Safety and Efficacy of Image-Guided Totally Implanted Central Venous Catheter Insertion in Cancer Patients

***Running title*:** Image-Guided Totally Implanted Venous Catheter Insertion.

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Abstract

Background and Objective:

Repetitive administration of the antineoplastic agents through peripheral veins eventually destroys venous integrity and decreases the ability to obtain venous access. We conducted this study to determine the safety and efficacy of totally implanted central venous catheters (TIVADs) in the administration of chemotherapy and to detect the advantages of using ultrasound and fluoroscopy to insert (TIVADs).

Methods:

The study enrolled 104 cancer patients who received image-guided, totally implanted port insertion in the period from October 2019 to September 2023 at the interventional radiology units.

All patients were analyzed prospectively regarding their characterization, technical factors, patency, and acute and late complications during device implantation.

Results:

We reported a 100% insertion success rate. The total complication rate was 13.5% (n=14), divided into early complications (within 30 days of the procedure) developed in 2.9% (n=3) of the patients, and late complications occurred later on in 10.6% (n=11) of the cases.

The most observed complication was port pocket infection, which occurred in 4.8% (n=5) of the patients. Catheter dysfunction due to late catheter-related central venous thrombosis was observed in 3.8% (n=4) of the cases. Catheter-related bloodstream infection, chemotherapy extravasation, mechanical dysfunction due to catheter kink, wound dehiscence, and skin necrosis; each of these complications occurred once in our study.

Conclusion:

Image-guided insertion of totally implanted venous access devices (TIVADs) showed high technical and clinical success rates with low complication rates, which could provide safe, practical, and life-long venous access for the administration of cytotoxic agents.

Keywords:

Totally implanted venous ports, porta Cath, central catheters, IV lines

Introduction:

The modern approach to the treatment of oncological patients with new chemotherapy combinations and more complex multimodal intravenous therapy put great demands on repeated venous access (1,2). Repetitive administration of the antineoplastic agents through peripheral veins destroys venous integrity, and accessibility becomes more and more difficult (3). Accordingly, central venous access devices (CVADs) represent a reliable option for delivering cytotoxic drugs, blood

transfusion, rehydration, and blood sampling (4,5).

Totally implanted venous access devices (TIVADs) are preferred to other central venous access devices due to the advantages of long indwelling time, reduced risk of complication, ease of nursing, less interference with daily activity, and less distortion of body image (6,7).

Since the first attempt of insertion by John Niederhuber in 1982 (8) using an open surgical technique, there have been many advances in the insertion techniques of TIVADs aiming for the reduction of associated complication rates. These advances include blind percutaneous insertion by anatomical landmarks or with ultrasound guidance using the Seldinger technique (9). Subsequently, we conducted this study to determine the efficacy and safety of using ultrasound and fluoroscopy for insertion port-a-cath.

Patients and Methods:

This case-series prospective study was conducted from October 2019 to September 2023 at the interventional radiology units in our university hospitals. This study was approved by our ethical committee, having IRB number: 17100902.

Written informed consent was obtained from each patient for participation and publication after receiving information about the details of the study.

All cancer patients of all age groups with accepted coagulation profile (prothrombin concentration > 70%, platelet counts > 70 000/µl), clear chest wall (with no signs of wounds or infection), and patent central venous system (detected by Doppler examination) were included in this study. Patients with severe uncorrectable coagulopathy (INR > 1.5), low platelets count < 70 000 /µl and any active infection were excluded.

Technique:

Interventional radiologists performed all port catheter implantations by using a Port-a-Cath kit (Dignity® Medcomp), (Celsite®, B. BRAUN, France) or (IN-PORT®, FB medical) either Titanium or plastic ports, 9.5F, 9F, or 8.5F polyurethane catheters.

