



# Impact of subcutaneous tunnels on peripherally inserted catheter placement: a multicenter retrospective study

Il Jung Kim<sup>1</sup> · Dong Jae Shim<sup>2</sup>  · Jae Hwan Lee<sup>3</sup> · Eung Tae Kim<sup>4,5</sup> · Jong Hyun Byeon<sup>2</sup> · Hun Jae Lee<sup>6</sup> · Soon Gu Cho<sup>7</sup>

Received: 3 August 2018 / Revised: 15 October 2018 / Accepted: 23 November 2018 / Published online: 17 December 2018  
© European Society of Radiology 2018

## Abstract

**Objective** To evaluate the impact of subcutaneous tunneling on peripherally inserted central catheter (PICC) placement in terms of central line-associated bloodstream infections (CLABSIs).

**Methods** Our dual-facility central institutional review board approved this retrospective study. We compared 302 of 327 consecutive recipients (mean age [ $\pm$  SD],  $68.0 \pm 15.9$  years; men, 134; women, 168) of tunneled PICCs (October 2017 to May 2018) with 309 of 328 consecutive recipients (mean age,  $68.7 \pm 14.6$  years; men, 142; women, 167) of conventional PICCs (April 2016 to September 2017). Tunnels were made near puncture sites ( $\sim 1$  in. away) using hemostats or puncture needles. In each group, procedure times and rates of complications, including CLABSI, entry-site infection, dislocation, thrombophlebitis, and occlusion, were examined. Risk factors for CLABSI were analyzed via logistic and Cox regression models.

**Results** Subcutaneous tunnels were achieved in all patients, enabling successful peripheral vein cannulations. Group procedure times were similar ( $p = 0.414$ ). CLABSI proved to be significantly less frequent after tunneling (8/6972 catheter-days) than after conventional (28/7574 catheter-days) PICC placement (adjusted hazard ratio = 0.328; 95% confidence interval, 0.149–0.721). Other risk factors (i.e., age, gender, comorbidity, PICC duration, veins, hospital stay, and intensive care unit stay) showed no significant correlations with CLABSI.

**Conclusions** Compared with conventional means, a subcutaneous tunneling approach for PICC placement significantly reduces the rate of CLABSI.

## Key Points

- Subcutaneous tunnels created to place peripherally inserted central catheters significantly reduced catheter-associated bloodstream infections.
- Subcutaneous tunnel creation did not significantly prolong procedural time.
- There were no subcutaneous tunnel-related complications.

**Keywords** Catheter-related infections · Central venous catheter · PICC placement · Catheterizations · Peripheral

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00330-018-5917-x>) contains supplementary material, which is available to authorized users.

✉ Dong Jae Shim  
inharad@naver.com

<sup>1</sup> Department of Radiology, Bucheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

<sup>2</sup> Department of Radiology, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 56, Dongsu-ro, Bupyeong-gu, Incheon 21431, Republic of Korea

<sup>3</sup> Center for Liver Cancer, National Cancer Center, Goyang-si, Gyeonggi-do, Republic of Korea

<sup>4</sup> Department of Radiology, Hanyang University Guri Hospital, Guri-si, Gyeonggi-do, Republic of Korea

<sup>5</sup> Department of Radiology, College of Medicine, Kangwon National University, Chuncheon, Gangwon-do, South Korea

<sup>6</sup> Department of Social and Preventive Medicine, College of Medicine, Inha University, Michuhol-Gu, Incheon 22212, Republic of Korea

<sup>7</sup> Department of Radiology, College of Medicine, Inha University, Incheon, Republic of Korea

## Abbreviations

CLABSI	Central line–associated bloodstream infection
cPICC	Conventional peripherally inserted central catheter
PICC	Peripherally inserted central catheter
tPICC	Tunneled peripherally inserted central catheter

## Introduction

Peripherally inserted central catheters (PICCs) are widely used in contemporary medicine, given their ready accessibility, safety, versatility, and cost-effectiveness [1]. Although, previous studies have also indicated that a relatively low rate of infection may contribute as well to this broader usage [2, 3], recent data from hospitalized patients reveal high infection rates, comparable to standard central venous catheters [1, 4]. PICC-associated bloodstream infections have been reported at rates of 0.07–2.46 per 1000 catheter-days and are more frequent in patients with intensive care unit (ICU) stays or with hematologic malignancies [3, 5–9].

