Original Article

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The relationship between the tip position of an indwelling venous catheter and the subcutaneous edema

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Summary **The present observational study aimed to clarify the relationship between the tip position of an indwelling venous catheter and the subcutaneous edema using ultrasonography images. Data were obtained before catheter removal in a medical ward of a university hospital in Tokyo, Japan. Two hundred peripheral intravenous catheters (PIVCs) from 154 patients were observed just before removal. We analyzed data for 194 PIVCs from 150 patients. Subcutaneous edema was observed in 43.8% of ultrasonography images. According to the univariate analysis, insertion site, PIVC tip contact with the vessel wall, and irritant drug's presence were selected as independent variables for logistic regression analysis. Both irritant drug and PIVC tip contact were associated with the presence of subcutaneous edema [adjusted odds ratio (OR) = 2.68, 95% confidence interval (CI) = 1.14-6.33; and OR = 2.01, 95% CI = 1.04-3.88, respectively]. To the best of our knowledge, this is the first study to use ultrasonography to simultaneously observe PIVC tip position and subcutaneous edema. Using ultrasonography to observe PIVC may be a useful method to understand these mechanisms. Medical staff should select an appropriate vein and indwelling catheter to avoid contact of PIVC tip with the vessel wall. Further studies exploring the causality of the relationship between subcutaneous edema, catheter placement, and thrombus formation is required. In addition, further development of nursing skills and medical devices to reduce mechanical stress is required.**

Keywords: Intravenous therapy, peripheral intravenous catheters, subcutaneous tissue, ultrasonography

1. Introduction

Intravenous therapy using a peripheral intravenous catheter (PIVC) is a common and useful method for peripheral venous administration of medicine or fluid (*1-3*). However, treatment interruptions frequently occur in intravenous therapy because of accidental removal or signs and symptoms indicating complications (*4-6*). These problems not only lead to uncomfortable experiences for patients but are also costly in terms of repeated PIVC insertion (*7,8*).

Infiltration is one of the problems of intravenous therapy, because it can result in serious complications, including skin loss and necrosis (*9*). A report from the Veterans Administration of Puget Sound Health Care System showed that 33.7% of all complications during IV therapy with PIVC occurred because of infiltration (*10*). Therefore, clarifying the causes of infiltration can help prevent catheter failures.

The Infusion Nurses Society Standards of Practice Infiltration Scale defines infiltration as inadvertent leakage of a non-vesicant solution into surrounding

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tissue; grade 1 clinical criteria is edema of < 1 inch (2.5 cm) in any direction (*11*). Edema is observed as swelling surrounding the insertion site of an indwelling catheter. In contrast, subcutaneous edema surrounding the insertion site of an indwelling catheter can also be observed using ultrasonography (US) (*12*), a portable, non-invasive method that does not result in radiation exposure.

Doellman *et al*. reported that risk factors for infiltration and extravasation have been commonly regarded as mechanical factors (vein size and condition, catheter size and stability, insertion site, patient activity, insertion frequency, and power injector use), physiological factors (clot formation, thrombus, fibrin sheath, and lymphedema), and pharmacological factors (pH, osmolarity, vasoconstrictive potential, and cytotoxicity) (*13*). In the present study, we focused on mechanical factors because the subcutaneous tissue and vessel wall are damaged by inserting the needle, and an indwelling catheter might also continuously stimulate the vessel wall during placement. PIVC directly injures the subcutaneous tissue and vessel walls, followed by repairing of the vessel wall by blood clotting (*14*) and occurrence of edema as an inflammatory reaction in the subcutaneous tissue. Stimulation due to catheterization, particularly the catheter tip position, may be directly related to subcutaneous edema.

We used US to observe the situation of the indwelling catheter in the vein just before catheter removal. Clarifying the relationship between the position of an indwelling catheter in the vein and complications such as subcutaneous edema can facilitate the development of catheter placement skills and devices to prevent stimulation of the vessel wall. Therefore, the present study aimed to clarify the relationship between the tip position of an indwelling venous catheter and the image of subcutaneous edema using US.

