An Appraisal of Totally Implantable Venous Access Devices in Pediatric Cancers

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ABSTRACT

Objective: To appraise the experience of a pediatric cancer center in Thailand regarding employment of totally implantable venous access devices (TIVAD).

Methods: The records of consecutive patients aged less than 15 years diagnosed with malignancy and underwent an implantation from the years 2010 to 2018 were reviewed with the main focus on effective duration and complications of the device. Changes in our practice in perioperative care were also reviewed.

Results: A total of 150 lines in 144 patients (103 hematologic malignancies and 41 solid tumors) were included with average age 6.4 years. Neck vein access was used in 62 lines, subclavian vein access in 88 lines. The median follow-up period was 973 days. Immediate complications occurred in 13 cases (9.4%). Excluding cases with death from unrelated causes, the overall TIVAD survival was 985.1 days while event-free device survival was 797.6 days. In cases of hematologic malignancies, which were the main users, 1000-day overall survival and event-free survival of TIVAD were 83.7% and 78.2%, respectively. Catheter-related infections and mechanical obstruction were the 2 most prevalent problems, occurring in 0.20 and 0.08 events/1,000 catheter days, respectively. Infection occurred in 23 patients and gram-negative bacilli were most common. Moreover, subclavian access was significantly related with infectious complications when compared to the neck vein approach.

Conclusion: A TIVAD can be used for chemotherapy longer than 3 years without serious complications. Refinement of surgical techniques and improving care process may improve the longevity of the line.

Keywords: Totally implantable venous access device; longevity; complications; pediatric cancer (Siriraj Med J 2020; 72: 95-102)

INTRODUCTION

A totally implantable venous access device (TIVAD) is a type of tunneled central venous catheter that provides venous system accessibility and prevents extravasation of hypertonic parenteral fluid and vesicant medications.[1] With an aim to improve quality of life (QOL) during chemotherapy[2], TIVAD are frequently used in pediatric cancer patients who require long-term intermittent therapy, especially those with hematologic malignancies.[3] TIVAD not only improves QOL, but also improves compliance to the treatment by reducing complications associated with difficult venous access.[4] Recent studies have shown that the preferred technique used in TIVAD implantation is percutaneous venipuncture, commonly via the subclavian the internal jugular vein.[5-7] If a venipuncture is not possible, open venesection is an alternative approach. Although TIVAD was designed to reduce catheter-related infections by tunneling the catheter within the subcutaneous plane,

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infectious complications can occur when the line has been used for a long period.[8,9] Moreover, mechanical complications, especially luminal obstruction, are common problems which might compromise TIVAD longevity.[10,11]

TIVAD has been practiced in Songklanagarind Hospital, one of the largest referral centers for pediatric oncology cases in southern Thailand, since 2010. After the procedure was partially subsidized by the Universal Health Coverage scheme, the number of implantations increased. The implantation was considered primarily in hematologic malignancies and in selected cases of pediatric solid tumor who were expected to receive chemotherapy for more than one year. The implantation surgical techniques and continuing post-operative care by a multidisciplinary team were continuously refined with an aim to achieve a 'best practices' program.

In this study, we appraised the longevity and the complications of TIVAD implantations in our institute and also analyzed the factors determining event-free usage longevity. Problems encountered and improvement of both surgical techniques and care processes during the period were also reviewed.

MATERIALS AND METHODS

Patient selection

The Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University approved the study as a retrospective review (EC-59-371-10-1). The records of all pediatric patients who underwent a TIVAD implantation by the pediatric surgical team at Songklanagarind Hospital from January 2010 to December 2018 and were taken care of by the pediatric oncology team either at our hospital or another hospital were reviewed.

