Analysis Of Related Complications Of Totally Implantable Venous Access Ports In Children's Chemotherapy - Single Center Experience

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Research Article

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Abstract

Background: Totally implantable venous access ports (TIVAP) have become important infusion channels for children with tumors. With the popularization of TIVAP, its related complications have gradually received clinical attention. However, few studies have investigated the complications of TIVAP in children. Therefore, this study aimed to systematically analyze the risk factors of complications in children's infusion ports to provide a basis for guiding clinical prevention and intervention.

Methods: A total of 182 children who underwent TIVAP implantation and required long-term chemotherapy in our hospital between January 2018 and January 2021 were included. Based on the demographic data, basic disease status, and operation-related data obtained through ERS, SEC, and manual follow-up, the complications and related influencing factors after implantation and implantation were summarized and analyzed. The SPSS software was used to analyze the influencing factors between the complication and control groups.

Results: There were 182 children implanted in the intravenous infusion port, of whom 71 had complications. Infection was the most common complication in 50 cases, followed by catheter blockage in 23 cases. Among the infection factors, catheter-related bloodstream infection accounted for the highest proportion (31 cases,17.0%), and Staphylococcus epidermidis was the most common pathogen. Nineteen cases were pulled out early, and the unplanned pull-out rate of catheter-related bloodstream infection was the highest. In the analysis of influencing factors, age showed significant differences in catheter-related infection, all complications, and no complications ($P < 0.05$).

Conclusion: The overall incidence of complications associated with the use of TIVAP in children undergoing chemotherapy is high, and infection is the most common complication, among which catheter-related blood flow infection is the most common cause of unplanned pullout. A younger age may be associated with a higher incidence of complications.

1. Background

A totally implantable venous access port (TIVAP) is widely used in clinics because of its advantages of long-term retention, easy management, and low infection rate[1]. Although TIVAP has a higher acceptance than traditional peripheral intravenous chemotherapy, infusion port-related complications still occur during long-term use. The occurrence of complications will prolong the length of stay, increase additional hospitalization expenses, and lead to additional pain for children[2, 3]. An increase in unplanned port pulling will inevitably lead to secondary puncture, increase the risk of vascular injury and recurrent complications, and increase the medical burden. At present, the time of TIVAP implantation in developing countries is still short, and there are few studies specifically aimed at the related complications in children who need long-term chemotherapy for TIVAP. Based on the clinical data of 172 children who underwent TIVAP implantation at our center, this study evaluated the related complications and analyzed the risk factors, hoping to improve the awareness of early clinical prevention and treatment.

2. Methods

2.1. Patients

From January 2018 to January 2021, children who received TIVAP implantation and required long-term chemotherapy at the People's Hospital Affiliated to Ningbo University were included in this study. This study was approved by the Human Research Ethics Committee. All patients in the same group underwent surgery. All children were identified by an expert group before surgery according to the indications for TIVAP implantation[4]. Preoperative routine examinations showed no abnormal blood coagulation or contraindications before the operation.

2.2 Surgical technique of TIVAP placement

All children were under general anesthesia in the operating room. The venous access port device was manufactured by a bard company in the United States. It is a single-lumen catheter with a guidewire and peel-away sheath. We used an ultrasonography (USG)-guided surgical technique. We chose the internal jugular vein as the puncture site. The patient was in a supine position with the neck tilted to the opposite side and the shoulder slightly raised with support. First, we marked the body surface(Fig. 1) and made a 2–3 cm transverse incision 2 cm on the anterolateral aspect of the chest. A subcutaneous pocket is created on the inferior aspect to accommodate the port. The neck marking point is the ideal location for the puncture of the internal intravenous vein. A subcutaneous tunnel was created connecting both incisions, and the catheter was guided along the tunnel. USG-guided venepuncture is then performed through which the guidewire is inserted. The tract was then dilated using serial dilators. Gently rotate along the guide wire, insert the stripping sheath, and remove the sheath stylet. At this time, the pressure blood may gush out, and the operator can block the sheath with his thumb to block the bleeding and then quickly insert the catheter. During the operation, bedside radiography was used to determine the appropriate position of the catheter head, the excess length was cut off, and the catheter was connected to the port and placed in the reserved subcutaneous pocket. Patency and reflux were ensured by injecting a heparin solution (10 U/ml)[5] and suction. Finally, we sutured the incision of the neck and chest (Fig. 2). After the operation, TIVAP was maintained according to the consensus of Chinese experts[4]. The catheter was flushed and sealed according to the operating program. The catheter was flushed once every four weeks during the infusion interval.

