Original Article

DOI: 10.5582/ddt.2022.01108

Verification study on the catheterization of an upper arm vein using the new long peripheral intravenous catheter to reduce catheter failure incidence: A randomized controlled trial

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SUMMARY Intravenous infusion using a peripheral intravenous catheter (PIVC) is often complicated by catheter failure (CF). We hypothesized that catheterization of an upper arm vein instead of a forearm vein may help prevent CF. This study was designed to compare the incidence of CF in patients receiving hyper-stimulant drugs when catheters are placed in the forearm using short PIVCs (SPCs) with that when catheters are placed in the upper arm using the new long PIVCs. Patients admitted to a university hospital in Tokyo, Japan were enrolled in this study and were assigned to the SPC or the new long PIVC group. The primary outcome was the incidence of CF until 7 days. The secondary outcomes were the number of CFs per 1,000 days, the duration of the indwelling catheter, and the presence of thrombi and subcutaneous edema. Forty-seven patients were analyzed (median age, 67.0 years). The incidence of CF was 0% in the new long PIVCs and 32.0% (8 catheters) in the SPCs ($p = 0.007$), and the number of CF per 1,000 days was 0/1,000 and 81.7/1,000 days, respectively ($p = 0.001$). A significant difference in the duration of the indwelling catheter until CF occurrence was observed between the two groups ($p = 0.004$). Thrombi and subcutaneous edema were observed more frequently in the SPC group ($p < 0.001$). Catheterization of an upper arm vein using the new long PIVC to administer a hyper-stimulant drug might reduce CF compared with catheterization of a forearm vein using SPC.

Keywords Catheter failure, vascular access device, adverse event, catheterization site, intravenous infusion therapy

1. Introduction

Intravenous infusion therapy is a widely used treatment modality worldwide, with peripheral intravenous catheter (PIVC) devices being used frequently, in > 70% of hospitalized patients (*1,2*). Despite the usefulness of intravenous infusion therapy, catheter failures (CFs) are common, characterized by signs and symptoms, including redness, swelling, pain, and occlusion (insufficient infusion volume), and CF makes it difficult to continue infusion *via* PIVCs (*3*). The incidence rates of CF have been reported to range from 30-69% (*4-6*). We previously reported that approximately 18% of catheters were removed because of CF in adult inpatient wards at a tertiary university hospital in Japan (*7*). CFs lead to patient suffering, healthcare provider workload, and higher healthcare costs; thus, the prevention of CFs is critically important (*8*).

The main cause of CF is damage to vascular endothelial cells due to mechanical stimulation by the catheters and chemical stimulation by the infusate (*9-12*). To minimize mechanical and chemical stimulation to vascular endothelial cells, it is recommended that the catheter is placed in a vessel with a larger diameter and abundant blood flow. The veins of the upper arm can meet these conditions better than those of the forearm

(*13*). However, no guidelines recommend a specific venous site in the upper arm for PIVC placement during chemotherapy even though forearm veins are exposed to chemical stimuli, such as irritants and vesicant drugs. To compare different insertion sites, different PIVCs are needed; PIVCs with sufficient length (long PIVC: 6-15 cm in length) (*14*) should be used for upper arm veins, which are generally deeper than forearm veins, to reach the blood-flow-rich axillary area, whereas short peripheral catheters (SPCs) are sufficient and suitable for forearm veins.

This study designed to compare the incidence of CFs between different insertion sites in patients receiving hyper-stimulant drugs: SPCs placed in a forearm vein versus new long PIVCs instead into an upper arm vein.

2. Methods

2.1. Trial design

This study adopted a parallel group open-label randomized trial design. Randomization was performed using the stratified permutated block method, where the stratification factor was the administration of anticancer drugs or other irritant drugs.