Surgical techniques and care processes

Pediatric patients aged less than 15 years with hematologic malignancies, lymphoma, or other pediatric solid tumors were considered for TIVAD. Cases with a solid tumor were selected for implantation when they were expected to receive intermittent intravenous chemotherapy for longer than 1 year. Percutaneous venipuncture using the 'catheter under the sheath' method (Seldinger technique) was attempted first when feasible.[12,13] Puncture sites were either the right subclavian or right internal jugular vein. During the initial years of implantation in our institute, the pediatric surgeons generally preferred an approach through the right subclavian vein without ultrasonographic guidance. Around 2016, as our service quality review and other studies showed that immediate complications were lower when the internal jugular vein was used as an access point, the team revised our protocol to begin with percutaneous venipuncture through the internal jugular vein under real-time ultrasonography. In cases where a percutaneous venipuncture was not successful or not suitable, open venesection was the main alternative choice. On the open venotomy, the right external jugular or the right internal jugular was the most preferred access sites. The tip of the catheter was passed though the superior vena cava (SVC) to be located around the junction between the SVC and the right ventricle, and the location was confirmed by intraoperative fluoroscopy. (To reduce catheter misplacement as an immediate complication, strict positioning under fluoroscopy has been implemented as a quality check point since 2017.) Together with the positioning regimen, all implanted catheters were checked for their functions using 'push and pause' infusion test before fixation. The catheter was tunneled along the subcutaneous plane and the port was placed at the right chest wall cranial to the ipsilateral nipple and fixed to the pectoral fascia using 4-0 polypropylene. The skin incision was closed by a subcuticular mattress using 5-0 polydioxanone. In general, the implanted TIVAD wass left 7-10 days before the first puncture test was performed by the surgical team. The catheters thereafter were taken care of by a multidisciplinary team.[14,15] The bundles of care process were divided into 3 steps: (1) needle insertion and chemotherapy administration, (2) monthly NSS flushing to prevent mechanical obstruction, and (3) needle removal and supervised home care for the patients and their parents. The care team provided a logbook and a pamphlet to each patient's caregivers, in which events and complications were recorded. When the patients finished their intravenous chemotherapy and had no relapse of disease for at least 1 year, the device was removed by the pediatric surgical team.

As the study aimed to apprise the longevity and complications in our TIVAD practice, we also focused on the learning curve and continuous adaptation of the operative techniques through a quality assurance process of the care team. Apart from the major change in the preferential puncture site, the TIVAD clinical practice guideline has been modified several times, and the current one reflects our best practice.

Data collection

Data were retrieved from our electronic medical records including age at implantation, gender, diagnosis of malignancy, anthropometry (weight and height) at implantation, site and techniques of central venous access, size of catheter, immediate complications, type of long-term complications (catheter-related infections,

mechanical obstruction), onset of complications. Diagnosis of catheter-related blood stream infections (CRBSI) was considered when there were positive microbiological reports of hemoculture collected from both peripheral blood and catheter blood drawn at different times more than 2 hours apart[16]. Neutropenia was diagnosed when the patient had an absolute neutrophil count less than 500 cells/cm^3. Date and reasons for catheter removal were also recorded. An immediate complication was defined as an event occurring within 7 days after implantation.[17,18]

Statistical analysis

Demographic data were described by crude value and representative percentage. Categorical data were stratified by various factors and compared by chi-square test, while continuous data were compared with t-test. The log-rank test was used to calculate time to event with regard to event-free usage and overall implantation. Events per catheter day was calculated as the number of events (i.e. CRBSI, obstruction) per 1,000 overall catheter days. Statistical significance was considered at a p-value of <0.05.

RESULTS

A total of 150 devices in 144 patients (103 hematologic malignancies and 41 solid tumors) were included in the analysis. The average age of the patients was 6.4 years with 66 cases (45.8%) aged less than 5 years and 38 cases (26.4%) less than 3 years. There was an increasing trend of TIVAD use in those with hematologic malignancy when use in solid tumors gradually decreased with time (Fig 1).

Considering the access sites, neck veins were used in 62 lines and subclavian veins in 88 lines. The 26 neck-accessed lines (41.9%) were approached by an open venesection. There was a trend toward changing from subclavian access to neck vein access over the study time period (Fig 2), especially during the last years 2017-2018. Immediate complications including obstruction, displacement, arterial puncture, hydrothorax and intraoperative bleeding occurred in 13 cases (8.7%), 6 of which (46.1%) required a surgical revision (Fig 3). The median follow-up period was 973 days (interquartile range 501-1,732 days).