Central line–associated bloodstream infection (CLABSI) prolong hospitalizations, inflicting high costs and serious consequences in critically ill patients [9]. However, subcutaneous tunneling is generally applied for central venous catheter placement in instances of extended use (i.e., permanent hemodialysis, tunneled cuffed centrally inserted central catheters, or implantable venous ports) and is known to reduce infection rates significantly [10–12]. In 2001, Selby Jr. et al reported on the technical feasibility of peripherally inserted tunneled catheters [13], presuming that tunneling without a Dacron cuff may not effectively reduce infection rates. We have instead maintained that, without a cuff, subcutaneous tunneling alone may reduce infection rates.

The purpose of this study was to evaluate the impact of subcutaneous tunneling on PICC-associated bloodstream infection.

## Materials and methods

The central institutional review board of our two hospitals approved this retrospective study. Medical records from 302 of 327 consecutive patients receiving tunneled PICCs (tPICCs) between October 2017 and May 2018 were collected from two tertiary institutions. As a control group, 309 of 328 consecutive patients receiving conventional PICCs (cPICCs) between April 2016 and September 2017 were also reviewed. Overall, 235 tPICCs (78%) and 241 cPICCs (78%) were performed at Incheon St. Mary's Hospital, with 67 tPICCs (22%) taking place between October 2017 and April 2018 and 68 cPICCs (22%) performed between May 2017 and September 2017 at Bucheon St. Mary's Hospital.

Patients who transferred early and those with short indwelling times (<2 days), unusually poor peripheral veins, and infections with other intravascular catheters were excluded (Fig. 1). The latter was excluded because it could potentially obscure the precise origins of infections. Medical records were reviewed for patient demographics, purpose and duration of catheterization, comorbidities, technical success, complications, and cause of catheter removal.

A total of 302 patients comprised the tPICC group, after excluding 25 patients for peripheral vein cannulation failures ( $n = 8$ ), infections related to other intravascular catheters ( $n = 3$ ), or brief indwelling times (<2 days,  $n = 14$ ). In the cPICC group, 309 patients qualified for the study, following exclusion of 3 patients with failed peripheral vein cannulations, 3 with infections acquired from other intravascular devices, and 13 who were immediately transferred.

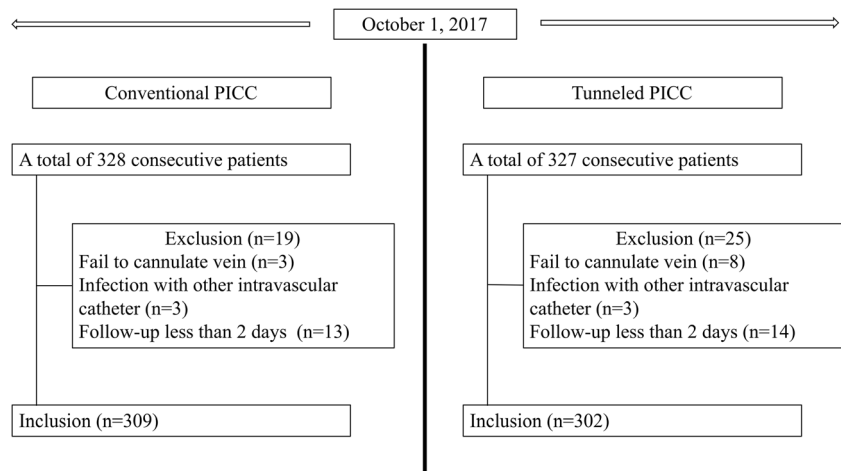
## Definition

Technical success was defined as successful PICC placement via tunneling, once achieving venous access. Adverse events were designated as follows: immediate/procedure related, delayed, or tunnel associated. Immediate procedure-related complications were adverse events occurring within 12 h after PICC insertion, including bloody oozing or neuropathy necessitating additional care. Delayed complications included CLABSI, entry-site infection, thrombophlebitis, dislocation, and occlusion. Local hematoma or pain in vicinities of tunnels constituted tunnel-associated complications.