2.2. Study setting and participants

This study was conducted at the Hematology and Oncology Department of the University of Tokyo Hospital, Tokyo, Japan, between August 2021 and March 2022. The inclusion criteria were as follows: hospitalized patients over 19 years old who underwent the first catheterization at the hospitalization and had planned administration of hyper-stimulant drugs, such as those with an osmotic pressure ratio ≥ 3, or irritant or vesicant drugs, including anticancer drugs. The exclusion criteria were as follows: patients who were scheduled for a chemotherapeutic regimen with continuous administration of vesicant drugs for more than 24 h, those with skin disorders at the planned puncture site, those with preexisting peripheral neuropathy, those with a history of thrombosis, those with stage ≥ stage G3a chronic kidney disease, those with abnormal blood coagulation test or bleeding tendency (prothrombin-international normalized ratio (PT-INR) ≥ 1.5; activated partial thromboplastin time (APTT) ≥ 36.1 s, or the use of anticoagulant or antiplatelet drugs), and those who were scheduled to undergo invasive procedures (*e.g.*, endoscopy and bronchoscopy). Other patients judged to be inappropriate for participation in this study by the physician in charge were also excluded.

All participants were given the explanation for this study, read the study's description, and signed a consent form. The study protocol was approved by the Research Ethics Committee of the Graduate School of Medicine and Institutional Review Board, The University of Tokyo (2021502SP). The trial protocol was registered and published in the Japan Registry of Clinical Trials: jRCT (protocol number: jRCTs032210224).

2.3. Intervention

The participants were assigned to the long PIVC group (New-PIVC group) placed in the upper arm vein and the short PIVC group (SPC group) placed in a forearm vein.

Long PIVC group (New-PIVC group) We used new-PIVCs (Terumo Corp. Tokyo, Japan) as long PIVCs (New-PIVCs). Because there are no approved long catheters in Japan and the safety of these new-PIVCs has been confirmed, we decided to use them, although they are unapproved vascular access devices (VAD) (*15*). The catheter length was 88 mm to enable us to reach the upper arm vein and place the catheter tip near the vicinity of the axillary vein. The size was 22 gauge (outer diameter: 0.9 mm); the catheter was made of polyurethane and did not have a built-in guidewire. With the two-person method, trained nurses performed the catheterization procedure using a tourniquet and applied the aseptic/no-touch technique with 1% chlorhexidine alcohol under ultrasound guidance.

Short PIVC group (SPC group) We used plastic cannula-type sterile puncture needles (Surshield® Surflo® ii, Terumo Corp. Tokyo, Japan) as short PIVCs (SPCs). The length/gauge of the catheter was 25 mm/22 gauge (outer diameter: 0.9 mm) or 19 mm /24 gauge (outer diameter: 0.7 mm). Physicians performed the catheterization procedure with a tourniquet and applied the aseptic/no-touch technique with 0.2% chlorhexidine gluconate or 81.4 vol% ethanol under inspection and palpation, according to the usual routine practice of the department.

2.4. Outcomes

The primary outcome of this study was the incidence of CF. CF was defined as unscheduled catheter removal due to signs and symptoms such as pain, swelling, redness, and occlusion before the completion of treatment until 7 days (24 h × 7 days), which was judged by physicians or staff nurses.

The secondary outcomes were the number of CFs per 1,000 days, the duration of the indwelling catheter until CF occurrence, and the presence of a thrombus in the vessel and subcutaneous edema. Catheter placement and pain when the needle was punctured, during the insertion of the catheter and during postural changes during catheter placement were subjectively evaluated. Although the period of indwelling was set at 24 h × 7 days in the protocol, there were cases in which the catheter continued to be used thereafter within the day of removal, at the discretion of the physician in charge. In such cases, the survival analysis was censored at 24 h × 7 days. Ultrasonographic images were obtained to