TABLE 1. Demographic characteristics of the patients comparing between hematologic malignancy cases and solid tumor cases.

	Hematologic malignancy	Solid tumors	Total
Patients (cases)	103	41	144
Sex			
Male	64 (62.1%)	26 (63.4%)	90 (62.5%)
Female	39 (37.9%)	15 (36.6%)	54 (37.5%)
Age (years)			
(mean ± S.D.)	6.7±3.6	5.6±5.0	6.4±4.1
Age			
> 5 years	60 (58.3%)	18 (43.9%)	78 (54.2%)
3-5 years	27 (26.2%)	1 (2.4%)	28 (19.4%)
< 3 years	16 (15.5%)	22 (53.7%)	38 (26.4%)
Weight (kg.)			
(mean ± S.D.)	23.1±12.6	21.0±19.5	22.5±14.9
Weight percentile			
<P10	17 (16.5%)	13 (31.7%)	30 (20.8%)
P10-P50	38 (36.9%)	19 (46.3%)	57 (39.6%)
P50-P90	32 (31.1%)	3 (7.3%)	35 (24.3%)
>P90	16 (15.5%)	6 (14.7%)	22 (15.3%)

Abbreviations: S.D.= standard deviation, kg.= kilograms, P= percentile

TABLE 2. Data of the 150 totally implantable venous access devices (TIVAD) used in this study.

	Hematologic malignancy	Solid tumors	Total
TIVAD (lines)	108	42	150
Insertion site			
Neck vein	43 (39.8%)	19 (45.2%)	62 (41.3%)
Subclavian vein	65 (60.2%)	23 (54.8%)	88 (58.7%)
Venous approach			
Venipuncture	94 (87.0%)	29 (69.1%)	123 (82.0%)
Venesection	14 (13.0%)	13 (30.9%)	27 (18.0%)
Immediate complications	8	5	13
Intraoperative bleeding	-	1	1
Arterial puncture	2	1	3
Displacement	4	1	5
Occlusion	1	2	3
Hydrothorax	1	-	1
Revision	5/8 (62.5%)	1/5 (20.0%)	6/13 (46.1%)
Late complications			
Infection	18 (17.5%)	5 (14.3%)	23 (16.7%)
Mechanical obstruction	6 (5.8%)	2 (5.7%)	8 (5.8%)

TABLE 3. Mechanical obstruction and catheter-related blood stream infections of TIVAD by venous access site.

Venous access site	Mechanical obstruction (events/1,000 catheter days)	Catheter-related blood stream infections (events/1,000 catheter days)
Neck vein	0.01	0.01
Subclavian vein	0.06	0.24

TABLE 4. Infectious complications in the study patients.

	Cases (n=23)	Percentage
Onset of infection		
During chemotherapy	12	52.2%
Post-chemotherapy	7	30.4%
Fever prior to admission	4	17.4%
Neutropenia	11	47.8%
Identified organism		
Acinetobacter baumannii	4	17.4%
Enterobacter cloacae	4	17.4%
Pseudomonas aeruginosa	4	17.4%
Stenotrophomonas maltophilia	3	13.1%
Staphylococcus aureus	2	8.7%
Candida albicans	2	8.7%
Cryptococcus neoformans	2	8.7%
Escherichia coli	1	4.3%
Rhodococcus equi	1	4.3%