All the procedures were done in an interventional radiology suit under local anesthesia with 10 cc of Xylocaine 2% and proceeded as follows:

Puncture of the internal jugular or subclavian veins was obtained by the puncture needle involved in the Port-a-Cath kit under ultrasound guidance (Acuson x300, Siemens, Germany) with a linear probe (4-10 MHz). In some cases, a convex probe (3-5 MHz) was used to access the subclavian vein. The short axis/out-of-plane or the long axis/ in-plane methods were used for venipuncture. **(Figure 1)**

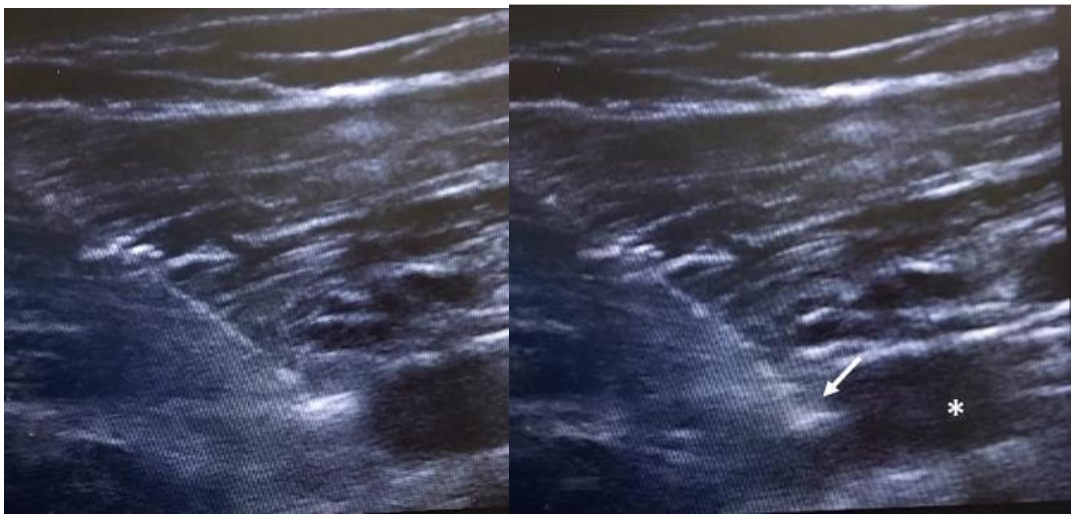

Figure 1: Inserting the puncture needle under sonographic guidance using a long axis/in-plane technique. Puncture needle tip (arrow), access vein (asterisk).

"J-shaped" guide wire (.038" x 70cm) was introduced through the puncture needle under the fluoroscopy (Artis Zee Celling Siemens Germany) to make sure that the proper site of the guide wire is in the central venous system and right atrium. **(Figure 2)**

The creation of the port pocket was done after subcutaneous local anesthesia with approximately 20 cc of Xylocaine, 2% mixed with diluted Epinephrine. An incision ± 2 cm was made over the chest wall two fingers below the mid aspect of the clavicle, and the pocket was made by blunt dissection. We tend to make the incision over a rib to provide a firm support base for later palpation and puncture.

After securing the port's connection to the catheter and testing the junction for leakage, we inserted the port to be tightly engaged in the pocket. Then, a tunnel through the subcutaneous tissue was made from the port pocket to the puncture site.

The peel-away sheath was then introduced over the guide wire under fluoroscopic guidance. The proper length of the catheter was estimated by using the guide wire as a measuring tape with its tip at the junction between the superior vena cava and right atrium by subtracting the length of the external tip of the peel-away sheath, then insertion of the catheter through the peel-away sheath into the central venous system. **(Figure 3)**

In some patients, we used another pathway (catheter first technique), starting with inserting the peel-away sheath over the guide wire. The catheter is introduced through the peel-away sheath, and its tip is adjusted to lie at the atriocaval junction under fluoroscopic guidance, with the other end connected to the tunneler. This is followed by creating the port pocket, tunneling the catheter from the puncture site to the port pocket, and connecting the catheter to the port in the port pocket (10). **(Figure 4)**

In some patients, we had to fix the port to the subcutaneous tissue by interrupted sutures using resorbable 4-0 vicryl sutures to prevent port migration or rotation due to a wide pocket or abundant loose fatty tissue. In most patients, we got enough by making the port pocket precisely fit the port size without port fixation (11). **(Figure 5)**