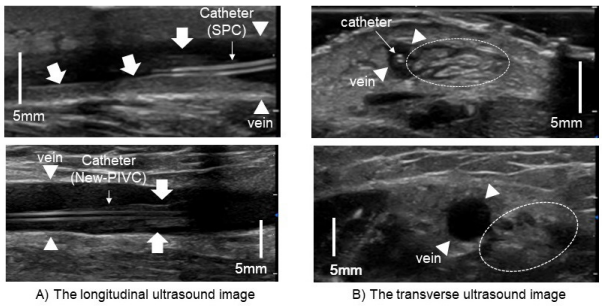

Figure 1. Samples of cases with the intravenous thrombus or the subcutaneous edema: SPCs on top; New-PIVCs on bottom. (**A**) Allow shows the intravenous thrombus: a marked echogenic mass with an uneven surface on the vessel wall or surround body or tip of catheter (*16*). (**B**) Dotted circle shows the subcutaneous edema (Mild or Severe): 1) Normal: the superficial fascia was clearly confirmed with no thickened subcutaneous fat layer, 2) Mild: the superficial fascia was confirmed with an unclear layered structure and a thickened subcutaneous fat layer, 3) Severe: a thickened subcutaneous fat layer was confirmed by a homogeneous cobblestone appearance in the subcutaneous fat layer, caused by excessive fluid in the interstitium (*17*).

detect thrombi in the vessel and subcutaneous edema at catheter removal. These images of subcutaneous tissue and vessel between the puncture point and catheter tip were taken using ultrasonography with two-dimensional linear-array transducers (6-13 MHz, FC1-X VA; Fujifilm, Tokyo, Japan) by research nurses trained for probe manipulation and interpretation of an image by a sonographer. Intravenous thrombi and subcutaneous tissue were assessed based on the classification described previously (Figure 1) (*16,17*). The removed catheter was documented photographically, and the angle of the base of the catheter was measured using ImageJ (National Institutes of Health: NIH). Painful catheterization was subjectively evaluated and confirmed using questionnaires with the visual analog scale.

We obtained data on the patients' characteristics (*i.e.*, diagnosis, medical history, oral medication, age, sex, body mass index, and the number of past regimens), blood test data on admission (*i.e.*, total protein, albumin, hematocrit, platelet count, differential white blood cell counts, C-reactive protein, prothrombin time, PT-INR, APTT, and fibrinogen), the length of hospital stay, and the rate and dosage of the infusate from the clinical records. We obtained data on the catheters and their insertion procedures, including catheter size, the number of punctures, and the distance between the elbow joint and the puncture point.

2.5. Sample size

We set the rate of CF occurrence as 5% in the New-PIVC group and 40% in the SPC group, with an effect size of 35%, according to our previous studies, which showed a CF incidence of 43.2% using SPCs (*12*) and 0% using the new PIVCs inserted into the upper arm vein (no events in eight cases) (*15*). With a two-sided statistical significance level of 0.05, and a power of 0.8, we estimated that the number of indwelling catheters needed would be 26 for each group.

2.6. Randomization and blinding

The Electronic Data Capture (EDC) system (ViedocTM 4) of the University Hospital Clinical Trial Alliance Clinical Research Support System was applied for an assignment; therefore, sequence generation and allocation concealment mechanisms were conducted automatically. While the staff nurses, physicians, and patients were not blinded because this was difficult due to the nature of the intervention, the research nurses interpreting the ultrasound images were blinded.

2.7. Research procedure

Informed consent was obtained from the patients with confirmed eligibility, who were subsequently assigned to either group by the EDC system. The patients in the New-PIVC group underwent the catheterization procedure in the treatment room, and those in the SPC group underwent the catheterization procedure at the bedside. After catheter fixation, a photograph of the insertion site was taken, and the patient responded to the subjective evaluation questionnaire. Staff nurses observed the puncture site and the surrounding area thrice a day until 24 h after catheter removal, and the researchers macroscopically observed the same area and interviewed patients and staff nurses once a day to get information on the signs and symptoms of CFs. When the catheter required removal, the insertion site was documented by photographs, and the vessel and subcutaneous tissues were observed using ultrasonography at removal. The research nurses took a photograph of the removed catheter for analysis.

2.8. Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (ver. 23.0; IBM Corp., Armonk, NY, USA) and SAS (ver. 9.4; SAS Institute Inc., Cary, NC, USA). Statistical significance was set at a two-tailed p-value < 0.05.

