADs) during the course of treatment (Wiener et al., 1992). Manipulating and managing TVADs primarily is the responsibility of nurses and, sometimes, of carefully trained parents. In many, but not all, clinical settings, heparinized solutions regularly are instilled into TVADs to maintain patency. Because the heparinized solution might affect results of some coagulation tests, blood samples for such tests usually are drawn by venipuncture according to institutional policy. Venipuncture is a painful and troubling procedure for children and adolescents. When a TVAD is in place, patients and their family members prefer that blood samples be collected from that device. At times, the pleas of patients and their parents have persuaded healthcare providers to ignore policy and instead collect blood samples for coagulation tests from a TVAD. Indeed, nurses and physicians have described instances when they chose varying amounts of discarded blood from a TVAD before collecting a coagulation sample. Laboratory technicians have described processing coagulation samples with suspicion as to the sample source; they say that unusual values are common and second draws often become necessary. Coagulation values from TVADs might be aberrant and, if they are not recognized as spurious, might lead to inappropriate medical decisions. If standard procedures used to manage TVADs could be altered safely to yield accurate coagulation values, patients could avoid venipuncture. The purpose of this single-site study was to determine whether measured values of coagulation indicators (activated partial thromboplastin time [aPTT], prothrombin time [PT], and fibrinogen [FBG]) differed significantly for samples collected sequentially through a TVAD from those collected by venipuncture.

Literature Review

The first published report of the relationship between coagulation abnormality and use of an indwelling catheter appeared in the *New England Journal of Medicine* in 1970 in the form of a letter to the editor by C.J. Bark, MD, clinical pathologist. The letter reported that tests on a blood sample obtained through a heparinized device used for monitoring the central venous pressure of a patient undergoing postoperative dialysis revealed a prolonged aPTT (Bark, 1970). An initial diagnosis of heparin overdose was made but later was refuted when a subsequent sample obtained by venipuncture revealed a normal aPTT. This clinical experience prompted Bark to draw normal citrated plasma through the patient's heparinized IV line. The aPTT of this plasma sample was abnormally prolonged, yet a sample taken after the line was flushed with 50 ml of normal saline yielded a normal aPTT. Bark called this finding a "type of coagulation nondisease" (p. 1214).

In the 25 years that have followed the introduction of the phenomenon of "coagulation nondisease," numerous studies have been conducted (primarily on adult patients) to test the accuracy of coagulation studies on samples obtained from heparinized catheters. For the purpose of this review, the authors selected articles that evaluated coagulation studies on samples obtained from arterial and venous routes. Although the results cannot be generalized beyond catheter type, patient population, or methodology used in each study, the principles of the effects of heparin on blood coagulation were the physiologic framework for each reviewed study.

Coagulation Studies From Arterial Routes

The literature review revealed seven studies (Gregersen, Underhill, Dettter, Schmer, & Lax, 1987; Kaplow, 1988; Konopad, Grace, Johnston, Noseworthy, & Shustack, 1992; Merenstein, 1971; Molyneaux, Papciak, & Rorem, 1987; Reinhardt, Tonneson, Brace, & Goodnough, 1987; Richiuse, 1998) that concluded that accurate coagulation studies for certain indicators could be obtained from arterial lines if an adequate discard volume was obtained prior to sampling. The consistent factor of each study was the concept of catheter dead space, defined operationally as "the arterial lumen and the stopcock from which the blood samples are drawn" (Laxson & Titler, 1994, p. 16). The studies differed with regard to the procedure used to obtain arterial blood samples and the volumes needed to clear the dead space (see Table 1).

An in vitro study conducted in 1971 investigated the accuracy of aPTT and PT values obtained from umbilical artery catheters with a dead space of 0.8 ml. The study used heparin concentrations of 1 u/ml and tested discard volumes ranging from 0–4.5 ml. The study found that a volume equal to five times the catheter's dead space, which was 4 ml, was needed to obtain accurate aPTT and PT values (Merenstein, 1971).

Two in vitro studies tested the accuracy of arterial catheters with a dead space of 0.8 ml, using heparin concentrations of 2 u/ml. The first published study measured aPTT values from 60 paired samples obtained from 24 patients (Molyneaux et al., 1987). Discard volumes tested ranged from 1.6–4.8 ml, which was six times the catheter's dead space. The second study, published five years later, measured both aPTT and PT values from a sample of critically ill adults (N = 41) who had venipuncture samples obtained simultaneously and served as their own control (Konopad et al., 1992). Discard volumes of 3 ml, 5.3 ml, and 7.6 ml were tested. Statistically significant differences between the arterial and venipuncture samples for all three discard volumes were found. Despite that, the authors argued that the differences, although statistically significant, were not necessarily clinically significant. The authors concluded that a 3 ml discard for obtaining accurate PT values from an arterial catheter and a 5.3 ml discard for accurate aPTT values was sufficient.

