

Original Article

Anaphylaxis and anaphylactoid reactions associated with the insertion of peripherally inserted central catheters: A multiyear comparative retrospective cohort study

Christina S. Thornton PhD, MD¹, Jody Dumanski RN², Cherylanne Margherit RN², Sandra Vaz-Gonsalves BN, RN², Sheryl McDiarmid RN, MBA, MEd, BScN³, Michael D. Parkins MD, MSc^{1,4} and John M. Conly MD^{1,4,5,6}

¹Department of Medicine, University of Calgary and Alberta Health Services, Calgary, Alberta, Canada, ²Advanced Venous Access Service, Alberta Health Services, Calgary, Alberta, Canada, ³The Ottawa Hospital and Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, ⁴Department of Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, Alberta, ⁵Snyder Institute for Chronic Diseases, Cumming School of Medicine, University of Calgary and Alberta Health Services, Calgary, Alberta, Canada and ⁶Department of Pathology and Laboratory Medicine, University of Calgary and Alberta Health Services, Calgary, Alberta, Canada

Abstract

Objective: Peripherally inserted central catheters (PICCs) are a mainstay of nonpermanent vascular access devices. In this study, we assessed patients displaying anaphylaxis or anaphylactoid reactions to the PowerPICC SOLO and Groshong PICC (Bard Access Systems) using the Sherlock tip locating system (TLS).

Methods: Patients from 2 tertiary-care hospitals were systematically monitored over 4 years for adverse events following the insertion of a PICC using the Sherlock TLS. Insertion data were also collected using the BioFlo PICC (Angiodynamics) from a third hospital site and from The Ottawa Hospital over 4 years as an additional comparator. Three definitions of anaphylaxis and anaphylactoid reactions were utilized, and the Cohen κ was used to assess interrater agreement. Analysis of reactions among the patient cohorts was performed using the χ^2 test with Yates correction or the Fisher exact test as appropriate.

Results: Among 8,257 insertions using the TLS PICCs, 37 potential reactions (0.45%) were recorded. Using specific definitions for anaphylaxis or anaphylactoid reactions, 54.1%–91.9% met criteria. Comparator populations using data from Calgary ($n = 491$) and Ottawa ($n = 7,889$) using the BioFlo PICC insertion found no reactions. Anaphylactic or anaphylactoid reactions were significantly associated with the PowerPICC SOLO and Groshong PICC with the TLS compared to the BioFlo PICC ($P < .0001$) across all definitions. The largest subset of patients experiencing adverse reactions had cystic fibrosis (CF) ($n = 4$, 10.8%).

Conclusion: Our study results demonstrate significant adverse events associated with the PowerPICC SOLO and Groshong PICC using the Sherlock TLS inserted across a range of patient populations. The incidence rate of anaphylaxis or anaphylactoid reactions in the CF population at our center is significantly higher than in non-CF patients ($P < .001$).

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Central venous catheters (CVCs) are frequently used for vascular access, most often using the subclavian or internal jugular vein in patients requiring intensive care or prolonged medication administration. Disadvantages of CVCs include the requirement for specific training for insertion by physicians; line occlusion; and serious complications including pneumothorax, inadvertent arterial puncture, and nerve damage.¹ Peripherally inserted central catheters (PICCs) are a type of central catheter that serve as nonpermanent vascular access devices.² Advantages of PICCs compared to CVCs include fewer serious complications because the upper thoracic veins are avoided and cost was reduced because specially trained

nurses or other healthcare professional staff may insert them.¹ Previously, PICC lines were considered to be associated with reduced infection rates but more recent studies have demonstrated similar rates between PICCs and other central-line catheters.^{3,4} Additional benefits of PICCs include the ability to retain the access for months at a time, compared to midline catheters, which often require replacement after a month.² Indications for PICC insertion include delivery of long-term intravenous antibiotics, chemotherapeutic agents, and parenteral nutrition. Despite the multitude of benefits for PICCs, side effects may include pain at the insertion site (39.9%), bleeding (20%), dislodgment (20%), superficial thrombophlebitis (7%), infection (6%–10%), and leakage (6%).^{2,5}

Although most adverse events appear to be relatively minor, limited reports have been published of other serious adverse events including deep venous thrombosis, bloodstream infection, hypersensitivity reactions, and anaphylaxis.^{6–9} Haworth et al⁷ described 3 patients who, after insertion of an Ohmeda Hydrocath, became

Author for correspondence: John M. Conly, Email: John.Conly@albertahealthservices.ca.

