



Complications and management strategies of totally implantable venous access port insertion through percutaneous subclavian vein

Perkütan subklaviyen ven yoluyla tamamen implante edilebilir venöz erişim portu yerleştirilmesinin komplikasyonları ve tedavi stratejileri

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ABSTRACT

Background: The aim of this study was to present clinical characteristics, peri-procedural outcomes, early and late complications, and management strategies in patients undergoing totally implantable venous access port insertion through percutaneous subclavian vein.

Methods: A total of 2,084 port devices were inserted to 2,000 cancer patients (1,066 males, 934 females; mean age 58.4±12.7 years; range, 18 to 88 years) through subclavian vein using percutaneous landmark method between March 2012 and June 2018. Medical data including demographic features, primary diagnosis, technical success, procedural time, duration of device use, reasons for the device removal, and early and late complications were retrospectively analyzed.

Results: The most common type of cancer was colon cancer in males and breast cancer in females. Technical success rate of the procedure was 98.5%. Right subclavian vein was accessed in the majority of patients (92.4%). Early complications including inadvertent arterial puncture, catheter malposition, superficial hematoma, and pneumothorax occurred in 143 patients (6.9%), while late complications including infection, catheter occlusion, venous thrombosis, wound problems, catheter migration and embolization and pinch-off syndrome was developed in 118 patients (5.7%). Inadvertent arterial puncture in 63 patients (3%) was the most common early complication, while infection in 44 patients (2.1%) was the most common late complication. A total of 192 devices were removed due to the completion of chemotherapy or development of complications.

Conclusion: Our study confirmed the safety and tolerability of totally implantable venous access port insertion through percutaneous subclavian vein with high technical success and low complication rates.

Keywords: Complication, percutaneous, port catheter, subclavian vein, totally implantable venous access device.

ÖZ

Amaç: Bu çalışmada perkütan subklaviyen ven yoluyla tamamen implante edilebilir venöz erişim portu yerleştirilen hastaların klinik özellikleri, periprocedürel sonuçları, erken ve geç komplikasyonları ve tedavi stratejileri sunuldu.

Çalışma planı: Mart 2012 - Haziran 2018 tarihleri arasında perkütan landmark yöntemi ile subklaviyen ven yoluyla 2000 kanser hastasına (1066 erkek, 934 kadın; ort. yaş: 58.4±12.7 yıl; dağılım, 18-88 yıl) toplam 2084 port cihazı yerleştirildi. Demografik özellikler, primer tanı, teknik başarı, işlem süresi, cihazın kalma süresi, cihazın çıkarılma nedenleri ve erken ve geç komplikasyonlar dahil olmak üzere tıbbi veriler retrospektif olarak incelendi.

Bulgular: En sık görülen kanser türü erkeklerde kolon kanseri, kadınlarda meme kanseri idi. İşlemin teknik başarı oranı %98.5 idi. Hastaların çoğunda (%92.4) sağ subklaviyen ven üzerinden erişim sağlandı. Arteriyel ponksiyon, kateter malpozisyonu, yüzeysel hematoma ve pnömotoraks gibi erken komplikasyonlar 143 hastada (%6.9) gözlenir iken, 118 hastada (%5.7) enfeksiyon, kateter tıkanması, venöz tromboz, yara problemleri, kateter göçü ve embolizasyonu ve pinch-off sendromu gibi geç komplikasyonlar gelişti. En sık erken komplikasyon 63 hastada (%3) hatalı arteriyel ponksiyon iken, 44 hastada (%2.1) enfeksiyon en sık görülen geç komplikasyondur. Kemoterapinin tamamlanması veya komplikasyon gelişmesi nedeniyle toplam 192 port cihazı çıkarıldı.

Sonuç: Çalışmamız yüksek teknik başarı ve düşük komplikasyon oranları ile perkütan subklaviyen ven yoluyla tamamen implante edilebilir venöz erişim portu yerleştirilmesinin güvenliğini ve tolerabilitesini doğrulamıştır.

Anahtar sözcükler: Komplikasyon, perkütan, port kateter, subklaviyen ven, tamamen implante edilebilir venöz erişim cihazı.

