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ORIGINAL ARTICLE

Retrospective evaluation of totally implantable venous access port devices: Early and late complications

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Summary

Purpose: *The role totally implantable vascular devices (TIVAD) have an important role in providing care to cancer patients who require continuous or frequent venous access route either for their primary or supportive care treatments. This retrospective study aimed to analyze the efficacy of TIVAD and device-related complications.*

Methods: *A total of 324 consecutive patients (185 male,139 female, median age 56 years, mean 48 ± 10.91; min:16, max:87) who were implanted with TIVAD between January 2012 – May 2014 were included. We retrospectively assessed all TIVAD complications and focused on early and late complications.*

Results: *A total of 324 devices were implanted successfully without major complications. The overall complication rate was 33.95% (N=110). Of them, 87 (26.85%) were early and 23 (7.09%) were late complications. In total, 39 (11.23%) catheters were removed, in 8 (2.30%) patients due to complication and in 31 (9.56%) due to the end of treatment.*

Conclusion: *Most of the complications of TIVAD were early without requiring removal. Port catheters for chemotherapy are safe and well tolerated with acceptable complication rates.*

Key words: *cancer, chemotherapy, complication, totally implantable venous access device*

Introduction

After the use of partially implantable venous access devices, TIVADs became available. Niederhuber et al. were the first surgeons to apply such a device in 1982 by placing it into the cephalic vein by surgical technique [1]. In 1992 TIVAD was percutaneously applied in an angiography unit with radiological assistance for the first time [2].

The routine use of TIVADs was a silent revolution for the treatment of many cancer patients who needed frequent and long-duration intravenous access for their chemotherapy. Along with cancer patients there are many patient groups, such as patients with chronic diseases like cystic fibrosis, hemophilia with patients needing urgent rapid transfusion of coagulation factors, and also patients with diseases that require frequent blood examinations benefited greatly from this invention [3]. Among its many potential advantages both for the patient and the healthcare provider are TIVAD implantation requiring only local anesthesia, being cosmetically acceptable, with same-day discharge from the hospital . Although they have much less infection risk in the long-term when compared to percutaneous venous catheters, the occurrence of various complications either at the time of implantation or during long-term use can be problematic [4]. Along with procedural complications such as pneumothorax, hemothorax and late-term complications like infection, thrombosis, catheter dysfunction and catheter migration can be seen [3,5].

In this study we reviewed our experience with subcutaneous venous port implantation and reported the outcomes of patients who developed

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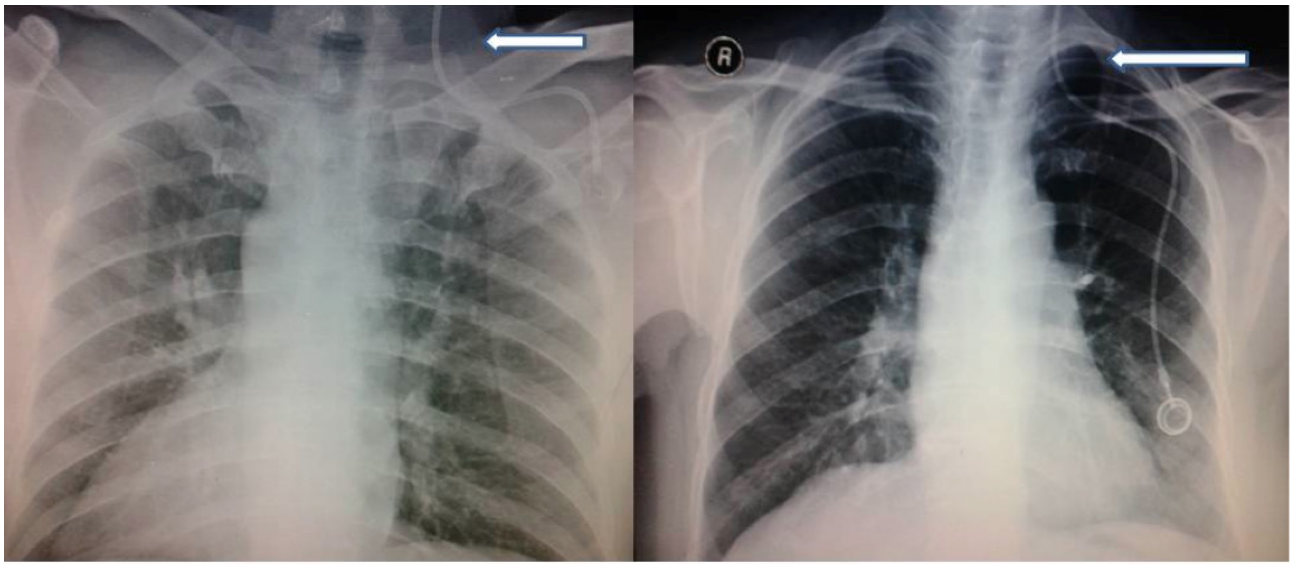