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profoundly unwell (including hypotension, respiratory distress, bronchospasm, tachycardia and flushing), requiring immediate catheter removal and administration of epinephrine and hydrocortisone in 1 case.⁷ Specific reactions to elastomeric hydrogel midline and PICC catheters^{6,9–11} have also been recorded, but the Haworth study⁷ highlighted unusual reactions to polyurethane that had not been reported previously.

PICC insertions have increasingly been utilized as an effective means of long-term parenteral therapies. Post licensing, studies have suggested that while uncommon, significant side effects including life-threatening clinical adverse events continue to occur.^{12,13} In early 2010, nursing staff from 3 adult acute-care hospitals began noting severe hypersensitivity-type reactions immediately following PICC insertion in groups of patients requiring them predominantly for long-term antimicrobial administration. In our current study, we sought to characterize serious adverse events within a diverse group of adult patients in tertiary-care hospitals within our health region.

Methods

Study background, setting, and rationale

The Calgary Health Zone provides all medical services to the city of Calgary, Alberta, Canada, and several surrounding communities, resulting in a catchment area of ~1.4 million individuals. PICCs are placed by a team of specialized nurses in each of the 4 tertiary-care adult hospitals. In early 2010, the Calgary Health Zone adopted the PowerPICC SOLO catheter (Bard Access Systems, Salt Lake City, UT) along with the Groshong PICC (Bard Access Systems) with a magnetized stylet wire, the Sherlock TLS (Bard Access Systems). The components of the catheter stylet tip were elucidated via a search of the US patent registry (magnetized stylet neodymium-iron-boron mixture, US patents 8388541 CR Bard and 5879297 Lucent Medical Systems). Prior to this implementation, adverse events were minimal and were noted to consist of rare vasovagal reactions. Following the adoption of the Sherlock TLS, significant adverse events suggestive of anaphylaxis and anaphylactoid reactions occurring during or postinsertion were noted by experienced nursing staff prompting a prospective site-based monitoring for adverse events.

Data sources and study design

From October 2010 to November 2014, patients at 2 tertiary-care hospitals in Calgary were systematically monitored prospectively for significant adverse events following insertion of the PowerPICC SOLO catheter or the Groshong PICC with the Sherlock TLS. Detailed data about the patients, the indication for PICC insertion, the type of catheter, and the nature of any serious reactions with the details of the symptoms and signs, time of onset and management required (oxygen administration, positioning, catheter removal, fluid resuscitation) were recorded in the nursing notes and later transcribed to a database (Excel version 10.0 software, Microsoft, Redmond, WA). As a comparator, insertion data were also collected prospectively from a new adult tertiary-care hospital site that had opened in February 2013 but using the BioFlo PICC (Angiodynamics, Latham, NY) without a magnetized stylet tip. In addition, to increase the robustness of the comparative analysis, data were also collected prospectively from a cohort of patients at The Ottawa Hospital, in Ottawa, Ontario, which had a longstanding PICC service and had a purpose-built Microsoft Access PICC database that recorded data

from 2008 onwards, including reactions on PICC insertions. They had used both the PowerPICC SOLO catheter but exclusively without the magnetized stylet and the BioFlo PICC.¹⁴ Furthermore, from April 2010 to November 2014, adverse events, defined as any clinical compromise prompting intervention or further management, were concurrently collected and recorded.¹⁵