Continuous variables were expressed as means with standard deviations (SD) or medians with interquartile ranges (IQR). Statistical differences in the nominal variables between the two groups were tested using Pearson's chi-square test or Fisher's exact test, and those in the continuous variables were tested using Student's t-test or Mann-Whitney U-test after the confirmation of normal distribution.

The incidence rate of CFs and the number of CFs per 1,000 days were calculated as the number of CFs divided by the number of catheters used for infusion of irritant drugs (%) and per 1,000 catheter days. The risk difference and its two-sided 95% confidence interval

(CI) were calculated. Furthermore, the difference in CFs per 1,000 catheter days between the two groups was calculated using Poisson regression in which the treatment arm was included as a covariate. The duration of the indwelling catheter until CF occurrence in each group was shown using the Kaplan-Meier method. Survival was compared between the groups using the log-rank (Mantel-Cox) test.

3. Results

3.1. Participant flow

The number of patients who agreed to participate in the study was 52. Two of them did not meet the inclusion criteria; therefore, 50 patients were enrolled in this study and were randomly assigned to the New-PIVC (n = 25) or SPC (n = 25) groups. Three patients were excluded because one did not start the infusion of irritant drugs *via* the New-PIVC, one failed the new-PIVC placement, and one started anticoagulants. Finally, 47 patients (22 in the New-PIVC group and 25 in the SPC group) were analyzed (Figure 2).

3.2. Baseline characteristics

The median age of the patients was 67.0 ± 28.0 years; of the 47 patients, 61.7% were male, and their median body mass index was 22.0 ± 5.7 kg/m^2. The data on blood tests were as follows: PT-INR was 1.00 ± 0.07, and APTT was 28.44 ± 3.12 s. Malignant lymphoma accounted for 72.3% of the diagnoses of all patients. The baseline characteristics were generally comparable between the groups (Table 1).

Indwelling catheter sizes were 22 gauge (40.0%) and 24 gauge (60.0%) in the SPC group. All the new-PIVCs were placed in the basilic vein in the upper arm; 18 (72.0%) catheters among the SPCs were placed in the cephalic vein in the forearm. The mean distance between the elbow joint and the puncture point was 93.0 ± 25.8 mm in the New-PIVC group. Anticancer drugs were administered to all patients, except for two patients in the SPC group who received amino acid and glucose injections with electrolytes and vitamin B1 (BFLUID®). The rate of successful initial puncture of the new-PIVCs and the SPCs did not differ (18 (81.8%) *vs.* 13 (52.0%); p = 0.063) (Table 1).

3.3. Outcome measures

The incidence of CF was 0% in the New-PIVC group and 32.0% (8 catheters) in the SPC group; the difference between the two groups was significant (p = 0.007). The risk difference between the New-PIVC and SPC groups was −32.0% with a 95% CI of −50.3 to −13.7%. There was a case in which a catheter made of different materials was used, and the analysis excluding that case (n = 46) also showed a significant difference between the New-PIVC (0 cases) and SPC (7 cases, 29.2%) group (p = 0.013). The risk difference was −32.0% with a 95% CI of −50.3 to −13.7%.

The number of CFs per 1,000 days was 0/1,000 days (95% CI: 0-24.0/1,000 days) in the New-PIVC group and 81.7/1,000 days (95% CI: 35.2-160.8/1,000 days) in the SPC group (p = 0.001). The median duration of the indwelling catheter was 8,112.5 ± 7,045.0 min in the New-PIVC group (n = 22) and 4,665.0 ± 5,693.0 min in the SPC group (n = 25) (p = 0.141) (Table 2). In the Kaplan-Meier analysis of the duration of the indwelling catheter until CF occurrence, a significant difference in the results of the log-rank test was observed (p = 0.004) (Figure 3).

