



Safety and Efficacy of Peripherally Inserted Central Catheter Placement by Surgical Intensivist–Led Vascular Access Team

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Purpose: This study aimed to evaluate the safety and efficacy of bedside peripherally inserted central catheter (PICC) placement under ultrasonography (USG) guidance in the general ward by a surgical intensivist–led vascular access team versus that of PICC placement in the intensive care unit (ICU) or fluoroscopy unit.

Materials and Methods: We conducted this retrospective study of all patients who underwent PICC placement between March 2021 and May 2022. Clinical, periprocedural, and outcome data were compared for PICC placement in the ICU, general ward, and fluoroscopy unit groups, respectively.

Results: A total of 354 PICC placements were made in 301 patients. Among them, USG-guided PICC placement was performed in 103 and 147 cases in the ICU and general ward, respectively, while fluoroscopy-guided PICC placement was performed in 104 cases. USG-guided PICC placement more often required post-procedural catheter repositioning than fluoroscopy-guided PICC placement ($P<0.001$), but there was no significant difference in any adverse events ($P=0.796$). In addition, USG-guided PICC placement in the general ward was more efficient than fluoroscopy-guided PICC placement (0.73 days vs. 5.73 days, respectively; $P<0.001$). In the multivariate analysis, previous PICC placement within 6 months was an independent risk factor for a PICC-associated bloodstream infection (odds ratio, 2.835; 95% confidence interval, 1.143–7.034; $P=0.025$).

Conclusion: USG-guided PICC placement in the general ward by a surgical intensivist–led vascular access team has comparable safety and efficiency to that of USG-guided PICC placement in the ICU or fluoroscopy-guided PICC placement.

Key Words: Central venous catheter, Peripherally inserted central catheter placement, Catheter-associated infection, Ultrasonography, Vascular access device

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INTRODUCTION

Since the 1950s, central venous catheter (CVC) insertion has been performed to deliver high-dose vasopressors or electrolytes that are difficult to administer through peripheral veins, central parenteral nutrition, chemotherapy, mas-

sive transfusion, and hemodialysis [1]. Among the various central venous access devices for short-term use, an acute 15 to 20-cm CVC is implanted in the internal jugular vein (IJV), subclavian vein, or femoral vein. However, peripherally inserted central catheter (PICC) placement has been extensively adopted because it can be used for a long period

of 2 weeks to several months, has a low incidence of mechanical complications and central bloodstream infection (BSI), and is more convenient for patients [2].

Conventionally, interventional radiologists perform fluoroscopy-guided PICC placement. However, with the increasing adoption of bedside ultrasonography (USG), USG-guided PICC placement has also been widely implemented by vascular access teams. However, performing fluoroscopy-guided PICC placement in the intensive care unit (ICU) is frequently challenging because of patient transport limitations such as mechanical ventilation or hemodynamic instability. Therefore, intensivists frequently perform USG-guided PICC placement for central vascular access in critically ill ICU patients.

Compared with that of the ICU or interventional unit, performing aseptic PICC placement in the general ward can be challenging, as the bed or patient makes it inconvenient for the operator and real-time monitoring of the patient's condition is frequently difficult. However, because of the high-flow nasal oxygen therapy application, which cannot be converted to non-rebreather mask oxygen; fluoroscopy units that cannot be used immediately because of reserved patients; and economic reasons, some patients in general wards are difficult to transport to the fluoroscopy unit for PICC placement. Therefore, a certain percentage of PICC insertions should be performed in general wards. However, studies of the safety and efficacy of USG-guided PICC insertion performed by surgical intensivists in the general wards are limited. Therefore, here we aimed to evaluate the safety and efficacy of bedside USG-guided PICC placement in the general ward by a surgical intensivist-led vascular access team versus PICC placement in the ICU or fluoroscopy unit.

MATERIALS AND METHODS

1) Study population

We conducted this retrospective study of all patients who underwent PICC placement at Kyungpook National University Chilgok Hospital between March 2021 and May 2022. Overall, 409 PICC insertion attempts were made during the study period. Among them, 15 patients were aged <18 years, the puncture was impossible due to poor patient cooperation in five cases, and guidewire or catheter insertion was impossible in seven cases due to intravenous thrombus, hematoma after first puncture failure, or a mass around the superior vena cava. The catheter was removed within 2 days or the patients were discharged from the hospital within 2 days in 28 cases. After the exclusion of 55 cases, 354 cases were included in this study. This study was

approved by the Institutional Review Board of Kyungpook National University Chilgok Hospital (no. 2022-07-011), which waived the need for informed consent because of the retrospective study design.

