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Catheter-related complications in children with cancer receiving parenteral nutrition: Change in risk is moderated by catheter type

Melissa A. Shenep, BSc[1,*], **Mary R. Tanner, MD**[1,*], **Yilun Sun, MS**[2], **Tina Culley, BSc**[1], **Randall T. Hayden, MD, PhD**[3], **Patricia M. Flynn, MD, MSc**[1], **Li Tang, PhD**[2], and **Joshua Wolf, MBBS, BA, FRACP**[1,4,**]

[1]Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, Tennessee

[2]Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, Tennessee

[3]Department of Pathology, St. Jude Children's Research Hospital, Memphis, Tennessee

[4]Department of Paediatrics, University of Melbourne, Parkville, Victoria, Australia

Abstract

Background—Long-term central venous catheters (CVCs) are essential to the care of pediatric oncology patients, but complications, such as occlusion and central line–associated bloodstream infection (CLABSI), are common. Although administration of parenteral nutrition (PN) increases the risk of complications, the effect of CVC-type on this increase is unknown.

Methods—This was a retrospective matched cohort study of pediatric oncology patients who received PN through subcutaneous ports or external CVCs. Complication rates were compared between CVC-types and between PN and non-PN periods using a log-negative binomial model.

Results—The risk of CLABSI was higher during PN than non-PN periods for children with ports (RR 39.6, 95% CI 5.0–309; 3.6 vs. 0.1 events/1000 days) or external CVCs (RR 2.9, 95% CI 1.1–7.4; 2.7 vs. 0.7 events/1000 days). The increase in risk during PN was significantly greater for ports than for external CVCs (RRR = 13.6, 95%CI 1.4–130.5). The relative increase in occlusion risk during PN was also significantly greater for ports than external CVCs (RRR 4.9, 95% CI 1.6–14.5; RR 10.0 vs. 2.0). Because of this, absolute complication rates were similar during PN.

Conclusion—Despite advances in supportive care, children with cancer who receive PN are at increased risk of CLABSI and occlusion. The risk increase is greatest in children with ports, with a 40-fold increase in infection risk and 10-fold increase in occlusion risk. Due to the more severe

**Corresponding author: Dr. Joshua Wolf, Department of Infectious Diseases, St. Jude Children's Research Hospital, 262 Danny Thomas Pl, Memphis, TN 38105, USA, Tel: 901 595 3300, Fax: 901 595 3099, Joshua.Wolf@stjude.org.

*Equal contribution

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clinical consequences of port-related complications, an external CVC is preferred for children with cancer who require PN.

Keywords

Child; Parenteral nutrition; Central venous catheter; Catheter-related infection; Venous thrombosis

Introduction

Long-term central venous catheters (CVCs) are an essential component of medical care for pediatric oncology patients. They provide reliable venous access for medication and fluid administration, collection of blood for laboratory testing, and nutritional support with parenteral nutrition (PN) when required. However, complications related to CVCs cause significant morbidity among pediatric patients with cancer; these complications include central line–associated bloodstream infection (CLABSI), occlusion of the CVC, and intravascular thrombosis.[1, 2] Past studies have indicated that PN administration is an important risk factor for many catheter-related complications.[3, 4]

There is limited information about risk factors for catheter-related complications during PN treatment in pediatric oncology patients. In other patient populations, the catheter type may contribute to the risk; for example, some studies of patients receiving PN found that the risk of CLABSI was higher in those with ports than in those with external CVCs[5–7], but others have found the opposite[8–10] or no apparent difference.[11–13] Under usual conditions, pediatric oncology patients with ports have a much lower rate of catheter-related complications than those with external CVCs, so the use of ports is preferred where feasible.[1, 14–16] However, clinical consequences of port complications are more serious because infections are more difficult to eradicate and surgery to replace the devices is more complicated.[17, 18] However, the effect of CVC type on the relative risk of complications in pediatric oncology patients during PN administration has not been well explored, so there is insufficient evidence to guide CVC choice in that setting.[3] This study was designed to assess the effect of CVC type and other clinical variables on CVC-related complications during PN administration in children with cancer.

