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Using Ultrasonography for Vessel Diameter Assessment to Prevent Infiltration

ABSTRACT
Small veins are a risk factor for infiltration. However, there are no data regarding the ideal vein diameter for preventing infiltration. Using ultrasound, vessel diameter and calculated ratios of the vessel diameter to the catheter gauge were measured. The relationship between the ratio and infiltration was assessed to establish a cutoff point. The mean ratio of the infiltration group was significantly smaller than that of the no-infiltration group ($P < .01$), and the ratio was an independent risk factor according to the multivariable analysis. The ratio of 3.3 was determined to be the cutoff point that enables health care professionals to identify veins appropriately.
Key words: catheters, infiltration, intravenous infusions, ultrasonography, vessel diameter

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Peripheral intravenous (IV) catheters, or short peripheral catheters (SPCs), are commonly used in hospitalized patients for the delivery of fluids, electrolytes, and/or medications. They are used in up to 70% of patients undergoing treatment in acute care settings.[1] SPCs frequently fail before the end of treatment for a broad number of reasons.[2] *Infiltration* is defined as the accidental leakage of a nonvesicant drug into surrounding tissue,[3,4] and it is one of the most common complications of infusion therapy.[5] A previous study has found that 33.7% of all complications associated with SPCs were caused by infiltration,[6] which can result in local tissue irritation, inflammation, and compartment syndrome.[7-10] Therefore, appropriate interventions are important to prevent infiltration.

A number of risk factors have been implicated in the development of infiltration, including patient-specific, catheter-specific, pharmacologic, and other factors.[11] One patient-specific risk factor is small veins, and 1 catheter-specific risk factor is larger catheter size relative to vein size.[11] Hadaway has suggested that health care professionals need to choose the smallest gauge that will accommodate the prescribed therapy and identify an appropriate vein large enough relative to the catheter to prevent infiltration.[7] However, the assessment can be difficult because the literature doesn't indicate appropriate vein size relative to the catheter gauge quantitatively. The provision of a cutoff point of the ratio of the vessel size to the catheter gauge may enable health care professionals to identify the right vein for SPC insertion.

B-mode ultrasonography (US) is an efficient, repeatable, radiation-free, and noninvasive test in real time. Because of this, not only radiologists but also nurses have begun to use US imaging for peripheral venous access.[12,13] US can be used to examine catheterized peripheral veins,[14] and Everitt stated that "B-mode ultrasound was used to determine vein calibre and proved to be a useful means for serial examination during intravenous infusion."[15(p109)] As a result, research was undertaken at a university hospital in Japan to investigate whether US might be an optimal assessment tool in a clinical setting for preventing SPC complications.

Accordingly, vessel diameter in patients was measured immediately after catheterization using US examination, and the ratio of vessel diameter to the size of the catheter placed in the vein was calculated. The aim was to reveal any differences in mean ratios between veins with infiltration and those without infiltration, and to see if the cutoff point of the ratio could be estimated to prevent infiltration.

PATIENTS AND METHODS

Participants and Study Setting

Participants were patients admitted to a medical ward of a university hospital between January 2014 and June 2014 and had received SPCs. Exclusion criteria were patients who were undergoing chemotherapy, were younger than 20 years of age, did not have approval from their attending physician, or had low cognition levels. SPCs had been inserted and maintained in accordance with the policies of the facility, including completion of therapy, regular replacement of infusion equipment, and clinically indicated catheter removal. Infusions were delivered through ethylene tetrafluoroethylene catheters (Surshield Surflo2, Terumo Corporation, Tokyo, Japan) inserted 19 to 32 mm into forearm veins. Demographic data (age, gender, body mass index [BMI], diagnosis, diabetes) and type of admission were collected from medical records. Information about types of solutions for each SPC also was collected from the medical records. The solutions were categorized into vasoconstrictive potential, lower or higher pH solution (< 5 or > 9), and hyperosmotic solution (> 600 mOsm/L), which have been suggested as pharmacologic risk factors for infiltration.[7,11] US video recordings for measuring vessel diameter were taken immediately after catheter insertion. Swelling around the insertion site was visually confirmed and recorded by 2 trained researchers before catheter removal. The researchers were in the medical ward on call weekdays between 6 AM and 9 PM. The study protocol was approved by the research ethics committee of the university's graduate school of medicine and faculty of medicine. Written informed consent to participate in the study was obtained from all patients or their family. Participants were always free to retract the consent and were encouraged to report any pain or discomfort during the US examination.