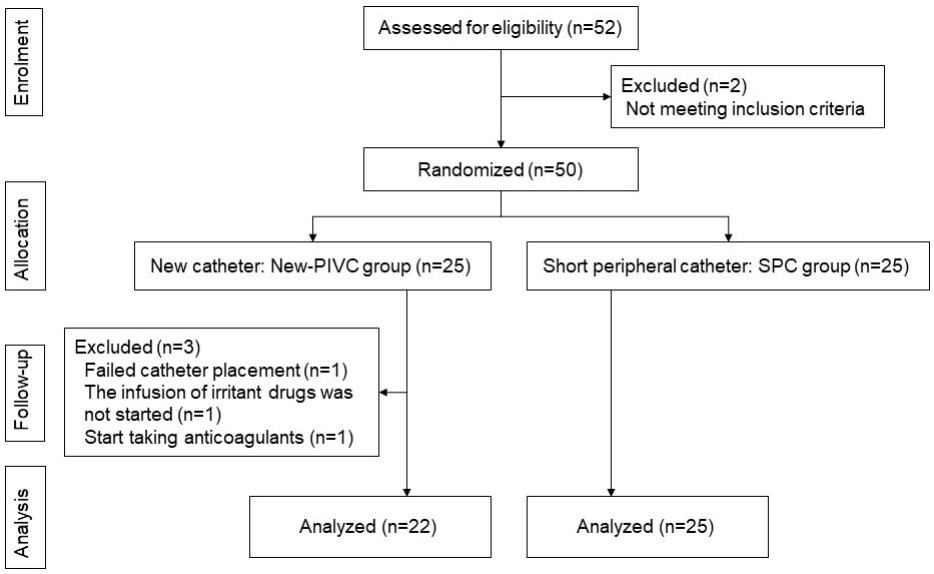

Figure 2. Study flow diagram.

Table 1. Patient and catheter characteristics

Items	All (n = 47)	New-PIVCs [a] (n = 22)	SPCs [a] (n = 25)	p-value
Age (years)	67.0 (28.0)	71.0 (32.0)	66.0 (20.0)	0.693 [h]
Sex (male)	29 (61.7)	11 (50.0)	18 (72.0)	0.144 [i]
Body Mass Index (kg/m^2)	22.0 (5.7)	21.7 (4.1)	22.6 (6.0)	0.201 [h]
Length of hospital stay	23.0 (14.0)	23.5 (16.5)	23.0 (13.0)	0.881 [h]
Number of regimens (past)	2.0 (6.0)	2.0 (5.3)	2.0 (6.0)	0.965 [h]
Blood test items[b]: mean (SD)				
Total protein (g/dL): mean (SD)	6.77 (0.76)	6.83 (0.56)	6.72 (0.91)	0.621 [j]
Albumin (g/dL)	4.10 (0.70)	4.15 (0.63)	4.10 (0.80)	0.486 [h]
Hematocrit (%): mean (SD)	34.81 (5.46)	36.12 (4.92)	33.66 (5.75)	0.125 [j]
Blood platelet count (×10^4/μL)	23.20 (15.60)	23.75 (14.90)	21.80 (15.65)	0.609 [h]
White blood cell count (×10^3/μL)	4.60 (3.40)	4.80 (2.73)	4.50 (4.85)	0.949 [h]
C-reactive protein (mg/dL)	0.30 (0.92)	0.14 (0.39)	0.46 (1.29)	0.117 [h]
Prothrombin (%): mean (SD)	101.63 (12.59)	105.47 (12.02)	98.26 (12.33)	0.049 [j]
PT-INR[c] : mean (SD)	1.00 (0.07)	0.98 (0.06)	1.02 (0.07)	0.046 [j]
APTT (seconds)[d] : mean (SD)	28.44 (3.12)	28.09 (2.97)	28.74 (3.27)	0.480 [j]
Fibrinogen (mg/dL) : mean (SD)	345.57 (103.32) [f]	329.43 (91.58) [f]	359.12 (112.29)	0.337 [j]
Diagnoses[e]				
Malignant Lymphoma	34 (72.3)	15 (68.2)	19 (76.0)	
DLBCL		9 (40.9)	8 (32.0)	
FL		2 (9.1)	4 (16.0)	
PCNSL		2 (9.1)	0 (0.0)	
BL		1 (4.5)	0 (0.0)	
MZL		1 (4.5)	2 (8.0)	
CLL		0 (0.0)	2 (8.0)	
cALCL		0 (0.0)	1 (4.0)	
PIOL		0 (0.0)	1 (4.0)	
WM		0 (0.0)	1 (4.0)	
Leukemia	13 (27.7)	7 (31.8)	6 (24.0)	
AML		6 (27.3)	4 (16.0)	
MDS		1 (4.5)	2 (8.0)	
Catheter size: gauge (G): 22 G / 24 G (%)		22 (100) / 0	10 (40.0) / 15 (60.0)	< 0.001 [i]
Number of successful initial punctures	31 (66.0)	18 (81.8)	13 (52.0)	0.063 [i]
Catheterized vein				
Basilic	25 (53.2)	22 (100.0)	3 (12.0)	
Cephalic	18 (38.3)	0	18 (72.0)	
Others (median: 3, hand: 1)	4 (8.5)	0	4 (16.0)	
Distance between the elbow joint and the puncture point (mm): mean (SD)		93.0 (25.8)	105.6 (41.0)	0.210 [j]
Total volume of irritant drugs: (mL)		910.0 (1470.0)	800.0 (640.0)	0.455 [h]
Administrated irritant drugs				
Anticancer drugs		22	23	
BFLUID[f]		0	2	