Definitions

To elucidate anaphylaxis or anaphylactoid (anaphylactic-like) reactions, 3 definitions were utilized from the literature (Table 1).^{16–18} We have used the terms anaphylaxis and anaphylactoid reactions interchangeably for our purposes because the criteria are similar (with IgE-mediated events being considered anaphylaxis and non IgE-mediated events being considered anaphylactoid reactions).¹³ We used 3 definitions because the symptoms and signs of anaphylaxis or anaphylactoid reactions can mimic many other conditions; we attempted to reduce bias in overinterpretation of observed clinical reactions and to allow comparisons of event rates based on the different definitions. Minor modifications to inclusion criteria were any patients that had severe chest pain, had abdominal pain, or required an intensive care code to be activated due to the severity of the symptoms and signs exhibited by the patients. Notably, 2 of the definitions^{14,16} listed the onset of the symptoms and signs to have occurred either within minutes to hours or within 60 minutes of the inciting event. The third definition from the Joint Council of Allergy, Asthma, and Immunology listed 3 scenarios in their definitions,¹³ one of which required the onset within minutes to hours, and we chose the latter for consistency within our definitions. One of the definitions¹² explicitly indicated that no other etiology was considered to be responsible and the Joint Council of Allergy, Asthma, and Immunology definition¹³ had an annotation attached to their definitions that other diagnoses should be excluded. We used a consistent definition of acute onset within minutes to an hour following the inciting event, that is, insertion of the PICC line and that other diagnoses were considered unlikely (Table 1). Comparisons were then conducted with all event rates at the different study locations and between the various catheter types. Ethical approval was obtained through the University of Calgary Institutional Research Information Services Solution panel (no. REB18-0859).

Statistical analysis

Two expert clinicians (J.M.C. and M.D.P.) were used to assess interrater agreement using the Cohen κ to determine agreement between each independent raters' opinion.¹⁹ The κ coefficients were calculated as described previously, using the proportion of rate opinion and the expected proportion. Based on interpretations described, κ agreement was defined as near perfect (>0.90), strong ($0.80–0.90$), moderate ($0.60–0.79$), weak ($0.40–0.59$), minimal ($0.21–0.39$), and none ($0–0.20$).¹⁹

Event rates were summarized using frequencies and percentages for categorical variables. Assessments of lot numbers, patient profiles, and medications or conditions known to be associated with a higher likelihood of anaphylaxis or anaphylactoid reactions were also conducted. Analysis of the event rates in the comparison groups was performed using the Student t test for continuous variables and the χ^2 test for categorical variables, with Yates correction or the Fisher exact test for a cell size <5 as appropriate. Only 1 catheter insertion per patient was assessed.

Table 1. Definitions of Anaphylactic and Anaphylactoid-Like Reactions Utilized for PICC Insertion Reactions

Definition	Description of Reaction	κ Analysis	κ Agreement
Zinderman et al ¹⁸	Required the involvement of signs or symptoms from ≥ 2 body systems ^a , with ≥ 1 sign or symptom being hypotension, vasodilation, or respiratory difficulty; and onset within 60 minutes after insertion ^b	0.477	Weak
Office of Surveillance & Epidemiology, FDA ¹²	One of the following criteria satisfies the inclusion criteria for anaphylaxis or anaphylactoid reaction: 1. Clinical diagnosis of anaphylactic or anaphylactoid reaction 2. Signs of allergic process coupled with 1 or both of the following features: (a) respiratory difficulty and (b) cardiovascular symptoms Plus No other etiology was apparently responsible and symptoms occurred within minutes to hours.	0.578	Moderate
Lieberman et al ¹⁷	Defined anaphylaxis [†] as 1 of 3 clinical scenarios: 1. The acute onset of a reaction (minutes to hours) ^c with involvement of the skin, mucosal tissue or both and ≥ 1 of the following: (a) respiratory compromise or (b) reduced blood pressure or symptoms of end-organ dysfunction 2. ≥ 2 of the following that occur rapidly after exposure to a likely allergen for that patient: involvement of the skin/mucosal tissue, respiratory compromise, reduced blood pressure or associated symptoms and/or persistent gastrointestinal symptoms 3. Reduced blood pressure after exposure to a known allergen.	0.510	Moderate

Note. PICC, peripherally inserted central-line catheter.

^aCardiovascular (hypotension, vasodilatation, flushing, tachycardia, bradycardia), respiratory (tachypnea, wheezing, stridor, laryngeal edema, respiratory distress, dyspnea, chest pain), dermatologic (urticaria, lip or facial edema), gastrointestinal (nausea, vomiting, abdominal pain), other (anxiety, feeling of impending doom, diaphoresis).