2) Data collection

Clinical, periprocedural, and outcome data were retrospectively obtained by electronic medical record review. In addition, demographic data, including age, sex, body mass index (BMI), admission department, Charlson comorbidity index, Michigan Risk Score (MRS) [3], comorbidities, PICC placement history within 6 months, the presence of another CVC (for example, a preexisting dual-lumen catheter for hemodialysis), and length of hospital stay before PICC placement were analyzed. Furthermore, the reasons for PICC placement, laterality of the arm of PICC placement, vein of PICC placement, time taken for PICC placement, interval between PICC request and placement, frequency of catheter tip placement in the target range, PICC reposition rate, duration of PICC use, reason for PICC removal, and adverse events (catheter occlusion, PICC-associated BSI, and upper-extremity venous thrombosis [UEVT]) were also analyzed.

Because different landmarks were used as targets for catheter tip positioning in the USG- and fluoroscopy-guided techniques, the following two criteria were used to evaluate the optimal position. First, for the USG-guided technique, a tracheal carina was used as a landmark; in cases in which the catheter tip was located within 3 cm above and 4 cm below the carina, this range was recorded as the target range as described by Zhang et al. [4], who defined 3 cm above and 4 cm below the carina as the central vein. Next, the radiologic cavoatrial junction (CAJ), defined as the inflection of the right cardiac border, was used as a landmark, and cases in which the catheter tip was located within 3 cm above and 3 cm below the radiologic CAJ were recorded as the target range in the fluoroscopy-guided technique [5]. Finally, PICC-associated BSI was defined as a primary BSI unrelated to an infection at another site in a patient with a PICC in place for more than 48 hours and infection with a recognized pathogen (identified from one or more central blood or tip specimens by a culture-based microbiological test). In addition, patients with symptoms of UEVT, such as pain and swelling, underwent Doppler USG for evaluation.

3) Procedures

A vascular access team comprising a trained nurse and two surgical intensivists performed the USG-guided PICC placement in the ICU or general ward. The fluoroscopy-guided PICC placement was performed by interventional

radiologists or anesthesiologists in the fluoroscopy unit. Three PICC types were used according to operator preference: Turbo-Ject Power-Injectable PICC (Cook, Bloomington, MN, USA), PowerPICC catheter (Bard Access Systems, Salt Lake City, UT, USA), and Pro-PICC catheter (Medcomp, Harleysville, PA, US), all of which were 5 Fr in diameter with a double lumen. Standard aseptic precautions were applied in all placements with maximal sterile barriers and 2% chlorhexidine gluconate for skin decontamination.

USG-guided PICC placement was determined using the Michigan Appropriateness Guide for Intravenous Catheters [6]. A nurse prepared the patient for the procedure and performed the monitoring, and a surgical intensivist was in charge of the procedure from skin decontamination to catheter insertion. The distance from the carina to the clavicle was measured before the procedure and confirmed through chest radiography or computed tomography. The distance from the skin puncture site to the point where the clavicle and superior vena cava were expected to meet was measured to determine the final catheter length. The basilic vein was preferentially used for PICC placement, and the brachial vein was used when the basilic vein diameter was <3 mm. Most PICC placements were performed in the right

arm, while the left arm was used only when the right arm was unavailable. After the procedure, the catheter tip was confirmed as not within the IJV using USG. Two surgical intensivists confirmed the catheter tip position on post-procedural chest radiography. Furthermore, initial catheter repositioning was performed at the bedside when the catheter tip was positioned in the subclavian vein or IJV, and an additional guidewire was used as necessary. After the initial catheter repositioning, the vascular access team repeated it in the fluoroscopy unit when necessary and considered difficult or failed at the bedside.

Alternatively, the catheter tip was determined using inserted guidewire length during the procedure in the case of fluoroscopy-guided PICC placement, and additional chest radiography was performed to confirm catheter tip position. Finally, a StatLock catheter stabilization device (Bard Access Systems) was used to hold the PICC line, and the catheter site was covered with 3M Tegaderm chlorhexidine gluconate IV (3M Health Care, Saint Paul, MN, USA).