Measurement of Vessel Diameter Using US

US equipment (Noblus, Hitachi Aloka Medical, Tokyo, Japan) was used with a linear-array (5-18 MHz) transducer. Echo gain and dynamic range were set at 25 and 65, respectively. Focal range and image depth were changed within 15 to 20 mm, depending on vessel depths. Images were acquired using a sufficient amount of ultrasound gel (Aquasonic100, Parker Laboratories, Fairfield, NJ) to avoid pressure on the vessel by the transducer. A gel stand-off pad (Sonar Pad, Nippon BXI, Tokyo, Japan) was used on the insertion site covered by an IV transparent dressing to reduce friction during transducer operation. Short-axis US videos were taken including the SPC tip and preserved on a hard disk in the US equipment.

All examinations were performed by 2 well-trained researchers. US images were captured from US videos at the SPC tip position for measurement of vessel diameter (Figure 1). Vessel diameter was defined as D (D = [major axis + minor axis]/2). The major axis was the longest diameter. The minor axis was perpendicular to

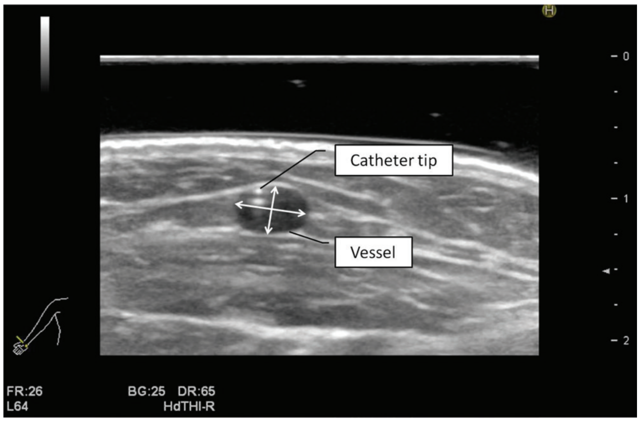

Figure 1 A short-axis sonographic image of a vein with an inserted SPC tip. Arrows indicate the major and minor axis lengths. *Abbreviation: SPC, short peripheral catheter.*

the major axis. The major and the minor axes were measured 3 times from the US image (0.04 mm/pixel) by a single researcher using ImageJ, a publicly available image-processing platform.[16]

The single researcher was blinded to the presence of infiltration. The mean of 3 measurements was used for calculating D. To determine test-retest reliability, the single researcher measured on 2 days, approximately 1 week apart. Test-retest reliability for 2 parameters (the major and minor axes) was investigated with intraclass correlation coefficients (ICCs). ICCs (mean value) and 95% confidence intervals (CIs) were calculated from 10 random samples of US images. ICCs (1, 3) of the 2 parameters (the major and the minor axes) were 0.99 (0.95-1.00) and 0.99 (0.95-1.00), respectively. Test-retest reliability for the 2 parameters on 2 days was considered excellent.

Data Analysis

Infiltration was defined as swelling extending at least 10 mm from the insertion site by referring to the grading scales developed by the Infusion Nurses Society.[4] Ratios were calculated by dividing vessel diameter D by the outside diameter of SPCs placed in the vein. The outside diameters of 20 gauge (G), 22 G, and 24 G SPCs were 1.1 mm, 0.9 mm, and 0.7 mm, respectively. Student's *t* test was used to compare the infiltrated veins and the noninfiltrated veins. Univariate analyses for each independent variable were performed by the χ^2 test or the Fisher exact test for categorical variables and Student's *t* test for continuous variables. The odds ratios and 95% CIs of independent variables for infiltration were estimated using logistic regression analyses. The variables were subjected to multiple logistic regression analyses when the *P* value was less than 0.1. Receiver operating characteristic (ROC) analysis[17] was performed to determine the sensitivity and specificity of cutoff points of the ratios in distinguishing between noninfiltrated and infiltrated veins. The area under the curve (AUC) was calculated to quantify the accuracy of the classification. Statistical analysis was performed with SPSS v22.0 (IBM, New York, NY). A *P* value of less than .05 was considered statistically significant.