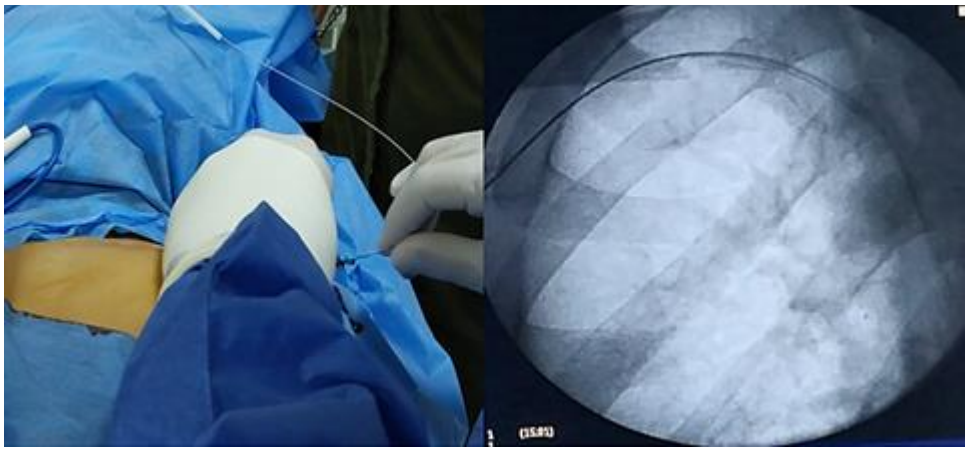

Figure 2: A "J-shaped" guide wire was introduced through the puncture needle under fluoroscopy to ensure that the proper site of the guide wire was in the central venous system and right atrium.

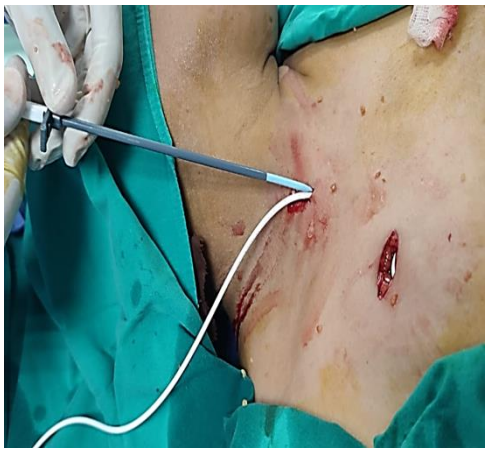

Figure 3: Insertion of the port first, then the catheter through the peel-away sheath.

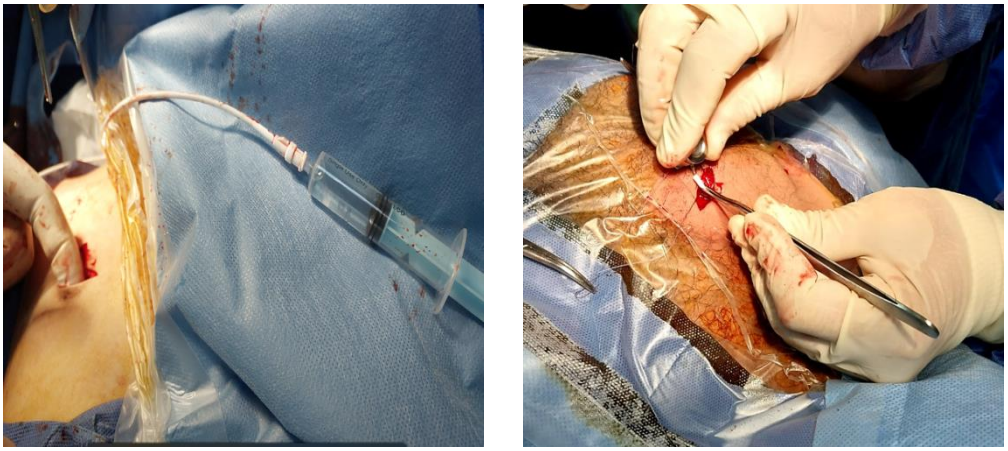

Figure 4: Insertion of the catheter was carried out first in this case, then creating the port pocket by blunt dissection and connecting the port to the catheter in the port pocket.

