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【 ORIGINAL ARTICLE 】

Changes in Central Venous Catheter Use in the Hematology Unit with the Introduction of Ultrasound Guidance and a Peripherally Inserted Central Venous Catheter

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Abstract:

Objective A central venous catheter (CVC) is often needed to treat hematologic diseases, but it is accompanied by many complications. Ultrasound guidance (USG) or a peripherally inserted central venous catheter (PICC) can reduce such complications.

Meterials We collected data of patients with attempted CVC placement in our hematology unit in 2012 (before introduction of USG and PICC) and 2018 (after introduction) and compared both periods.

Results In total, 187 CVC insertions were attempted in 2018 and 198 in 2012. USG was used 154 times (82%) in 2018 and 4 times (2%) in 2012 ($p<0.001$). The success rates of insertion were 95% in 2018 and 89% in 2012 ($p=0.063$). The incidence of acute complications was 4.3% in 2018 and 9.1% in 2012 ($p=0.069$). The incidence of CVC removal owing to delayed complications was 26% in 2018 and 21% in 2012 ($p=0.327$). The sites of approach in 2018 and 2012 were the internal jugular in 42 (22%) and 54 (27%), subclavian in 52 (28%) and 128 (65%), brachial (PICC) in 89 (48%) and 14 (7%), and femoral in 4 (2%) and 2 (1%), respectively ($p<0.001$).

Conclusion USG has become commonplace since its introduction. The landmark-based subclavian approach was largely replaced by PICC with USG in 2018. USG and PICC can help improve success rates and safety profiles.

Key words: central venous catheter, complication, ultrasound guidance, peripherally inserted catheter, hematologic disease

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Introduction

Central venous catheters (CVCs) have been indispensable in modern hematology practice. However, the catheterization procedure is invasive and can lead to serious and sometimes life-threatening complications. According to past reports, over 15% of patients who underwent catheterization experienced complications (1-3). In particular, patients who undergo catheterization in hematology units are often exposed to risks such as thrombocytopenia, coagulation disorders, and immunosuppression. Although there have been several relevant reports focusing on patients with disorders of hemostasis and/or hematologic malignancies, the results have been varied due to differing patients' backgrounds (4-6).

A number of recent meta-analyses have described the usefulness of ultrasound guidance (USG) for reducing complications linked to catheterization (7-11). In addition, CVC centers providing imaging modalities for catheterization have started up in many academic centers of Japan (12-14). In some of these facilities, experienced radiologists or anesthesiologists perform most catheterization procedures. Such efforts have clearly contributed to a reduction in complications, and USG has become a standard procedure. However, we propose that a safe and reliable catheterization technique is essential for physicians, as specialists are not available at

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all times or in all settings.

In our unit, we perform approximately 200 catheterizations using a CVC for patients with hematologic disease annually, and we purchased an ultrasound device for CVC insertion in 2014. Around the same time, the peripherally inserted central venous catheter (PICC) using USG was introduced. Because we had collected data on the clinical use of CVCs in 2012, before the introduction of USG and PICCs (presented at the 75th annual meeting of the Japanese Society of Hematology in Sapporo, Japan), we decided to collect data after the introduction of USG and PICCs in a similar manner. We then compared both periods to assess the safety of CVC use and the effectiveness of using USG or PICC in the hematology unit.

Materials and Methods

Study design and patients

This observational study was conducted between April 1, 2018, and March 31, 2019, in the hematology unit of Japanese Red Cross Narita Hospital, a 60-bed facility that includes a ward for hematopoietic stem cell transplantation. We included all inpatients in whom insertion of a CVC was attempted during the study period. Similarly, the control group was all patients requiring a CVC between April 1, 2012, and March 31, 2013.

This study was approved by the ethics committee of Japanese Red Cross Narita Hospital, and written informed consent for catheterization was obtained from all patients or their proxies. Data were collected in accordance with the Law Concerning the Protection of Personal Information (Law No. 57, 2003) of Japan.