We applied the National Healthcare Safety Network surveillance definition of CLABSI [14]. CLABSI was defined as a laboratory-confirmed bloodstream infection where central line was in place for >2 days and must meet one of the following criteria: Patient had a recognized pathogen identified from one or more blood specimens by a culture or non-culture-based microbiologic test and organism identified in blood was not related to an infection at another site. Two reviewers confirmed the diagnosis by reviewing medical records and microbiologic data, reaching an agreement on the final diagnosis. If laboratory studies failed to substantiate bacteremia under highly probable circumstances, forcing physicians to remove the catheters, such instances were deemed suspicious of CLABSI. To estimate tunneling time (for group comparisons), we subtracted guidewire insertion time from catheter placement completion time in minutes, using the Picture Archiving and Communication System.

ICU status was equated with any ICU care required during hospitalization. The time from insertion to removal of PICCs corresponded with PICC duration. The purpose of PICC placement was based on initial indication, such as antibiotic or chemotherapy delivery.

**Fig. 1** Schematic of patient selection process



Thrombophlebitis was signaled by arm swelling or pain along a PICC route without signs of infection and was subdivided by local thrombophlebitis and PICC-related venous thrombosis. Local thrombophlebitis was defined when local tenderness and palpable cord without ultrasound evidence of venous thrombosis. PICC-related venous thrombosis was specified by arm swelling and pain along a PICC route without signs of infection and confirmed by ultrasound. Entry-site infection was marked by erythema, induration, and/or tenderness within 2 cm of a catheter entry site, with or without infectious signs and symptoms (i.e., pus or fever) [5].

## Technique

All PICCs (PowerPICC [Bard Access Systems Inc.] and Pro-PICC [Medcomp Inc.]) were inserted by interventional radiologists using a specialized suite and standard aseptic protocol. All were commercially available dual-lumen products of 5-Fr caliber that were placed under ultrasound guidance. Before the puncture, the vein diameter was measured by ultrasound. Poor peripheral vascularity was considered to be related to high risk of catheter-associated thrombosis and technical difficulty (more than 45% of catheter to vessel ratio) [15]. Then, the PICCs were placed at central vein and the patients were excluded in this study. After successfully inserting the guidewire into a vein, small skin nicks were made at venous puncture and tunnel entry (2–3 cm distal) sites. The tunnels were created in two ways. First, subcutaneous fat was undermined using a hemostat. The catheter was subsequently pulled by hemostat and inserted via peel-away sheath. This technique, previously reported by Selby Jr. in 2001 [13] (Fig. 2 and Video 1), was used at Incheon St. Mary's hospital. The second method involved a puncture needle. After guidewire placement, the needle served to undermine the subcutaneous layer, and the guidewire was inserted backwards. The peel-away sheath was then passed through the tunnel to the cannulated vein, and the PICC catheter was

placed via peel-away sheath [16] (Fig. 3 and Video 2). This method was used at Bucheon St. Mary's Hospital. [Online supplementary materials](#) are available. The two puncture sites were closed by applying *N*-butyl cyanoacrylate (NBCA; Histoacryl, B. Braun Surgical). Regular device checks and flushing with normal saline took place daily. Insertion-site care entailed weekly film-covered dressing changes and new gauze application every other day.