Methods

Setting and Institutional Review

This retrospective matched cohort study was conducted at St. Jude Children’s Research Hospital, a 68-bed pediatric oncology referral center located in the southeast United States. The study was approved by the hospital’s Institutional Review Board before data collection was initiated (XPD14-043).

Selection of Participants

The study included two cohorts: Cohort 1 consisted of patients receiving PN through a port, and Cohort 2 consisted of a matched group of patients receiving PN through an external CVC. The external CVCs included peripherally inserted central catheters (PICCs) and external tunneled catheters (Hickman® or Broviac®). To identify eligible participants, the

pharmaceutical database was queried for all PN orders entered between January 1, 2006, and May 2, 2014, and the results were compared against a list of documented CVC types. The type of CVC in place during PN administration was verified by manual chart review. Fifty consecutive individuals were identified for Cohort 1 (PN administered through a port), and matched participants were sought by chart review to complete Cohort 2 (PN administered through an external CVC), according to an algorithm developed to identify a well-matched cohort. The participants were matched on a 1:1 basis. The algorithm accounted for the patient's age at diagnosis (± 5 years), the type of malignancy, whether the patient had undergone hematopoietic stem cell transplantation (HSCT), and the presence of severe malignant disease (defined as relapsed malignancy, chemotherapeutic treatment failure, or death from malignancy during the study period). Supplementary Figure 1 shows the branched matching algorithm.

Data Collection

Data were collected concerning the demographics, comorbidities, and treatment of the primary malignancy of each participant. The study period was defined as the period from the first PN dose until censoring for each participant. The censoring indications were death, loss to follow-up, change to the other type of CVC, CVC removal without replacement, removal of the last CVC through which PN was administered, and the end of the study. Death and CVC removal were regarded as competing risks. The dates of PN administration and the characteristics of the prescription were collected during the PN period. CVC-related complications, including bloodstream infection, catheter occlusion, drug extravasation, and intravascular thrombosis, were collected for the entire study period. The "PN period" included all the days on which PN was received and up to 14 days after PN was administered. The "non-PN period" included all days in the study period that did not meet those criteria.

To identify all the episodes of CLABSI, all positive blood cultures obtained during the study period were reviewed and categorized. CLABSI was defined according to the National Healthcare Safety Network (NHSN) criteria, with a modification to include episodes in which a common skin contaminant was isolated from a single blood culture and the treating clinician elected to treat the infection as CLABSI.[19] This modification is necessary to account for the usual practice in many pediatric oncology units whereby only one blood culture-set is collected from a single-lumen CVC before initiating parenteral antibiotics.[20] To identify episodes of occlusion, the institutional pharmaceutical database was queried for all orders for tissue plasminogen activator (TPA) entered during the study period; episodes of TPA administration were assumed to indicate CVC occlusion. Urokinase and other thrombolytic agents were not routinely used to treat CVC occlusion at the hospital during the study period

Statistical Analysis

The demographic characteristics of the matched cohorts were examined with the Wilcoxon signed-rank test for continuous variables or McNemar's test for categorical variables. To minimize the discrepancy among patient characteristics other than the variable of interest, the two matched cohorts were used to compare the absolute event rates for the ports and

external CVCs. Conversely, the entire cohort was used to assess the differences in risk between the PN period and non-PN period, as each cohort could act as their own control.