Catheterization procedure

The indications for catheterization and the choice of the site of approach were assessed by each attending physician during clinical practice. A cervical or subclavian approach was impossible in patients with a major blood coagulation disorder that could not be corrected within a short time (i.e. untreated acute promyelocytic leukemia, acquired hemophilia). In patients with either a low platelet count ($<30\times10^3$/μL), a prolonged prothrombin time (>1.6 times the normal range, or a partial thromboplastin time (>2 times the normal range), the blood products were transfused to compensate for these abnormalities. During each catheterization procedure, a CVC was inserted into the selected site by an attending physician with more than 5 years of clinical experience, or by a supervised senior (2 to 5 years' clinical experience) or junior (less than 2 years' clinical experience) resident. Maximum sterile barrier precautions were taken, including the use of large sterile drapes; surgical antiseptic hand wash; careful skin cleaning of the patient followed by the sterilization with chlorhexidine-based or povidone-iodin solutions; and a sterile gown, gloves, mask, and cap. Catheter kits including a 22-gauge puncture needle (Safe Guide Micronee-dle Seldinger kit®; Covidien, Tokyo, Japan) were used for internal jugular, subclavian, or femoral approaches. The use of an ultrasound device (SonoSite S-Nerve™; FUJIFILM Medical, Tokyo, Japan) was recommended, as necessary. For the brachial approach, an NXT Groshong® Catheter (Medicon, Osaka, Japan) with USG was used in 2018, and an Argyle™ PICC kit (Cardinal Health, Dublin, USA) for direct puncture of a superficial vein was used in 2012. Residents were instructed to memorize the procedure completely before catheterization and to switch the operator to an attendant staff member if the initial few venipuncture attempts were unsuccessful, as in a past report (15). The catheter was used for a variety of purposes, including the administration of intravenous fluids, medications, total parenteral nutrition, and blood products.

Data collection and definition

We aggregated the procedure and patient characteristics and compiled a composite of acute complications as the primary endpoint from the database prepared for this study, as described by the operators or attending physicians. A failed attempt at catheterization was specifically defined as the inability by the operator to complete the intended procedure owing to being unable to successfully catheterize the primarily intended vessel.

From our review of the literature and a consensus among our group, we defined an acute complication as any composite of the following outcomes: arterial puncture, pneumothorax, hematoma, and misplacement (3, 16, 17). An arterial puncture was judged to have occurred when a physician aspirated pulsatile arterial (bright red) blood into a locator syringe. The presence of pneumothorax or misplacement was determined using plain chest or abdominal X-ray. A physician or nurse documented a hematoma if an area of bruising or swelling was noted around the insertion site. A delayed complication was defined as any of the following events that compelled a physician to remove the catheter: accidental removal, infection, obstruction, and breakage of the catheter. Accidental removal was defined as the unexpected removal of the catheter without any medical decision to do so. An infection was documented when a physician suspected infection and decided to remove the catheter regardless of the result of a microbiological examination.

Statistical analyses

All statistical analyses were performed with EZR version 1.20 (Saitama Medical Center, Jichi Medical University), which is a graphical user interface for R version 3.02 (The R Foundation for Statistical Computing, Vienna, Austria) (18). To identify factors affecting the outcomes of catheterization, we used the chi-squared test or Fisher's exact test for categorical variables and the Kruskal-Wallis test for the continuous variables of interest. A p value <0.05 was considered statistically significant. All tests were two-sided.

Table 1. Characteristics of Patients in Whom Central Venous Catheter Insertion was Attempted.

Year		2012		2018		
N		198		187		p value
Female sex, n (%)		89	(45)	80	(43)	
Median age, y (range)		63	(22-84)	64	(21-91)	
Disease, n (%)	Acute leukemia	89	(45)	80	(43)	0.123
	Lymphoma	41	(21)	55	(29)	
	Myeloma	27	(27)	15	(8)	
	Other	39	(20)	37	(20)	
Median platelet count, $10^4/\mu L$ (range)		6.2	(0.1-44)	10.0	(0.1-80)	0.030

Table 2. Characteristics Related to the Procedure.

Year		2012		2018		
N		198		187		p value
Ultrasound-guided approach		4	(2)	154	(82)	<0.001
Success		176	(89)	177	(95)	0.063
Operator	Junior resident	43	(22)	41	(22)	0.236
	Senior resident	50	(25)	61	(33)	
	Attending physician	105	(53)	85	(45)	
Site	Internal jugular	54	(27)	42	(22)	<0.001
	Subclavian	128	(65)	52	(28)	
	Brachial	14	(7)	89	(48)	
	Femoral	2	(1)	4	(2)	

Values in the table are n (%) unless otherwise noted.