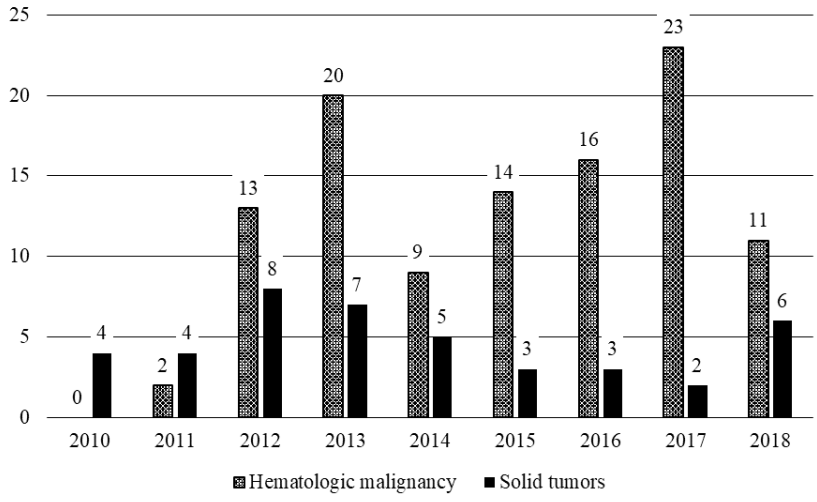

Fig 1. Total TIVAD implantation during the study period.

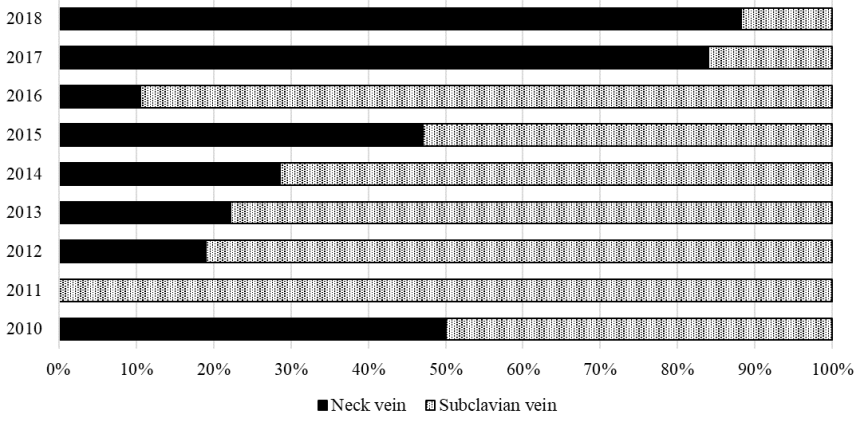

Fig 2. Site of TIVAD implantation stratified by year of implantation.

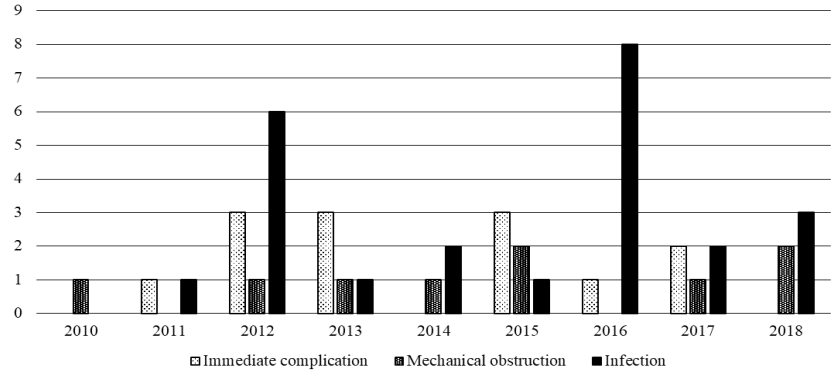

Fig 3. Immediate and long-term complications of TIVAD stratified by year of implantation.

Excluding cases with death from unrelated causes and those removed because of immediate complications, the overall TIVAD longevity was 985.1 days while event-free device longevity was 797.6 days. In cases of hematologic malignancies, 1000-day overall survival and event-free survival of TIVAD were 83.7% and 78.2%, respectively (Fig 4).

Catheter-related infections and mechanical obstruction were the 2 most common problems occurring with the device, occurring in 0.2 and 0.08 events/1,000 catheter days, respectively (Fig 5). Infectious complications occurred in 23 pediatric patients, usually developing during the chemotherapy session (52.2%) and commonly found in neutropenic condition. Gram negative bacilli was the most common organism in CRBSI (56.7%) and there were 4 cases of fungal infection. Subclavian access was related to infectious complications at a significantly higher frequency when compared to the neck vein approach (25.4% vs 9.1%, p-value 0.02). Lines with either mechanical complication or infection had significantly poorer longevity compared to uneventful implantations.