^bRevised from infusion in the original definition to insertion of PICC line for this study.

^cOnset within minutes to hours scenario was chosen and allowed for consistency with the other 2 definitions.

[†]For consistency, exclusion of other diagnoses was used across all definitions.

Results

Patients at 2 tertiary-care hospitals in Calgary were identified between 2010 and 2014 that experienced adverse clinical reactions following insertion of the PowerPICC SOLO or Groshong PICC using the Sherlock TLS. There were 5,957 insertions from site A and 2300 from site B during this period ($n = 8,257$). In total, using the PowerPICC SOLO or Groshong PICC, 32 reactions from site A (0.54%) and 5 reactions from site B (0.22%) were observed that were noted to represent significant adverse events (mean event rate, 0.45%). Notably, all 37 reactions occurred within minutes of PICC insertion. Several definitions (Table 1) were used to determine whether individual events met criteria for anaphylaxis or anaphylactoid reactions. From all reactions recorded, those meeting criteria included 34 of 37 (91.9%) using definition 1, 30 of 37 (81.8%) using definition 2, and 20 of 37 (54.1%) using definition 3.

To elucidate interrater significance between 2 clinical experts, patients who met criteria for anaphylactic or anaphylactoid reactions were weak agreement for criteria 1 and moderate agreement for both criteria 2 and 3. In general, using definition 2 had the highest κ agreement, where a range of 51%–59% of patients met criteria for anaphylactic or anaphylactoid reactions following PICC insertion.

To further determine whether anaphylactic or anaphylactoid reactions were limited to a single delivery system, a comparison population was used by PICC insertion using the BioFlo PICC across centers in Ottawa ($n = 7,889$) and Calgary ($n = 491$). Again, using all 3 definitions, none met criteria for anaphylactic or anaphylactoid reactions.

To determine whether differences in reactions occurred between the varying PICC insertion systems, reactions using the PowerPICC SOLO or Groshong PICC without the magnetized stylet versus the BioFlo PICC were compared; no difference was observed ($P > .05$).

In contrast, anaphylactic or anaphylactoid reactions were significantly more likely to occur using the PowerPICC SOLO with the magnetized stylet as compared to The Ottawa Hospital cohort (0 of 15,252) without the magnetized stylet ($P < .0001$), with significance maintained across all 3 definitions. Finally, anaphylactic or anaphylactoid reactions were significantly associated with the PowerPICC SOLO or Groshong PICC with the magnetized stylet as compared to the BioFlo PICC ($P < .0001$), again across all definitions.

All those with significant adverse reactions ($n = 37$) were identified, and demographic and treatment information was extracted (Table 2). The median age of patients was 46.5 years old (IQR, 18–76), and most were female (31, 79.5%). The indications for PICC insertion consisted primarily for the provision of long-term intravenous antibiotics (25 of 37, 67.6%), venous access (8 of 37, 21.6%), parenteral nutrition (1 of 37, 2.7%), and chemotherapy (1 of 37, 2.7%). Of patients with reactions, over half had documented preceding drug and environmental allergies (21 of 37, 56.8%), with one-third demonstrating multiple allergic responses (13 of 37, 35.2%). Only 2 of 37 patients were on angiotensin converting enzyme inhibitors. All sites in both Calgary and Ottawa used identical skin preparations, buffered lidocaine, flushes, and similar dressings. No apparent deviations in aseptic technique were identified at any of the sites and type of infusion between sites was similar.

Among those with reactions, the largest subset of patients experiencing adverse reactions had cystic fibrosis (CF) ($n = 4$, 10.8%). All 4 patients met criteria for anaphylactic or anaphylactoid reactions across all 3 definitions, and 2 patients (50%) were described as having serious reactions. Patients 20 and 28 both incurred significant respiratory compromise during PICC insertion, resulting in a severe clinical demise requiring activation of