4) Statistical analysis

Categorical and continuous variables are presented as

Table 1. Baseline characteristics of enrolled patients

Variable	USG-guided PICC in the ICU (n=103)	USG-guided PICC in the general ward (n=147)	Fluoroscopy-guided PICC (n=104)	P-value
Age (y)	67.40±12.81	67.86±13.49	66.02±11.82	0.225
Sex, male	67 (65.0)	93 (63.3)	60 (57.7)	0.315
Body mass index (kg/m ²)	23.27±4.84	20.88±5.02	20.44±3.77	<0.001*
Admission at medical department	86 (83.5)	80 (54.4)	64 (61.5)	0.001*
Charlson Comorbidity Index	4.41±2.25	5.89±2.74	6.69±2.64	<0.001*
Michigan risk score	2.05±1.53	2.86±1.71	3.17±1.55	<0.001*
Comorbidities				
Hypertension	43 (41.7)	47 (32.0)	29 (27.9)	0.035*
Diabetes mellitus	37 (35.9)	37 (25.2)	20 (19.2)	0.007*
Chronic obstructive pulmonary disease	7 (6.8)	12 (8.2)	7 (6.7)	0.984
Congestive heart failure	7 (6.8)	8 (5.4)	2 (1.9)	0.101
Chronic kidney disease	11 (10.7)	12 (8.2)	5 (4.8)	0.118
Venous thromboembolism	4 (3.9)	5 (3.4)	8 (7.7)	0.200
Transplantation	3 (2.9)	4 (2.7)	0 (0.0)	0.132
Solid tumor	28 (27.2)	98 (66.7)	84 (80.8)	<0.001*
Hematologic malignancies	3 (2.9)	10 (6.8)	7 (6.7)	0.236
COVID-19	51 (49.5)	1 (0.7)	0 (0.0)	<0.001*
History of PICC placement	7 (6.8)	15 (10.2)	36 (34.6)	<0.001*
Presence of another central venous catheter	36 (35.0)	0 (0.0)	3 (2.9)	<0.001*
Length of hospital stay before PICC placement	9.84±13.55	18.77±27.39	43.69±52.00	<0.001*

Values are presented as mean±standard deviation or number (%).

USG, ultrasonography; PICC, peripherally inserted central catheter; ICU, intensive care unit.

*Statistically significant P<0.05.

number and percentage or mean with standard deviation, respectively. One-way analysis of variance or the Kruskal–Wallis test was performed according to normality for comparing the ICU, general ward, and fluoroscopy groups. Since the time taken for PICC placement in the fluoroscopy group was not included in the electronic medical records and the time difference between the PICC request and placement in the ICU group was identified, the Mann–Whitney U-test was used to compare the two variables. Moreover, logistic regression analysis was performed to

identify the risk factors for complications associated with PICC placement. Variables with values of $P < 0.1$ that tended to be associated with the univariate analysis were considered in the multivariable regression models. Finally, the odds ratios are reported with 95% confidence intervals for each variable. Statistical significance was set at $P < 0.05$. All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) software version 23 (IBM Corp., Armonk, NY, USA).

