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Article

Protocol to Control the Bedside Ultrasound-Guided Peripherally-Inserted Central Catheter-Related Infection in Elderly Intensive-Care-Unit Patients in a Small-Volume Center in Korea

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Abstract

We performed a retrospective analysis of the data from a total of 241 patients (n=241). A total of 161 (66.8%) patients received the peripherally-inserted central catheter (PICC) for long-term intravenous access, 172 (71.4%) had no past history of receiving catheters and 142 (58.9%) received the PICC on the right side. Target veins include basilic vein (42.7% [103/241]), brachial vein (41.9% [101/241]) and cephalic vein (15.4% [37/241]). There were a total of five cases (2.1%) of the PICC-related infection. Of these, one case (0.4%) was the PICC-related bloodstream infection; *Candida parapsilosis* was identified from both the PICC tip and blood samples. A total of 224 patients (92.9%) had optimal positions of the PICC tip. Male sex (OR 0.183; 95% CI 0.050-0.675, *p*=0.011), the length of a catheter (OR 0.794; 95% CI 0.657-0.960, *p*=0.017) and right side (OR 4.711; 95% CI 1.227-18.091, *p*=0.024) were significant risk factors of non-optimal positions of the catheter. Time-to-events are estimated at 56.02±1.37 days (95% CI 53.33-58.71). Here, we describe our single-center, retrospective experience with bedside ultrasound (US)-guided PICCs in elderly ICU patients in a small-volume center.

Keywords: peripherally inserted central catheters; catheterization; central venous; ultrasonography; interventional; intensive care units; catheter-related infections; bloodstream infection

1. Introduction

A central catheterization using a central venous catheter (CVC) or a peripherally-inserted central catheter (PICC) is referred to as an intravascular access to deliver injectate into a large central vein. Patients requiring medications that irritate smaller peripheral veins, parenteral nutrition and chemotherapies or the measurement of central venous pressure are indicated in a central catheterization[1]. The PICC is defined as a medical device for central vascular access and it is inserted in the extremity and then advanced until its tip is positioned in the vena cava[2]. It is a medium-to-long-term venous access that is placed through a peripheral vein, such as basilic vein, brachial vein or cephalic vein, serving as a standard, cost-effective alternative to the CVC[3],[4]. Since first introduced in 1975, it has gained popularity because of its advantages such as convenience of placement and cost-effectiveness[5],[6]. Indeed, it has become an integral part of treatment modalities in the realm of mainstream medicine[2]. The use of PICC was approved by the United States Food and Drug Administration (FDA) for up to 3-12 months. After inserted, most of the PICCs are maintained at the site of placement for several months. But there is a variability in the actual period of use of PICC depending on its type, the method of insertion, a patient's compliance and the technical expertise of a healthcare professional[7].

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The PICC has been conventionally performed under fluoroscopic guidance[8–10]. But critically-ill patients may present with adverse effects during transport if they have respiratory failure or hemodynamic instability[11–13]. In particular, intensive-care-unit (ICU) patients should run a risk while being transferred to other places because they are in need of specific management including diverse monitoring, continuous drug administration and ventilator support. According to a previous study, 37% of ICU patients presented with complications while being transferred to other places; the rate of such complications including worsening pulmonary function was approximately 2-fold higher as compared with normal controls[14],[15]. The safe use of PICC in unstable patients at the bedside would be mandatory. It can therefore be inferred that considerable efforts should be made to prevent the occurrence of such complications during transfer of critically-ill patients. From this context, attempts have been recently made to perform an ultrasound (US)-guided PICC at the bedside, thus termed as bedside US-guided PICC, for critically-ill patients[11],[16–21].