Table 2. Demographics of Patients Exhibiting Reactions to PICC Insertion

Patient	Age	Gender	Clinical Background	PICC Indication	Allergies	Anxiety	Facial Flushing ^a	CP	SOB ^b	Doom ^c	Diaphoresis
1	35	F	Ovarian abscess	Antibiotic therapy	Penicillin, latex	+	–	+	+	–	–
2 ^d	54	M	Emphysema	Antibiotic therapy	NKDA	–	N/A	–	+	–	–
3	30	F	Lumbar spine infection	Antibiotic therapy	Morphine, cefazolin, nickle, adhesive, chlorhexidine, betadine	N/A	+	+	+	–	N/A
4	46	F	Breast cancer	Chemo-therapy	Penicillin	N/A	+	N/A	–	+	–
5 ^e	21	F	Cystic fibrosis	Antibiotic therapy	Tape, chlorhexidine	–	+	N/A	–	N/A	+
6	26	F	VP shunt infection and spina bifida	Antibiotic therapy	Diphenhydramine, codeine, sulfamethoxazole, vancomycin, latex, cephalixin	–	+	N/A	+	–	–
7	64	F	Pituitary tumor and acromegaly	Venous access	Meperidine, morphine, latex, nicotine patch	+	+	N/A	–	+	
8	53	F	Aneurysms	Antibiotic therapy	Penicillin	+	+	N/A	–	+	+
9	31	F	Facial osteomyelitis	Antibiotic therapy	NKDA	N/A	+	+	–	+	N/A
10	66	M	Sarcoma	Venous access	NKDA	–	N/A	+	N/A	+	–
11	57	M	Osteomyelitis discitis	Antibiotic therapy	NKDA	–	+	–	–	+	–
12	64	F	Pseudomyxoma	Antibiotic therapy	NKDA	N/A	+	–	–	–	+
13	33	F	Crohn's Disease	Antibiotic therapy	Morphine	N/A	+	+	+	+	+
14	68	F	L3-S1 Fusion	Antibiotic therapy	NKDA	–	+	–	+	+	+
15	65	F	Thymectomy	Antibiotic therapy	Penicillin, egg	–	+	+	N/A	+	+
16	37	F	Breast Cancer	Venous access	NKDA	–	–	+	–	–	–
17	18	F	Small bowel obstruction	Venous access	NKDA	N/A	+	N/A	+	+	–
18 ^e	46	F	Cystic fibrosis	Antibiotic therapy	NKDA	–	+	N/A	+	+	–
19 ^d	56	M	Pancreatic Cancer	Venous access	Sulfamethoxazole, penicillin	–	–	–	+	–	–
20 ^{de}	42	F	Cystic fibrosis	Antibiotic therapy	Tape	–	–	+	–	+	–
21	63	F	Sarcoma	Antibiotic therapy	NKDA	–	+	+	+	–	+
22	69	F	Colon Cancer	Venous access	Penicillin	N/A	+	–	+	–	–
23	78	M	Infected right TKR	Antibiotic therapy	NKDA	–	+	–	–	+	+
24	39	F	Klatskin tumour	Antibiotic therapy	Diphenhydramine, morphine, hydromorphone	N/A	+	+	N/A	N/A	+
25	26	M	Paraganglioma	Venous access	NKDA	–	+	+	+	–	+
26	35	F	C-section	Antibiotic therapy	Sulfamethoxazole	–	+	+	+	+	–
27	32	F	Left hip infection	Antibiotic therapy	NKDA	N/A	+	+	–	–	–
28 ^{de}	27	F	Cystic fibrosis	Antibiotic therapy	Tape	–	+	–	–	+	+
29	45	F	Post-op spine infection	Antibiotic therapy	Penicillin, morphine	–	+	–	+	+	+
30	68	F	Crohn's Disease	Enteral nutrition	Penicillin, eggs	–	+	N/A	N/A	–	+
31	44	F	Nesidioblastosis	Antibiotic therapy	Sulfamethoxazole, Morphine	–	+	+	+	–	+
32	57	F	Peritonitis	Antibiotic therapy	NKDA	–	+	–	+	N/A	+
33	68	F	Infected Tibia and Fibula	Antibiotic therapy	Dust, feathers	+	+	+	+	+	–
34	71	F	HSV Meningitis	Antibiotic therapy	Clindamycin, metronidazole, tetracycline, cefazolin, anileirdine, nitrofurantoin	+	+	+	+	–	–