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Totally implantable venous access devices (TIVADs) are used not only for repeated chemotherapy administration, but also for blood sampling, parenteral nutrition, blood product transfusions, and administration of other intravenous medications. These devices are useful to improve the quality of life of patient and to reduce adverse conditions including pain, phlebitis, frequent needle penetration, and cosmetic problems.^[1,2]

Currently, different TIVAD insertion techniques are performed by the surgeons or interventional radiologists. Surgeons usually prefer cut-down or percutaneous access to the cephalic, subclavian or jugular vein, while interventional radiologists usually prefer puncturing the jugular or subclavian vein under the ultrasound guidance.

In our hospital, TIVAD insertion has almost always been performed for the percutaneous subclavian vein access using the landmark-based approach. In the present study, we aimed to evaluate the clinical features, peri-procedural outcomes, early and late complications and management strategies, and to present our experiences in patients undergoing TIVAD insertion through the percutaneous subclavian vein in a relatively large cohort.

PATIENTS AND METHODS

Between March 2012 and June 2018, a total of 2,084 TIVADs were implanted to 2,000 adult oncology patients (1,066 males, 934 females; mean age 58.4 ± 12.7 years; range, 18 to 88 years) through the percutaneous subclavian vein access using the landmark-based approach, and these cases were included in this study. Data were collected through electronic file scanning, and their medical records were reviewed retrospectively. Data including age, gender, primary diagnosis, total number of implanted TIVAD per patient, accessed subclavian vein (right or left), technical success, procedure time, duration of device use, reasons for the device removal, and early and late complications were recorded. Patients under 18 years old, patients with a high risk of bleeding (platelet count $< 80,000/\text{mm}^3$, international normalized ratio [INR] > 1.5), those whose subclavian vein was punctured under the ultrasound guidance, and those in whom the access was other than the subclavian route were excluded from this study. A written informed consent was obtained from each patient. The study protocol was approved by the Bolu Abant İzzet Baysal University Clinical Researches Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. Early complications were defined as those related to the intervention and

those occurred within the first 24 h post-interventional period. Late complications were defined as those occurred at least 24 h following the intervention, such as TIVAD-related infections, venous thrombosis, catheter occlusion, migration, embolization, and pinch-off syndrome.

Procedure

Coagulation parameters of the patients including prothrombin time, INR, activated partial thromboplastin time, and platelet count were examined before the procedure. During the procedure, all patients were non-invasively monitored using arterial blood pressure, electrocardiography, and fingertip oxygen saturation. A single lumen TIVAD (Celsite, B. Braun Medical, Boulogne Cedex, France) was implanted to all patients. As the first choice, the right subclavian vein was preferred due to the convenience of access and satisfactory cosmetic outcomes. For patients who had a history of right mastectomy, receiving radiotherapy on the right thoracic side, or in the presence of unavailability of right subclavian vein for vascular access due to the several causes, the left subclavian venous route was used.

All procedures were performed under local anesthesia with sterile conditions in the operating room. The subclavian vein was percutaneously punctured using the Seldinger needle through blind landmark technique without any ultrasound guidance. Using this technique, the needle entrance site was determined 1 to 2 cm below and one third lateral of the clavicle. The needle was placed under the inferior margin of the clavicle in a horizontal plane and gingerly directed with negative aspiration toward the anterior margin of the trachea at the level of the suprasternal notch. Following the aspiration of venous blood, a 0.035-inch guidewire was inserted through the needle, until an arrhythmia trace was seen on the monitor. If an arrhythmia trace was not seen or there was a suspicion on guidewire location, a fluoroscopic examination was performed to detect the location of the wire. A subcutaneous pocket was created 3 to 4-cm below the clavicle for the placement of port reservoir through making a transverse incision with a size of approximately 3 cm. A tunnel was formed between the puncture site and subcutaneous pocket. A silicone catheter with a diameter of 7 or 8 F was inserted through the tunnel, and a tip of the catheter was connected to the reservoir placed into the subcutaneous pocket. A peel-away sheath combined with a vascular dilator was passed over the guidewire. Following the dilator and guidewire removal, the catheter was inserted through the sheath. The function of the TIVAD was

checked after withdrawal of venous blood from the port reservoir by using the Huber needle (Cytocan, B. Braun Medical, Boulogne, France). The reservoir and catheter were washed with a 20-mL isotonic sodium chloride solution and, then, the reservoir was filled with a 5-mL isotonic sodium chloride solution containing 100 U/mL of unfractionated heparin. The base of the reservoir was fixed to the fascia of the pectoralis major muscle with the absorbable sutures, and the skin was sutured using the polypropylene threads.