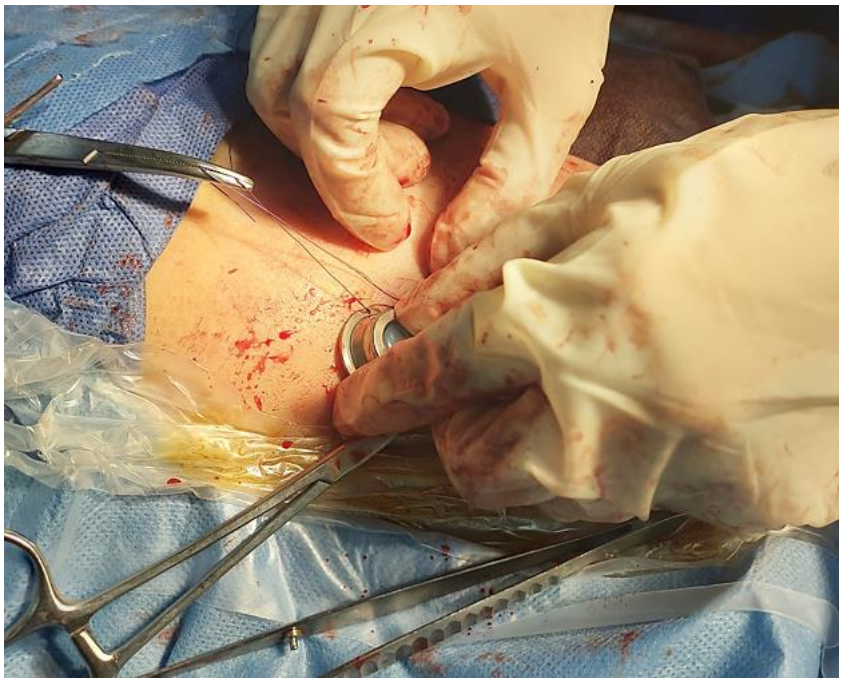

Figure 5: Fixation of the port to the subcutaneous tissue using interrupted absorbable sutures.

Finally, verifying the function of the port by aspiration of blood and injection of saline using the non-coring needle provided in the device kit, then closure of the port pocket was done using three to four interrupted deep subcutaneous sutures and by running subcuticular resorbable sutures by using 4-0 vicryl sutures (12,13).

After the closure of the port pocket, the system is locked by injecting about 10 ml of heparinized saline 50 units/ml through the port system.

All patients were analyzed prospectively regarding their characterization, technical factors, early (within 30 days after the procedure) complications, and late complications (after 30 days after the procedure) during device implantation.

Statistical Analysis*:*

Patients' characteristics and technical and follow-up data were collected and analyzed using statistical software of IBM Statistical Package for the Social Sciences (SPSS, IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

Numerical data was expressed in the form of mean ± SD, while categorical data was expressed in the form of percentage and frequency.

Results

Patients' Characteristics*:*

This study included 104 patients. The mean age of the patients was 49 years ± 12.8(SD) (18–76 years). Males comprised 37.5% (n=39) of the patients and 63.5% (n=65) were females.

The mean weight of the patients was 70.14 Kg +/- 11.83 (SD), while the mean basal metabolic rate (BMI) was 24.72 kg/m2 +/- 3.90(SD). Most of our patients were overweight (BMI more than 25kg/m2 and less than 30 kg/m2), representing 41.3% (n=43) of the patients.

Breast cancer was the most common malignancy, representing 32.7% (n=33) of our patients, followed by Gastrointestinal malignancies representing 21.2% (n=22).

Other comorbidities rather than malignancy were reported in 45.2% (n=47) of the patients. The most common comorbidity was hypertension, which was reported in 18.3% (n=19) of the patients.