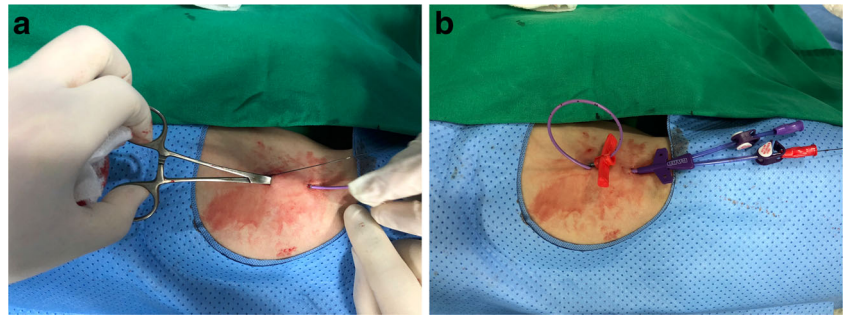
## Statistical analysis

To compare the two study groups, we used the independent sample *t* test for continuous variables and the Chi-square test for categorical variables. The CLABSI rate was multiplied by 1000 and divided by total catheter-days, using Chi-square or Fisher's exact test for between-group comparisons. Odds ratios with 95% confidence intervals (CIs) were estimated for every complication, including CLABSI, entry-site infection, thrombophlebitis, dislocation, and occlusion. Logistic regression served to analyze risk factors for CLABSI, and hazard ratios were generated by Cox regression analysis, focusing on PICC duration and CLABSI. Statistical significance was set at  $p < 0.05$ . All computations relied on standard software (SPSS v17.0; SPSS Inc). Numbers needed to treat were calculated for CLABSI alone, infections of bloodstream and entry site, and all infections with bloody oozing.

## Results

Once venous access was achieved, subcutaneous tunnels were feasible in all patients (100% technical success). The sum of total catheter indwelling times was 6972 days and 7574 days with median durations of 15.5 days (range, 2–188 days) and 16.0 days (range, 2–134 days) in tPICC and cPICC groups, respectively. The right arm and basilic vein were the most

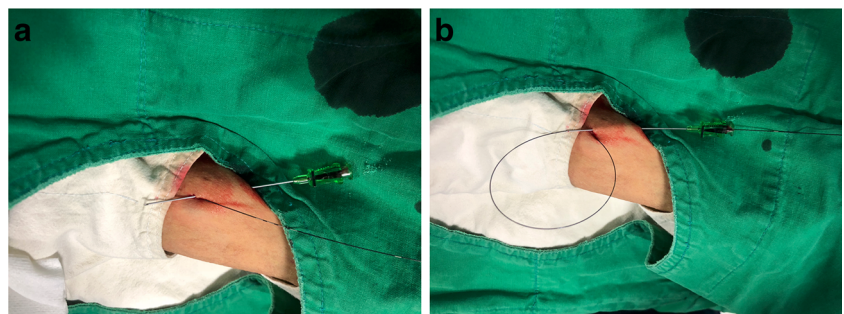
**Fig. 2** Serial photographs showing subcutaneous tunneling of peripherally inserted central catheter in a 43-year-old man: **a** hemostat used to undermine subcutaneous fat and pull catheter through tunnel created; and **b** insertion of catheter into vein (via peel-away sheath) once passed through subcutaneous tunnel



preferred insertion sites in both groups. Patient characteristics are summarized in Table 1.

Intravenous antibiotic delivery was the most common reason for PICC insertion, followed by intravenous fluid infusion and parenteral nutrition. However, the purpose for PICC placement differed significantly by group ( $p = 0.008$ ). Further analysis for each purpose demonstrated significant differences in the groups for antibiotics therapy ( $p = 0.041$ ), chemotherapy ( $p = 0.041$ ), and surgery ( $p = 0.026$ ). The most common comorbidity was malignant solid tumor, followed by diabetes mellitus, and both groups were similar in this regard. ICU stays (vs general ward or outpatient treatment) significantly different by group ( $p = 0.002$ ), but hospital stays in the tPICC (median, 32 days; range, 3–337 days) and cPICC (median, 33.5 days; range, 0–544 days) groups were similar ( $p = 0.574$ ). The average time between guidewire insertion and catheter placement was slightly longer in tPICC (vs cPICC) group, although not significantly different (tPICC,  $3.1 \pm 2.6$  min; cPICC,  $2.9 \pm 2.7$  min;  $p = 0.414$ ). CLABSI occurred in 28 patients of the cPICC group (3.71/1000 catheter-days) and in 8 patients of the tPICC group (1.15/1000 catheter-days), representing a significant reduction for the tPICC group in terms of patient numbers (OR = 0.273; 95% CI, 0.122–0.609) and catheter-days (OR = 0.310; 95%, 0.141–0.680). In the absence of laboratory-confirmed bloodstream infection, there were another 16 patients in cPICC group and 10 patients in the tPICC group whose catheters were removed due to suspicion of CLABSI. All thrombophlebitis were related with venous thrombosis and the occurrence rates were not different in both groups. Other delayed complications did not differ significantly by group (Table 2).