In another study, researchers compared simultaneously obtained venous samples with those drawn from the sampling port of Lab-Site® high-pressure tubing. Within the sample population of 25 critically ill patients who were in an intensive care unit or recently had undergone surgery, the researchers concluded that both aPTT and PT values could be obtained accurately from the specified brand of sampling ports (Cicala, Cannon, Larson, & Fabian, 1988). In a study by Lew, Hutchinson, and Lin (1991), the accuracy of a central venous pressure (CVP) line also was considered. The authors concluded that the PT values differed significantly for the discard volume of dead space plus 5 ml in the CVP samples when compared to venipuncture. They found no significant differences in aPTT values. The third of the 0.6 ml dead space studies investigated aPTT and thrombin time (TT) values within a sample of adult patients with cardiac disease (N = 30) and reported that a 5.1 ml discard volume was necessary to obtain accurate aPTT values. Furthermore, the authors concluded that TT values only could be obtained accurately by venipuncture (Gregersen et al., 1987).

Table 1. Summary of Published Studies of Coagulation Tests Using Blood Drawn Through Arterial Catheters

Investigator	Dependent Variable	Catheter Dead Space (ml)	Heparin Concentration (u/ml)	Sample Size	Discard Volume(s) Tested	Recommended Method or Discard Volume
Merenstein, 1971	aPPT PT	0.8	1	0 (in vitro study)	0 ml, 0.9 ml, 1.8 ml, 2.7 ml, 3.6 ml, 4.5 ml	5 x DS
Kajs, 1986	aPTT	0.6	6	24 patients	3 ml, 6 ml	Venipuncture indicated
Gregersen et al., 1987	aPTT TT	0.6	4	30 patients	0.6 ml, 5.1 ml, 9.6 ml, 14.1 ml, 18.6 ml	5.1 ml for aPPT tests; venipuncture indicated for TT tests
Molyneux et al., 1987	aPTT	0.8	2	24 patients	1.6 ml, 3.2 ml, 4.8 ml	6 x DS
Reinhardt et al., 1987	aPTT PT TT	0.65	1, 2, or 4	9 dogs	2 x DS, 4 x DS, 6 x DS, 8 x DS, 10 x DS, 12 x DS, 14 x DS	5 x DS
Kaplow, 1988	aPTT PT	1.0	1	50 patients	10 ml	10 x DS
Cicala et al., 1988	aPTT PT	0.1	1	25 patients	NA	NR
Lew et al., 1991	aPTT PT	0.6	1, 2	60 patients	3.1 ml (2.5 ml + DS) 5.6 ml (5.0 ml + DS) 12.5 ml (10.0 ml + DS)	NR
Konopad, et al., 1992	aPTT PT	0.8	2	41 patients	3 ml 5.3 ml 7.6 ml	3 ml for PT tests 5.3 ml for aPTT tests
Hancock, 1993	aPTT	2.5	2	35 patients	10 ml 12.5 ml 15.0 ml	Venipuncture indicated
Richiuso, 1998	aPTT	0.85	NR	16 patients	8 ml 12 ml	14 x DS

aPTT—activated partial thromboplastin time; DS—dead space; NA—not applicable; NR—not reported; PT—prothrombin time; TT—thrombin time

A canine study (N = 9) evaluated aPTT, PT, and TT values to determine whether heparin concentrations of 1 u/ml, 2 u/ml or 4 u/ml could be cleared from the arterial catheter dead space of 0.65 ml (Reinhardt et al., 1987). Discard volumes tested ranged from 2–14 times the catheter's dead space. The finding of this study supported that accurate aPTT, PT, and TT values could be obtained using a discard volume of five times the dead space.

Kaplow (1988) compared aPTT and PT venipuncture values in arterial samples from 50 acutely ill adult patients with various oncologic or medical diagnoses. The arterial catheter dead space was 1.0 ml. The heparin concentration was 1 u/ml. No significant differences were found when a 10 ml discard volume was obtained prior to sampling.

The largest arterial catheter dead space studied was 2.5 ml (Hancock, 1993). The only variable considered in the experiment was aPTT values. The study tested heparin 2 u/ml and discard volumes ranging from 10–15 ml in 35 subjects who had

experienced percutaneous transluminal coronary angioplasty. The findings of this study disagreed with those of the eight previously reviewed studies by concluding that venipuncture was the indicated route for obtaining accurate aPTT values.