In all our patients, the indication of TIVAD insertion was for administration of chemotherapy as a curative, eradicative treatment in 61.5% (n=64) of the patients, while 38.5% (n=40) of the patients were on chemotherapy as a palliation for an advanced stage of the disease. **(Table 1)**

Table 1: Patients' characterizations

Parameter	**Mean ± SD/ percentage (n=)**
Age (years)	49 ±12.8
Sex	
Male	37.5% (n=39)
Female	63.5% (n=65)
Weight (Kg)	70.14 ± 11.83
BMI	24.72 ± 3.90
Under-weight (BMI < 20kg/m^2)	14.4% (n=15)
Average weight (BMI 20:25kg/m^2)	37.5% (n=39)
Over-weight (BMI 25:30kg/m^2)	42.3% (n=43)
Obese (BMI >30kg/m^2)	6.7% (n=7)
Inpatients	24.1% (n=26)
Outpatients	72.2% (n=76)
Malignancy	
Breast	33 (32.7%)
Gastrointestinal	22 (21.2%)
Hematologic	16 (15.4%)
Lung	8 (7.7%)
Pancreas	7 (6.7%)

Head and neck	7 (6.7%)
Gynecological	5 (4.8%)
Hepatic	2.9% (n=3)
Sarcomas	1.9% (n=2)
Melanoma	0.9% (n=1)
Comorbidities	45.2% (n=47)
Hypertension	18.3% (n=19)
Diabetes Mellitus	13.5% (n=14)
Chest disease	7.7% (n=8)
Cardiac diseases	3.8 (n=4)
Brucellosis	0.9 % (n=1)
Burger's disease	0.9 % (n=1)
Chemotherapy mode	
Palliative	38.5% (n=40)
Curative	61.5% (n=64)

Technical Data:

Technical Success Rate:

All the ports were implanted successfully under ultrasound and fluoroscopic guidance. 100% of the catheters were implanted at the first trial.

Access Site:

The right internal jugular vein was accessed in half of the cases 50% (n=52). The left internal jugular veins comprised 23.1% (n=24) of the access sites. The right subclavian vein was used in 18.3% (n=19) of the patients, while the left subclavian vein was used in 8.7%(n=9).

The right side was used in 68.3% (n=71) of the patients, while the left was used in 31.7% (n=33).

Operation Time*:*

The operation time was estimated from the venipuncture till the last suture, with the meantime of the procedure in this study being 43.31 minutes ± 4.17(SD).

Follow-up Data*:*

A total of 56.7% (n=59) of patients reached the end of the thesis in September 2023 with functioning ports. Patients who did not reach the deadline due to death comprised 30.8% (n=32); none of the deaths were reported to be port-related. 9.6% (n=10) of devices had been removed in the observed period, and 7.7 % (n=8) of the cases because of complications. In two cases (1.9%), the catheter was removed because the need for central venous access no longer existed, and the patients decided to undergo an elective port explantation**.**

Three patients (2.9%) were lost to follow-up; two were missed after one year of insertion, and one patient missed after four months.

Complications*:*

Complications occurred in 13.5% (n=14) of the cases, 2.9% (n=3) occurred as early complications (within 30 days of the procedure), and 10.6% (n=11) occurred after one month of insertion.

In the current study, the most observed complication was infection, which occurred in 5.8% (n=6) of the patients, divided into early port-pocket infections observed in 1.9% (n=2) **(Figure 6)** and late port pocket infection was observed in 2.9% (n=3). One case (0.9%) showed late catheter-related bloodstream infection (CRBSI). All the infected ports required premature explantation after the failure of port salvage therapy.

Catheter dysfunction due to late catheter-related central venous thrombosis was the second most common complication observed in 3.8% (n=4) of the cases. The four cases occurred in the late stage (after 30 days of insertion).

One of the patients developed early wound dehiscence after 20 days of port insertion. A failed trial of edge trimming and resuturing compelled us eventually to remove the device.