Table 2. Procedural characteristics and clinical outcomes of PICC placement

Variable	USG-guided PICC in the ICU (n=103)	USG-guided PICC in the general ward (n=147)	Fluoroscopy-guided PICC (n=104)	P-value
Reason for PICC placement				
Difficult venous access	18 (17.5)	35 (23.8)	18 (17.3)	0.972
Chemotherapy	1 (1.0)	9 (6.1)	4 (3.8)	0.292
Central total parenteral nutrition	52 (50.5)	55 (37.4)	28 (26.9)	<0.001*
Vasopressor	30 (29.1)	1 (0.7)	0 (0.0)	<0.001*
Hospice care	0 (0.0)	19 (12.9)	20 (19.2)	<0.001*
Arm of PICC placement				
Right	95 (92.2)	121 (82.3)	92 (88.5)	0.424
Left	8 (7.8)	26 (17.7)	12 (11.5)	
Vein of PICC placement				
Basilic vein	102 (63.7)	148 (67.3)	70 (74.3)	0.154
Brachial vein	37 (36.3)	48 (32.7)	18 (25.7)	
Time required for PICC placement (min)				
	11.84±5.50	11.49±7.20	-	0.139
Time difference between request and placement of PICC (d)				
	-	0.73±1.10	5.73±4.98	<0.001*
Catheter tip in the target range				
	83 (80.6)	116 (78.9)	79 (76.0)	0.419
PICC reposition				
	15 (14.6)	9 (6.1)	0 (0.0)	<0.001*
Duration of PICC use (d)				
	19.93±21.83	25.47±23.31	30.66±32.27	0.013*
Reason for PICC removal				
	96	124	90	0.226
The patient died	37 (38.5)	41 (33.1)	31 (34.4)	
Hospital discharge	21 (21.9)	43 (34.7)	21 (23.3)	
Only fever	9 (9.4)	9 (7.3)	2 (2.2)	
No longer needed	8 (8.3)	10 (8.1)	3 (3.3)	
PICC-associated infection	6 (6.3)	9 (7.3)	9 (10.0)	
Catheter occlusion	5 (5.2)	2 (1.6)	5 (5.6)	
Upper extremity venous thrombosis	3 (3.1)	0 (0.0)	1 (1.1)	
Self-removal	2 (2.1)	4 (3.2)	12 (13.3)	
Unintended removal	3 (3.1)	1 (0.8)	4 (4.4)	
Unknown	2 (2.1)	5 (4.0)	2 (2.2)	
All adverse events				
	12 (11.7)	11 (7.5)	11 (10.6)	0.796
Catheter occlusion	3 (2.9)	2 (1.4)	2 (1.9)	0.611
PICC-associated bloodstream infection	7 (6.8)	9 (6.1)	8 (7.7)	0.797
Upper extremity venous thrombosis	2 (1.9)	0 (0.0)	1 (1.0)	0.445

Values are presented as number (%) or mean±standard deviation.

PICC, peripherally inserted central catheter; USG, ultrasonography; ICU, intensive care unit.

*Statistically significant $P < 0.05$.

RESULTS

During the study period, 354 PICCs were placed in 301 patients for 8,792 catheter days. The baseline characteristics of the enrolled patients are shown in Table 1. USG-guided PICC placement was performed in 103 and 147 cases in the ICU and general ward, respectively, while fluoroscopy-guided PICC placement was performed in 104 cases. Age and sex were not significantly different among groups ($P=0.225$ and $P=0.315$, respectively). However, the ICU group had a higher BMI ($P<0.001$), more patients in the medical department ($P=0.001$), and a lower MRS than the other groups ($P<0.001$). The Charlson comorbidity index was the highest in the fluoroscopy group and lowest in the ICU group ($P<0.001$). The ICU group included more patients with hypertension and diabetes mellitus than the fluoroscopy group ($P=0.042$ and $P=0.008$, respectively). Conversely, the fluoroscopy group had the most patients with solid tumors, followed by the general ward group and the ICU group ($P<0.001$). In addition, the ICU group had a higher proportion of patients with coronavirus disease 2019 ($P<0.001$) and CVC than the other groups ($P<0.001$). Furthermore, the proportion of patients who had undergone

two or more PICC placements in the previous 6 months was higher in the fluoroscopy group than in the other groups ($P<0.001$). After hospitalization, USG-guided PICC placement in the ICU was performed first, followed by USG-guided PICC placement in the general ward and fluoroscopy-guided PICC placement ($P<0.001$).

Table 2 shows the procedural characteristics and clinical outcomes of PICC placement. PICC placement was used more often in the ICU group than in the fluoroscopy group to enable a central parenteral nutrition supply ($P=0.001$), while placement for vasopressor administration was more common in the ICU group than in the other groups ($P<0.001$). USG-guided PICC placement in the ICU group was immediately performed when necessary. In addition, USG-guided PICC placement in the general ward was implemented sooner than fluoroscopy-guided PICC placement ($P<0.001$). PICC repositioning was performed more frequently in the ICU group than in the other groups ($P<0.001$). Furthermore, catheters placed in the ICU group were removed sooner than those in the other groups ($P=0.013$). No significant intergroup differences were observed in PICC placement arm ($P=0.424$), PICC placement vein ($P=0.154$), time required for PICC placement ($P=0.139$), target range

Table 3. Risk factors for central line-associated bloodstream infection after PICC placement