Of the 11 studies reviewed, nine involved patients who were 18 years of age or older. Seven of the 11 studies using arterial catheters concluded that the results of coagulation tests performed on blood samples drawn through these catheters were accurate if adequate discard volumes were obtained before sampling, two concluded that venipuncture was indicated, and two made no recommendation. Three studies examined the accuracy of aPTT and PT results; a fourth study examined the accuracy of aPTT and TT results. Heparin concentrations varied from 1–6 u/ml. Reported discard volumes ranged from 0.1–18.6 ml. The largest dead space of any arterial catheter studied was 2.5 ml, and the smallest was 0.1 ml. Of the studies that indicated catheter type, site, or specific product name, none investigated the same kind of arterial catheter (see Table 1).

Coagulation Studies From Venous Routes

The use of a heparinized saline flush to maintain the patency of an indwelling central venous catheter also has prompted concerns about the accuracy of coagulation tests on blood obtained from such catheters. Of seven coagulation studies of samples obtained from heparinized central venous catheters, one study focused solely on aPTT values (Almadrones, Godbold, Raaf, & Ennis, 1987), two included PT values and aPTT studies (Ellis, 1993; Pinto, 1994), and four included aPTT, PT, activated clotting time (ACT), platelet count or FBG, and fibrin/fibrinogen degradation products (FDP) (Barton & Poon, 1986; Mayo, Dimond, Kramer, & Horne, 1996; Palermo, Andrews, & Ellison, 1980; van Genderen, Gomes, & Stibbe, 1994). Heparin concentrations

ranged from 1–100 u/ml, and discard volumes ranged from 0–25 ml. A dead space volume was reported only in two studies.

In the seven venous catheter studies, sample size ranged from 12–30 patients (see Table 2). Study samples were comprised of patients with cancer or patients waiting for open-heart surgery (their ages were not specified). Pediatric oncology and hematology patients were included in only one of the reviewed studies (Ellis, 1993). Findings and recommendations from the studies varied considerably. Only Palermo et al. (1980) concluded that an appropriate discard volume (defined as 1.5 ml) made it possible to obtain accurate coagulation studies from a heparinized central venous catheter. In contrast, four studies (Almadrones et al., 1987; Barton & Poon, 1986; Pinto, 1994; van Genderen et al., 1994) con-

Table 2. Summary of Published Studies of Coagulation Tests Using Blood Drawn Through Venous Catheters

Investigator	Dependent Variable	Dead Space (ml)	Heparin (u/ml)	Sample Size	Discard Volume(s) Tested	Recommended Method or Discard Volume
Palermo et al., 1980	aPTT PT ACT Platelet count	1.5	1 2	12 patients	1.5 ml, 2.5 ml, 3.5 ml, 5.5 ml	1.5 ml
Barton & Poon, 1986	aPTT FBG FDP PT	NR	100	12 patients	0 ml, 10 ml	Venipuncture indicated
Almadrones et al., 1987	aPTT	NR	10	30 patients	10 ml	Venipuncture indicated
van Genderen et al., 1992	aPTT AT-111 α2-AP TAT FM F1.2 FbDP TDP	NR	100	14 patients	10 ml	Venipuncture indicated
Ellis, 1993	aPTT PT	NR	100	25 patients	5 ml	5 ml + 4 µg/ml (or 1 ml) of protamine added to aPTT sample; PT should be omitted from coagulopathy screen.
Pinto, 1994	aPTT PT	0.5 2.0	100	12 patients	6 x DS	Venipuncture indicated
Mayo et al., 1995	aPTT PT FBG	NR	100	20 patients	5 ml, 10 ml, 15 ml, 20 ml, 25 ml	25 ml from TVAD in nonemergent situations; venipuncture for critical decisions

α2-AP—alpha-2 antiplasmin; ACT—activated clotting time; aPTT—activated partial thromboplastin time; AT-111—antithrombin 111; DS—dead space; F1.2—prothrombin activation fragment; FbDP—degradation products of fibrin; FBG—fibrinogen; FDP—fibrinogen degradation products; FM—soluble fibrin; NR—not reported; PT—prothrombin time; TAT—thrombin-antithrombin III complexes; TDP—total degradation products; TVAD—tunneled venous access device

cluded that venipuncture was the only appropriate route for obtaining aPTT, FBG, FDP, and PT. The remaining two studies came to situation-specific conclusions. One concluded that only venipuncture should be used for critical clinical decisions but that a 25 ml discard could be sufficient in nonemergent situations. The second study concluded that accurate PT values could not be obtained accurately from TVADs but that accurate values of aPTT could be obtained if protamine was added to samples.