RESULTS

During the 6-month study period, 292 subjects with 529 SPCs were enrolled. A total of 125 subjects with 323 SPCs for whom we could not obtain US videos immediately after insertion of the SPCs were excluded from the analysis. In addition, 95 subjects with 127 SPCs for whom we could not observe macroscopic findings around the insertion site before SPC removal were excluded (Figure 2).

Complete data were obtained for 79 SPCs from 72 subjects (50 males, 22 females) with a mean ± SD age of 68.5 ± 13.4 years. Sixty-six subjects (91.7%) were in the gastroenterology wards. Five subjects (6.9%) and 1 subject (1.4%) were in the geriatric and the infectious diseases wards, respectively. Seven subjects were assessed twice, with each second catheterization in the contralateral arm. Clinical characteristics of the subjects are displayed in Table 1. Most subjects had neoplasms (72.2%).

Fifteen SPCs (19%) were diagnosed with infiltration. In this study, 3 SPC gauge sizes were used. Table 2 shows the comparison of mean D for each SPC gauge between the infiltrated and noninfiltrated veins. In the veins inserted with 22 G SPCs, the mean D in the infiltrated veins was significantly smaller than that in the noninfiltrated veins. On the other hand, the D in the infiltrated vein (n = 1) was larger than the mean D in the noninfiltrated veins with 24 G SPCs. Mean ratios (SD) in the infiltrated and noninfiltrated groups were 1.9 (0.6) and 2.9 (1.0), respectively; the ratio in the infiltrated group was significantly smaller than that in the noninfiltrated group ($P < .01$).

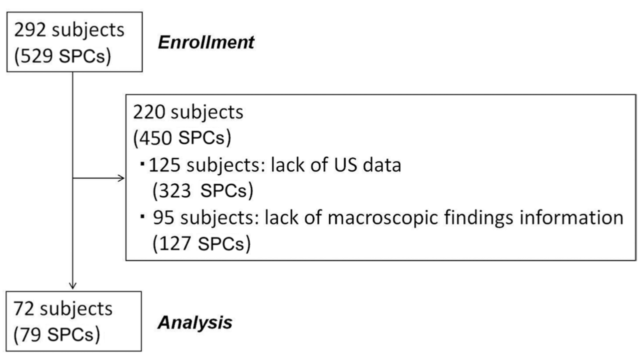

Figure 2 Participant flowchart throughout enrollment and analysis. *Abbreviations: SPC, short peripheral catheter; US, ultrasound.*

TABLE 1

Characteristics of the Subjects (N = 72)

Characteristic	n	(%)
Gender		
Male	50	(69.4)
Female	22	(30.6)
Age, years	68.5	± 13.4
History of present illness		
Neoplasms	52	(72.2)
Digestive disease	14	(19.4)
Certain infections	2	(2.8)
Circulatory disease	3	(4.2)
Respiratory disease	1	(1.4)

Note: n (%), mean ± SD. History of present illness was classified based on International Classification of Diseases-10.

The results from univariate analyses for each independent variable are shown in Table 3. No subjects received vasoconstrictive medication. The variables, including BMI, vein/catheter ratio, and hyperosmotic solution, were found to be possible candidates for multivariable analysis. Among these candidates, the multicollinearity was confirmed, and no correlations were found. As a result, age, BMI, vein/catheter ratio, and hyperosmotic solution were entered into the multivariate model. Multivariate analysis demonstrated that vein/catheter ratio was significantly associated with infiltration (Table 4).

ROC analysis was performed (Figure 3). The AUC was calculated (AUC, 0.80; 95% CI, 0.68-0.91). The value of 0.80 was considered good in its ability to predict infiltration. Using the ROC analysis, several cutoff points of the ratio were presented (Table 5). The balance between sensitivity and specificity changes, depending on the cutoff points.