**Fig. 3** Serial photographs showing subcutaneous tunneling of peripherally inserted central catheter in a 76-year-old man: **a** Puncture needle re-used, creating 1-in. subcutaneous tunnel after guidewire placement into target vein; and **b** guidewire passed through puncture needle forming a loop, resolved by a snap of pull back



Immediate oozing of blood was likewise significantly reduced (OR = 0.221; 95% CI, 0.089–0.544) in the tPICC (vs cPICC) group. Procedure-related pain and possible neuropathy occurred in two patients of the cPICC group and one patient of tPICC group ( $p = 1.0$ ). In Cox regression analysis, subcutaneous tunneling was the only variable to correlate significantly with CLABSI (adjusted hazard ratio = 0.328; 95% CI, 0.149–0.721) (Table 3 and Fig. 4). There were no subcutaneous tunnel-associated adverse events. Numbers needed to treat were 13.8 for CLABSI, 11.7 for CLABSI and entry-site infection, and 5.5 for all infections and oozing of blood.

## Discussion

In this comparative study, PICC-associated bloodstream infections in patients with subcutaneous tunnels (vs conventional moorings) proved to be significantly fewer ( $p = 0.002$ ). Oozing of blood was also significantly reduced although largely controlled by manual or sandbag compression. Procedure times did not differ significantly by group.

The use of subcutaneous tunnels in placing intravascular catheters is not a new concept, and the effects are well documented [10–12]. However, this method is not widely applied to PICC placement; many physicians perhaps consider PICCs relatively safe and infection-free. Several recent reports have nonetheless indicated that the complication rates of PICCs are as high as those of standard central venous catheters [1]. Another drawback is that subcutaneous tunnels have not been evaluated due to commercial unavailability of PICC with tunneller and Dacron cuffs. In

**Table 1** Patient characteristics

Characteristics	Tunneled PICC ( <i>n</i> = 302)	Conventional PICC ( <i>n</i> = 309)	<i>p</i> value
Mean age, years ± SD	68.0 ± 15.9	68.7 ± 14.6	0.546
Gender			
Male:female	134:168	142:167	0.694
Arm			
Right:left	258:44	263:46	0.912
Peripheral vein			0.104
Basilic	186	176	
Brachial	107	113	
Cephalic	9	20	
Duration of PICC, days	6972 15.5 [2–188] <sup>†</sup>	7574 16.0 [2–134] <sup>†</sup>	0.463
Purpose of catheter			0.008
Antibiotics therapy	151	129	0.041
Parenteral nutrition	37	43	0.542
Chemotherapy	5	14	0.041
Surgery	19	8	0.026
Intravenous infusion	90	115	0.052
Comorbidities			0.170
None	111	103	
Diabetes mellitus	59	56	
Malignant solid tumor	85	94	
Immune compromise (hematology malignancy, ANC* < 500, organ transplant recipient, or AIDS)	9	22	
Multicomorbidity	38	34	
Admission type			0.002
General condition (general ward/outpatient treatment)	252 (252/0)	226 (214/12)	
Intensive care unit	50	83	
Combined intravascular device	20	11	0.085
Hospitalization, days	32 [3–377] <sup>†</sup>	33.5 [0–544] <sup>†</sup>	0.574

*p* value generated via independent sample *t* test and  $\chi^2$  test

Unless otherwise indicated, data expressed as numbers of patients

\*Absolute neutrophil count

<sup>†</sup> Median [range]