Post-procedural follow-up and care

All patients were transferred to the regular ward at the end of the intervention, if there was no sign of a complication, and they were followed in the hospital setting at least 24 h after the intervention. Posteroanterior chest X-ray images were routinely obtained at two and 24 h following the intervention to evaluate both the localization of the catheter and the presence of any complications. After discharge, the patients were scheduled to the outpatient clinic for a routine follow-up on Days 10 to 14 after the procedure. During follow-up, they were evaluated in terms of any signs of infection and wound complications and the skin sutures were, then, removed. To prevent occlusion and dysfunction of port catheters, the catheters were flushed at regular intervals for long-term catheter care in patients who received regular chemotherapy. For those who did not receive chemotherapy, their current medical conditions were ascertained by telephone interviews.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean \pm standard deviation (SD) and median (min-max), while categorical variables were expressed in number and frequency.

RESULTS

A total of 2,084 devices were implanted to 2,000 patients. For all patients, TIVADs were implanted for the intention of intravenous chemotherapy administration. Primary malignancies of patients are listed in Table 1. The most common malignancies in our study population were colon and breast cancer. The TIVADs were implanted twice in 78 patients and three times in three patients. The procedure failed in 32 patients despite the attempt to access bilateral subclavian veins, and these patients were excluded from the study population. The technical success rate

was calculated as 98.5%. The right subclavian vein was primarily preferred for venous access. The TIVADs were inserted through the right subclavian vein in 1,926 patients (92.4%) and the left subclavian vein in 158 patients (7.6%). The mean procedure time was 27.7 ± 19.0 (range, 10 to 180) min. The mean duration of device use was 26.2 ± 14.8 (range, 1 to 75) months.

Early and late complications following TIVAD insertion are shown in Table 2. Early complications developed in 143 patients (6.9%) and included inadvertent arterial puncture, catheter malposition, superficial hematoma, and pneumothorax. The most common adverse event was inadvertent arterial

Table 1. Primary diseases of study population

| Cancer types | n | % |
|---|-----|-------|
| Colon cancer | 447 | 22.35 |
| Breast cancer | 414 | 20.7 |
| Gastric cancer | 260 | 13.0 |
| Rectal cancer | 189 | 9.45 |
| Lung cancer | 166 | 8.3 |
| Gynecological cancers | 126 | 6.3 |
| Genitourinary cancers | 88 | 4.4 |
| Pancreatic cancer | 81 | 4.05 |
| Esophageal cancer | 57 | 2.85 |
| Hepatobiliary cancers | 54 | 2.7 |
| Nasopharyngeal cancers | 42 | 2.1 |
| Other cancers (hematological, laryngeal, thyroid cancers, sarcomas, etc.) | 76 | 3.8 |

Table 2. Complications following totally implantable venous access device insertion

| | n | % |
|-------------------------------------|-----|------|
| Early complications | 143 | 6.9 |
| Inadvertent arterial puncture | 63 | 3.0 |
| Catheter malposition | 37 | 1.8 |
| Hematoma formation | 27 | 1.3 |
| Pneumothorax | 16 | 0.8 |
| Late complications | 118 | 5.7 |
| Infection | 44 | 2.1 |
| Catheter occlusion | 30 | 1.4 |
| Venous thrombosis | 26 | 1.2 |
| Wound dehiscence or skin necrosis | 12 | 0.6 |
| Catheter migration and embolization | 3 | 0.14 |
| Pinch-off syndrome | 3 | 0.14 |
| Total complications | 261 | 12.5 |