Despite the benefits of PICC, complications associated with its use have been described in the literature, thus termed as PICC-related complications. These include thrombophlebitis, catheter-related infection, particularly termed as the PICC-related infection, and thrombosis and mechanical complications (*e.g.*, occlusion and accidental withdrawal), all of which cause patient discomfort and additional health care costs[22–28]. Of these, the PICC-related infection is a less common complication as compared with serious thrombosis[29]. According to a review of literatures, the incidence of PICC-related infection is estimated at 0.4-0.8 per 1,000 catheter-days, although a majority of these cases are seen in a lower risk group of patients[30–35]. Moreover, severe cases of PICC-related complications include life-threatening bloodstream infection (BSI) and deep vein thrombosis (DVT)[36],[37]. It has been shown that the presence of a PICC line is closely associated with a high risk of PICC-related BSI[24],[38].

PICC-related infections are classified as local exit-site infection, bacterial colonization and PICC-related BSI. Local exit-site infection is defined as the presence of erythema, induration and/or tenderness within 2 cm of the exit site, showing a positivity for the bacteria culture for swabs of exit-sites showed positive but being excluded from the possibility of contamination in accordance with the Infectious Diseases Society of America recommendations[22]. Bacterial colonization is defined as the presence of ≥15 colony-forming units (CFUs) using the roll-plate technique or ≥1,000 CFUs by quantitative culture of pathogenic bacteria[39]. PICC-related BSI is defined as the presence of bacteremia arising from an intravenous catheter in the presence of clinical signs of infection, such as fever >38°C, chills, rigor and hypotension, and the absence of other sources of infection in accordance with the National Nosocomial Infections Surveillance System from the Centers for Disease Control and Prevention (CDC) (Atlanta, GA, USA) and from the Public Health Laboratory Service of the UK[22],[40]. It serves as the most common cause of nosocomial bacteremia[41]. A diagnosis of PICC-related BSI can be made according to the Clinical Practice Guidelines for the Diagnosis and Treatment of Intravascular Catheter-related Infection[23]. It can be established either based on the isolation of the same microorganism from ≥ one peripheral venous blood culture and from the catheter tip or from two blood culture samples each collected from a catheter hub and the peripheral vein[42]. It is estimated that 16.4-28.8% of patients receiving the PICC are at a risk of developing PICC-related BSI; they are vulnerable to an increase in the mortality, morbidity and medical costs[22,43,44]. Previous literatures have shown that there is a variability in the prevalence of PICC-related BSI, being estimated at 0.47-4.79 episodes per 1,000 catheter-days[45],[46]. More specifically, Maki DG, et al. estimated the prevalence of PICC-related BSI at 2.1 and 1.0 episodes per 1,000 catheter-days in hospitalized patients and outpatients, respectively[47].

According to a previous study, bedside US-guided PICC was a feasible, safe modality in ICU patients even in a single small-volume center in the pandemic era of the COVID-19[48]. Along the continuum of this previous literature, we have devised an evidence-based protocol to control the bedside PICC-related infection in elderly ICU patients receiving bedside US-guided PICC in a small-volume center. The elderly are vulnerable to an increase in the frequency and duration of hospitalization and often have multiple comorbidities. This justifies the importance of an effective,

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reliable venous access in the treatment of the elderly with geriatric diseases[49]. We therefore conducted this single-center, retrospective study to describe our protocol in a single small-volume center in an ICU setting in Korea.

1. Results

1.1. Baseline and clinical characteristics of the patients

A total of 241 patients (n=241) were finally included in the current study, who comprise 129 men (53.5%) and 112 women (46.5%) and whose mean age was 77.87±8.70 (66-99) years old. The age distribution of the patients showed that there were 103 patients (42.7%) in their 80s, 67 (27.8%) in their 70s, 53 (22.0%) in their 60s and 18 (7.5%) in their 90s. Baseline characteristics of the patients are represented in Table 1.

Table 1. Baseline characteristics of the patients (n=241).