**Table 2** Comparison of associated complications in tunneled (tPICC) and conventional (cPICC) PICC groups

	tPICC ( <i>n</i> = 302, 6972 days)	cPICC ( <i>n</i> = 309, 7574 days)	OR (tPICC/ cPICC)	95% confidence interval
Delayed complication				
CLABSI				
Per person	8	28	0.273	0.122–0.609
Per day	(1.15) <sup>†</sup>	(3.71) <sup>†</sup>	0.310	0.141–0.680
Thrombophlebitis	6	4	1.546	0.432–5.532
Dislocation	22	20	1.135	0.606–2.126
Occlusion	6	5	1.232	0.372–4.082
Hematoma	11	6	1.909	0.697–5.229
Entry-site infection	3	6	0.507	0.126–2.045
Immediate complication				
Bloody oozing	6	26	0.221	0.089–0.544
Neuropathy	1	2	0.510	0.046–5.654

All data per person (except CLABSI)

PICC peripherally inserted central catheter, OR odds ratio, CLABSI central line-associated bloodstream infection

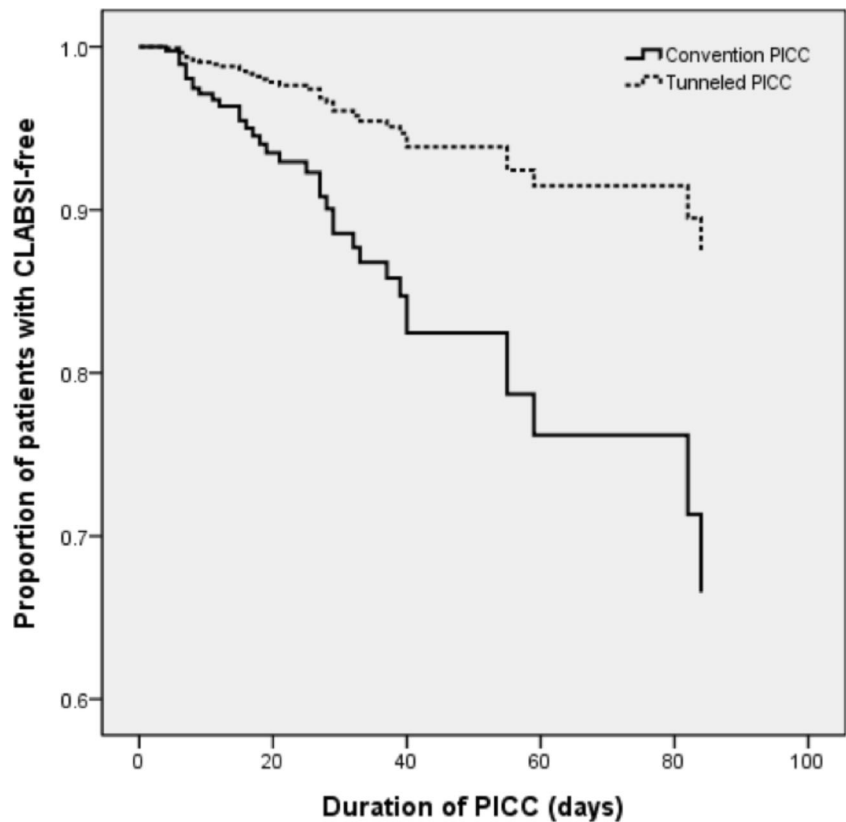
<sup>†</sup> Values per 1000 catheter-days

**Table 3** Logistic and Cox regression analyses of risk factors for central line-associated blood-stream infection

	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> value	aHR (95% CI)	<i>p</i> value
Age	0.997 (0.975–1.018)	0.754	1.006 (0.984–1.029)	0.592
Male/female	1.092 (0.556–2.143)	0.799	1.075 (0.559–2.069)	0.829
Tunnel/non-tunnel	0.273 (0.122–0.609)	0.002	0.328 (0.149–0.721)	0.006
PICC duration	1.004 (0.991–1.016)	0.587	N/A	
PICC purpose				
Antibiotics	1 (ref.)	0.218	1 (ref.)	0.254
TPN	0.316 (0.073–1.379)	0.125	0.299 (0.070–1.277)	0.103
Chemotherapy	2.313 (0.623–8.578)	0.210	2.263 (0.674–7.601)	0.187
Surgery	0.000 (0.000–.)	0.998	0.000 (0.000–.)	0.973
Intravenous infusion	0.632 (0.291–1.374)	0.247	0.784 (0.368–1.668)	0.527
Comorbidity				
No comorbidity	1 (ref.)	0.429	1 (ref.)	0.496
Diabetes mellitus	0.851 (0.315–2.302)	0.751	0.840 (0.319–2.214)	0.725
Solid tumor	1.012 (0.442–2.319)	0.977	1.011 (0.452–2.260)	0.979
Immune compromise	2.291 (0.697–7.533)	0.172	2.129 (0.691–6.562)	0.188
Multicomorbidity	0.442 (0.097–2.006)	0.290	0.504 (0.113–2.249)	0.369
Hospital stay	1.005(1.000–1.010)	0.051	0.999 (0.993–1.006)	0.853
ICU stay	1.370 (0.955–1.965)	0.087	1.642 (0.821–3.284)	0.161