The reviewed studies of arterial and venous catheters had methodologic differences and discrepant findings, and most involved adult patients; thus, a standard of care for collecting coagulation samples from TVADs in pediatric patients with cancer could not be derived from the reviewed studies. Therefore, the authors studied a group of pediatric patients to determine whether the results of coagulation tests performed on blood sampled sequentially from a TVAD that routinely was flushed first with heparinized saline differed statistically and clinically from the results of tests performed on samples drawn by venipuncture.

Methods

Setting

The study was performed at a comprehensive care center for children and adolescents with catastrophic diseases, primarily cancer. The center has 62 inpatient beds and almost 2,000 outpatient visits per week. About 200 single- and double-lumen TVADs had been placed during each of the five years preceding the study. In the year preceding this study, 6,622 coagulation tests were ordered, but determining how many were performed on blood drawn from TVADs or arterial lines is impossible.

Sample

Patients undergoing coagulation tests in this study were 2–20 years of age and had a diagnosis of cancer. Either a single- or double-lumen TVAD had been inserted previously. To be eligible for the study, patients could not have received a dose of asparaginase during the previous 14 days because of the documented influence of this agent on coagulation (Capizzi & Holcenberg, 1993; Nowak-Gottl, Werber, Ziemann, Ahlke, & Boos, 1996). Consent for study participation was obtained from parents or guardians, as appropriate, and the assent of the patients was obtained when possible.

Sample Size

To determine the sample size needed to achieve the study's objectives, the authors reviewed historical data on coagulation tests performed at the study setting during the preceding five years. During that time, 16,000 coagulation tests had been completed, but many patients had undergone such tests more than once. To avoid including multiple tests on the same patient, the authors only used the results of the first coagulation study for each patient. Therefore, only the results from 1,644 patient tests were used to determine the sample size. On the basis of these findings, the authors determined that a medium-effect size difference of 0.3 for each of the variables (PT, aPTT, FBG) would be appropriate. Type I error was controlled at the level of 0.05, and the desired power was set at 90%. When these factors were taken into consideration, the required sample size was set at 55 patients.

Procedure

Blood samples for coagulation tests first were obtained by venipuncture. Immediately thereafter, 3 ml of blood was withdrawn from a TVAD and discarded, then three 3 ml samples were drawn sequentially from the TVAD (sample 1, sample 2, and sample 3). All four samples (venipuncture sample and three TVAD samples) immediately were placed on ice and taken to the clinical laboratory for analysis. All study samples from each patient were collected within three minutes. The six nurses who shared responsibility for collecting blood specimens had completed competency training before initiating the study and repeated the training every four months during the two years of data collection. All samples were collected in accordance with the standard procedures of the institution.

The research nurse coded all collected samples by using a random-number coding scheme generated by the study biostatistician. With that, the laboratory technicians processing the samples were blinded to the source of each sample. PT and aPTT values were determined by the COAG-A-Mate X® (serial number 021X1596) during the first year of the study and then by the MLA1400C (serial number 721CE). FBG values were determined by the Fibrometer™ (serial number TOO452). The same reagents and laboratory standards were used during the entire study period. Using standard methods, a single technician processed all samples from the same patient. After completing the analyses on all four samples, the technician contacted the research nurse, who revealed which sample was the venipuncture sample. Only the values from the venipuncture sample were used for clinical care purposes.

Data Analysis

The one-sample Hotelling's T^2 test was used to determine whether the differences in PT, aPTT, and FBG results from the venipuncture samples and the sequentially collected TVAD samples were equal to zero. Because three comparisons were performed, the authors adjusted the p value by using the Bonferroni method. As a result, a comparison was significant if the p value was less than 0.017 (0.05 divided by 3). The same statistic was used to determine whether differences existed in the results of coagulation tests performed on the sequentially drawn TVAD samples, and the same correction was made for multiple comparisons. To determine whether significant clinical differences existed between the results of coagulation tests performed on the venipuncture samples and each of the sequentially drawn TVAD samples, each result was reviewed independently by three physicians and one nurse practitioner, who indicated whether any results were different enough from the others to have prompted a change in clinical care. The expert reviewers used the range of seconds to clot formation considered to represent normal findings at the study setting: PT = 10–15 seconds; aPTT = 26–40 seconds; FBG = 150–400 seconds.