puncture, which was seen in 63 patients (3%). Catheter malposition in 37 patients (1.8%) was the second most common early complication. In 33 patients with catheter malposition, the tip of catheter was accidentally placed into the contralateral or ipsilateral internal jugular vein. In such cases, repositioning was carried out under fluoroscopy in the angiography unit. Pneumothorax was the most serious early complication of TIVAD insertion, which was observed in 16 patients (0.8%). Among patients with pneumothorax, 14 needed tube thoracostomy for the treatment of a large pneumothorax, while only remaining two patients were managed conservatively. Late complications developed at a rate of 5.7% (n=118) and included TIVAD-related infection, catheter occlusion, venous thrombosis, wound healing problems, catheter migration, embolization, and pinch-off syndrome. The most common late complication was TIVAD-related infection, which was observed in 44 patients (2.1%). Among those 44 patients with infection, 36 needed TIVAD removal with antibiotic treatment, while the remaining eight were treated with conservative approaches without device removal. Catheter thrombosis or occlusion occurred in 30 patients (1.4%), and the catheters of these 30 patients were removed and, then, reinserted through the contralateral subclavian vein. Upper limb deep venous thrombosis on the TIVAD insertion side was seen in 26 patients (1.2%); among them, four relieved with appropriate anticoagulant therapy alone. However, 22 patients required device removal along with anticoagulant therapy. Catheter migration and embolization was an uncommon, yet life-threatening adverse event, which occurred in three patients (0.14%). Two of the three patients with catheter migration and embolization were managed endovascularly using the snare retrieval technique by an interventional radiologist, while the remaining case received no intervention due to his poor health condition with a very low life expectancy. Pinch-off syndrome was another

uncommon late complication of TIVAD insertion, which was experienced in three patients (0.14%). The device was removed and re-implanted at another site in two of these patients, while the remaining one patient was followed conservatively.

No procedure-related mortality was observed in any patients. However, death events related to primary malignancies were observed in 311 patients during follow-up period. In addition, complete follow-up was unable to be achieved in 63 patients due to unavailability of the patients (i.e., ceased, interrupted, or not possible).

Implanted TIVADs were removed in 192 patients due to the completion of chemotherapy, or complications including infection, catheter occlusion, venous thrombosis, wound problems, pinch-off syndrome, catheter migration, and embolization. The reasons for removal of TIVADs are summarized in Table 3.

DISCUSSION

The TIVADs or port catheters are the devices which are entirely placed under the skin and provide easy and safe vascular access, particularly for repeated chemotherapy administrations in cancer patients. Currently, these devices have been increasingly used in patients with difficulty in vascular access and who need long-term intravenous treatments. Many chemotherapeutic agents may cause damage at the vessel wall and obliteration of the vein, if peripheral veins are used for chemotherapy administration. In addition, if the agents leak into the surrounding tissue, they may result in cellulitis, phlebitis, or even tissue necrosis. The utilization of TIVADs can avoid the potential vascular damage caused by the chemotherapeutic agents in the peripheral veins. Placement under local anesthesia, discharging the patient on the same day which enables the continuation of the treatment at home, no restrictions of the daily life, minimal discomfort, not causing any cosmetic problems, and low complication rates are among the main advantages of TIVAD insertion. However, despite these merits, TIVADs are not completely free from complications. Inadvertent arterial puncture, pneumothorax, hemothorax, air embolism, cardiac arrhythmia, pericardial tamponade and brachial plexus injuries are the early complications related to TIVAD insertion. Late complications include TIVAD-related infection, venous thrombosis, catheter thrombosis, occlusion and dysfunction, catheter migration and embolization, local extravasation, and pinch-off syndrome.^[1-3]

Previous studies regarding the TIVAD insertion are summarized in Table 4. According to the existing

Table 3. Causes of device removal

| Cause | n | % |
|-------------------------------------|----|------|
| Completion of chemotherapy | 93 | 48.4 |
| Complications | 99 | 51.6 |
| Infection | 36 | 18.7 |
| Catheter occlusion | 30 | 15.6 |
| Venous thrombosis | 22 | 11.5 |
| Wound dehiscence or skin necrosis | 7 | 3.6 |
| Catheter migration and embolization | 2 | 1.0 |
| Pinch-off syndrome | 2 | 1.0 |

Table 4. Summary of literature studies in surgically implanted venous access port devices