(Continued)

Table 2. (Continued)

Patient	Age	Gender	Clinical Background	PICC Indication	Allergies	Anxiety	Facial Flushing ^a	CP	SOB ^b	Doom ^c	Diaphoresis
35	33	F	Hyperemesis gravidarum	Venous access	NKDA	–	+	–	+	–	–
36	82	F	Post-op infection hernia repair	Antibiotic therapy	Tape, tetracycline	N/A	+	–	–	N/A	+
37	38	F	Osteomyelitis of right jaw	Antibiotic therapy	NKDA	–	+	N/A	N/A	–	+

Note. NKDA, no known drug allergies; N/A, no available data from clinical records; CP, chest pain; SOB, shortness of breath.

^aFacial flushing noted as the physical sign of moderate to severe erythema of the facies with 1 patient noted to have urticaria in addition to facial erythema.

^b6 patients had documented desaturations (range, 51%–92%); additional 3 patients had tachycardia (range, 106–144).

^cDoom, a sense by the patient of impending clinical demise.

^dDenotes immediate life-threatening clinical compromise requiring calling of a code, or death within 30 d (all were code incidents and no deaths were recorded).

^eDenotes patients with cystic fibrosis.

the “code blue” system and intensive care unit (ICU) team intervention. In contrast, only 2 other patients from the remainder of the cohort (excluding CF patients) experienced similar severe reactions requiring ICU intervention (6.1%). A retrospective assessment of the Ottawa cohort revealed CF patients who did have PICC insertion, but no adverse reactions were noted, in contrast to this study.

At our center, in the CF population, the rate of PICC insertion is estimated to be 25–40 per year among a population of 160 patients. In addition, the incidence rate of anaphylactic or anaphylactoid reactions in the CF population at our center was 10%–16%, significantly higher than non-CF patients ($P < .001$). Of the 4 CF patients, 3 (75%) had documented allergies, notably all to tape or tape adhesive.

Discussion

Complications of PICC insertions have generally been described in the published literature as case reports, which may introduce bias with limited available evidence. To better understand the natural history of and risk factors associated with PICC adverse events, prospective observational studies are required. A recent large retrospective cohort study of 656 patients demonstrated catheter-related bloodstream infections (0.6%), deep venous thrombosis (1.5%), superficial venous thrombosis (2.1%), and requirement of thrombolytics for occluded catheters.¹⁴ The authors acknowledged lower rates of serious PICC-related complications than prior reports, in part due to expertise from trained nursing staff for insertion. Our study focuses specifically on anaphylactic or anaphylactoid reactions occurring exclusively with the use of the PowerPICC SOLO or Groshing PICCs with the magnetized Sherlock TLS. In Ottawa, from October 1998 to April 2012, of 12,585 PICC insertions, a total of 1,947 (15.5%) demonstrated complications, but no clear anaphylactic or anaphylactoid reactions occurred (personal communication, S McDiarmid, September 2015).

Compared to central venous catheters, midline catheters serve as an alternative for nonpermanent vascular access device toward noncaustic drug delivery with different anatomical endpoints for tip termination.² Despite the benefits listed, in 1990 the Food and Drug Administration (FDA) in the United States released data on Landmark midline reactions (Menlo Care, Menlo Park, CA) where multiple cases of adverse events (including 3 cardiac arrests and 2 deaths) were observed following their insertion.²⁰ Similarly, a

large prospective study by Mermel et al¹⁰ assessing midline catheter-related infections among hospitalized patients noted several severe clinical adverse events during insertion including erythroderma, hypotension, chest tightness, and shortness of breath. In total, Mermel et al¹⁰ found 53 cases of adverse events with prominent clinical features highlighting, urticaria, abdominal pain, and dyspnea.²⁰ The etiology behind these hypersensitivity reactions has been speculated to occur from sources including catheter components (intrinsic or extrinsic material), residual material associated with packaging of the catheter, injectable fluids and medications, or anatomic location.¹⁰ Notably, the authors concluded that these adverse events represented hypersensitivity as opposed to anaphylactic or anaphylactoid reactions, which have been limited to case reports in the literature.