2. Materials and Methods

2.1. *Study design and participants*

The present study used a prospective observational approach. Data were obtained just before catheter removal in a medical ward of a university hospital in Tokyo, Japan, from January to June 2014. The study sample included hospitalized adult patients who received IV therapy. Catheter removal was from 6:00 AM to 9:00 PM every weekday. Exclusion criteria were as follows: patients who received chemotherapy, those who were under 20 years of age, those who had low cognitive levels, and those who had a condition that made it difficult to cooperate with the research.

2.2. *Data collection procedure*

Researchers were notified by the nurse or physician when a catheter was to be removed due to catheter failure, routine replacement, or completion of IV therapy. US examination was performed at bedside just before catheter removal. Characteristics of PIVC placement, such as insertion site, catheter size, and catheterization duration, were also recorded.

In addition, the researchers observed signs, such as swelling, redness, induration, bleeding, and symptoms, such as pain. Patient characteristics, such as age, sex, and history of present illness and intravenous fluid therapy, were collected from patients' medical records.

2.3. *US scanning technique*

We used US diagnostic equipment (Hitachi Aloka Medical Ltd., Tokyo, Japan) with linear-array transducers (5-18.0 MHz). The focal range and image depth were set at 1.5-2 cm to determine the correct display range. Echo gain was set at 25 and the dynamic range at 65. Ultrasound gel (Aquasonic 100; Parker Laboratories Inc., Fairfield, NJ, USA) and gel pads (Sonar Pad; Nippon Bxi Inc., Tokyo, Japan) were used because transducer pressure resulted in vein disfiguration (Figure 1).

US examinations were performed by two researchers who received US training. The PIVC tip positions were the anatomic landmarks for identifying the US scanning point, with scanning starting at the insertion site and performed for more than 5 cm on both the short and long axes.

2.4. *Data analysis*

2.4.1. *US images analysis*

The PIVC tip position, intravenous thrombus, and edema of the subcutaneous fat layer were assessed by a certified sonographer with over 10 years of experience. The definitions of thrombus and subcutaneous edema were based on our previous study (*12*). Intravenous thrombus was defined as a marked echogenic mass with an uneven surface. Subcutaneous edema was defined by a homogeneous cobblestone appearance in the subcutaneous fat layer due to excessive fluid in the interstitium and a slightly edematous dermis. Presence or absence of subcutaneous edema and intravenous thrombus was determined using both transverse and longitudinal US images.

The PIVC tip position was defined as clear contact with the vessel wall; presence or absence of contact was determined using transverse US images.

2.4.2. *Statistical analysis*

Chi-square or Mann-Whitney *U* tests were used to compare PIVC placement between two patient groups (with and without subcutaneous edema).