Variables		Values
Age (years old)		77.87±8.70 (66-99)
	60-69	53 (22.0%)
	70-79	67 (27.8%)
	80-89	103 (42.7%)
	90-99	18 (7.5%)
Sex		
	Men	129 (53.5%)
	Women	112 (46.5%)
SAPS2		38.83±14.47
Status		
	Ventilator	95 (39.4%)
	CRRT	40 (16.6%)
Length of ICU stay (days)		23.75±27.39
Length of hospital stay (days)		39.89±41.88

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Causes of ICU admission		
	CNS disorders	
	Brain hemorrhage	16 (6.6%)
	Brain infarction	9 (3.7%)
	Infectious diseases	3 (1.2%)
	CVS disorders	
	HF	27 (11.2%)
	ACS	10 (4.1%)
	PTE	2 (0.8%)
	Infectious diseases	2 (0.8%)
	AD	2 (0.8%)
	Pulmonary system disorders	
	Pneumonia	102 (42.3%)
	COPD	4 (1.7%)
	Tuberculosis	2 (0.8%)
	Lung cancer	6 (2.5%)
	Hepatobiliary system disorders	
	Liver cirrhosis	2 (0.8%)
	rHCC	3 (1.2%)
	Spleen injury	1 (0.4%)
	Cholecystitis/Cholangitis	11 (4.6%)

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Pancreatitis	1 (0.4%)
Gastrointestinal system disorders	
Bleeding	7 (2.9%)
Perforation	11 (4.6%)
Obstruction	3 (1.2%)
IBD	2 (0.8%)
Renal system disorders	
AKI	15 (6.2%)
Causes of ICU discharge	
Transfer to a ward	138 (57.3%)
Transfer to other hospital	35 (14.5%)
Death of a patient	68 (28.2%)
Causes of hospital discharge	
Return to home	54 (22.4%)
Transfer to other hospital	113 (46.9%)
Death of a patient	74 (30.7%)

Abbreviations: SAPS2, Simplified Acute Physiology Score II; CRRT, continuous renal replacement therapy; ICU, intensive care unit; CNS, central nervous system; CVS, cardiovascular system; HF, heart failure; ACS, acute coronary syndrome; PTE, pulmonary thromboembolism; AD, aortic dissection; COPD, chronic obstructive pulmonary disease; rHCC, ruptured hepatocellular carcinoma; IBD, inflammatory bowel disease; AKI, acute kidney disease. Values are mean±standard deviation with range or the number of the patients with percentage, where appropriate.

Characteristics of the PICC are summarized in Table 2. A total of 161 (66.8%) patients received the PICC for long-term intravenous access, 172 (71.4%) had no past history of receiving catheters and 142 (58.9%) received the PICC on the right side. Target veins include basilic vein (42.7% [103/241]), brachial vein (41.9% [101/241]) and cephalic vein (15.4% [37/241]).

Table 2. Characteristics of the peripherally-inserted central catheter (n=241).

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Variables	Values
Purposes of PICC	
Long-term intravenous access	161 (66.8%)
Use of non-peripherally compatible infusate	80 (33.2%)
The number of previous catheters	
0	172 (71.4%)
≥1	69 (28.6%)
Side of PICC and the length of a catheter	
Right side	142 (58.9%)
Length (cm)	38.59±2.81
Left side	99 (41.1%)
Length (cm)	43.58±3.30
Target veins	
Brachial vein	101 (41.9%)
Basilic vein	103 (42.7%)
Cephalic vein	37 (15.4%)
Length of procedure time (min)	14.32±7.46
Length of catheter indwelling time (days)	16.49±10.48
Causes of PICC removal	
Improvement of a patient's condition	93 (38.7%)
Death of a patient	51 (21.2%)

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Transfer to other hospital with PICC	32 (13.3%)
Accidental removal	8 (3.3%)
Replacement with new catheter	31 (12.9%)
Suspicious catheter-related infection	6 (2.5%)
Non-function	5 (2.1%)
Swelling or hematoma	11 (4.6%)
Malposition	4 (1.7%)

Abbreviations: PICC, peripherally-inserted central catheter; Values are mean±standard deviation with range or the number of the patients with percentage, where appropriate.

1.1. Cases of the PICC-related infection

In our series, there were a total of five cases (2.1%) of the PICC-related infection. Of these, one case (0.4%) was the PICC-related BSI; *Candida parapsilosis* was identified from both the PICC tip and blood samples (Table 3).

Table 3. Summary of cases of the peripherally-inserted central catheter-related infections (n=5).