Results

Patients

Sixty patients were enrolled in the study. However, the sequentially drawn samples of one patient were combined mistakenly in the laboratory before analysis, the research nurses were unable to obtain samples through the TVADs of two patients, the recorded test results for three patients could not be located, and one patient exceeded the age criterion for

eligibility. Therefore, the final study sample consisted of 53 patients, most of whom were male and Caucasian (see Table 3). Most had a double-lumen TVAD, and the TVAD dead space ranged from 0.6–1 ml as reported by the manufacturers and confirmed by the surgeons who inserted them. The most frequently represented diagnoses were neuroblastoma and acute myelocyticleukemia. The heparin flush concentration used daily to maintain patency was 10 u/ml. The majority of TVADs were flushed and clamped at the time of data collection; only eight had infusions (normal saline hydration fluids) that were interrupted briefly for this study.

Coagulation Tests

All 53 patients underwent venipuncture. PT and aPTT values were determined for all patients, and FBG values were determined for 48. However, because the laboratory labeled one PT sample, one FBG sample, and five aPTT samples sequentially drawn from TVADs as “unable to calculate,” the number of comparisons varies (see Table 4). Coagulation tests performed on samples drawn through TVADs showed that PT and aPTT values decreased with each sequential sample; the results of tests on sample 3 were closest to those of tests performed on samples obtained by venipuncture. The venipuncture PT values and the sequential TVAD PT values were moderately to strongly correlated; the correlation coefficient increased with each sequential sample (see Table 5). The venipuncture FBG values and the sequential TVAD FBG values were strongly correlated (see Table 6). The venipuncture aPTT values and the TVAD aPTT values were moderately correlated (see Table 7).

Table 3. Demographic Characteristics

Characteristic	n	%
Sex		
Male	29	55
Female	24	45
Race		
Caucasian	37	70
African American	9	17
Hispanic	5	9
Other	2	4
Diagnosis		
Neuroblastoma	18	34
Acute myeloid leukemia	10	19
Acute lymphoblastic leukemia	5	9
Other malignant neoplasms	3	6
Myelodysplastic syndrome	3	6
Medulloblastoma	2	4
Non-Hodgkin's lymphoma	2	4
Osteosarcoma	2	4
Chronic myelogenous leukemia	2	4
Other leukemia	1	2
Germ cell tumors	1	2
Wilms tumor	1	2
Choroid plexus carcinoma	1	2
Central nervous system neoplasms	1	2
Other	1	2
Type of line		
Double lumen	42	79
Single lumen	11	21

N = 53

Note. Because of rounding, percentages may not total 100.

Table 4. Seconds to Coagulation During Tests on Blood Samples Drawn by Venipuncture and Three Samples Sequentially Drawn Through a Tunneled Venous Access Device

Coagulation Indicator	n	\bar{X}	SD	Median
Prothrombin time				
Venipuncture	53	11.83	1.18	11.6
TVAD-sample 1	52	12.66	1.60	12.1
TVAD-sample 2	52	12.19	1.25	11.9
TVAD-sample 3	53	12.09	1.24	11.8
Fibrinogen				
Venipuncture	48	311.33	85.23	286.5
TVAD-sample 1	48	294.06	78.28	271.0
TVAD-sample 2	47	302.23	81.99	271.0
TVAD-sample 3	47	301.70	83.05	281.0
Activated partial thromboplastin time				
Venipuncture	53	31.59	4.76	31.2
TVAD-sample 1	45	54.17	29.67	42.0
TVAD-sample 2	48	38.49	10.11	36.8
TVAD-sample 3	50	36.00	10.59	33.1

TVAD—tunneled venous access device

N = 53

Despite these linear correlations, however, significant differences existed among the coagulation indicators for each TVAD sample (see Table 8). To identify the source of the differences, the authors compared the values of each coagulation indicator by using an analysis of variance procedure. The findings indicated that all TVAD values differed significantly from the venipuncture values (see Table 9). These results were confirmed by using a paired t-test statistic. In addition, no differences were noted for any of the PT, aPTT, or FBG blood draws between single- and double-lumen TVADs ($p = 0.16$ – 0.92). No differences were found in any of the blood draws by length of time since a TVAD had been surgically placed ($p = 0.14$ – 0.93).

Clinical Significance

The panel of four clinicians agreed that 51 of the 53 sets of PT values were similar enough that no change in practice would have been recommended. Three of the four reviewers found that two comparison sets of PT values were so discrepant that either

Table 5. Correlations Between Results of Tests of Prothrombin Time: Venipuncture versus TVAD

	Venipuncture	TVAD Sample 1	TVAD Sample 2	TVAD Sample 3
Venipuncture	1.000	0.60 (n = 52)	0.79 (n = 52)	0.85 (n = 53)
Sample 1	–	1.000	0.86 (n = 51)	0.73 (n = 52)
Sample 2	–	–	1.000	0.90 (n = 52)