The duration of the PN and non-PN periods and the counts of CVC-related complications during each period were calculated for each patient by summing the days, and categorizing each event by time period. The rate of each complication was defined as the number of observed events in each time period divided by the total duration of that time period, with one day being added to the observed period for purposes of statistical analysis. To control for correlated observations or matching effect, log-negative binomial models with a generalized estimating equation (GEE) framework were used to estimate the relative complication rates for the PN and non-PN periods and for children with ports and those with external CVCs during each period.[21–23] The same technique was used to calculate 95% confidence intervals for the relative rates, which were considered to be statistically significant if the confidence interval did not include the value 1. Cumulative incidence analyses, stratified by CVC-type, were used to compare the incidence of CLABSI according to dichotomous variables, including gender, race (white vs. non-white) and age (greater vs. less than the median). Because of concerns regarding competing risks and potential violation of the proportional hazards assumption, a modified Fine-Grey analysis was applied.[24, 25] Death and line-removal were considered to be competing risks, as each would preclude the occurrence of CLABSI. When there were no events in at least one group, Fisher's exact test was used without regard to time-at-risk; this applied only to the type of malignancy (hematological vs. solid) for both ports and external CVCs, and to patient age for external CVCs. Unadjusted *P*-values of less than 0.05 were considered statistically significant for all analyses. Statistical analyses were performed using SAS (SAS Institute, Cary, NC), Windows version 9.3.

Results

Study Population

During the study period, 50 patients who had received PN through ports were identified for inclusion. The characteristics of this population are presented in Table 1. A matched cohort of 40 patients who received PN through external CVCs was identified by using the algorithm described above (Cohort 2). No matches were found for 10 patients. The characteristics of the matched cohorts are also shown in Table 1. Although children with external CVCs were somewhat younger and received PN for longer periods than those with ports, matching was otherwise effective in reducing the apparent differences between the two groups.

Of the 50 participants with ports, 8 (16%) experienced at least one episode of CLABSI during the PN period, and 21 (42%) experienced at least one episode of occlusion. The median time from the initiation of PN to the first CLABSI was 58.5 days (range, 22–84 days). Other catheter-related complications that occurred during the PN period included thrombosis (1 episode) and extravasation of PN fluid into the port pocket (4 episodes in 3 participants). One participant developed perforation of the posterior port hub requiring device removal. The CLABSI rate was markedly higher during the PN period than during the non-PN period (RR = 39.6; 95%CI 5.0–309; 3.6 vs. 0.1 events/1000 days). The rate of occlusion was also significantly higher during the PN period (RR = 10.0, 95%CI 4.4–22.8;

11.3 vs. 0.6 events/1000 days). The event rates for each of these complications during the non-PN period were similar to those in published data for ports in children with cancer (0.11–0.68 for CLABSI[14, 26–28] and 2.2 for occlusion[29]).

Effect of Catheter Type on Risk of Complications during Parenteral Nutrition

Using the entire cohort ($n = 90$), we compared the relative increase in the rates of complications between the PN and non-PN periods for each CVC type. As with ports, external CVCs showed an increase in the rate of both CLABSI (RR 2.9 95%CI 1.1–7.4; 2.7 vs. 0.7 events/1000 days) and occlusion (RR 2.0, 95%CI 1.0–4.1; 12.7 vs. 3.7 events/1000 days) during the PN period. However, the relative increase in risk of CLABSI during the PN period was significantly greater in children with ports than in those with external CVCs (RR 39.6 vs. 2.9; RRR = 13.6, 95%CI 1.4–130.5; $P = 0.02$). Likewise, the relative increase in the rate of occlusion during PN was significantly greater in children with ports than in those with CVCs (RR 10.0 vs. 2.0; RRR = 4.9, 95%CI 1.6–14.5; $P = 0.004$).

To determine whether the absolute risk of catheter-related complications during PN administration was affected by catheter type, we compared the rates of these events in the 80 participants constituting the matched cohorts. During the non-PN period, the CLABSI rate was lower in children with ports than in those with external CVCs (RR 0.2; 95%CI 0.01–1.2; 0.2 vs. 0.7 events/1000 days). However, during the PN period, the rate of CLABSI was paradoxically higher in children with ports, though this difference was not statistically significant (RR = 1.4; 95%CI 0.5–3.7; 4.6 vs. 2.7 events/1000 days). Similarly, during the non-PN period, the rate of occlusion was significantly lower in children with ports (RR = 0.2, 95%CI 0.06–0.7; 0.6 vs. 3.7 events/1000 days) but during the PN period, the rate was not significantly different (RR 0.7; 95%CI 0.3–1.5; 8.5 vs. 12.7 events/1000 days).