We observed only one case of chemotherapeutic agent extravasation, late skin necrosis, and catheter dysfunction due to catheter kink, and each of these complications was managed conservatively without the need for catheter removal. **(Figures 7 & 8)**

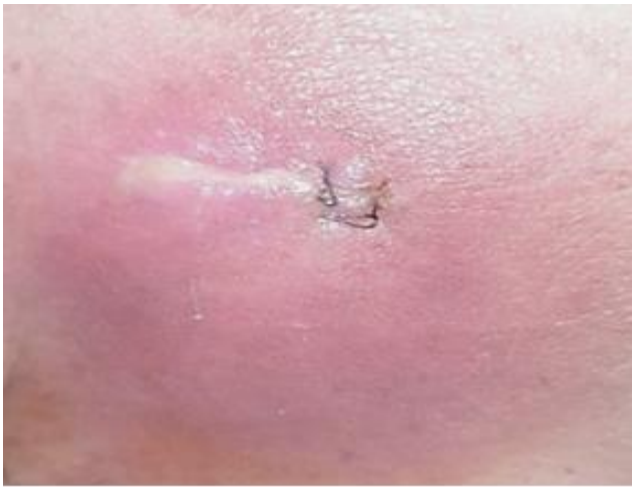

Figure 6: Infected port pocket presented by hotness, redness, and pus discharge at the port pocket site.

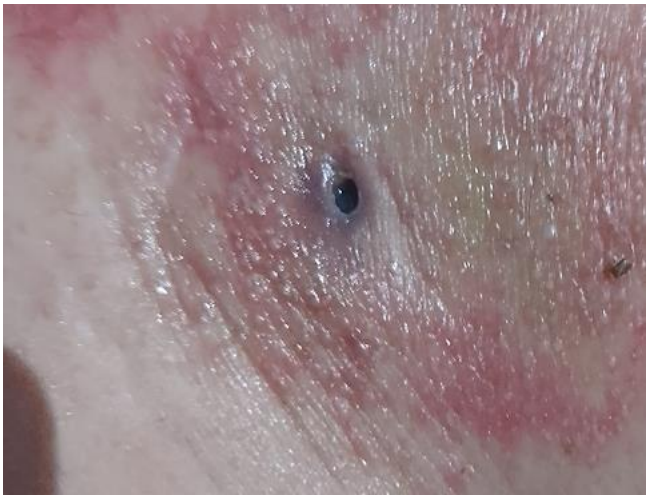

Figure 7: A case of skin necrosis over the port after 11 months of port insertion.

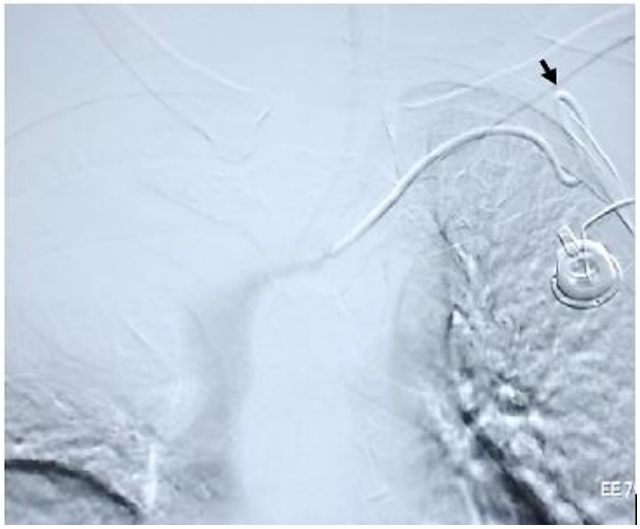

Figure 8: Digital subtraction angiography showing catheter kink (arrow) at venipuncture site with free passage of contrast media through the catheter

Discussion

Most chemotherapeutic agents are associated with significant venous toxicity, often leading to venous thrombosis or thrombophlebitis of the peripheral veins. In contrast, central venous catheters are usually associated with less venous toxicity because wide caliber veins immediately dilute administered medication and reduce the risk of vascular damage (12).