TVAD—tunneled venous access device

N = 53

Note. All correlations significant at 0.0001

Table 6. Correlations Between Results of Tests of Fibrinogen Levels: Venipuncture Versus Tunneled Venous Access Device

	Veni-puncture	TVAD Sample 1	TVAD Sample 2	TVAD Sample 3
Venipuncture	1.000	0.96 (n = 48)	0.98 (n = 47)	0.98 (n = 47)
Sample 1	–	1.000	0.97 (n = 47)	0.96 (n = 47)
Sample 2	–	–	1.000	0.98 (n = 46)

TVAD—tunneled venous access device
N = 53
Note. All correlations significant at 0.0001

a second test would have been ordered or a change in care would have been made for those two patients. One of the discrepancies was between the venipuncture values and the values for TVAD sample 2; the other was between the venipuncture values and the values for TVAD sample 3. The clinical experts agreed as to the similarity among the 48 sets of FBG values and concluded that no change in care was indicated by those values. Two or more of the clinical experts found that 19 of 53 sets of aPTT values were different enough that a second test or a change in care would have been indicated (see Table 10). Twelve of these discrepancies were found between the venipuncture values and the values for TVAD sample 2, and seven were found between the venipuncture values and the values for TVAD sample 3.

Discussion

The stimuli for this study were the patients’ and family members’ objections to the potentially painful procedure of venipuncture to obtain coagulation samples and the reluctance of nurses to attempt venipunctures for ordered coagulation studies because of patient and parent protestations. The motivation of the study team was to demonstrate the need for venipuncture to obtain accurate coagulation values or to demonstrate the scientific basis for not needing to rely only on values obtained by venipuncture. The findings of this study indicate that the results

Table 7. Correlations Between Results of Tests of Activated Partial Thromboplastin Time: Venipuncture Versus Tunneled Venous Access Device

	Veni-puncture	TVAD Sample 1	TVAD Sample 2	TVAD Sample 3
Venipuncture	1.000	0.17 p = 0.26 (n = 45)	0.54 p = 0.0001 (n = 48)	0.50 p = 0.0002 (n = 50)
Sample 1	–	1.000	0.73 p = 0.0001 (n = 44)	0.38 p = 0.01 (n = 44)
Sample 2	–	–	1.000	0.77 (n = 47)

TVAD—tunneled venous access device
N = 53

Table 8. Differences in Results of Coagulation Tests Between Samples Drawn by Venipuncture and Each of Three Samples Sequentially Drawn Through a Tunneled Venous Access Device

Venipuncture	N	F	p
and sample 1	41	17.60	0.0001
and sample 2	44	14.10	0.0001
and sample 3	45	6.81	0.0008

N = 53

of PT, aPTT, and FBG tests performed on blood obtained from pediatric patients through heparinized TVADs that have the same or similar dead space, are maintained by similar flushing techniques, and where sampling includes the same discard volume are unreliable for clinical use. Although the discard volume used in this study was 6–12 times the dead space, a volume equal to or greater than those reported in earlier studies using venous catheters (Palermo et al., 1980; Pinto, 1994), these volumes still did not prevent statistically and clinically significant differences in the results of PT and aPTT tests performed on blood drawn by venipuncture and through TVADs. Thus, these study findings indicate that venipuncture is the recommended method of obtaining blood samples for coagulation studies in this patient population under these or similar conditions.

This conclusion is the same as that reported by four previous studies but different from those reported by Palermo et al. (1980) and Ellis (1993), who concluded that, in a slight majority of patients and with certain manipulations, satisfactory coagulation test results could be achieved when blood was drawn through TVADs or central venous lines. In both of those studies, protamine sulfate was added to the TVAD samples to neutralize the heparin. Ellis concluded that even with that adjustment, venipuncture still was the preferred approach for about 52% of pediatric patients with cancer. He warned that false-positive test results limited the use of protamine sulfate. Given these qualifying comments, his recommendation to use TVADs for coagulation indicators in routine clinical practice situations might be premature.

Although caution is merited in using TVADs to draw blood for coagulation studies, certain trends should be considered in the relationship between the results of tests on blood drawn by venipuncture and through TVADs. The results of PT and aPTT tests on sequentially drawn TVAD samples became more similar descriptively to those of such tests on blood drawn by venipuncture. That is, in the current study, the results of tests performed on TVAD sample 3 were more similar to the results of tests on blood drawn by venipuncture than were the results of such tests performed on samples 1 and 2. The results of coagulation tests performed on each subsequent TVAD sample tended to become more similar to the results of tests performed on venipuncture samples. Finally, the size and significance of the difference between the venipuncture values and the TVAD values decreased with each subsequent sample. These trends suggested that as discard volumes increase, the results of coagulation tests on samples drawn through TVADs are more likely to be similar to the results of such tests on samples drawn by venipuncture.