Note. Median (IQR) or n (%); IQR, interquartile range; SD, standard deviation. [a]New-PIVCs, the new peripheral intravenous catheter group; SPCs: the short peripheral intravenous catheter group. [b]Blood test values on the closest day before catheter placement. [c]PT-INR, prothrombin time and/or international normalized ratio. [d]APTT, activated partial thromboplastin time. [e]DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; PCNSL, primary central nervous system lymphoma; BL, Burkitt lymphoma; MZL, marginal zone lymphoma; CLL, chronic lymphocytic leukemia; cALCL, primary cutaneous anaplastic large cell lymphoma; PIOL, primary intraocular lymphoma; WM, primary macroglobulinemia/Waldenström macroglobulinemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndromes. [f]n = 46 (in all), n = 21 (in New-PIVCs). [g]BFLUID (amino acid and glucose injection with electrolytes and vitamin B1). [h]Mann-Whitney U-test. [i]Fisher's exact test. [j]t-test.

Table 2. Outcome measures

Items	New-PIVCs (n = 22)	SPCs (n = 25)	p-value
Catheter failure (CF): n (%)	0 (0.0)	8 (32.0)	0.007[a]
CF per 1000 days (95%CI)	0 (0-24.0)	81.7 (35.2-160.8)	0.001[b]
Catheter dwelling time: median ± IQR (min)	8112.5 ± 7045.0	4665.0 ± 5693.0	0.141[c]
Presence of the thrombus in the vessel: n (%)	10 (45.5)	22 (95.7)[f]	< 0.001[a]
Presence of the mild or severe subcutaneous edema: n (%)	4 (18.2)	18 (78.3)[f]	< 0.001[a]
The angle of the base of the removed catheter: mean ± SD (degrees)	20.0 ± 7.2	10.2 ± 6.3[g]	< 0.001[d]
Subjective assessment of catheter placement: median (range)[e]			
Pain when the needle punctures the skin surface	10.5 (0-54.0)	36.0 (9.0-89.0)	< 0.001[c]
Pain when inserting a catheter into a blood vessel	0.5 (0-37.0)	14.0 (0-88.0)	0.008[c]
Painful due to posture during catheter placement	0 (0-52.0)	0 (0-26.0)	0.039[c]

Note. [a]Fisher's exact test; [b]Poisson regression; [c]Mann-Whitney U-test; d) t-test. [e]visual analogue scale: 0, no pain; 100, maximum pain. [f]n = 23; [g]n = 22.