PICC peripherally inserted central catheter, OR odds ratio, aHR adjusted hazard ratio, CI confidence interval, TPN total parenteral nutrition, ICU intensive care unit, N/A not applicable

**Fig. 4** Survival curve showing cumulative CLABSI-free survival according to indwelling time of conventional and tunneled PICCs



2001, Selby Jr. et al first reported on the safety of tunneled PICCs using 29 catheters with Dacron cuffs and 14 conventional catheters. These researchers insisted that tunneling requires no additional effort and is likely to prevent dislocation and infection, provided cuffs were used [13]. Pittiruti et al also introduced the usefulness of tunneling in placement of PICC especially for pediatric patients or atypical sites of insertion [16, 17]. To our knowledge, there has been no related large-scale study in the absence of cuffs until now. Physicians often prefer the easy access and removal of a PICC, which Dacron cuffs may thus hinder. Ostroff et al have described use of a modified Seldinger method to create subcutaneous tunnels in 50 patients [18]. Although evaluated solely for technical feasibility, this may be another viable method for venous access via subcutaneous tunnel. Regarding inadvertent dislocation, subcutaneous tunnel without Dacron cuff was not so effective for prevention. However, the use of anchoring device (SecurAcath; Interrad Medical Inc.) may be helpful for securing PICC even without Dacron-cuffed device.

The present study has several limitations, the first being that its retrospective design is subject to selection bias. Still, we included all consecutive patients in both study groups, which aside from tunneling were otherwise fundamentally quite similar. We believe that a randomized controlled study would yield more promising outcomes. Second, the use of NBCA may be a confounder herein. To close skin nicks, sutures or topical NBCA application are needed; and NBCA was our preference, despite a somewhat higher cost. By firmly securing the skin and catheter (unlike more movable conventional PICCs), we may have simulated the effects of a Dacron cuff. Oozing immediately after procedures was also diminished, likely due to glue applied at entry sites. Third, we only considered CLABSI, not catheter-related bloodstream infection (CR-BSI) which is more thorough definition of term used when the source of infection is identified from the catheter. This could result in overestimation of the true incidence of CR-BSI [19]. Finally, the cPICC group unintentionally included more ICU-based patients, potentially predisposing to CLABSI [3]. In Cox regression analysis, however, neither ICU care nor hospital stay emerged as a significant risk factor for CLABSI.

In summary, subcutaneous tunneling is a technically feasible and safe means of PICC placement, without prolonging procedures times. Even with an absent Dacron cuff, tunneled PICCs reduce the likelihood of CLABSI. Although a Dacron-cuffed catheter may be more effective in preventing dislocation and infection, access and retrieval may suffer. The use of a cuff in this setting merits further investigation.

**Acknowledgements** We thank Pyunghwa Kim for assisting with data collection.

**Funding** This research was supported by a Grant of Translational R&D Project through Institute for Bio-Medical convergence, Incheon St. Mary's Hospital, The Catholic University of Korea.

## Compliance with ethical standards

**Guarantor** The scientific guarantor of this publication is Dong Jae Shim.

**Conflict of interest** The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

**Statistics and biometry** One of the authors (Hun Jae Lee, College of Medicine, Inha University) has significant statistical expertise.