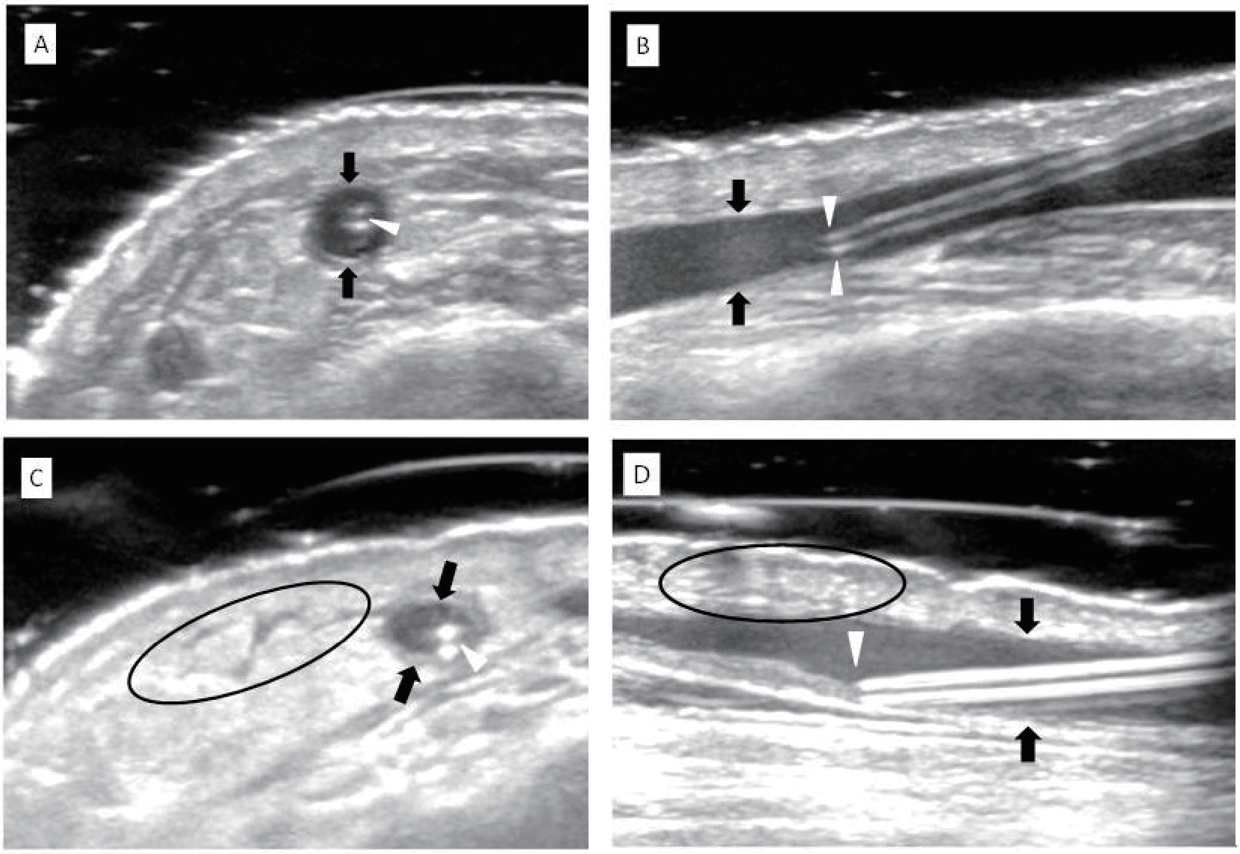

Figure 1. Ultrasonography findings of subcutaneous tissue, blood vessel, and peripheral intravenous catheter placement. **A:** Normal findings (transverse image), **B**: Normal findings (longitudinal image), **C**: PIVC tip in contact with the vessel wall (transverse image), **D**: PIVC tip in contact with the vessel wall (longitudinal image). Ultrasonography images showing the vessel wall (arrows), PIVC tip (arrowheads), and subcutaneous edema (circle).

The insertion site was classified as forearm or others (upper arm, dorsum of hand, wrist, cubital fossa and dorsum of foot) and the duration of catheterization was classified as < 96 h or ≥ 96 h based on the study facility's policy as specified by the Guidelines for the Prevention of Intravascular Catheter-Related Infections (*15*).

The subjective observation of the presence or absence of infiltration [edema (swelling), pain, cool-to-touch] was based on the Infusion Nurses Society Standards of Practice Infiltration Scale, with presence being more than grade 1 criteria (*11*).

Information about intravenous fluids, including antibiotic and irritant drug administration, was collected from patients' medical charts. We defined an irritant drug as having a pH < 5 or a ratio of osmotic pressure ≥ 3, based on the Infusion Nursing Standards of Practice (*16*). Multivariate logistic regression analysis was used to define the relationships between each factor in the univariate analysis that showed $p < 0.2$ with subcutaneous edema.

All two-tailed *p*-values of < 0.05 were considered significant. Data were analyzed using the Statistical Package for Social Sciences Version 21.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

2.5. *Ethical considerations*

Before participation, all patients and their families were informed about the purpose of the study, methods of measurement, management of individual information, consideration of safety, and right to withdraw from participation at any time. Written consent was obtained from all participating patients.

This study was approved by the Research Ethics Committee of the Graduate School of Medicine at the University of Tokyo (#10348).

3. Results

3.1. *Participants and PIVC characteristics*

In total, 293 patients consented to participate in the present study. Two hundred PIVCs from 154 patients were observed just before removal. Six PIVCs were excluded from analysis because US images were not obtained. Data for 194 PIVCs from 150 patients were analyzed. Of the participants, 88 (58.7%) were male; the mean age was 69.7 years, with a standard deviation

(SD) of 12.7 years (range, 25-92 years). In addition, 81 patients (54%) had neoplasms (Table 1).