Variable	Univariate analyses			Multivariate analyses		
	OR	95% CI	P-value	OR	95% CI	P-value
Age ≥ 75 y	0.338	0.099–1.160	0.085			
Surgical department	0.922	0.383–2.220	0.857			
Malnutrition (BMI <18.5 kg/m ²)	1.409	0.580–3.423	0.449			
Obesity (BMI ≥ 25 kg/m ²)	1.118	0.400–3.124	0.831			
PICC for chemotherapy	2.409	0.507–11.442	0.269			
PICC for central TPN	1.406	0.611–3.234	0.423			
PICC for vasopressor	0.944	0.211–4.216	0.939			
PICC for hospice care	0.334	0.044–2.545	0.290			
Solid tumor	1.724	0.696–4.270	0.239			
Hematologic malignancies	0.712	0.091–5.556	0.746			
COVID-19	0.509	0.116–2.233	0.371			
History of PICC placement	2.800	1.138–6.890	0.025*	2.835	1.143–7.034	0.025*
Presence of another central venous catheter	0.720	0.163–3.186	0.665			
Procedure type						
USG-guided procedure in the ICU			0.888			
USG-guided procedure in the general ward	0.894	0.322–2.484	0.830			
Fluoroscopy-guided procedure	1.143	0.399–3.276	0.804			
Arm of PICC placement, left	0.275	0.036–2.090	0.212			
PICC repositioning	3.100	0.967–9.937	0.057	3.167	0.971–10.332	0.056
Catheter tip not in the target range	1.395	0.462–4.212	0.555			

PICC, peripherally inserted central catheter; OR, odds ratio; CI, confidence interval; BMI, body mass index; TPN, total parenteral nutrition; USG, ultrasonography; ICU, intensive care unit.

*Statistically significant $P<0.05$.

catheter tip placement ($P=0.419$), reasons for PICC removal ($P=0.226$), or adverse events ($P=0.796$).

Of the total PICC placements, 24 PICC-associated BSI occurred over 8,792 days, equivalent to 2.73 per 1,000 catheter days. The incidence of PICC-associated BSI per 1,000 catheter days was highest in the ICU group (3.56), followed by the fluoroscopy group (2.51) and the general ward group (2.47). However, the PICC-associated BSI rates did not differ significantly among the three groups ($P=0.888$). A previous PICC placement was a significant risk factor for PICC-associated BSI, and it differed significantly among groups in the univariate analyses ($P=0.025$; Table 3). Old age (≥ 75 years) ($P=0.085$) and PICC repositioning ($P=0.057$) showed marginally significant intergroup differences. Moreover, no significant difference in PICC-associated BSI was observed among the three groups ($P=0.888$). In the multivariate analysis, previous PICC placement was the only independent risk factor for a PICC-associated BSI. Furthermore, in the multivariate analyses, no other independent risk factors were identified for all adverse events, catheter occlusion, and UEVT.

DISCUSSION

In this study, we evaluated the safety and efficacy of PICC placement by surgical intensivist-led vascular access teams in the general ward by analyzing clinical and procedural characteristics in three different clinical settings. Although differences were observed among groups regarding reasons for PICC placement, post-procedural catheter repositioning, and PICC use duration, no significant differences were found in the overall adverse events or detailed complications, including catheter occlusion, PICC-associated BSI, and UEVT. Moreover, multivariate analyses were performed to identify the risk factors for overall adverse events and detailed complications. A history of PICC placement was the only risk factor for PICC-associated BSI.

Interventional radiologists traditionally performed fluoroscopy-guided PICC placement. However, PICC placement is easy to insert, is safe, and has a lower complications rate than other CVC insertions. Therefore, this safe and cost-effective procedure is widely performed at the bedside by experienced nurses or technicians [7,8]. However, unexpected events, including bleeding due to vessel injury, nerve injury, ischemia, and arrhythmia, may occur [9,10], and the surgical intensivist is more likely to resolve it more quickly than other medical personnel. For example, in two severely obese patients of this study, the guidewire became stuck in the muscle and cut in the middle. The surgical intensivist safely removed the fragmented guidewire in the muscle under local anesthesia. In our hospital, a puncture needle

and guidewire are inserted into the brachial vein. However, the guidewire could not be smoothly inserted through the needle in these cases. An attempt was made to remove the guidewire; however, it was caught in the muscle layer and could not be removed or cut in the middle. After additional local anesthesia, the surgical intensivist removed the entire fragmented guidewire by safely examining the muscle layer. In addition, since the intensivist was familiar with performing various USG examinations and procedures in the ICU, USG-guided PICC placement in the general ward could be easily and safely performed.