The four clinicians’ assessments of clinical significance did not concur with the statistical conclusions about FBG values but did concur with the statistical conclusions about aPTT values.

Table 9. Differences in Results of Coagulation Tests Performed on Samples Drawn by Venipuncture and Three Samples Sequentially Drawn Through a Tunneled Venous Access Device

Coagulation Indicator	n	F	p
Prothrombin time			
Venipuncture—TVAD sample 1	41	20.03	0.0001
Venipuncture—TVAD sample 2	44	16.14	0.0002
Venipuncture—TVAD sample 3	45	6.98	0.0114
Fibrinogen			
Venipuncture—TVAD sample 1	41	24.32	0.0001
Venipuncture—TVAD sample 2	44	15.25	0.0003
Venipuncture—TVAD sample 3	45	8.97	0.0045
Activated partial thromboplastin time			
Venipuncture—TVAD sample 1	41	25.81	0.0001
Venipuncture—TVAD sample 2	44	30.42	0.0001
Venipuncture—TVAD sample 3	45	10.32	0.0025

TVAD—tunneled venous access device
N = 53

With regard to the FBG values, the ratings of the four clinicians indicated that they found the venipuncture values similar enough to all three of the TVAD values that they would not have recommended a change in care or ordered a second test. This difference between statistical and clinical significance estimates is difficult to explain but might be a result of the relatively large range of FBG values that are considered to be within clinically normal limits. With regard to aPTT values, the ratings of the four clinicians indicated that more than a third of the TVAD values were beyond the normal clinical range, an outcome that probably would have prompted change in care or a retest. These clinical estimates support the findings of the statistical analysis.

Limitations

This study had stricter eligibility criteria, a more explicit data collection procedure, and a larger sample size than previously reported studies; nevertheless, certain limitations were apparent. The majority of participating patients did not have infusions at the time of data collection; thus, the influence of continuous infusions on accuracy of coagulation indicators cannot be determined. The variables of TVAD flush (e.g., heparin concentration, amount of flush, number of times the TVAD had been flushed in the previous 24 hours) were not studied. The potential usefulness of protamine sulfate also was not considered.

Future studies certainly could be designed to include a larger discard volume. However, as the discard volume increases, the need to reinfuse the discarded blood will become more likely in pediatric participants. Reinfusion adds a step to the blood-collection process and might increase the likelihood of error or contamination. Alternatively, adding protamine sulfate or another product to neutralize the heparin could be considered. However, because these agents increase the possibility of false-positive readings and inconsistent laboratory findings, they are unlikely to be clinically useful in the near future. In rare clinical situations, a venipuncture might not be preferable and coagulation samples might need to be drawn from a TVAD. If venipuncture were mandated by institutional policy, a medical order would be needed to legitimize drawing the samples from a TVAD. The nurse also would need to document the source of the sample (TVAD) and the reasons for the policy exception. The nurse should explain this change in care as an exception to the patient, family members, and staff. Given all of these considerations, the authors recommend that venipuncture continue to be used for collecting blood for coagulation studies and that nurses and other healthcare providers alert patients and parents to the scientific basis for this practice recommendation when they are considering venous access device placement. In addition, future research about the accuracy of coagulation indicators drawn from TVADs should include study of the heparin flush (e.g., volume, timing, frequency) and the influence of continuous infusions (e.g., type, duration).

The authors acknowledge the contributions to this work of Kattie Pring, MSN; Belinda Mandrell, MSN, PNP; Bassem Razzouk, MD; Gregory Hale, MD; and Linda Watts-Parker.

Author Contact: Pamela S. Hinds, PhD, can be reached at pam.hinds@stjude.org, with copy to editor at rose_mary@earthlink.net.

Table 10. Descriptive Summary of the Clinical Experts' Ratings of Discrepant Results of Coagulation Tests Performed on Samples Drawn by Venipuncture and Through a Tunneled Venous Access Device

	# of Patient Sets of Values Compared N	# of Agreements Recommending No Practice Changes n (%)	# of Agreements Recommending Practice Change n (%)		
			4 Raters	3 Raters	2 Raters
PT	53	51 (96)	1 (2)	1 (2)	0
FBG	48	48 (100)	—	—	—
aPPT	53	34 (64)	10 (19)	3 (6)	6 (11)

aPPT—activated partial thromboplastin time; FBG—fibrinogen; PT—prothrombin time
N = 53