2.3 Data collection

We obtained the general clinical data of patients through EMR and HIS, including sex, age, tumor type, chemotherapy received before operation, failure of the first puncture, time from completion of TIVAP to first use, absolute number of neutrophils, and operation time. These patients were followed up until the end of chemotherapy or unplanned port removal, and their complications were recorded, including infectious and non-infectious factors.

2.4 Statistical analysis

Data were analyzed using the Statistical Product and Service Solutions (SPSS) package (SPSS 13.0, for Macintosh. The measurement data are expressed as median (m), and the comparison between groups was performed using t-test; the counting data were in cases (%), the comparison between groups was used the χ 2 test or Fisher exact probability method, and logistic regression analysis was carried out for meaningful influencing factors. Differences were considered statistically significant ($P < 0.05$).

3. Results

3.1 General information

A total of 182 children (99 men and 83 women) with a median age of 45 (21–216) months were included in this study. The majority of patients in this group had haematological malignancies (123 cases, 67.6%). The first chemotherapy session in 89 children was performed after TIVAP implantation. The median time from TIVAP implantation to the beginning of chemotherapy was 3 (0–28)days. 93 children had received chemotherapy via other channels before TIVAP implantation, and the median time from TIVAP implantation to the beginning of chemotherapy was 10 (1–39) days.

3.2 Complications

In this group, 71 patients (71 / 182,39%) had complications, with 88 cases, of which infection-related complications were the most common, with 50 cases (50 / 88,56.8%). Staphylococcus epidermidis is the most common pathogen causing catheter-related bloodstream infections. Among all patients with complications, 19 had TIVAP removed due to complications, of which 16 had TIVAP removed due to concurrent infection (10 had catheter-related blood stream infection (CRBSI); 6 had local infection), and 3 cases were due to catheter obstruction. Further details are provided in Table 1.

Table 1
Port related complications and removal rate of complications

Complication	Number of cases occurred (n/%)	underwent port removal(n/%)
Infection factors		
Skin infections around the port	31(17.0%)	6(19.4%)
Catheter-related bloodstream infection	19(10.4%)	10(52.6%)
Non infectious factors		
Catheter blockage	23(12.6%)	3(13.0%)
Bleeding or hematoma	7(3.8%)	0(0)
Drug extravasation	2(1.1%)	0(0)
Turnover of port	1(0.5%)	0(0)

3.3 Analysis of risk factors for complications

There was a significant difference in age between 71 patients with infusion port-related complications and 111 patients without complications (P = 0.02). There were no significant differences in sex, tumor type, preoperative chemotherapy, first puncture failure, time from completion of TIVAP to first use, absolute number of neutrophils, or operation time between the case and control groups (P > 0.05) (Table 2). Logistic regression analysis showed that age was significantly associated with the occurrence of complications (P = 0.024), and the relative risk was 0.945(Table 3).