DISCUSSION

This is the first study to reveal the relationship between the ratio of the vessel diameter to the SPC gauge and infiltration by examining catheterized peripheral veins using US. Additionally, ROC curves were charted to determine recommended cutoff values. The ratio equal to 3.3 was determined to be the best variable for differentiating normal veins from infiltrated veins as an objective reference for vessel evaluation.

In this study, US was used to measure the diameter of peripheral veins. Because peripheral veins are prone to compression by US transducers, a sufficient amount of ultrasound gel was used to avoid compression. Also, a single researcher blinded to the presence of infiltration measured vessel diameters, which helped ensure reliability for the study. The ICC was more than 0.9, and test-retest reliability was excellent.

Infiltration occurred more frequently when catheters were inserted into small veins with the mean ratio less than 1.9 (eg, in case 22 G SPC is used, small veins are less than 1.7 mm); the ratio was an independent risk factor according to the multivariable analysis. Although univariate analysis ($P = .02$) indicated hyperosmotic solution was a risk factor for infiltration, multivariate analysis did not ($P = .16$). It was assumed this was due to hyperosmotic solution used for patients who had low BMI and small veins, because only hyperosmotic solution was for peripheral parenteral nutrition: glucose-added electrolyte and amino acid solution with vitamin B_1 (approximately 850 mOsm/L). These independent factors, BMI and hyperosmotic solution, were weakly

TABLE 2

Comparison of Mean Vessel Diameter for Each Gauge of Short Peripheral Catheter Between Infiltrated Veins and Noninfiltrated Veins (N = 79)

	Infiltration Group (n = 15)		No-Infiltration Group (n = 64)		
SPC Gauge	n	Mean (SD), mm	n	Mean (SD), mm	*P*
20 G (n = 2)	0	—	2	2.3 and 3.0	—
22 G (n =68)	14	1.6 (0.5)	54	2.7 (0.9)	< .01
24 G (n = 9)	1	2.1	8	1.7 (0.9)	—

Student's t test.
Abbreviations: SD, standard deviation; SPC, short peripheral catheter.

TABLE 3
Patient Factors and Risks of Infiltration (N = 79)

	Infiltration (n = 15)	No Infiltration (n = 64)	Total (n = 79)	OR	95% CI	*P*
Age, years	70.9 ± 16.7	68.3 ± 12.8	68.5 ± 13.4	1.02	0.97-1.06	.49
BMI						
≤ 18	2 (13)	1 (2)	3 (4)	9.60	0.79-116.40	.08[a]
19-24 (reference)	10 (67)	48 (75)	58 (73)	1.00		
≥ 25	3 (20)	15 (23)	18 (23)	0.96	0.23-3.95	.96
Diabetes						
Yes	6 (40)	14 (22)	20 (25)	2.38	0.72-7.83	.19
No (reference)	9 (60)	50 (78)	59 (75)			
Hyperosmotic solution						
Yes	5 (33)	5 (8)	10 (13)	5.90	1.44-24.15	.02[a]
No (reference)	10 (67)	59 (92)	69 (87)			
Lower or higher pH solution						
Yes	0 (0)	1 (2)	1 (1)	0.81	0.73-0.90	1.00
No (reference)	15 (100)	63 (98)	78 (99)			
Vein/catheter ratio	1.9 ± 0.6	2.9 ± 1.0	2.7 ± 1.0	0.24	0.10-0.62	< .01[a]

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.
[a]$P < .1$ for bivariate association. n (%), mean ± SD. The ORs and 95% CIs of infiltration were estimated using logistic regression analyses.

correlated. This result indicates that infiltration could be affected more by mechanical factors than pharmacologic ones and that veins with low ratios (< 1.9) can be a cause of infiltration. One of the causes of infiltration has been associated with thrombus.[7] In a previous study, fluid leakage from the veins occurred more often when a small vein was used, because small, fragile, and mobile veins require multiple needle punctures.[18] The endothelium regulates the balance between intravascular thrombosis and thrombolysis,[19] with endothelial damage shifting the balance toward thrombosis.[20] After multiple venipuncture attempts, a clot can form inside the vein lumen. A larger catheter relative to the vein decreases blood flow,[21] which would promote thrombus growth. Thrombus may lead to complete occlusion of the vein. Continued infusion in the presence of thrombus increases internal pressure in the vein, resulting in fluid leaking from the puncture site into the subcutaneous tissue. This result supports the necessity of selecting a vein large enough to accommodate the gauge of the SPC.