Table 3. Acute Complications (during Insertion).

Year	2012		2018		
N	198		187		p value
Total events, n (%)	18	(9.1)	8	(4.3)	0.069
Misplacement	10	(5.1)	3	(1.6)	0.086
Arterial puncture	4	(2.0)	2	(1.1)	0.686
Hematoma	3	(1.5)	2	(1.1)	1
Pneumothorax	1	(0.5)	0	0	1
Other	0	0	1	(0.5)	1

Results

The cohort in this study consisted of 187 CVC attempts during a 1-year period from April 1, 2018, to March 31, 2019 (“2018” group). The control group included 198 CVC attempts from April 1, 2012, to March 31, 2013 (“2012” group). The characteristics of the patients are shown in Table 1. More than 75% of patients had a hematologic malignancy and were in treatment. Underlying diseases affecting fewer than five patients were grouped together as “Other” and included aplastic anemia, myelodysplastic syndrome, chronic myeloid leukemia, immune thrombocytopenic purpura, hemolytic anemia, and non-hematologic malignancy. Platelet concentrates were administered in 18 cases during 2018 and 71 cases during 2012, just prior to catheterization.

Characteristics related to the procedure are summarized in Table 2. USG was used in 158 cases (82%) during 2018 and 4 cases (2%) during 2013. There were 10 failed catheterization attempts (5%) in 2018 and 22 (11%) in 2012. The proportion of experienced operators did not differ markedly between the two periods. The choices of the site of approach in 2018 and 2012 were the internal jugular in 42 (22%) and 54 (27%), subclavian in 52 (28%) and 128 (65%), brachial (PICC) in 89 (48%) and 14 (7%), and femoral in 4 (2%) and 2 (1%), respectively.

Acute complications are summarized in Table 3. Although there were no significant differences in occurrence between 2018 and 2012, fewer acute complications were seen in 2018, especially misplacement. There were no cases of either pneumothorax or hemothorax that required drainage during 2018, while there was one such case in 2012. No patients required any treatment other than manual astriction, none were left with physical impediments, and no patients died owing to complications during either period. Although one patient undergoing PICC insertion in 2018 complained of fulminant pain owing to suspected nerve injury during venous puncture, the pain improved within a few minutes without any subsequent nervous disorders.

Table 4 shows the complications during clinical use (delayed complications). In 177 cases of successful catheterization in 2018 and 176 in 2012, the median duration of catheter placement was 33 days (total 9,613 catheter-days) and 38 days (total 10,022 catheter-days), respectively. There were 45 catheter removals in 2018 and 37 in 2012 owing to de-

Table 4. Delayed Complications (during Clinical Use).

Year	2012		2018		
N (Successfully catheterized cases)	176		177		p value
Total events, n (%)	37	(21.0)	45	(25.5)	0.378
Infection	25	(14.3)	27	(15.2)	0.881
Occlusion	2	(1.1)	12	(6.8)	0.011
Breakage	2	(1.1)	4	(2.3)	0.685
Accidental removal	5	(2.8)	1	(0.6)	0.121
Other	3	(2.8)	1	(0.6)	0.371
Median duration of insertion, days (range)	38	(0-274)	33	(0-383)	0.329

layed complications, showing no statistically significant difference. Catheter obstruction was more frequently seen in 2018 than in 2012. Other delayed complications included thrombosis in three cases and accidental catheter contamination without infection in one case.

Discussion

Because using a brachial approach with a PICC carries no risk of pneumo- or hemothorax and it is easy to perform manual astriction if bleeding occurs, physicians in our hematology unit have come to choose this rather than a subclavian approach, which had otherwise been considered the first choice in many cases. This safety profile also made it possible to avoid the need to perform prophylactic transfusions. In our study, the incidence of acute complications was 4.3% among 187 CVC insertions in 2018 and 9.1% among 198 CVC insertions in 2012, with no significant difference. Fewer occurrences of misplacement were seen in 2018 than in 2012 because we were able to confirm the catheter position using an ultrasound device during catheterization and corrected the position at the same time in cases with malpositioning. The rates of arterial puncture, hematoma, and pneumothorax were not markedly reduced after the introduction of USG, with a low occurrence noted even in the control group, compared with a previous report (1-3). This is partly because the CVC kits used have 22-gauge puncture needles and are designed to provide minimal puncture resistance, which reduces the risk of damaging blood vessels (19, 20). Based on evidence from lung biopsies, the use of fine needles has also been reported to reduce the occurrence of pneumothorax (21-23).