Table 2
Analysis of risk factors of complications

Categorical variables	Complication group(n = 71)	Control group(n = 111)	Statistical value	P-value
Gender			$\chi^2 = 0.639$	0.423
Male	36	63		
Female	35	48		
Tumor type			$\chi^2 = 0.408$	0.815
Leukemia	48	75		
Lymphoma	3	7		
Malignant solid tumor	20	29		
Received chemotherapy before operation			$\chi^2 = 2.576$	0.108
No	40	49		
Yes	31	62		
The first puncture failure			$\chi^2 = 0.033$	0.855
No	68	107		
Yes	3	4		
Age(month)	41.84 ± 33.56	56.89 ± 46.85	t = 2.347	0.020
Time from completion of TIVAP to first use(day)	9.15 ± 12.54	12.85 ± 26.12	t = 1.113	0.267
Absolute number of neutrophils($\times 10^9$/L)	2.84 ± 3.58	2.69 ± 2.32	t = 0.343	0.731
operation time(min)	45.21 ± 19.58	48.59 ± 20.64	t = 1.099	0.273

Table 3
Logistic regression analysis of risk factors for complications

Variable	B	S.E.	Wald	P	OR
Age(month)	-0.052	0.022	5.021	0.024	0.945

There were significant differences in age (P = 0.015) and absolute number of neutrophils (P = 0.006) between the 19 patients with CRBSI and the 111 patients without complications. There were no significant differences in sex, tumor type, preoperative chemotherapy, first puncture failure, time from completion of TIVAP to first use, or operation time between the case and control groups (P > 0.05) (Table 4). The results showed that younger age was significantly associated with CRBSI (P = 0.035), the relative risk was 0.964, and the number of neutrophils was not significant (P = 0.054) (Table 5).

Table 4
Analysis of risk factors for catheter-related bloodstream infection

Categorical variables	CRBSI group(n = 19)	Control group(n = 111)	Statistical value	P-value
Gender			χ^2 = 0008	0.926
Male	11	63		
Female	8	48		
Tumor type			χ^2 = 1.379	0.501
Leukemia	13	75		
Lymphoma	0	7		
Malignant solid tumor	6	29		
Received chemotherapy before operation			χ^2 = 1.049	0.305
No	6	49		
Yes	13	62		
The first puncture failure			χ^2 = 0543	0.819
No	18	107		
Yes	1	4		
Age(month)	26.52 ± 25.94	56.89 ± 46.85	t = 2.748	0.006
Time from completion of TIVAP to first use(day)	8.84 ± 11.25	12.85 ± 26.12	t = 0.657	0.512
Absolute number of neutrophils($\times 10^9$/L)	3.98 ± 3.65	2.69 ± 2.32	t = 2.038	0.043
operation time(min)	44.74 ± 18.46	48.59 ± 20.64	t = 0.762	0.447

Table 5
Logistic regression analysis of risk factors for catheter-related bloodstream infection

Variable	B	S.E.	Wald	P	OR
Age(month)	-0.027	0.015	4.256	0.035	0.964
Absolute number of neutrophils($\times 10^9$/L)	0.168	0.078	3.754	0.054	1.179

4. Discussion

In this study, the incidence of complications related to the use of TIVAP in children's chemotherapy was 39%, which is higher than the 14.7–33% reported in foreign children's studies[6, 7], which may be related to the short duration of TIVAP use in our hospital. Infectious complications were the most common. TIVAP-related infection generally results from skin infection at the puncture point, microorganisms migrating into the catheter along the port, or blood flow infection from other distant parts of the body, and there are also very few possible sources of pollution caused by infusion liquid[8]. The results of a meta-analysis[9] showed that infection prevention strategies and the education and training of professional nursing staff are the most effective means of preventing infection. The incidence of TIVAP-related infection complications in this group was 27.4%, which is higher than the 6.5% – 17.9% reported in the literature[7, 10], which may be related to the short operation time and insufficient experience in preventive nursing education in our hospital. A more recent study in the literature[7, 10] reported a lower incidence rate of infectious complications, suggesting that a large number of cases, surgical and maintenance procedures, and standardized care reduced the incidence of infection. In previous studies, coagulase-negative Staphylococcus (Staphylococcus epidermidis, human staphylococcus, and Staphylococcus saprophytes) were the most common infectious microorganisms, among which Staphylococcus epidermidis is the most common[8, 11]. Similar results were observed in this study. Coagulase-negative Staphylococcus is a common skin microorganism, suggesting that the infection may originate from the puncture site, which is consistent with the pathogenesis of infection complications. In this study, intravenous anti-infection therapy was administered after catheter infection with an effective rate of 75%.