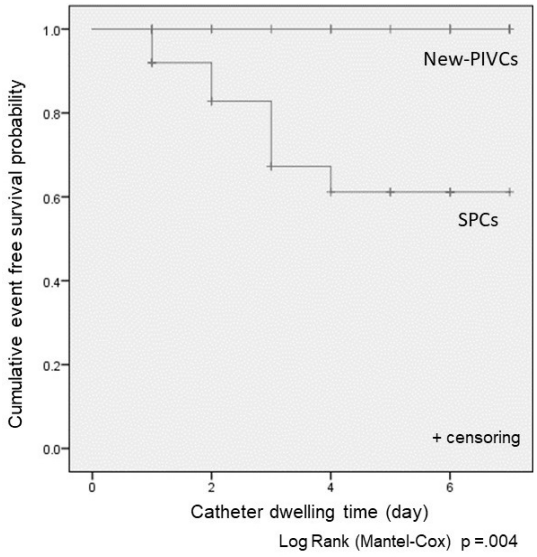

Figure 3. The duration of the indwelling catheter until catheter failure occurrence.

The number of patients for whom ultrasonographic images were obtained at catheter removal was 22 in the New-PIVC group and 23 in the SPC group. The frequency rate of thrombosis at catheter removal was 45.5% in the New-PIVC group and 95.7% in the SPC group ($p < 0.001$). Subcutaneous edema was observed in 18.2% and 78.3% of the patients of the New-PIVC and SPC group, respectively ($p < 0.001$). The signs and symptoms of CF seen in the SPC group were occlusion (insufficient infusion volume or inability, $n = 6$) and redness, swelling, and pain ($n = 2$). Catheter-related bloodstream infections, thrombophlebitis, and extravasation did not occur.

The number of patients for whom the catheter was removed was 22 in the New-PIVC group and 22 in the SPC group. The mean angle of the base of the removed New-PIVCs and SPCs differed significantly (20.0° ± 7.2° *vs.* 10.2° ± 6.3°; $p < 0.001$) (Table 2).

According to the visual analog scale (100 points is the maximum pain), the pain scores due to needle puncture on the skin surface and catheter insertion into the vessel in the New-PIVC group were lower than those in the SPC group ($p < 0.001$, and $p = 0.008$, respectively). Pain score associated with postural changes during catheter placement was higher in the New-PIVC group than in the SPC group ($p = 0.039$) (Table 2).

4. Discussion

This study revealed that the incidence of CF can be reduced by catheterizing the upper arm vein using a new long catheter instead of catheterizing the forearm vein using a short catheter in patients receiving hyper-stimulant drugs. The results suggest that CF is reduced by selecting the upper arm vein instead of the forearm vein for PIVC placement, particularly when a chemical stimulus is likely to damage vascular endothelial cells. Therefore, the characteristics of the upper arm vein (deep and invisible or unpalpable) should be considered in selecting VAD and catheterization should be assisted by visualization devices.

Recently, the PIV5RightsTMBundle was proposed to prevent complications associated with catheter placement and to preserve vessels (*18*). Although there have been reports of high puncture success rates, long indwelling periods, and decreased complications with the PIV5RightsTMBundle, it has been highlighted that vessel selection in terms of blood flow (hemodilution ratio) was not considered (*19*). Blood vessels are probably repeatedly exposed to chemical stimuli, particularly when irritant or vesicant agents are used in chemotherapy. The patients in this study had been treated with anticancer drugs in the past. Therefore, for vascular preservation, indwelling and infusing at sites with high blood flow volume (*e.g.*, an upper arm vein among upper extremity) seems important to reduce drug exposure. Although there have been several reports investigating the differences in CF incidence and catheter survival time when PIVCs using different catheter lengths were placed, few studies have directly compared whether the upper arm or forearm was a more appropriate insertion site to prevent CFs. Additionally, few reports have clearly described the irritancy of infusates (*20,21*). Therefore, in this study, we compared the incidence of CFs between patients receiving hyper-stimulant drugs *via* the upper arm and those receiving hyper-stimulant drugs *via* the forearm.