**Informed consent** Written informed consent was waived by the Institutional Review Board.

**Ethical approval** Institutional Review Board approval was obtained (IRB approval number: XC18REDI0032).

## Methodology

- retrospective
- observational
- multicenter study

## References

1. Chopra V, O'Horo JC, Rogers MA, Maki DG, Safdar N (2013) The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 34:908–918
2. Gunst M, Matsushima K, Vanek S, Gunst R, Shafi S, Frankel H (2011) Peripherally inserted central catheters may lower the incidence of catheter-related blood stream infections in patients in surgical intensive care units. *Surg Infect (Larchmt)* 12:279–282
3. Chopra V, Ratz D, Kuhn L, Lopus T, Chenoweth C, Krein S (2014) PICC-associated bloodstream infections: prevalence, patterns, and predictors. *Am J Med* 127:319–328
4. Safdar N, Maki DG (2005) Risk of catheter-related bloodstream infection with peripherally inserted central venous catheters used in hospitalized patients. *Chest* 128:489–495
5. Bouzad C, Duron S, Bousquet A et al (2016) Peripherally inserted central catheter-related infections in a cohort of hospitalized adult patients. *Cardiovasc Intervent Radiol* 39:385–393
6. Grau D, Clarivet B, Lotthé A, Bommart S, Parer S (2017) Complications with peripherally inserted central catheters (PICCs) used in hospitalized patients and outpatients: a prospective cohort study. *Antimicrob Resist Infect Control* 6:18
7. McDiarmid S, Scrivens N, Carrier M et al (2017) Outcomes in a nurse-led peripherally inserted central catheter program: a retrospective cohort study. *CMAJ Open* 5:E535–E539
8. Walshe LJ, Malak SF, Eagan J, Sepkowitz KA (2002) Complication rates among cancer patients with peripherally inserted central catheters. *J Clin Oncol* 20:3276–3281
9. Advani S, Reich NG, Sengupta A, Gosey L, Milstone AM (2011) Central line-associated bloodstream infection in hospitalized children with peripherally inserted central venous catheters: extending risk analyses outside the intensive care unit. *Clin Infect Dis* 52:1108–1115

10. Randolph AG, Cook DJ, Gonzales CA, Brun-Buisson C (1998) Tunneling short-term central venous catheters to prevent catheter-related infection: a meta-analysis of randomized, controlled trials. *Crit Care Med* 26:1452–1457
11. Timsit JF, Sebille V, Farkas JC et al (1996) Effect of subcutaneous tunneling on internal jugular catheter-related sepsis in critically ill patients: a prospective randomized multicenter study. *JAMA* 276:1416–1420
12. Timsit JF, Bruneel F, Cheval C et al (1999) Use of tunneled femoral catheters to prevent catheter-related infection: a randomized, controlled trial. *Ann Intern Med* 130:729–735
13. (2001) *Peripherally inserted tunnelled catheters: a new option for venous access*. Springer, Milano
14. Centers for Disease Control (CDC)/National healthcare Safety Network (NHSN) (2018) Protocol for definition of central-line associated bloodstream infection. Available at: [http://www.cdc.gov/nhsn/PDFs/pseManual/4PSC\\_CLABScurrent.pdf](http://www.cdc.gov/nhsn/PDFs/pseManual/4PSC_CLABScurrent.pdf). Accessed 10 July 2018
15. Sharp R, Cummings M, Fielder A, Mikočka-Walus A, Grech C, Esterman A (2015) The catheter to vein ratio and rates of symptomatic venous thromboembolism in patients with a peripherally inserted central catheter (PICC): a prospective cohort study. *Int J Nurs Stud* 52:677–685
16. Sandrucci S, Mussa B (2014) *Peripherally inserted central venous catheters*. Springer
17. Pittiruti M, Scoppettuolo G (2017) *The GAVeCeLT manual of Picc and midline: indications, insertion, management*. Edra
18. Ostroff MD, Moureau NL (2017) Report of modification for peripherally inserted central catheter placement: subcutaneous needle tunnel for high upper arm placement. *J Infus Nurs* 40:232–237
19. O’Grady NP, Alexander M, Burns LA et al (2011) Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 52:e162–e193