There are many reasons for TIVAP catheter blockage, which can be divided into catheter factors such as catheter discount, compression or improper end position, catheter tip sticking to the vessel wall or catheter displacement, and non-catheter factors such as precipitation caused by parenteral nutrition infusion, blood products, and drug interactions during use. Mechanical blockage is often caused by catheter discount or compression. Pinch off syndrome is the most serious mechanical blockage and is common in subclavian vein catheterization. The catheter is compressed between the clavicle and the first rib for a long time, resulting in fragmentation of the catheter wall and debris falling off and moving to the central vein, right atrium, right ventricle, and pulmonary artery. It is a rare, but serious complication[12]. In this study, internal jugular vein puncture was performed, and no such complications were found. Endothelial injury, the hypercoagulable state of malignant tumors, and chemotherapy itself are all factors that lead to thrombosis in cancer patients. Thrombosis can occur around or in veins at the top of the catheter. The manifestations of catheter-related thrombosis may be asymptomatic, with or without pain or swelling of the ipsilateral limb[13]. Therefore, the evidence of thrombosis may not be clinically clear, but it is usually the most common cause of catheter blockage. In some studies, heparin treatment was compared with urokinase treatment, and urokinase treatment was found to be significantly associated with a lower thrombosis rate[14]. In this study, 91.3% of the children with catheter obstruction improved after thrombolytic therapy with heparin or urokinase, suggesting that thrombolytic therapy with heparin and urokinase may reduce the risk of thrombosis. In the past, the incidence of thrombosis was reported to

be 1.6-7%[10]. No thrombosis cases were found in this study, which may be related to the small sample size of this study and the lack of routine regular vascular ultrasound follow-up of patients.

The literature reports that the incidence of drug extravasation is 0.26-6%[15] The severity of lesions caused by extravasation depends on the nature, volume, concentration, and location of extravasation drugs and the contact time required for extravasation drugs to damage surrounding tissues. Prevention of drug extravasation complications should be emphasized. Training of the nursing team should be strengthened to prevent serious skin damage caused by chemotherapy drug extravasation and delay tumor treatment. In this study, there were 2 cases of drug extravasation. No serious consequences were observed after local symptomatic treatment or nursing. The literature reported that the incidence of catheter fracture ranged from 0.4–1.8% [16], which was not found in this study.

In a retrospective analysis of pediatric patients, Hung et al.[17] found that younger patients had a higher risk of infection after TIVAP implantation. The results of the logistic regression analysis in this study suggest that the lower the age, the higher the risk of complications, which is consistent with the reported results and may be related to the nursing difficulties of low-age patients. Delaying catheter use has been reported[18] that delaying the use of catheter can reduce the risk of infection. It is suggested that one week between the placement of TIVAP and the start of use can reduce the incidence of complications and the risk of unplanned port removal, which may be related to the healing time of incision after implantation. This study did not find an impact of the start time of TIVAP on the incidence of complications, and prospective studies with larger sample sizes are needed. Some studies have pointed out that the occurrence of complications is unrelated to the timing of TIVAP surgery, and others have pointed out that the risk of infection in children undergoing TIVAP surgery in the early stage of induction remission treatment of acute lymphoblastic leukemia will increase[19]. It has been reported that neutropenia is a risk factor for catheter-related infection[20]. In this study, it was found that neutrophils in the infection group were higher than those in the control group, and the difference was statistically significant, which is inconsistent with previous reports because the chemotherapy time and intensity of leukemia patients were higher than those of solid tumor patients; therefore, the degree and duration of potential neutropenia were also higher than those of solid tumors. We found that the incidence of clinical sepsis in the leukemia group was very high. However, because Hong Kong blood was not collected from all patients with sepsis for culture, the infection rate of catheter-related blood influenza in the leukemia group may be underestimated.