Figure 1. Catheter malposition to internal jugular vein during insertion (arrows).

early and late complications in our clinic.

Methods

This retrospective study was approved by the Local Ethics Committee of the Namik Kemal University Hospital (protocol number 2013/53/05/02; date of approval 30/05/2013). Included were 347 patients who presented to Namik Kemal University Hospital, Cardiovascular Surgery Clinic, for TIVADS implantation between January 2012–May 2014. The medical records of the patients were scanned from the hospital's database and current information about the status of the patients were obtained by telephone. Twenty three patients who could not be reached by telephone were left out of the study group. All the invasive procedures were done by two experienced cardiovascular surgeons in sterilized operation room. Signed informed consent was taken from all of the patients. Possible vascular entrance routes (subclavian, jugular, upper extremity veins) were thoroughly examined before the procedure. All patients had their blood count and coagulation parameters checked before the operation. In all patients single lumen venous port was used (Celsite, B.Braun Medical, Boulogne Cedex, France). The right subclavian vein was preferred because of ease of access and better cosmetic results. In patients who had mastectomy, received radiotherapy on the right side or venous entrance could not be accessed for various reasons, contralateral subclavian or jugular veins were chosen.

Except for the first 50 cases , intraoperative fluoroscopy was used in all cases. During the operation ECG, finger tip oxygen saturation and arterial pressure were non invasively monitored. All patients received nasal oxygen 4-6 l/min. After sterile barrier precautions taken and under local anesthesia with 1% lidocaine, central vein was cannulated. If the subclavian vein was chosen, the puncture was made 1-2 cm below and 1/3 lateral to the clavicle; if the jugular vein was chosen, the entrance was made medially between the two heads of sternocleidomastoid muscle. Puncture was made by using the "Huber needles" designed for vascular ports. A 0.035 inch thick guidewire was passed through the needle and positioned near the right atriocaval junction. Intraoperative fluoroscopic guidance was used to ensure whether the wire was in the right atrium. After placing the guidewire, a 'peel away' sheath combined with the dilatator was passed through the guidewire . An incision was made under local anesthesia 3-4 cm below the clavicle and with the use of electrocauterization a subcutaneous pocket was formed. The guidewire was then removed and the distal tip of the catheter was passed through the 'peel-away' sheath. The distal tip of the catheter was inserted into the central vein by splitting and pulling out the 'peel-away' sheath. The base of the port was then fixed to the pectoral fascia with non absorbable sutures. After testing by aspiration if the blood was in the lumen, both the port and the catheter were washed with normal saline and then the catheter was filled with 100U/ml diluted heparin. Two hours after the completion of the procedure a chest x-ray was taken for controlling the position and location of the catheter.