| Study | Publication year | No. of inserted devices | Accessed vein | Technical success | Device removal for complication | | Catheter malposition | Pneumothorax | Infection | Thrombosis | Catheter malfunction | Pinch-off syndrome | Overall complication | |
|--|------------------|-------------------------|------------------|-------------------|---------------------------------|-----|----------------------|--------------|-----------|------------|----------------------|--------------------|----------------------|---|
| | | | | | % | % | | | | | | | % | % |
| Koek <i>et al.</i> ^[4] | 1998 | 1500 | SV, IJV, CV | NS | 11.9 | 2.4 | 0.3 | 3.2 | 2.5 | 2.8 | NS | NS | 12.8 | |
| Guth ^[5] | 2001 | 513 | SV, IJV | 98.2 | 0.2 | 1.5 | 1.2 | NS | NS | NS | NS | NS | 3.1 | |
| Yildizeli <i>et al.</i> ^[6] | 2004 | 225 | SV | NS | 4.4 | 3.1 | 1.3 | 2.2 | 1.3 | 1.8 | NS | NS | 12.4 | |
| Araujo <i>et al.</i> ^[7] | 2008 | 1231 | SV, IJV | NS | NS | 1.2 | 0.8 | 3.5 | 1.3 | 6.8 | NS | NS | 15.1 | |
| Narducci <i>et al.</i> ^[8] | 2011 | 815 | CV, EJV | NS | 6.7 | 0.9 | 0 | 5.4 | 0.7 | NS | NS | NS | 16.1 | |
| Keum <i>et al.</i> ^[9] | 2013 | 245 | SV | 100 | 7.8 | 2.4 | 0 | 2.9 | 1.6 | 1.2 | 0 | 0 | 9.4 | |
| Seok <i>et al.</i> ^[10] | 2014 | 165 | SV, IJV | 97 | 17 | 0.5 | 0.5 | 9 | 2 | 4 | 0 | 0 | 21.2 | |
| Nagasawa <i>et al.</i> ^[11] | 2014 | 233 | SV, IJV | 95.7 | 8.2 | 0.4 | 1.7 | 4.3 | 0.9 | 2.6 | NS | NS | 12.9 | |
| Aziret <i>et al.</i> ^[12] | 2015 | 122 | SV | 97.5 | 3.2 | 2.4 | 1.6 | 3.3 | 0 | 6.6 | 0 | 0 | 14.7 | |
| An <i>et al.</i> ^[13] | 2015 | 397 | SV, IJV | 97 | 4.3 | 0.8 | 0 | NS | 0 | 0.3 | 0 | 0 | 8.3 | |
| Gurkan <i>et al.</i> ^[14] | 2015 | 324 | SV, IJV | 100 | 2.3 | 1.2 | 0.9 | 1.2 | NS | 4 | 0.6 | 0.6 | 33.9 | |
| Ma <i>et al.</i> ^[15] | 2016 | 2996 | SV, IJV | 98.7 | 2.7 | 0.9 | 0.3 | 1.66 | 0.8 | 2.6 | 0.2 | 0.2 | 6.8 | |
| Zerati <i>et al.</i> ^[16] | 2016 | 1255 | SV, IJV, EJV, FV | NS | NS | NS | 0.1 | 13 | 2.2 | 3.1 | NS | NS | 19.8 | |
| Feo <i>et al.</i> ^[17] | 2017 | 527 | SV | NS | NS | 1.3 | 0.6 | 1.3 | 0.2 | 0.8 | 0 | 0 | 4.2 | |
| Bazine <i>et al.</i> ^[18] | 2018 | 852 | SV, IJV, CV, EJV | NS | NS | 0 | 1.9 | 2.8 | 1.8 | 1.3 | 0 | 0 | 10.8 | |
| Yank <i>et al.</i> ^[19] | 2018 | 3000 | SV, IJV | 99 | 7.3 | 0.2 | 1 | 3 | 1 | 0.4 | 0.06 | 0.06 | 9.6 | |
| Kim <i>et al.</i> ^[20] | 2019 | 843 | SV, IJV | 100 | 0.2 | 0.3 | 0 | 1.4 | 0.5 | 1 | 0 | 0 | 4 | |

SV: Subclavian vein; IJV: Internal jugular vein; CV: Cephalic vein; EJV: External jugular vein; NS: Non-specified.

literature, the overall complication rate following TIVAD insertion ranges from 3.1 to 33.9%.^[4-20] The overall complication rate in our study population was 12.5%, consistent with the results reported in previous studies.

Inadvertent arterial puncture was the most common complication in our study with a rate of 3%. In the course of subclavian venous access, inadvertent arterial puncture may develop in 6 to 8% of all attempts.^[21] Although the rate of inadvertent arterial puncture during subclavian venous catheterization was higher, when ultrasonography guidance was not used as in our series, our lower rate compared to the literature can be attributed to our meticulous work and high level of experience.