TIVAP, a device that can easily provide long-term venous access, is safe for pediatric malignant tumors. Special attention is required in the process of surgical placement and operation. Therefore, surgeons and nursing teams require professional training. The incidence of complications in this study was 39%, and there were no deaths due to complications at the infusion port. Infection is the most common complication, and CRBSI is the most common cause of unplanned pullout. Younger age may be a risk factor for CRBSI and complications.

Declarations

Ethics approval and consent to participate: The study was approved by the ethics committee of The Affiliated People's Hospital of Ningbo University (No.2018-058, May 15, 2018). Informed consent was obtained from each patient's parent / local guardian.

Consent for publication: Not applicable.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions Songze Zhang analyzed and interpreted the patient data and draft the preparation. Zhangsheng Xiao and Feibiao Yang involved in the surgeries, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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References

1. Parienti J J, Mongardon N, Megarbane B, et al. Intravascular Complications of Central Venous Catheterization by Insertion Site[J]. N Engl J Med,2015,373(13):1220–1229.
2. Samaras P, Dold S, Braun J, et al. Infectious port complications are more frequent in younger patients with hematologic malignancies than in solid tumor patients[J]. Oncology,2008,74(3–4):237–244.
3. Ahn S J, Kim H C, Chung J W, et al. Ultrasound and fluoroscopy-guided placement of central venous ports via internal jugular vein: retrospective analysis of 1254 port implantations at a single center[J]. Korean J Radiol,2012,13(3):314–323.
4. Xiaoyi D, Fang D, Yonggang W, et al. Shanghai expert consensus on totally implantable access ports 2019[J]. Journal of Interventional Medicine,2019,2(04):141–145.
5. Rosenbluth G, Tsang L, Vittinghoff E, et al. Impact of decreased heparin dose for flush-lock of implanted venous access ports in pediatric oncology patients[J]. Pediatr Blood Cancer,2014,61(5):855–858.
6. Chandrasekaran A, Somasundaram J. Surgical placement of totally implantable venous access device-an institutional experience[J]. Indian J Pediatr,2014,81(9):866–870.
7. Pinon M, Bezzio S, Tovo P A, et al. A prospective 7-year survey on central venous catheter-related complications at a single pediatric hospital[J]. Eur J Pediatr,2009,168(12):1505–1512.
8. O'Grady N P, Alexander M, Burns L A, et al. Guidelines for the prevention of intravascular catheter-related infections[J]. Clin Infect Dis,2011,52(9):e162-e193.