Other Risk Factors for CLABSI During Parenteral Nutrition

During the PN period, children with solid tumors had a higher risk of CLABSI than those with hematological malignancies regardless of CVC-type (22% vs. 0%; $P = 0.01$). For children with external CVCs only, the risk of CLABSI was significantly greater in younger than older patients (29% vs. 0%; $P = 0.03$). However, age was not a significant predictor of CLABSI risk in children with ports ($P = 0.2$). There were no significant differences in the risk of CLABSI by gender ($P = 0.6$) or race ($P = 0.7$).. Patients with solid tumors had a PN period of longer mean duration than that of those with hematological malignancies (76 vs. 54 days), as did younger children with external CVCs (93 vs. 85 days).

Discussion

This study confirms that, despite significant advances in supportive care, children with cancer who receive PN are still at markedly elevated risk of developing CVC-related complications.[3, 4, 30, 31] The two most frequent complications identified were CLABSI and CVC occlusion. These complications are important, as both are associated with morbidity and mortality in this patient population.[26, 32–34]

Consistent with the published data, both CLABSI and occlusion appeared to be less frequent in children with ports than in those with external CVCs during the non-PN

period.[14, 18, 30, 35] However, during the PN period, there was no significant difference in the absolute complication rates according to CVC type. This resulted from the markedly greater increase of risk in children with ports. As shown in Table 2, previous investigations of the effect of device type on CVC complications have yielded conflicting results, but in this study, the usual difference in complication rates between CVC types was eliminated during PN administration. This supports the findings of those studies suggesting that device type does affect the relative risk of complications during PN.

Central Line–Associated Bloodstream Infection

Current evidence suggests that the development of CLABSI in patients with long-term CVCs is related to the development of luminal aggregations of microorganisms in complex communities called biofilm.[36] This biofilm allows microorganisms to remain sessile on the surface of the device, protected from immune and antibiotic killing. The increased risk of CLABSI associated with PN in all CVC types might be related to the sugar and nutrient content of the PN fluid or to increased handling of the CVC during PN administration. Similarly, the greater relative increase in patients with ports could be related to the increased duration or frequency of transcutaneous needle access, which allows microorganisms access to the luminal surface.[8]

This increased risk of CLABSI is important because these infections are associated with additional antibiotic exposure, chemotherapy delay, sepsis, and even mortality.[2] Attributable mortality in pediatric oncology patients is usually estimated at around 2%[26] but has been reported to be as high as 9.6%.[33] In US pediatric oncology patients, CLABSI results in a mean attributable length of hospital stay of 21 days and a mean cost of $69,332.[37] The greater increase in the risk of infection associated with PN use in children with ports is important because this change eliminates the lower infection risk that is one of the primary advantages of these subcutaneous devices. Furthermore, previous studies have definitively demonstrated that outcomes of CLABSI are significantly worse for patients with ports. Specifically, infections are more likely to be prolonged, the rate of relapse is up to 5-fold higher than for patients with external CVCs, and the surgical procedures required to remove or replace ports are much more complex.[17, 18]

Because of the high risk of infection, adjunctive methods of prevention and treatment of CLABSI in pediatric oncology patients with ports should be considered during PN. However, currently available treatments, such as lock therapy with antibiotics or hydrochloric acid, are not well supported by available data.[2, 38–40] A recent study showed that weekly ethanol lock therapy (ELT) can reduce the risk of CLABSI in pediatric oncology patients but the investigators did not report whether any participants received PN, and other studies have raised concerns that ELT could damage ports with polyurethane catheters.[41–43]

Patients with solid tumors had a higher incidence of CLABSI than did those with hematological malignancies. This is interesting, because, under normal circumstances, the ratio is usually reversed[47, 48] or equal.[14] The reason for this is unclear, but it might be related to the different reasons for PN being required, such as oromotor incoordination in children with brain tumors leading to external contamination of the CVC with oral secretions.