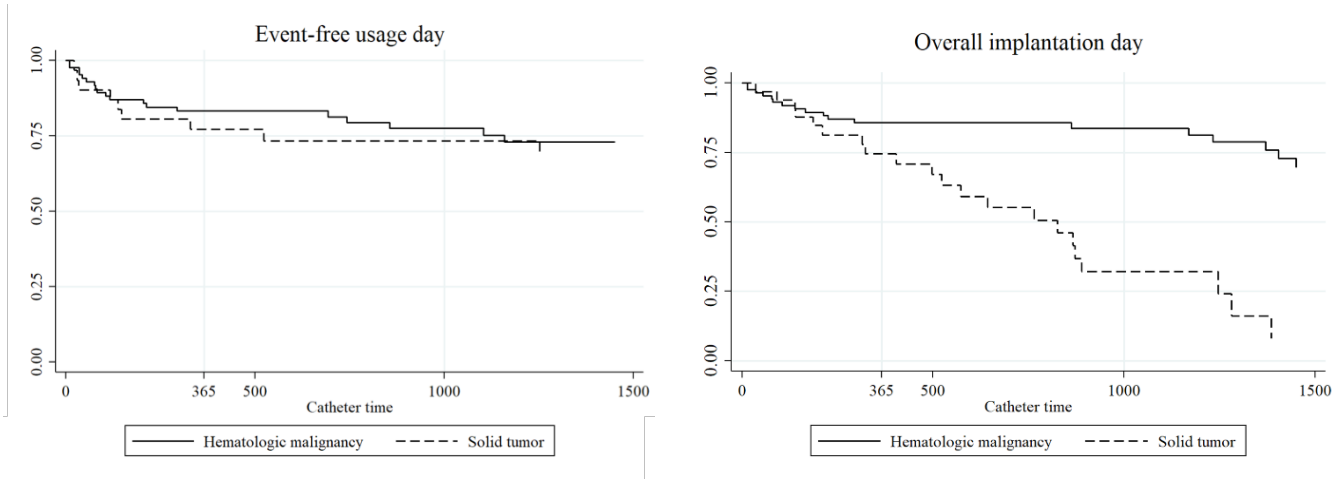

Fig 4. Kaplan Meier curves of event-free usage and overall implantation day of TIVAD stratified by type of malignancy.

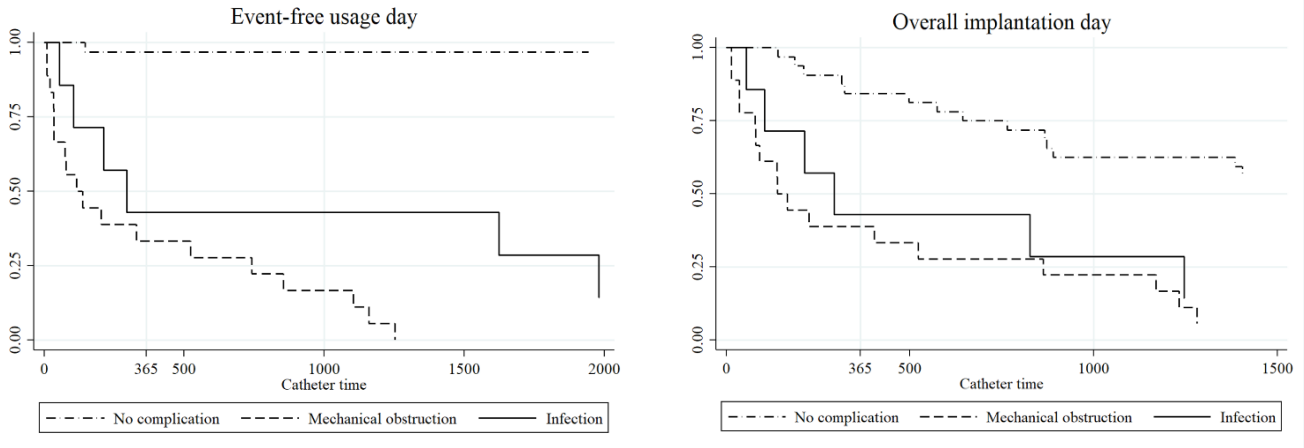

Fig 5. Kaplan Meier curves of event-free usage and overall implantation day of TIVAD stratified by type of complication.