Variables	**Values**			
N	7 (2.6%)			
Case #	Age /Sex	Length of catheter indwelling time (days)	Pathogens isolated from the tip culture	Pathogens isolated from the blood culture
1	91/M	28	*Staphylococcus capitis*	Negative
2	66/M	28	*Candida carapsilosis*	*Candida parapsilosis*
3	84/F	14	*Streptococcus mitis, S. oralis* and	Negative

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				Corynebacterium species	
	4	66/M	28	*Staphylococcus epidermidis*	Negative
	5	78/F	16	*Stenotrophomonas maltophilia*	Negative

Note: N, the total number of cases; F, female; M, male.

1.1. Locations of the PICC tip and risk factors of its non-optimal position

In our series, a total of 224 patients (92.9%) had optimal positions of the PICC tip (Table 4). A logistic regression analysis showed that male sex (OR 0.183; 95% CI 0.050-0.675, *p*=0.011), the length of a catheter (OR 0.794; 95% CI 0.657-0.960, *p*=0.017) and right side (OR 4.711; 95% CI 1.227-18.091, *p*=0.024) were significant risk factors of non-optimal positions of the catheter (Table 5).

Table 4. Locations of a catheter tip (n=241).

Variables	Values
Optimal position	224 (92.9%)
Suboptimal position	
RA	6 (2.5%)
Tributaries of the SVC	5 (2.1%)
Malposition	
Ipsilateral IJV	2 (0.8%)
Ipsilateral SCV	1 (0.4%)
Arm vein	2 (0.8%)

Abbreviations: RA, right atrium; SVC, superior vena cava; IJV, internal jugular vein; SCV, subclavian artery. Values are the number of the patients with percentage.

Table 5. Risk factors of non-optimal positions of a catheter tip (n=241).

Variables	OR 95% CI	P-value

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Age	1.013 (0.951-1.080)	0.684
Male sex	0.183 (0.050-0.675)	0.011*
SAPS2	1.009 (0.970-1.050)	0.656
Long-term intravenous access	0.568 (0.173-1.861)	0.350
Length of procedure time	0.972 (0.892-1.059)	0.515
Length of a catheter	0.794 (0.657-0.960)	0.017*
Number of previous catheters	1.680 (0.555-5.090)	0.359
Right side	4.711 (1.227-18.091)	0.024*

Note: OR, odds ratio; CI, confidence interval. **Abbreviation:** SAPS2, Simplified Acute Physiologic Score II. *Statistical significance at P<0.05.

1. Discussion

Since the early 1990s, a PICC has been used in a clinical setting. It remains problematic, however, that adverse effects may occur at a higher incidence during intra-hospital transport in critically-ill patients[50],[51]. This justifies the rationale of performing the bedside PICC placement for them[52],[53]. In 2001, Lee DS, et al. described the results of a preliminary report about the US-guided PICC performed by an intensivist in an ICU setting in a large-volume center in Korea[11].

In 1989, the FDA published a precautionary statement as to the positioning of CVCs to the effect that the catheter tip cannot be placed in or migrate into the heart[54]. In 1998, the National Association of Vascular Access Networks published a statement about the positioning of PICCs, thus recommending that the tip of a PICC should be located within the lower 1/3 of the SVC, close to the SVC-RA junction[55].

It is a general rule that the PICC is blindly inserted based on anatomical measurements of estimated distance[56]. The conventional use of anatomical landmarks provides the estimated length between the puncture site and the SVC-RA junction. Its advantages include relatively lower financial costs and acceptable performance. It can therefore be considered as the first-line of choice in patients with poor economic status. It is disadvantageous, however, in that patients are exposed to radiation and burdened with additional costs because of post-procedural chest X-rays[57]. Moreover, the success rate of the PICC based on the conventional use of anatomical landmarks is estimated at approximately 80%, which may not be regarded as a satisfactory outcome[3,58,59]. This explains why we routinely perform the PICC under US guidance in our institution. The utility of US guidance in bedside PICC has been advocated by several previous reports[60–64]. The success rate of conventional PICC varies, ranging from 65% to 75%, because there is a limited availability of the site of PICC (1.5 inches above to 1.5 inches below the antecubital fossa). But the success rate of US-guided PICC increases to 91-94%[2]. This is in agreement with our results showing that the rate of optimal position was 92.9% (224/241).