In this study, several cutoff points were presented using ROC analysis. Despite low specificity, the ratio equal to 3.3 would be a better cutoff point. If we select the other cutoff point with higher specificity (with lower sensitivity), the number of selectable veins in patients

TABLE 4
Independent Risk Factors for Infiltration (N = 79)[a]

	OR	95% CI	*P*
Age, years	1.01	0.97-1.06	.59
BMI	7.28	0.45-117.37	.16
Hyperosmotic solution	3.54	0.66-18.97	.16
Vein/catheter ratio	0.28	0.11-0.72	< .01

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio.
[a]Findings are from a multivariate logistic model.

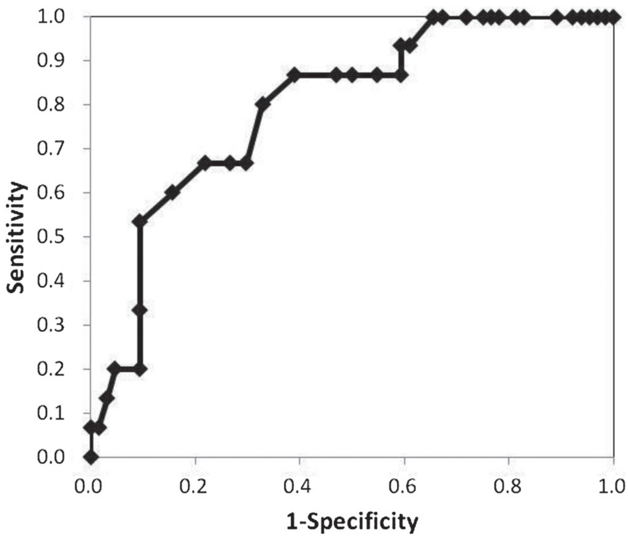

Figure 3 ROC curve of the ratios. *Abbreviation: ROC, receiver operating characteristic.*

would be increased. On the other hand, when patients have damage to their vein secondary to infiltration, their future vascular access would be reduced or eliminated around the vessel,[5] which could make it almost impossible for health care professionals to select suitable veins. The authors placed importance on the sensitivity rather than the specificity to prevent infiltration completely. The cutoff point of the ratio equal to 3.3 was generally consistent with European Society for Clinical Nutrition and Metabolism guidelines for the prevention of peripheral vein thrombophlebitis—that is, ideally the diameter of the catheter should be one-third or less the diameter of the vein, as checked by US.[22] Using the figure calculated by multiplying the outer diameter of the catheter by 3.3 can help health care professionals identify suitable veins for infusions using SPCs. If a large vein with the ratio greater than 3.3 is not detected in a patient, alternative catheters—such as peripherally inserted central venous catheters or midline catheters—need to be considered.[23,24] Consideration should be given to using SPCs with a gauge less than 24 G for patients with small forearm veins.

The small number of participants is a limitation of this study. With a larger sample size, specific associations between medication and infiltration and catheter-gauge and infiltration could be indicated. Further research with a larger sample size is needed to make conclusive determinations.

CONCLUSIONS

The results of this study show that the ratio in the infiltrated group was significantly smaller than that in the noninfiltrated group ($P < .01$). It is suggested that the cutoff point of the ratio equal to 3.3 would help health care professionals identify veins appropriately for preventing infiltration. Future studies with larger sample sizes are needed to reach definitive conclusions.

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TABLE 5

Sensitivity and Specificity of Several Cutoff Points of the Ratios and Ideal Vessel Diameter Calculated by Each Cutoff Point When 22 Gauge Is Used as an Example

Cutoff Point of the Ratio	Sensitivity	Specificity	Ideal Vessel Diameter Calculated by Cutoff Point When 22 Gauge (0.9 mm) SPC Is Used
1.9	60%	84%	0.9 mm × 1.9 = 1.7 mm
2.6	87%	61%	0.9 mm × 2.6 = 2.3 mm
3.3	100%	34%	0.9 mm × 3.3 = 3.0 mm

Abbreviations: SPC, short peripheral catheter; mm, millimeter.

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