DISCUSSION

The number of TIVAD implantations in our practice has been increasing in recent years, partly because of financial support from the Universal Health Coverage scheme of the Thailand health care system. The device is used with an aim to improve compliance with chemotherapeutic treatment by preventing extravasation and pain caused by difficult venotomies. Our study found that more than 80% of TIVAD could be used longer than 3 years. Considering its high cost, the majority of TIVAD (70%) were used primarily in hematologic malignancy cases in which the therapeutic course usually takes longer than 1-2 years. Eventually, complications developed during the period of utilization at the incidence of 0.3 events per 1,000 catheter days. The majority of complications were related to mechanical obstruction and catheter-related blood stream infections (CRBSI). There were 2-time peaks of complication occurrence, the first being immediate complications that occurred within days of implantation in which mechanical problems predominated and the second being infectious complications during the first year of catheter use. This high complication occurrence during the first year of use might be explained by the intensity of chemotherapy in that period. Our data also found that once a complication occurred, the longevity of the TIVAD was significantly compromised.

The TIVAD is a catheter of which the whole device is surgically implanted within the body, one end laid in the vena cava and the other end placed under the skin. Although this system has been proven to have less chance of infection when compared to the exteriorized catheter, CRBSI remain a concern. During the on-going period of this study, we found that the neck vein approach was superior to the subclavian approach in terms of a significantly lower incidence of CRBSI[7,19], and based on this finding we modified our surgical protocol to perform internal jugular venous puncture under ultrasonographic guidance as the first choice. Now in our institution the use of fluoroscopy and flow check before the end of a TIVAD procedure are mandatory. With that strategy

launched in 2017, the immediate complication rate reduced from 11% to 6% of total implantations and there were no immediate complications in 2018.

Risk reduction in TIVAD implantation and care involves not only the surgery and post-surgical care but also patient preparation and right surgical timing.[20] One lesson our team has learned in our early experience is that implantation should be avoided during the period that a patient remains in blast crisis or the bone marrow suppression phase. Implantation is scheduled when a leukemic patient enters a remission phase and his/her hematologic profile is within the normal range, usually between the first and second sessions of chemotherapy. Even though transfusion therapy might be able to quickly restore the number of platelet count to the normal limit, the risk of hemorrhagic complications and soft tissue infection are not substantially alleviated[21]. Concerning post-operative and long-term care, a multidisciplinary team approach is the key point[14]. The first puncture of a device is usually performed by the pediatric surgical team. Further maintenance is then in the hands of pediatricians and chemotherapeutic nurses in the pediatric cancer ward. Such care includes a log-book record and regular inspection and irrigation. With refinement of surgical techniques, the complication rate in our institution gradually decreased from 29.6/100 catheters to 15.6/100 catheters after the year 2017.[15]

Our next aim to improve the effective use of TIVAD is to reduce infectious complications. Our data showed that half of the CRBSI occur during the chemotherapeutic session. During the neutropenic period, even though a double culture technique was used, it was not easy to differentiate between systemic bacteremia and primary catheter infection. When blood culture is positive with gram negative bacteria or fungus, removal of the device is usually inevitable. Active surveillance of bacterial colonization within the device and avoiding its use during the neutropenic period may reduce the problems.

CONCLUSION

In conclusion, our study documents the continuous improvement of our practice in TIVAD implantation and care in pediatric malignancy cases. Over time, continually improving surgical techniques and multidisciplinary care reduced complications and improved longevity of TIVAD implantation.

Conflict of Interest: All authors have no conflict of interest

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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