Despite the efficiency of the PICC, it may be unavoidable that positioning of a PICC tip may cause complications; they can be classified as mechanical (obstruction) and organic (infections and/or thromboses) complications[65]. It would therefore be mandatory *not only* to position a PICC in the remote region where there is a sufficient blood flow with the endothelium far from the catheter *but*

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also to ensure that the tip cannot reach the RA, which is essential for minimizing a risk of such complications. In this regard, the SVC-RA junction serves as the optimal site of PICC[56],[66]. A tip malpositioning may raise a risk of PICC-related complications, such as venous thrombosis, vascular erosion, malfunction or arrhythmias[58,67,68]. If recognized at the earliest opportunities possible, however, a tip malpositioning would be corrected and this would be helpful for preventing the occurrence of serious complications[67],[68]. Special attention should therefore be paid to positioning of the catheter from the left side because a >40°-angle formed between the PICC tip and the wall of the SVC may cause the perforation of the vascular wall and the pericardium covering the last portion of the SVC, infection, malfunctioning and venous thrombosis[66]. Additionally, vascular erosion and early cardiac tamponade may also occur as a result of accidental vessel/heart perforation during the PICC placement[69]. An accurate technical PICC procedure would therefore be useful in improving its overall performance[70].

Previous studies have indicated that the major disadvantage of PICC is its association with possible risks of DVT and pulmonary embolism[71–76]. This is not surprising because PICCs occupy a large portion of the cross-sectional diameter of peripheral veins of the upper extremities and are involved in the onset of venous stasis[77]. Moreover, they are vulnerable to displacement. Therefore, the displacement of the PICC tip can also cause damages to the endothelium[78]. Thus, the PICC-related DVT account for up to 35% of all cases of DVT in the upper extremities[79]. Risk factors of the PICC-related DVT include severity of illness, malignancy, a past history of taking warfarin, that of venous thrombosis or thromboembolism; high body mass index (BMI), trauma, renal failure, the infusion of antibiotics, the external diameter of the PICC >4 F, the left-sided placement of PICC and the placement of PICC in the basilic vein[71],[79–82]. It is known that the degree of risk of DVT in the upper extremities is higher in association with the PICC as compared with the CVC[83]. This is supported by Winters JP, et al. who showed that patients receiving PICC are at a significantly greater risk of DVT in the upper extremities as compared with those receiving CVC (8.1 *versus* 4.8 per 1,000 admissions; $p<0.05$)[84]. In this regard, it is promising that there were no cases of DVT in our series.

To summarize, our results are as follows:

(1) A total of 161 (66.8%) patients received the PICC for long-term intravenous access, 172 (71.4%) had no past history of receiving catheters and 142 (58.9%) received the PICC on the right side. Target veins include basilic vein (42.7% [103/241]), brachial vein (41.9% [101/241]) and cephalic vein (15.4% [37/241]).

(2) In our series, there were a total of five cases (2.1%) of the PICC-related infection. Of these, one case (0.4%) was the PICC-related BSI; *Candida parapsilosis* was identified from both the PICC tip and blood samples.

(3) A total of 224 patients (92.9%) had optimal positions of the PICC tip. A logistic regression analysis showed that male sex (OR 0.183; 95% CI 0.050-0.675, $p=0.011$), the length of a catheter (OR 0.794; 95% CI 0.657-0.960, $p=0.017$) and right side (OR 4.711; 95% CI 1.227-18.091, $p=0.024$) were significant risk factors of non-optimal positions of the catheter.