Catheter Occlusion

This study confirms an increased risk of occlusion associated with PN. However, the significantly greater relative risk of occlusion during PN compared to non-PN periods in children with ports is a novel finding. This is important, because occlusion events are associated with clinically significant adverse outcomes. Specifically, up to 20% of occlusion events require CVC replacement, and attempts to clear the obstruction can lead to CVC fracture or rupture.[41, 49–51] Even after successful treatment of occlusion, the risk of CLABSI and venous thrombosis is significantly elevated.[34, 49, 52] Lastly, two separate studies have shown that pediatric oncology patients who experience CVC occlusion have a higher risk of all-cause mortality.[32, 34] In the context of excellent evidence for associated harm, the marked increase in the risk of occlusion with PN administration, especially in ports, is a major concern. There is some evidence that imminent CVC occlusion can be predicted by monitoring catheter resistance, so future studies of this method could focus on children receiving PN.[53, 54]

Other Complications

Although previous studies have suggested that intravascular thrombosis is more common in children receiving PN, there was no difference detected in this study as the absolute number of thrombotic events was low.[55] PN extravasation into the port pocket was seen in three patients, in one case being related to perforation of the port. Perforation of plastic ports has been described previously, but PN might have contributed to its occurrence in this case as it requires frequent, prolonged port access.[56]

Study Strengths and Limitations

This study has several limitations. The retrospective nature of the data collection means that some outcomes or exposures may have been missed. Similarly, retrospective matching is imperfect and may fail to account for unrecognized risk factors for outcomes of interest. In this study, the children with ports were slightly older than those with external CVCs, which might have affected the risk of CLABSI or occlusion. However, this would not be expected to affect the relative risk ratio between ports and external CVCs, as each cohort acted as their own control for that analysis. An alternative explanation of the strong temporal association between PN and CLABSI could be that the requirement for PN is a marker for gastrointestinal tract dysfunction, which in turn might lead to bacteremia by translocation rather than via CVC luminal biofilm. However, data from other studies suggest that most bloodstream infections in pediatric oncology patients are indeed CVC-related, and propensity score analysis in adult patients has identified PN as an independent risk factor for CLABSI.[4, 18] The use of TPA administration as a surrogate for CVC occlusion is imperfect and may miss some cases that self-resolved or received alternate management; however, this is unlikely to differ by CVC type. These findings could be affected by line-care regimens, such as the use of CVC for collection of blood samples for laboratory tests, and cleaning technique, which differs between institutions. The use of unadjusted *P*-values to determine the significance of differences between groups could increase the possibility of type 1 error. We did, however, predetermine that differences in the complication rates for CVC types

during PN administration would be the primary analysis, so interpretation of this outcome is not affected.

The main strengths of this study relate to the study design and statistical analysis. The relative homogeneity of these pediatric oncology patients treated contemporaneously at a single center reduced the risk that unrecognized variations in institutional practice would affect the results. Furthermore, using a carefully matched cohort to compare absolute complication rates ameliorated the effect of potential confounders, such as the type of malignancy, HSCT status, and patient age on the results. A generalized estimating equation framework was used for the analysis, allowing us to control for potentially correlated observations, such as an increased risk of subsequent CLABSI after a first episode, and to preserve statistical power. Similarly, using each cohort as their own control for the comparison of the relative risk of complications between ports and external CVCs reduced the risk of unrecognized differences between cohorts affecting the analysis. Finally, using the modified NHSN criteria for retrospective diagnosis of CLABSI allowed a pragmatic categorization of positive blood cultures that was not biased by the more frequent collection of paired blood cultures from external catheters than from ports.

Implications for Clinical Practice and Future Research

Guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN) for PN in adults and from ESPEN and the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) for PN in children both recommend preferential use of external CVCs in patients who will require medium- to long-term PN.[57, 58] However, the evidence provided to support these recommendations was limited. The pediatric guidelines state that the recommendation for avoidance of ports is Level of Evidence 2+, which is defined as being based on “well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal.” The adult guidelines state that “ports are appropriate…[for]…medium-term” use but that “for prolonged use and home parenteral nutrition (> 3 months)… requiring frequent (daily) access, a tunneled device is generally preferable.”