Notably, no CFs occurred in the 22 patents in the New-PIVC group, whereas CFs occurred in 32.0% of the patients in the SPC group, which are similar to the incidence rates reported previously (*22,23*). Six of the eight CF cases in the SPC group were occlusions (insufficient infusion volume or inability). Significantly higher rates of thrombus formation and subcutaneous edema formation at the time of catheter removal were observed in the SPC group using ultrasonography. These results suggest that mechanical and chemical stimuli to the forearm vessel are more severe than those to the upper arm vessel, possibly reflecting a more profound damage to endothelial cells.

Based on the results of this study, the upper arm should also be considered a site for catheter placement, at least in some cases. There seem to be three points to consider for catheterization into a vein in the upper arm. First, the angle of the base of the removed New-PIVCs was significantly larger than that of the removed SPCs because the needle reached the deep vessel. If external forces are applied to the catheter hub after fixation, through the movement of the subcutaneous tissue with joint movement or muscle contraction, the angle of the base of the catheter may further increase, leading to kinking of the catheter (*15*). Therefore, the site of catheter fixation should be far from the elbow joint

appropriately. Second, the pain score associated with needle puncture and catheter insertion into the vessel was lower in the New-PIVC group than in the SPC group. In contrast, pain due to postural changes during catheter placement was higher in the New-PIVC group than in the SPC group. Although, the median pain score was zero, some patients were uncomfortable during the catheterization of the upper arm vein. Therefore, we must consider the posture of the patient during catheter insertion at the upper arm. Third, the visualizing device (*i.e*., ultrasonography), as well as proper training of the operators, is needed to appropriately reach the upper arm vein.

5. Limitations

The external validity of the results should be considered because most irritants administered in this study were anticancer drugs, and the patients had hematologic and oncological diseases. Although catheter placement in the upper arm vein has been shown to be effective in preventing CF caused by vancomycin (*24*), its effect on other irritating agents (*e.g.*, peripheral parenteral nutrition agents) is unknown. Blom JW *et al.* reported that patients with cancer have a significantly increased risk of venous thrombosis, and those harboring factor V Leiden and prothrombin 20210A mutations appeared to have an even higher risk (*25*). Therefore, whether the difference in patient background and the quality of infused drugs may affect the risk reduction of CF in catheterization at the upper arm is unclear. However, it is noteworthy that the risk of CF was attenuated by catheterization at the upper arm, in especially high-risk patients harboring hematologic malignancy and undergoing high-risk medications, considering this is a quite prevalent clinical situation.

There was no echo-assisted catheter placement in the SPC group in our study. If ultrasonography had been used, the SPC group might have shown a higher puncture success rate (*26*) and reduced mechanical stimulation, which may have reduced the occurrence of CF (*22, 27*). However, the way how the SPCs were placed reflects the daily practice in the real world, possibly increasing the impact of our research in everyday clinical practice.

6. Conclusions

It was demonstrated that the use of the new long catheter inserted into the upper arm vein to administer a hyper-irritant drug could significantly reduce the occurrence of CF compared with the use of a short catheter inserted into the forearm vein.

Acknowledgements

The authors thank the head nurse Toshie Yamashita for managing the research environment of the wards.

Funding: The new catheter used in this study was developed in a collaborative research with Terumo Corp., which provided funding for the collaborative research. This work was supported by JSPS KAKENHI Grant Number JP20H03976.

Conflict of Interest: RM and MA-D belong to a laboratory (Department of Advanced Nursing Technology, Graduate School of Medicine, The University of Tokyo) supported by Terumo Corporation. Other authors declare that there are no conflicts of interest. The new catheter was provided to this study free of charge from Terumo Corp.

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Received November 26, 2022; Revised January 31, 2023; Accepted February 22, 2023.

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Released online in J-STAGE as advance publication February 28, 2023.