All patients were discharged the same day and were seen in the outpatient clinic for a routine follow up one week postprocedure. In the follow up visit physical examination for any signs of infection and wound complications were made and the sutures were removed. All of the complications recorded during the invasive procedures and those that occurred during the one-week period were defined as acute complications and the complications that occurred at a later time were defined as late complications.

Statistics

Data were analyzed using the PASW SPSS version

Table 1. Characteristics and cancer types of the study population

Characteristics	*N (%)*
No. of patients	347 (100)
Age (years), mean±SD	56.48 ± 10.91
Gender	
Male	185 (57.09)
Female	139 (42.91)
Cancer types	
Gastrointestinal system	154 (47.53)
Breast	67 (20.67)
Lung	33 (10.18)
Upper airway	28 (8.64)
Hematopoietic system	23 (7.09)
Genitourinary system	19 (5.89)
No.of ports	347
Port duration (days), mean±SD	271.92 ± 197.65
Range (days)	9 - 783

SD: standard deviation

Table 2. Totally implantable venous access port devices complications and indications for removal

Characteristics	*N (%)*
Total ports removed	39 (11.23)
Complication	8 (2.30)
Completion of treatment or patient request	31 (9.56)
Total complications	110 (33.95)
Early	87 (26.85)
Late	23 (7.09)
Early complications	
Arrhythmia	43 (13.27)
Accidental arterial puncture	17 (5.24)
Local inflammation	15 (4.62)
Pocket hematoma	5 (1.24)
Catheter malposition	4 (1.23)
Pneumothorax	3 (0.92)
Late complications	
Thrombosis or occlusion of the catheter	13 (4.01)
Infection	5 (1.24)
Catheter rupture or embolisation	3 (0.92)
'Pinch off syndrome'	2 (0.61)

18.0 (SPSS Inc., Chicago, IL, USA). Qualitative variables were expressed as median and range, and mean and standard deviation.

Results

Three hundred and twenty four patients (185 males,139 females, mean age 56.48±10.91; min:16, max:87) in whom TIVAD was applied in our center were included in this study. In 289 (89.19%) patients the right subclavian vein, in 26 (8.02%) the left subclavian vein and in 9 (2.77%) the right jugular vein were used for venous access. The total port implantation time ranged between 9 and 783 catheter-days, with a mean catheter functional duration time of 271.92±197.65 days and a total of 88.128 catheter-days for all ports.

Patients with gastrointestinal system cancers formed the largest group (47.53%), followed by breast, lung, upper airway, hematopoetic and genitourinary cancer patients (Table 1). Port implantation was successfully accomplished in all patients. In the first 50 patients fluoroscopy was not used during the implantation procedure. After the observation of a catheter malposition due to upward advancement of the guidewire through the jugular vein with the help of a chest x-ray taken following the completion of the operation, fluoroscopy and ultrasonography were used in all of the following cases (Figure 1). The position of the catheter was corrected in the cardiac angiography laboratory under fluoroscopy at the same day.

Complications were recorded in 110 (33.95%) patients; 87 (26.85%) of them were procedural and early complications, while there were 23(7.09%) late complications. The most common acute complication type was short-lasting cardiac arrhythmia not necessitating intervention, which was observed in 43 (13.27%) patients. Accidental arterial puncture in 17 (5.24%) patients was the second most common procedural complication. In 15 (4.62%) patients local inflammation which was treated without catheter removal was recorded in the 7th day of the follow up visit. In 5 (1.24%) patients pocket hematoma developed. Hematoma was resolved by compression alone in 2 of the cases. In all of these patients catheters remained functional. Catheter malposition and guidewire disposition was observed in 4 (1.23%) patients. One of these malpositions was corrected in the angiography laboratory and the other cases were instantly corrected as they were detected under fluoroscopy. The most serious early complication was pneumothorax. In 3 (0.92%) patients pneumothorax dev0eloped during the procedure. In all of these patients pneumothorax resolved spontaneously and no tube thoracostomy was needed.