Long-term totally implanted venous access devices (TIVADs) have been reported to be more durable and have a longer patency in terms of lower complication and malfunction rates than other central venous catheters (13,14).

In this study, we reported a 100% technical success rate and all catheters were inserted at the first trial, and none of the reported complications was puncture-related like arterial puncture or pneumothorax; this could be attributed to the usage of ultrasound guidance of insertion, which allows the real-time visualization of the needle tip and its advance through the wall of the access vein. This result is in accordance with other studies where ultrasound guidance was also used with zero technical failure rate (15).

The total operation time in our study was 43.31 minutes ± 4.17(SD), comparable to the results of other previously published studies with the operation time ranging between 10 minutes and 90 minutes (16,17) . The overall complication rate in the current study was 13.5%, which is comparable to what we found in the literature that ranged between 6.6% and 14% in the case of using ultrasound and fluoroscopic guidance, while for the anatomical landmark-guided insertion, the reported complication rates ranged from 5% to 24.6% (18,19). The complication rates of the surgical cut-down technique ranged from 16% to 21% (20).

In our series, the most observed complication was infection at 5.8 % (n=6); this was comparable to other studies in the literature, which reported that the infection rate ranged between 5.6% and 13% (21).

Despite our trials with conservative management, the port systems were eventually removed in all the infected cases. In the literature, catheter-related infection was the cause of premature catheter removal in 7.1–13.4% of cases (10). Failure of port salvage treatment was not exclusive to our study; Vidal et al. reported that 81% of infections required port removal, while conservative treatment and port salvage were feasible only in a few cases (22).

Late catheter-related deep venous thrombosis occurred in four cases (3.9%). Similar to previously reported results with incidence rate (2.7%-8%) (23), other reports revealed thrombosis as the most common complication (24). Three of the four cases were successfully treated with an anticoagulant. In only one case with thrombosis, the catheter had to be removed due to failure of conservative therapy.

One case (0.98%) developed a catheter kink manifested by catheter dysfunction in the form of inability to aspirate blood from the port with preservation of the infusive function; this conforms with other studies with a reported incidence between 0.8 and 9% (25).

Previous study reports showed that the incidence of wound disruption was 1% - 3% (25), which is comparable to our results as we only had one case with wound dehiscence that occurred after 20 days of port insertion (0.98%). The low incidence of wound dehiscence might be due to the closure of the subcutaneous tissue in all our patients with absorbable interrupted sutures in a strict aseptic condition that would relieve the skin sutures' tension. The failed trial of resuturing compelled us to eventually remove the device.

Skin necrosis occurred once (0.98%) in our study after 11 months of catheter insertion; in another study, the reported frequency of skin necrosis was 0.7% (26). The chemotherapy-associated debilitation and subsequent loss of the subcutaneous fat overlying the port device was the main cause of skin necrosis because the thin skin

layer becomes more prone to irritation and necrosis.

Similar to a recent series that observed a decreasing trend for major complications of TIVAD insertions (based on the Society of Interventional Radiology (SIR) consensus-based classification of complications) (4,27), We had not experienced any major complication due to puncture that was reported in other studies like accidental arterial puncture, pneumothorax or hemothorax. This could be attributed to the utilization of ultrasound and fluoroscopy in all our cases and the main operators' deep experience in dealing with ultrasound and fluoroscopic imaging.

Conclusion

Image-guided insertion of totally implanted venous access devices (TIVADs) showed high success and low complication rates, which could provide a safe, feasible, and life-long central venous access route for the administration of cytotoxic chemotherapeutic agents and the more complex multimodal intravenous therapies for cancer patients.

Using ultrasound and other technical advances played a major role in eliminating the fatal complications used to occur with central venous line insertion.

Limitations:

The major limitation of this study was the relatively low sample size due to financial issues. Nevertheless, a detailed case series study confirmed the safety of the radiological placement of totally implanted central access devices.

Another limitation was the lack of child cases, which made our cohort more homogenous and confined our description to adult cases.

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