9. Gastmeier P, Geffers C. Prevention of catheter-related bloodstream infections: analysis of studies published between 2002 and 2005[J]. J Hosp Infect,2006,64(4):326–335.
10. Shankar G, Jadhav V, Ravindra S, et al. Totally Implantable Venous Access Devices in Children Requiring Long-Term Chemotherapy: Analysis of Outcome in 122 Children from a Single Institution[J]. Indian J Surg Oncol,2016,7(3):326–331.
11. Chauhan A, Lebeaux D, Ghigo J M, et al. Full and broad-spectrum in vivo eradication of catheter-associated biofilms using gentamicin-EDTA antibiotic lock therapy[J]. Antimicrob Agents Chemother,2012,56(12):6310–6318.
12. Cho J B, Park I Y, Sung K Y, et al. Pinch-off syndrome[J]. J Korean Surg Soc,2013,85(3):139–144.
13. Vescia S, Baumgartner A K, Jacobs V R, et al. Management of venous port systems in oncology: a review of current evidence[J]. Ann Oncol,2008,19(1):9–15.
14. Bertoglio S, Solari N, Meszaros P, et al. Efficacy of normal saline versus heparinized saline solution for locking catheters of totally implantable long-term central vascular access devices in adult cancer patients[J]. Cancer Nurs,2012,35(4):E35-E42.
15. Azais H, Bresson L, Bassil A, et al. Chemotherapy drug extravasation in totally implantable venous access port systems: how effective is early surgical lavage?[J]. J Vasc Access,2015,16(1):31–37.
16. Doley R P, Brar P, Chaudhary S, et al. Port catheter fracture and migration in Internal Jugular Vein[J]. Am J Case Rep,2012,13:14–16.
17. Hung M C, Chen C J, Wu K G, et al. Subcutaneously implanted central venous access device infection in pediatric patients with cancer[J]. J Microbiol Immunol Infect,2009,42(2):166–171.
18. Narducci F, Jean-Laurent M, Boulanger L, et al. Totally implantable venous access port systems and risk factors for complications: a one-year prospective study in a cancer centre[J]. Eur J Surg Oncol,2011,37(10):913–918.
19. Mclean T W, Fisher C J, Snively B M, et al. Central venous lines in children with lesser risk acute lymphoblastic leukemia: optimal type and timing of placement[J]. J Clin Oncol,2005,23(13):3024–3029.
20. Freire M P, Pierrotti L C, Zerati A E, et al. Infection related to implantable central venous access devices in cancer patients: epidemiology and risk factors[J]. Infect Control Hosp Epidemiol,2013,34(7):671–677.

Figures

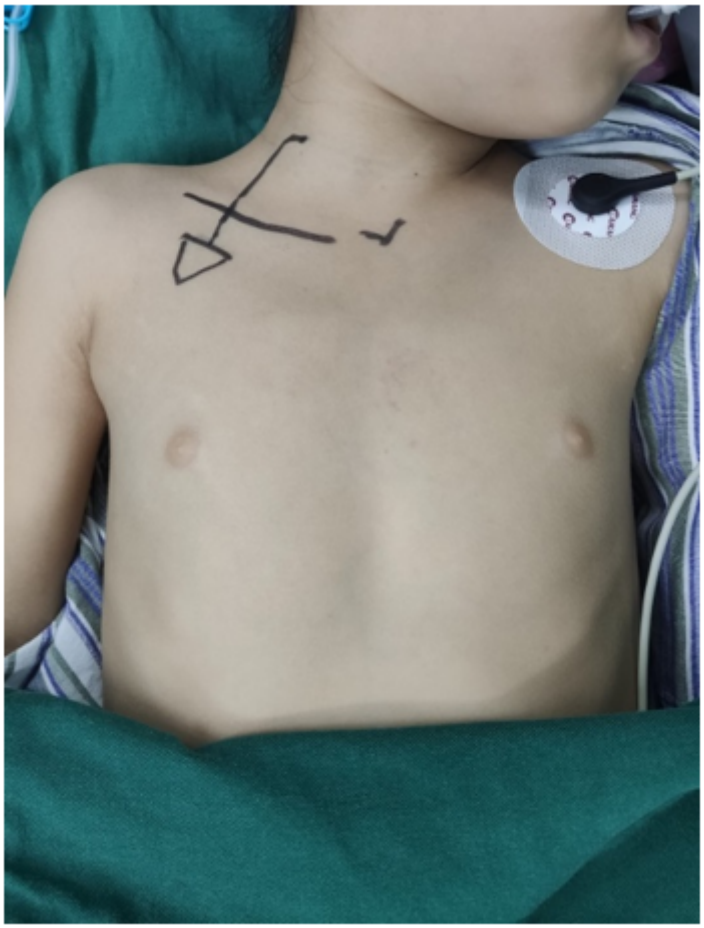

Figure 1

Preoperative body surface positioning of the puncture line

Figure 2

State after suturing the incision