The present study supports the recommendations in these guidelines. However, even relatively short-term administration of PN was associated with a significant complication risk in children with ports, with a median time to CLABSI of less than 2 months. Some options available for pediatric oncology patients with ports who subsequently require PN include removal and replacement of the port with an external CVC; insertion of a temporary external CVC; addition of adjunctive prophylaxis, such as ethanol or antibiotic catheter lock therapy; or close monitoring for complications without adjunctive therapy. There is currently insufficient evidence to support favoring any of these options, and more research examining these interventions during the PN period is needed.

Conclusions

There is a marked increase in the risk of CLABSI and CVC occlusion in pediatric oncology patients receiving PN. Although absolute risk of complications during PN did not differ by CVC-type, the increase in risk and clinical ramifications are significantly greater in children

with ports than in those with external CVCs. These complications are important, as they can have a major effect on the provision of chemotherapy and other life-sustaining care. Enteral feeding should be used wherever possible to reduce the requirement for PN, but this is often unachievable. The optimal management of pediatric oncology patients with ports who subsequently require initiation of parenteral nutrition remains unclear, but adjunctive preventive therapy should be considered. If a pediatric oncology patient is anticipated to require PN at the time CVC insertion is planned, strong consideration should be given to primary insertion of an external catheter to avoid the high risks of port-related complications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

95% CI	95% confidence interval
ALT	antibiotic lock therapy
CVC	central venous catheter
ELT	ethanol lock therapy
HSCT	hematopoietic stem cell transplantation
PICC	peripherally inserted central catheter
Port	subcutaneous port
RR	relative risk
RRR	ratio of relative risks

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Clinical Relevancy Statement

Pediatric oncology patients frequently require parenteral nutrition because of difficulties in swallowing or other impediments to enteral nutrition. The administration of parenteral nutrition increases the risk of catheter-related complications, such as bloodstream infection and catheter occlusion. This study examined the effect of catheter type on the frequency of these complications, comparing patients with totally implantable ports to those with external catheters.

Although the risk of complications was increased with all catheter types, the increase was greatest in patients with ports, who had a 40-fold increase in the risk of infection and a 10-fold increase in the risk of occlusion.

These findings should be considered when deciding which catheter type to use in pediatric oncology patients who are expected to require parenteral nutrition. The results also raise important questions about the optimal management of patients with ports who subsequently require parenteral nutrition.

Table 1

Characteristics of Included Participants.

Patient Characteristics	All Port Patients	Matched Patients		
	Port *n* = 50	Port *n* = 40	External CVC *n* = 40	
	Median (Range)	Median (Range)	Median (Range)	*P*=
Age (y)	7.3 0.7–24	6.5 0.7–24	2.6 0.5–22	0.38[b]
Study period (d)	162 5–823	134.5 5–823	211 30–864	0.62[b]
PN period (d)	35 5–229	37 5–229	55 25–343	0.06[b]
	n (%)	*n* (%)	*n* (%)	*P*=
Sex				0.83[c]
Female	23 (46)	18 (45)	19 (47.5)	
Male	27 (54)	22 (55)	21 (52.5)	
Race				0.11[c]
White	32 (64)	24 (60)	31 (77.5)	
Black	15 (30)	13 (32.5)	7 (17.5)	
Other or “mixed”	3 (6)	3 (7.5)	2 (5)	
CVC type[a]				N/A
Port	50 (100)	40 (100)	0	
External CVC				
Tunneled	0	0	38 (87.5)	
Non-tunneled	0	0	4 (12.5)	
Primary malignancy				1.0[c]
Hematologic				
ALL	8 (16)	4 (10)	6 (15)	
Lymphoma	4 (8)	1 (2.5)	1 (2.5)	
Other	3 (6)	3 (7.5)	1 (2.5)	
Solid tumor				
Brain tumor	13 (26)	13 (32.5)	12 (30)	
Bone tumor	6 (12)	5 (12.5)	5 (12.5)	
Other solid tumor	16 (32)	14 (35)	15 (37.5)	
HSCT	6 (12)	6 (15)	6 (15)	
Number of PN episodes				0.36[c]
1	42 (84)	32 (80)	31 (77.5)	
2	6 (12)	6 (15)	8 (20)	
3	2 (4)	2 (5)	0	
4	0	0	1 (2.5)	
PN Regimen				0.25[c]
Continuous	34 (68)	27 (67.5)	22 (55)	
Cycled or mixed	16 (32)	13 (32.5)	18 (45)	