The second most common early complication in the current study was the catheter malpositioning. Catheter malposition is defined as the catheter tip placement into a vein other than superior vena cava or right atrium, impingement with the lateral wall of superior vena cava ($>40^\circ$) and arterial cannulation. If not addressed, it may result in several adverse events such as venous thrombosis, erosion and perforation of vessel wall, catheter wedging, catheter dysfunction, and cranial retrograde injection in which the infusate is directed to the head instead of the central circulation. Therefore, it is advised that the catheter should be promptly repositioned, replaced or removed, when a catheter malposition occurs.^[21] In our patients with catheter malposition, most of the catheter tips were accidentally located into the contralateral internal jugular vein and, then, these catheters were repositioned immediately and accurately.

The development of hematoma is usually a result of either hemostatic disturbances or a technical fault. Risk factors which contribute to this adverse event are obesity, previous procedures and radiotherapy applications to the insertion area, multiple punctures, and inexperienced practitioner. Hematoma formation has been reported to occur with an incidence of 0.1 to 8%.^[22] Consistent with the literature, this adverse event occurred in 1.3% of our patients. These patients were conservatively followed without any additional intervention.

Among the early complications, pneumothorax is the most undesirable and feared one, since it may lead to severe clinical, economic, and psychological consequences. Although different rates of incidence of pneumothorax have been reported in the literature, its incidence following TIVAD insertion through percutaneous subclavian vein ranges between

0.5 and 4%.^[6,12,17,22-24] In the present study, we observed pneumothorax in 16 patients (0.8%), consistent with the reported incidences in the literature. Management of TIVAD insertion-related pneumothorax varies from simple observation to invasive tube thoracostomy, depending on the size of pneumothorax and presence of signs and symptoms. The majority of our patients with pneumothorax were managed with tube thoracostomy due to the large size of pneumothorax.

Infections are one of the most frequent and important complications of TIVAD insertion, which adversely affect morbidity and mortality and is associated with increased healthcare costs. Patients' primary malignancy itself and poor health status, delayed wound healing due to chemotherapeutic agents, intensive chemotherapy schedule, device insertion in hospitalized patients, device insertion through femoral vein, the obsolete technique of venous cannulation by venous cut-down, use of device for parenteral nutrition, frequent access to the device, and presence of an underlying hematologic and HIV-infected malignancies are considered to be risk factors associated with TIVAD-related infections.^[25] In cases of TIVAD-related infections, device removal along with antibiotic treatment was mostly applied, while conservative treatment (antibiotic treatment alone) was chosen in the minority of patients with TIVAD-related infections. In a recent study performed by Vidal et al.,^[26] 81% of patients with device-related infection required device removal, while conservative approach was suitable for the remaining patients. In our study cohort, we encountered TIVAD-related infection in 44 patients (2.1%) and the device was removed in 36 of them.

Catheter dysfunction caused by catheter thrombosis and occlusion is another frequent complication following TIVAD insertion. Inadequate catheter care, withdrawal of blood for confirming the place of the catheter prior to the use of the device, frequent blood transfusions, and blood sampling (blood withdrawals for laboratory tests) are all factors which increase the risk of catheter thrombosis and occlusion. Education of the nurses and other healthcare staff members as well as their attention and care can avoid withdrawal of blood during using the port catheter. If possible, minimizing the use of the port catheter for blood transfusion and blood sampling can decrease the risk of thrombosis and occlusion of the port catheter.^[27] Catheter dysfunction caused by intraluminal catheter thrombosis can be treated empirically with thrombolytic agents as the first therapeutic options. However, if this thrombolytic therapy fails and a permanent dysfunction occurs,

the device should not be left in place and the device removal should be performed to manage complications.

Due to the tendency of hypercoagulation, cancer patients are at high risk for venous thrombosis. The insertion of foreign materials to the vein further increases the risks. Endothelial damage during the insertion, low blood flow in the catheterized vein, characteristics of the administered fluids and chemotherapeutic agents, the material that the catheter is constructed, insertion site, and duration of the catheterization are all contributing factors for the formation of thrombosis.^[28] Venous thrombosis is usually asymptomatic or may occasionally manifest itself with ipsilateral limb and neck pain or swelling. Since it is usually asymptomatic, its true incidence is underestimated. Ignatov *et al.*^[29] reported the incidence of venous thrombosis as 7.5% in their study. It is known that the placement of the catheter tip in the upper half of the superior vena cava is the most important factor in the formation of thrombosis.^[30] In the current study, we routinely checked the location of catheter tip following TIVAD insertion using chest X-ray images in all cases. Nevertheless, symptomatic venous thrombosis developed in 26 patients (1.2%). When a venous thrombosis is diagnosed, it is recommended that anticoagulation should be immediately started for the acute treatment and, then, continued for at least three months or until the device is in place. Although the device removal is not mandatory for all cases with venous thrombosis, the device should be removed if it is non-functional or not necessary.^[3,18]