References

- Almadrones, L., Godbold, J., Raaf, J., & Ennis, J. (1987). Accuracy of activated partial thromboplastin time drawn through central venous catheters. *Oncology Nursing Forum*, 14(2), 15–18.
- Bark, C.J. (1970). Coagulation nondisease [Letter to the editor]. *New England Journal of Medicine*, 282, 1214.
- Barton, J.C., & Poon, M.C. (1986). Coagulation testing of Hickman catheter blood in patients with acute leukemia. *Archives of Internal Medicine*, 146, 2165–2169.
- Capizzi, R., & Holcenberg, J.S. (1993). Asparaginase. In J.F. Holland, E. Frei, R. Bast, D. Kufe, D. Morton, & R. Weichsebaum (Eds.), *Cancer Medicine* (3rd ed., pp. 796–805). Philadelphia: Lea and Febiger.
- Cicala, R.S., Cannon, K., Larson, J.S., & Fabian, T.C. (1988). Evaluation of coagulation studies from heparinized arterial lines with use of Lab-Site high-pressure tubing. *Heart and Lung*, 17, 662–666.
- Ellis, M.R., III (1993). Coagulopathy screening in children with heparinized central venous catheters. *Pediatrics*, 91, 1147–1150.
- Gregersen, R.A., Underhill, S.L., Detter, J.C., Schmer, G., & Lax, K. (1987). Accurate coagulation studies from heparinized radial artery catheters. *Heart and Lung*, 16, 686–693.
- Hancock, R.D. (1993). Venipuncture vs. arterial catheter activated partial thromboplastin times in heparinized patients. *Dimensions of Critical Care Nursing*, 12, 238–245.
- Kajs, M. (1986). Comparison of coagulation values obtained by traditional venipuncture and intra-arterial line methods. *Heart and Lung*, 15, 622–627.
- Kaplow, R. (1988). Comparison of two techniques for obtaining samples for coagulation studies: Venipuncture and intra-arterial line. *Heart and Lung*, 17, 651–653.
- Konopad, E., Grace, M., Johnston, R., Noseworthy, T., & Shustack, A. (1992). Comparison of PT and aPTT values drawn by venipuncture and arterial line using three discard volumes. *American Journal of Critical Care*, 1, 94–101.
- Laxson, C.J., & Titler, M.G. (1994). Drawing coagulation studies from arterial lines: An integrative literature review. *American Journal of Critical Care*, 3, 16–22.
- Lew, J.K., Hutchinson, R., & Lin, E.S. (1991). Intra-arterial blood sampling for clotting studies. Effects of heparin contamination. *Anaesthesia*, 46, 719–721.
- Mayo, D.J., Dimond, E.P., Kramer, W., & Horne, M.K. (1996). Discard volumes necessary for clinically useful coagulation studies from heparinized Hickman catheters. *Oncology Nursing Forum*, 23, 671–675.
- Merenstein, G.B. (1971). Heparinized catheters and coagulation studies. *Journal of Pediatrics*, 79, 117–119.
- Molyneaux, R.D., Papciak, B., & Rorem, D.A. (1987). Coagulation studies and the indwelling heparinized catheter. *Heart and Lung*, 16, 20–23.
- Nowak-Gottl, U., Werber, G., Ziemann, D., Ahlke, E., & Boos, J. (1996). Influence of two different *Escherichia coli* asparaginase preparations on fibrinolytic proteins in childhood ALL. *Haematologica*, 81, 127–131.
- Palermo, L.M., Andrews, R.W., & Ellison, N. (1980). Avoidance of heparin contamination in coagulation studies drawn from indwelling lines. *Anesthesia Analgesia*, 59, 222–224.
- Pinto, K.M. (1994). Accuracy of coagulation values obtained from a heparinized central venous catheter. *Oncology Nursing Forum*, 21, 573–575.
- Reinhardt, A.C., Tonneson, A.S., Bracey, A., & Goodnough, S.K. (1987). Minimum discard volume from arterial catheters to obtain coagulation studies free of heparin effect. *Heart and Lung*, 16, 699–705.
- Richiuso, N. (1998). Accuracy of aPTT values drawn from heparinized arterial lines in children. *Dimensions of Critical Care Nursing*, 17, 14–19.
- van Genderen, P.J., Gomes, M., & Stibbe, J. (1994). The reliability of Hickman catheter blood for the assessment of activation markers of coagulation and fibrinolysis in patients with hematological malignancies. *Thrombosis Research*, 73, 247–254.
- Wiener, E.S., McGuire, P., Stolar, C.J., Rich, R.H., Albo, V.C., Ablin, A.R., et al. (1992). The CCSG prospective study of venous access devices: An analysis of insertions and causes for removal. *Journal of Pediatric Surgery*, 27, 155–163.