Thrombosis of the catheter reservoir, intralu-

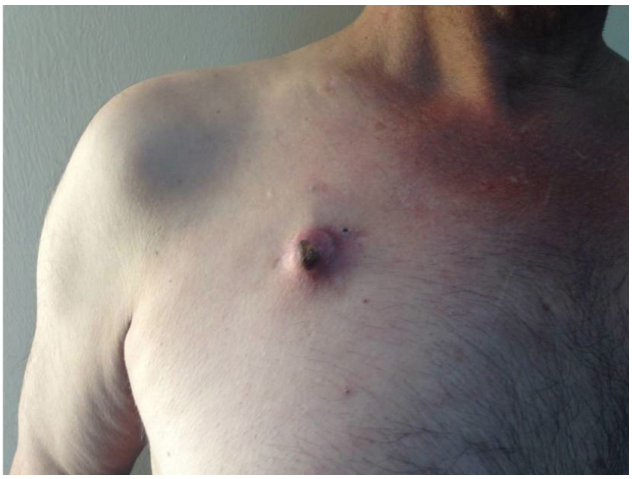

Figure 2. Port avulsion due to infection.

minal occlusion and fibrous sheath formation were the most common late complications. Thrombosis was seen in 13 (4%) patients and resolved without urokinase treatment or catheter removal. In 5 (1.24%) patients infection in the port region was detected and in 2 of these port avulsion occurred (Figure 2). All of these cases presented as late complications (259.4±116.94 days) and the catheter had to be eventually removed.

Catheter embolisation is a rare but life-threatening complication. In our series 3 patients were identified with this serious event. In one patient the emboli were removed subcutaneously and one was removed from the subclavian vein (Figure 3A-B). The other case was solved by endovascular methods because the catheter embolisation was into the pulmonary artery (Figure 3C). Another less common late complication observed in 2 patients was the "pinch off syndrome". Surgical intervention resolved the problem in these 2 cases.

During follow up 17 patients died of disease-related causes. No fatal complications occurred either during the invasive procedure or later in time in any of the patients. The catheter was removed in 31 patients because of treatment termination, in 3 patients because of rupture and in 5 patients because of infection (Table 2).