The most common catheter size was 22 gauge (81.4%) and almost all were inserted into the forearm (91.8%). The duration of catheterization was almost within 96 h (82.0%).

3.2. *US findings*

Subcutaneous edema was observed in 85 (43.8%) US images and was associated with the presence of infiltration ($p < 0.001$). Intravenous thrombus before PIVC removal was observed in 112 (60.9%) images, and PIVC tip was in clear contact with the vessel wall in 60 (33.3%) images.

Table 1. Participants characteristics

Items	(n = 150)
Age (years), mean (SD)	69.7 (12.7)
Sex, *n* (%)	
Male	88 (58.7)
Female	62 (41.3)
History of present illness, *n* (%)	
Neoplasms	81 (54.0)
Digestive system	50 (33.4)
Circulatory system	8 (5.3)
Certain infectious	5 (3.3)
Musculoskeletal system and connective tissue	3 (2.0)
Nervous system	2 (1.3)
Respiratory system	1 (0.7)

Note. History of present illness was classified based on ICD-10.

3.3. *Risk factors associated with subcutaneous edema*

Patient characteristics, such as age and sex, and PIVC characteristics, such as catheter size, insertion site, and catheterization duration, were not associated with subcutaneous edema. The number of PIVCs used to administer irritant drug during catheterization was 36 (18.6%), which was significantly associated with subcutaneous edema (p = 0.009) and thrombus (p = 0.001). In this research, all irritant drugs were BFLUID®. The presence of PIVC tip contact was also associated with subcutaneous edema (p = 0.038). Intravenous thrombus was associated with subcutaneous edema (p = 0.047) (Table 2).

Following univariate analysis, insertion site, irritant drug, and presence of PIVC tip contact's presence were included as independent variables for logistic regression analysis. The sex and age of patients were included as control variables. Multicollinearity was considered to be present between PIVC tip contact with the vessel wall and intravenous thrombus; therefore, intravenous thrombus was excluded. Administration of an irritant drug and presence of PIVC tip contact were associated with the presence of subcutaneous edema [adjusted odds ratio (OR) = 2.68, 95% confidence ratio

Table 2. Characteristics of peripheral intravenous catheter placement

Items	Total catheter (n = 194)	Without edema[a] (n = 109)	With edema[a] (n = 85)	p-value
Age (years), median [interquartile range]	72.5 [15.3]	73.0 [15.0]	72.0 [17.0]	0.321[d]
Sex, *n* (%)				0.377[e]
Male	115 (59.3)	68 (62.4)	47 (55.3)	
Female	79 (40.7)	41 (37.6)	38 (44.7)	
Catheter size, *n* (%)				0.418[d]
20 gauge	4 (2.1)	2 (1.8)	2 (2.4)	
22 gauge	158 (81.4)	87 (79.8)	71 (83.5)	
24 gauge	32 (16.5)	20 (18.3)	12 (14.1)	
Insertion site, *n* (%)				0.125[e]
Forearm	178 (91.8)	103 (94.5)	75 (88.2)	
Others[b]	16 (8.2)	6 (5.5)	10 (11.8)	
Duration of catheterization, *n* (%)				0.852[e])
< 96 hours	159 (82.0)	90 (82.6)	69 (81.2)	
≥ 96 hours	35 (18.0)	19 (17.4)	16 (18.8)	
Antibiotics, n (%)				0.312[e]
Presence	94 (48.5)	49 (45.0)	45 (52.9)	
Absence	100 (51.5)	60 (55.0)	40 (47.1)	
Irritant drug[c], *n* (%)				0.009[e]*
Presence	36 (18.6)	13 (11.9)	23 (27.1)	
Absence	158 (81.4)	96 (88.1)	62 (72.9)	
PIVC tip in contact with the vessel wall, *n* (%) (n = 180)				0.038[e]*
Presence	60 (33.3)	27 (26.5)	33 (42.3)	
Absence	120 (66.7)	75 (73.5)	45 (57.7)	
Intravenous thrombus, *n* (%) (n = 184)				0.047[e]*
Presence	112 (60.9)	57 (54.3)	55 (69.6)	
Absence	72 (39.1)	48 (45.7)	24 (30.4)	

[a] Presence of edema of the subcutaneous fat layer before catheter removal by ultrasound. [b] Others: upper arm, dorsum of hand, wrist, cubital fossa, dorsum of foot, [c] Irritant drug: pH < 5 or ratio of osmotic pressure ≥ 3, [d] Mann-Whitney *U* test, [e] χ^2–test. *$p < 0.05$.