In our study, we identified a disproportionate number of patients with CF who met the clinical criteria for anaphylactic or anaphylactoid reactions. Indeed, there are similar case series of CF individuals experiencing anaphylactoid reactions with vascular access device insertions in the literature.^{6,7} It is unclear why patients with CF appear to be disproportionately affected, and to our knowledge, there have been no other reports in the literature, apart from those presented here. We curtailed the use of PICCs with the use of the magnetized stylet at our centers following this analysis. Given the high rates of antibiotic allergy in the CF population compared to the general population, there may be an element of IgE-mediated immediate anaphylaxis.²¹ In the Haworth series, patient skin tests to water extracts from the line, guide wire, and gloves failed to provide a positive reaction. Additionally, IgE-specific antibodies to latex and ethylene oxide were normal, suggesting an alternative mechanism. In CF patients with allergic bronchopulmonary aspergillosis (ABPA), flow cytometry studies after exposure to antigen have shown that blood basophils are primed and subsequently hyperresponsive.²² Thus, there may be a role in antigen stimulation by PICC components in CF patients related to basophilic response; however, this is an area for future study.

One potential explanation for the anaphylactic or anaphylactoid reactions we observed may be related to the magnetized stylet component of the PowerPICC SOLO. Components within the magnet stylet (neodymium) have been shown to be a major stimulus for basophil and or mast cell degranulation.²³ Furthermore, heavy metals including silver and gold have been shown in vitro to potentiate mast cell activation.^{24,25} Potential leaching of the stylet components into a major vessel may

possibly implicated in the anaphylactic or anaphylactoid reactions observed in our study.

The discrepancy in anaphylactic or anaphylactoid reactions between 2 sites, Ottawa and Calgary, raises several points. A retrospective review confirmed similar procedures between the 2 sites: identical skin preparation, buffered lidocaine, saline flushes, and skin dressings. Within the Calgary Health Zone, there were no differences between devices manufactured at different times (ie, different lots). At all insertions, aseptic technique was utilized adequately as evaluated by independent infection and prevention control. The discordance may be in part due to a selected patient population who are prone to allergic manifestations, including CF individuals.

Our study demonstrates several limitations, including the use of a retrospective cohort analysis for the comparative population. Given that categories are nominal (ie, absent or present) for criteria to meet definitions for anaphylaxis or anaphylactoid reactions, there is always a concern with interpretation of more subtle clinical presentations. We acknowledge the possibility of other explanations for the observed clinical events, but we used 2 expert clinicians in a nonbiased observational manner to try to mitigate these concerns. In addition, the reporting of very similar reactions using the PowerPICC SOLO or Groshing PICC with the Sherlock TLS within the US FDA Center for Devices and Radiological Health Medical Product Safety Network (MedSun) and the Canadian Medical Devices Sentinel Network – Health Canada Reporting Project provides supportive evidence for our observations. Notably, the manufacturer was advised of the concerns and responded by updating its labeling to indicate that anaphylactic or anaphylactoid-like reactions occur in a small percentage of the population during placement, positioning, flushing of CVCs or cleaning of the catheter exit site. Alternative definitions, such as the accepted Brighton definition for anaphylaxis,²⁶ may increase specificity of true anaphylactic reactions but will require further quality control assessment. Additionally, our study lacked a control group and thus may limit the generalizability of results to other populations.

The clinician should be cognizant of the number of models and manufacturers of PICCs and the numerous proprietary materials. As such, findings pertaining to a particular type of product may not translate to others. Finally, the nature of the mechanism behind anaphylactic or anaphylactoid reactions in these patients may be multifactorial and requires further studies to discern biological plausibility.

In conclusion, this study highlights potential anaphylactic or anaphylactoid reactions with insertion of PowerPICC SOLO or Groshing PICC using the Sherlock TLS. Given the disproportionate rate of anaphylactic or anaphylactoid-like reactions following PICC insertion observed in CF patients (ie, 10- to 20-fold higher compared to the general population, 10%–16% vs 0.5%), our observations suggest the need for additional clinical vigilance in the CF population. Furthermore, these findings suggest that disease-specific reports of adverse reactions associated with medical devices may be important in identifying their biological basis.

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