Wound problems such as wound dehiscence, skin decubitus, and necrosis may develop following the TIVAD insertion due to the technical failure or patient-related causes. During the device implantation, the creation of subcutaneous pocket close to skin or the selection of inappropriate reservoir size for weak patients can lead to wound healing problems. To avoid these problems, the catheter should be inserted in the subcutaneous plane and to be sure that it is not superficially located. In addition to these precautions, the catheter should not be inserted under irradiated skin or previous mastectomy incision sites.^[3,31] On the other hand, in obese patients, excessive depth in the placement of the catheter may cause problems related to the palpation of the port catheter or insertion of the port needle. In our study population, wound problems occurred in only 12 patients (0.6%), as we paid a great attention to the related issues.

Catheter migration and embolization are rare complications of TIVAD insertion, which may usually develop due to the mechanical stress or, in rare cases,

these complications may develop due to technical problems during the device insertion. To avoid these problems during the procedure, the catheter-reservoir connection should be carefully checked while inserting the device. This is very important for the safety of the system.^[32] These adverse events may be asymptomatic and can be incidentally detected by routine chest X-ray imaging in certain cases. They may be also accompanied by catheter dysfunction or symptoms of local extravasation. In such a case, an intense pain may occur around the site, where the drug is administered, when the agent is being infused through the port reservoir. In addition, these complications may also manifest themselves with serious cardiac arrhythmias, and even death. The diagnosis is easily established using chest X-ray images.^[2,3,33] When diagnosed, the catheter should be removed as quick as possible to prevent the lethal consequences. In most cases, the catheter removal is usually performed using endovascular methods, while open surgery or even leaving the catheter in place can be considered as other management options in selected cases.^[2,33,34]

Pinch-off syndrome is defined as the compression of a long-term central venous catheter between the clavicle and first rib. The compression may lead to temporary obstruction of the catheter and impairment of the flow, total occlusion and malfunction of the catheter, and even breaking, transection and embolization of the catheter. This complication usually manifests itself first with the presence of a resistance during the utilization of the device. Its distinctive feature is intermittent catheter occlusion where the device activates by abduction of the ipsilateral arm. Additionally, it may cause some complaints including infraclavicular pain, swelling around the device, and paresthesia in the arm. The presence of catheter indentation that passes beneath the clavicle, which can be revealed on a chest X-ray image, as also known as the 'pinch-off sign', is pathognomonic. Since this complication possess the risk of catheter embolization and severe cardiac arrhythmias, the port catheter should be removed. The risk of pinch-off syndrome can be reduced performing the initial puncture laterally for subclavian vein access or introducing the catheter through the cephalic vein by a cut-down technique or using the internal jugular vein as vascular access site.^[35-37]

In our routine practice, we have been using the percutaneous landmark technique, also known as the 'blind technique' for TIVAD insertion for many years; therefore, we have become highly experienced. Moreover, we are very familiar with the anatomy of the chest and neck vasculature and can identify possible

procedure-related adverse events in a timely manner and treat them appropriately. In our study, we chose the right subclavian vein as the first option for vascular access route, since this route has several advantages such as ease of access, satisfactory cosmetic outcomes, good stability on the chest wall, and low infection risk. The left subclavian route was used, when the right subclavian access was unfavorable or failed. Of note, it is known that catheters employed on the right side are more durable and associated with less complication rates, compared to the catheters inserted on the left side.^[6,9,14,38]

The main strength of our study is that it includes a large cohort. However, the retrospective nature of data collection is the main limitation. The present study was mainly designed to present our extensive experiences on this topic.

In conclusion, totally implantable venous access device insertion through percutaneous subclavian vein is a safe and well-tolerated procedure with high technical success and low complication rates in experienced hands. Considering the great convenience for the patients, totally implantable venous access device insertion in patients receiving long-term chemotherapy is a valuable method which should be routinely preferred. Post-procedural long-term follow-up and care of the device is essential and should be carried out by a multidisciplinary team consisting of surgeons, medical oncologists, nursing staff, and patients themselves.

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