Our definition of catheter infection as a delayed complication included suspected cases, such as those with swelling or pain at the site of insertion, even without the detection of pathogenic microorganisms, and those that led to the removal of the catheter. Our practice guidelines recommend catheter removal even in suspected cases of infection in order to prevent progression to severe bacteremia. The incidence of catheter infection was 2.8 cases per 1,000 catheter-days in 2018 and 2.5 cases per 1,000 catheter-days in 2012. Cases diagnosed as catheter-related blood stream infection (CRBSI), according to the definition proposed in the Practical Clinical Guidelines for the Diagnosis and Treatment of Intravascular Catheter-related Infection: Revised by the Infectious Diseases Society of America in 2009 (24), occurred in 7 patients in 2018 and 8 in 2012, an incidence equivalent to 0.73 and 0.80 cases per 1,000 catheter-days, respectively. Previous reports of PICCs used in patients with hematologic diseases, who are compromised hosts, have indicated that the incidence of CRBSI is approximately 1-6 cases per 1,000 catheter-days, and use of a PICC did not increase the occurrence of CRBSI compared with a conventional CVC (25-27). Our study also demonstrated comparably low occurrence of CRBSI in 2018, when PICCs were used in many cases, which further supports these findings. However, an increased occurrence of catheter obstruction and breakage was seen in 2018. This is partly because a PICC has a small bore and long length and is made of soft and thin silicone rubber, whereas a conventional CVC is made of hard polyurethane. Complications may be reduced with maintenance suitable for a PICC, e.g. frequent and low-pressure flushing.

Some studies have reported the safety and usefulness of PICCs for hematologic diseases, including stem cell transplantation (25, 27-29); our study also showed safe and effective profiles. Although a PICC can be used in chemotherapy, blood transfusion, and parenteral nutrition to avoid problems associated with the use of a conventional CVC, PICCs were found to be inconvenient in cases in the present study requiring bolus injection, such as during intensive care, resuscitation, or stem cell infusion. Therefore, some hematologists in our unit still choose conventional CVCs rather than PICCs for patients scheduled to receive stem cell transplantation or intensive care. Refaei et al. reported that PICCs have a 2.5 times greater risk of catheter-related thrombosis than a conventional CVC in acute leukemia patietns (30). Although those results were not reproduced in our study, we agree that a PICC is not suitable for all cases in the hematology unit, and careful consideration and the use of the proper type of catheter is needed.

USG is considered the standard procedure, as demonstrated in several meta-analyses (7-11). In our study, the success rate of catheterization and the occurrence of acute complications tended to be better in 2018, when USG was used in over 80% of cases, than in 2012. However, one report suggested that catheterization procedures with USG conducted by inexperienced operators could increase the rate of complications (31). French et al. indicated that specific

pitfalls of USG were that it could led to overshoot of the needle or incorrect identification of the vessel with a short- and long-axis view, and Tokumine et al. highlighted the importance of proper technique and training to overcome these pitfalls (32). At our institution, starting in 2015, residents were required to attend hands-on training using a mannequin simulator to learn the techniques in order to ensure the safety of USG.

Several limitations associated with the present study warrant mention. First, this was an observational study based on clinical practice, and the data were derived from assessments made by the operators or attending physicians. There might have been oversight of events, resulting in the study being statistically underpowered. Second, this was not a precise comparative study of USG and PICC. Although we could have directly analyzed the effects of USG and PICC (and should do so in the future), selective biases are present because each operator had their own reason for using or not using these approaches, especially in 2018. Randomized trials may avoid biases, including latent ones; however, this is ethically problematic and currently difficult in this setting.

In conclusion, we found that the insertion and use of CVCs in hematology units have changed drastically with the introduction of USG and PICC. Use of USG has become commonplace in the insertion of CVCs. A PICC with USG replaced the landmark-based subclavian approach in many cases during 2018. The introduction of USG and PICC can contribute to better success rates and safety profiles of CVCs in hematology units.

The authors state that they have no Conflict of Interest (COI).

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