Table 3. Logistic regression analysis of risk factors associated with subcutaneous edema

Items	Odds ratio (95% CI)			
	Crude	*p*-value	Adjusted	*p*-value
Patient characteristics				
Sex (1: male, 0: female)	0.75 (0.42,1.33)	0.377	0.84 (0.44,1.60)	0.587
Age (years)	1.01 (0.99,1.03)	0.429	1.01 (0.99,1.04)	0.443
Insertion site (1: others, 0: forearm)	2.29 (0.80,6.57)	0.125	2.41 (0.80,7.29)	0.119
Irritant drug (1: presence, 0: absence)	2.74 (1.29,5.81)*	0.009	2.68 (1.14,6.33)*	0.025
PIVC tip in contact with the vessel wall (1: presence, 0: absence)	2.04 (1.09,3.82)*	0.038	2.01 (1.04, 3.88)*	0.038

n = 180, $^{*}p < 0.05$, Hosmer & Lemeshow test: p = 0.694.

(CI) = 1.14-6.33; and OR = 2.01, 95% CI = 1.04-3.88, respectively] (Table 3).

4. Discussion

To the best of our knowledge, this is the first study using US to simultaneously examine PIVC tip position and subcutaneous edema. We found that the PIVC tip position was associated with subcutaneous edema.

We focused on mechanical factors, one of the risk factors for infiltration and extravasation, because the subcutaneous tissue and vessel wall get damaged by inserting the needle. An indwelling catheter may also continuously stimulate the vessel wall during placement. Everitt prospectively observed intravenous catheters (fine-bore polyurethane) and vein caliber using B-mode ultrasound (7.5 MHz transducer), and suggested that the complication of infusion might be related to intravenous thrombus and that the initiating event was venous endothelial trauma by venipuncture and abrasion at the catheter tip or delivery of the feed (*17*). However, Everitt made no reference to the presence or absence of subcutaneous edema. In contrast, LaRue and Peterson suggested that the toxicant is no more diluted when a catheter's tip is positioned perpendicularly to the vessel wall; therefore, it may promote the incidence of chemically-induced phlebitis and subcutaneous edema (*18*). However, they did not observe the position of the catheter within the vein.

Our results showed that one third of PIVC tip was clearly in contact with the vessel wall. It is noteworthy that the presence of subcutaneous edema was not only associated with irritant infusate but also associated with PIVC tip contact. This suggests that venous endothelial cells are directly damaged by mechanical stimulation from PIVC tip. Consequently, subcutaneous edema may have been formed as an inflammatory reaction to mechanical stimulation. In addition, venous endothelial cells might be damaged by chemical stimulation from PIVC tip positioned near the vessel wall. Extreme pH and high osmolarity relative to blood also affect venous endothelial cell damage and cause the infusate to escape venous circulation (*13,19*).

Although a relationship between the mechanism of the vessel wall damage and an increase in complications has not yet been revealed in detail (*20*), healthcare providers should carefully consider PIVC placement and the tip position in the vein. PIVC observation using US may be a useful method to develop understanding of these mechanisms. Medical staff should select an appropriate vein and indwelling catheter to avoid contact between PIVC tip and the vessel wall. Furthermore, even if PIVC tip is in contact with the vessel wall, developments in catheter design or material might reduce stimulation and inflammatory reactions.

As we performed US observation just before catheter removal, we could not determine how long PIVC tip had stimulated a vascular wall. Moreover, it is not known exactly how PIVC position leads to complications. Further study exploring the causality of the relationship between subcutaneous edema, catheter placement, and thrombus formation is needed. In addition, further development is needed in nursing skills and medical devices to reduce mechanical stress.

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