HSCT, hematopoietic stem cell transplantation; TPN period, sum of the number of days on which PN was received, or up to 14 days after receiving PN during the study period; ALL, acute lymphoblastic leukemia.

[a] 4 participants had both tunneled and non-tunneled external catheters during the study period

[b] Wilcoxon signed rank test

[c] McNemar's test

Table 2a

Studies of the Effect of CVC Type on Risk of Infectious Complications during PN.

Study	Study Design	Population (Age)	No. of Patients (Port vs. External CVC)	Infection Risk (Port vs. External CVC)	*P*-value
Santarpia *et al.*	Prospective consecutive	All PN patients (38–76 y)	159 vs. 71	23% vs. 10%	$P = 0.03$
Shirotani *et al.*	Retrospective chart review	All PN patients (46–75 y)	23 vs. 45	0.5 vs. 0.5/1000 d	$P = 0.4$
Pomp *et al.*	Retrospective and prospective	All PN patients (24–66 y)	15 vs. 21	0.4 vs. 2.5/1000 d	NR
Cotogni *et al.*	Prospective	Adult patients with cancer (29–85 y)	72 vs. 45	0.5 vs. 0.7/1000 d	NR
Buchman *et al.*	Retrospective chart review	All PN patients (6–87 y)	318 vs. 66	0.7 vs. 0.4/1000 d	$P = 0.001$
Christensen *et al.*	Prospective	Pediatric patients with cancer (0.1–21 y)	16 vs. 79	31% vs. 38%	$P = 0.78$
Bozzetti *et al.*	Retrospective questionnaire	All PN patients (20–89 y)	44 vs. 403	27% vs. 15%	$P = 0.04$
Gaggioti *et al.*	Retrospective chart review	Patients with both devices (32–65 y)	6 vs. 6	0.9 vs. 3.3/1000 d	NR
Howard *et al.*	Retrospective chart review	All PN patients (13–74 y)	27 vs. 48	0.6 vs. 0.7/1000 d	NR
Present study	Retrospective chart review	Pediatric patients with cancer (0.5–24 y)	40 vs. 40	4.6 vs. 2.7/1000 d	$P = 0.52$

PN, parenteral nutrition; CVC, central venous catheter; CLABSI, central line–associated bloodstream infection; NR, not reported; d, day; y, year. Where data were provided separately for the PN period, this is reported. Most studies combined data on site and bloodstream infection, but where CLABSI data were provided separately, this is the figure reported.

Table 2b

Studies of the Effect of CVC Type on Risk of Mechanical Complication during PN.

Study	Study Design	Population (Age)	No. of Patients (Port vs. External CVC)	Occlusion Risk (Port vs. External CVC)	*P*-value
Bozzetti *et al.*	Retrospective questionnaire	All PN patients (20–89 y)	44 vs. 403	25% vs. 2%	$P = 0.001$
Howard *et al.*	Retrospective	All PN patients (13–74 y)	27 vs. 48	0.1 vs. 0.3/1000 d	NR
Cotogni *et al.*	Prospective observational	Adult patients with cancer (29–85 y)	72 vs. 45	0.8 vs. 0.2/1000 d	NR
Present study	Retrospective chart review	Pediatric patients with cancer (0.5–24 y)	40 vs. 40	8.5 vs. 12.7/1000 d	$P = 0.35$

PN, parenteral nutrition; CVC, central venous catheter; CLABSI, central line–associated bloodstream infection; NR, not reported; d, day; y, year. Where data were provided separately for the PN period, this is reported.