Various procedures such as percutaneous drainage, chemoport insertion, and embolization are performed in the interventional fluoroscopy unit. In our hospital, because of limited interventional fluoroscopy unit resources, PICC placement was generally delayed for other scheduled or emergency procedures, taking an average of 5.73 days from request to placement. Furthermore, critical care required in the ICU can make it challenging for surgical intensivists to perform PICC placement in the general ward. However, when PICC placement preparation and post-procedure care are performed by trained nurses in the vascular access team, PICC placement can be performed sooner in the general ward. In this study, PICC placement in the ICU or general ward groups took 11.84 and 11.49 minutes, respectively, with 70.7% and 86.3% completed within 10 and 15 minutes, respectively. Therefore, the time interval between the request and implementation of PICC placement in the general ward was a mean 0.73 days.

Moreover, a difference was observed in the cost of the procedure excluding the materials. In most cases, fluoroscopy-guided PICC placement is more expensive than USG-guided PICC placement because of the high cost of angiographic equipment and contrast; therefore, USG-guided PICC placement is more cost-effective. Moreover, USG-guided PICC placement has the advantages of no contrast agent use and no radiation exposure compared to fluoroscopy-guided PICC placement.

In this study, USG-guided PICC placement required more post-procedural repositioning than fluoroscopy-guided PICC placement. However, no significant intergroup differences were observed in the incidence of catheter occlusion, PICC-associated BSI, UEVT, and all adverse events, and post-procedural repositioning was not an independent risk factor for every adverse event, consistent with the study findings of Baxi et al. [11]. This may be because no significant intergroup differences were noted in target range catheter tip placement, and all post-procedural repositioning sessions were performed under aseptic precautions with sterile barriers.

According to Kim et al. [12], previous PICC placement

was a risk factor for PICC-associated BSI and catheter-related infection in patients undergoing hemodialysis [13], findings that are consistent with our findings. A history of PICC placement within the previous 6 months was an independent risk factor for PICC-associated BSI. Therefore, more attention should be paid to PICC placement or line management in long-term hospitalized patients with poor peripheral veins or if repeated PICC placement is required for periodic chemotherapy to prevent PICC-associated BSI.

In this study, the Michigan Compatibility Guide for Intravenous Catheters was followed to reduce PICC overuse as follows: 1) delivery of peripherally compatible infusates when the proposed duration of such use is 6 days or longer; 2) delivery of non-peripherally compatible infusates regardless of proposed duration of use; and 3) infusions or palliative treatment during end-of-life care [6]. In our study, there were 35 (9.9%) cases of PICC removal within 5 days, of which 17 (4.8%) had difficult venous access to deliver non-peripherally compatible infusates. Most of these cases were strongly desired by patients who had long-term peripheral vein access difficulty, which is assumed to be because PICC placement is more comfortable and convenient than repetitive peripheral intravenous lines [14,15].

This study has some limitations. First, it was a single-center retrospective study; therefore, there may have been selection bias. Second, the incidence of catheter-related UEVT was reportedly 38.5% to 66% [16,17]. In the present study, without routine monitoring for UEVT, we performed Doppler ultrasound only in patients with symptoms such as pain or swelling; therefore, the incidence of UEVT was very low (<1%) compared with other studies. Finally, 44 patients (12.4%) were discharged with the PICC for further treatment at another hospital; therefore, all post-procedural complications could not be analyzed.

CONCLUSION

USG-guided PICC placement in the general ward by a surgical intensivist–led vascular access team has safety and efficiency comparable to those in the ICU or under fluoroscopic guidance. Therefore, we recommend that a surgical intensivist–led vascular access team perform PICC placement in appropriate patients in the general ward, particularly when it is challenging to transfer a patient to a fluoroscopy unit or the fluoroscopy unit is unavailable within a short time.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHOR CONTRIBUTIONS

Conception and design: BY. Analysis and interpretation: BY. Data collection: all authors. Writing the article: all authors. Critical revision of the article: JH. Final approval of the article: all authors. Statistical analysis: BY. Overall responsibility: JH.

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