Limitations of the current study are as follows: First, we conducted it under retrospective design. Second, we included a small series of the patients. Third, we evaluated the patients who had been admitted to an ICU of a secondary referral center. Therefore, the possibility of selection bias could not be completely ruled out. Fourth, there was no control group in the current study. Fifth, we failed to analyze the learning curve of bedside ultrasound-guided PICCs in ICU patients in a small-volume center. It remains difficult to improve skills in performing bedside ultrasound-guided PICCs in ICU patients[60]. Nevertheless, there is a paucity of literatures showing the learning curve for acquisition of this capacity, although a recent study showed that the PICC is a well-established procedure with a small learning curve[85,86]. This is supported by Lassen K, et al. showing that the safety and efficacy of PICC are achieved without a learning curve[87]. Moreover, according to Kleidon TM, et al., it would be mandatory consider the variability in the learning curve in employing a new medical device into a healthcare service[88].

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Here, we describe our single-center, retrospective experience with bedside US-guided PICCs in elderly ICU patients in a small-volume center.

Based on our results, it can be concluded that bedside US-guided PICCs would be recommendable in the elderly if it is possible to control risk factors of PICC-related infection *as well as* tip malpositioning and thereby to prevent the occurrence of serious complications. But further large-scale case-controlled studies are warranted to corroborate our results.

1. Materials and methods

1.1. Study patients and setting

A total of 273 patients (n=273) received PICC at a 21-bed ICU of our 291-bed medical institution (H Plus Yangji Hospital in Seoul, Korea) between January of 2021 and June of 2022. Their age distribution is shown in Figure 1.

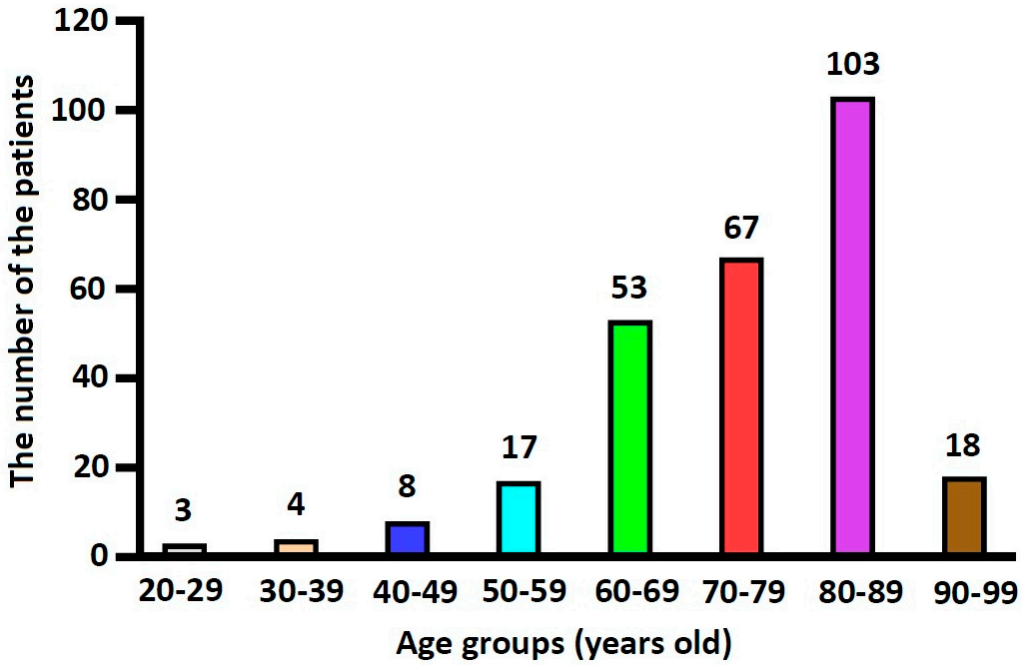


Figure 1. Age distribution of the study population.

We included only the Korean elderly aged 60 years or older but excluded those lost to follow-up.

We therefore included a total of 241 patients (n=241) in the current study; it was conducted in compliance with the relevant ethics guidelines following the approval by the Institutional Review Board (IRB) of H Plus Yangji Hospital in Seoul, Korea (IRB approval #: HYJ 2022-07-017). All procedures described herein were performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. But informed consent was waived due to its retrospective nature, as granted by the IRB of H Plus Yangji Hospital in Seoul, Korea.

1.1. An evidence-based protocol to perform bedside US-guided PICC and to control its related infection

In our series, bedside US (GE LOGIQ-e Ultrasound Machine; GE Healthcare, Milwaukee, WI)-guided PICC was performed, as previously described (Figure 4)[48]. All the procedures were performed using a 5-Fr Dual Lumen Power PICC (Bard Access System Inc., Salt Lake City, UT, USA). Lack of timely control of catheter-related infection would lead to an increase in the incidence of

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further infection and mortality[89]. It would therefore be mandatory to identify methods for reducing or eliminating the bedside PICC-related infection.

The patients were placed in a supine position. But the patients with dyspnea were placed in a sitting position with the arm abducted, and they had a tourniquet applied to the upper arm. The patients underwent PICC placement under maximal barrier precautions using 2% chlorhexidine for skin preparation, surgical drapes, a surgical cap, sterile gown and gloves. Thus, the procedure was performed using the microintroducer technique at the patients' bedside under ultrasound guidance[90–92].

To determine the side of PICC insertion, the site without previous catheterization was selected. Moreover, the site on the right arm was initially selected for PICC insertion in the patients with no past history of catheterization. For puncture, large-sized veins were selected so that they might not be less compressed during the procedure under ultrasound guidance. Therefore, brachial and basilic veins rather than cephalic veins were selected[93–95].

The length of catheter was measured based on a sum of the distance from the insertion site to the axilla, that from the axilla to the sternum and that from the sternum to the 4th intercostal space[96]. After the completion of PICC, the internal jugular vein was scanned under US guidance to ensure the correct placement of the catheter. This was followed by chest X-ray to confirm the location of the catheter[97].

After the procedure, the patients were evaluated on routine surveillance at a weekly follow-up and the PICC was daily flushed using a 10 mL saline[98].

1.1. Patient evaluation and criteria

Baseline characteristics of the patients include age, sex, Simplified Acute Physiology Score II (SAPS2), status at the time of ICU arrival (ventilation and continuous renal replacement therapy [CRRT]), length of ICU stay, length of hospital stay, reasons for ICU discharge (transfer to a ward or other hospitals and death) and reasons for hospital discharge (discharge to home, transfer to other hospitals and death).

Causes of ICU admission include central nervous system problems, cardiovascular system problems, pulmonary diseases, hepatobiliary problems, gastrointestinal problems and renal problems.

PICC-related characteristics of the patients include purposes of PICC placement, number of previous catheters, side of PICC placement, length of PICC, veins for PICC placement, length of procedure time, length of indwelling time, rates of PICC-related infections and reasons for PICC removal.

The position of the catheter tip was classified into the optimal position, the suboptimal position and the malposition. The optimal position was defined as the placement of catheter tip in the areas extending from the distal 2/3 of the superior vena cava (SVC) to the right atrium (RA). Moreover, the suboptimal position was defined as the placement of catheter tip into tributaries of the SVC connecting to the right atrium. Finally, the malposition was defined as the placement of catheter tip into other veins than the abovementioned ones. For the PICC insertion, the suboptimal position was maintained but the malposition was corrected[99,100].

1.1. Statistical analysis

All data was expressed as mean±standard deviation or the number of the patients with percentage, where appropriate. Continuous and categorical variables were analyzed using the Student's *t*-test and χ^2-test, respectively. Moreover, a logistic regression analysis was performed to identify risk factors of the non-optimal position of catheter tip. A *p*-value of < 0.05 was considered statistically significant. All statistical analyses were performed using the IBM SPSS Statistics Version 28.0.1.1 (IBM, Armonk, NY).

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Institutional review board statement: The current study was conducted in compliance with the relevant ethics guidelines following the approval by the Institutional Review Board (IRB) of H Plus Yangji Hospital in Seoul, Korea (IRB approval #: HYJ 2022-07-017). All procedures described herein were performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. But informed consent was waived due to its retrospective nature, as granted by the IRB of H Plus Yangji Hospital in Seoul, Korea.

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