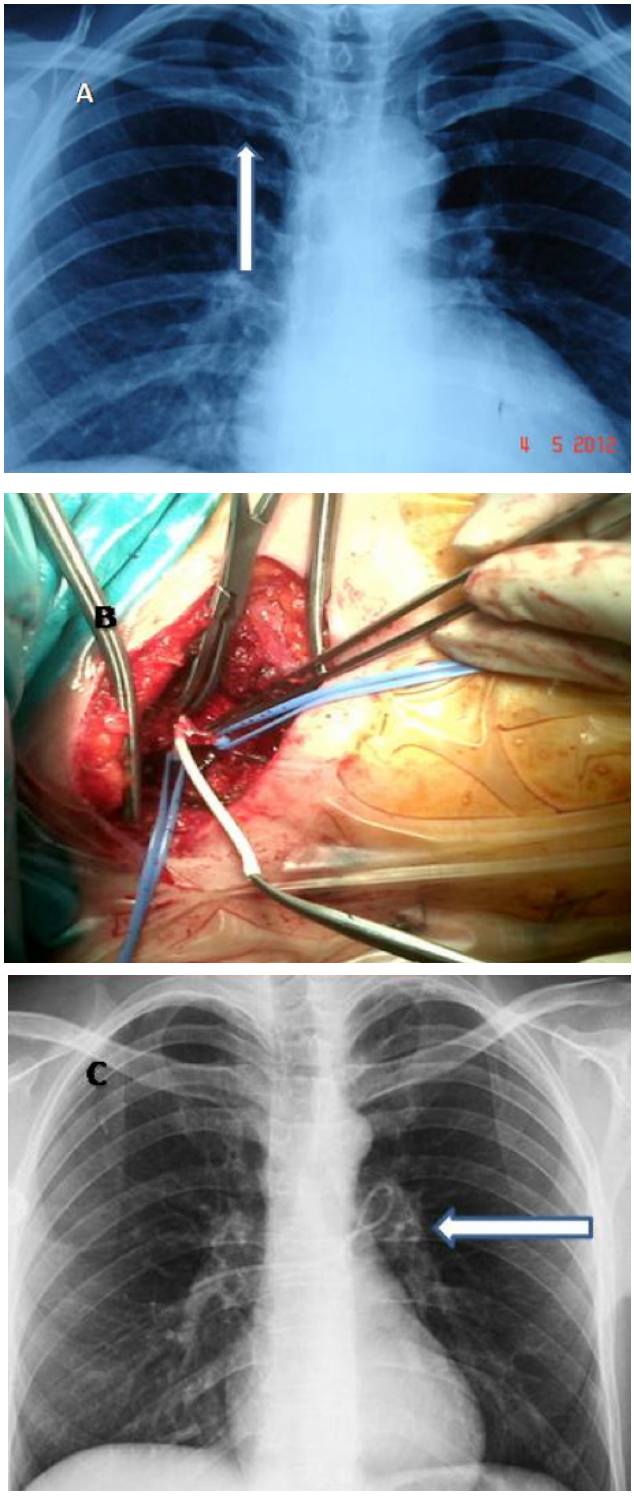

Figure 3. A: Catheter rupture and embolisation to subclavian vein (arrow). **B:** Surgical extirpation of the catheter from subclavian vein. **C:** Catheter fracture and embolisation to the pulmonary artery (arrow).

Discussion

Subcutaneously implanted venous ports offer substantial benefits in cancer patients who need long-term intravenous chemotherapy. These ports are not seen from outside and are easily accepted by the patient. They do not limit daily and physical activities such as taking a bath or swimming; besides, the incidence of catheter-related infection is rather low [6]. However, despite these advantages, various complications can occur either during the implantation procedure or later in the follow up. In this study we retrospectively assessed the outcomes and complications related with TIVAD implantation in our center.

Cephalic vein, internal jugular vein, subclavian vein or lower extremity veins can be used for TIVAD implantation. We preferred the right subclavian vein for implantation in the majority of the patients. Ease of access, more cosmetically acceptable results and because it is not making a 90 degrees angle with the vena cava superior were the main reasons behind our preference for the right subclavian vein. In contrast, the left subclavian vein makes a 90 degree angle with the superior vena cava which can lead to intima damage or rupture of the vein during the advancement of the catheter or the guidewire. The close proximity of the subclavian vein to the lung parenchyma can excessively increase the risk of pneumothorax in inexperienced hands. The expected incidence of pneumothorax during the procedure is 1–4% [3,7].

Catheter-related thrombosis may lead to pain and swelling in the upper extremity. In addition, repeated compression in long-term catheters can lead to "pinch off" syndrome [8]. Some experts advocate use of internal jugular vein for implantation because it makes a more straight line with the superior vena cava and also has low thrombosis, pneumothorax and hemothorax complication rates. However, in a randomized trial no significant differences in terms of early and late complication rates were found between internal jugular vein, cephalic vein and subclavian vein. The lowest rate of complications was observed in ultrasonography-guided subclavian catheterization [9].

Although the total complication rate in our study was relatively high (33%), most of these complications occurred early, were minor and did not result in any major problems. The rate of complications which resulted in catheter removal was substantially low.

Complications that can be seen during the procedure can be listed as pneumothorax, hemothorax, catheter malposition, puncture of the artery, cardiac arrhythmia, pericardial tamponade and brachial plexus damage. Imaging guidance during the invasive procedure can decrease the complication rate significantly [9,10]. Ultrasonography-guided puncture is important for the prevention of pneumothorax, hemothorax and arterial puncture. Fluoroscopy and x-ray use during the procedure help determine the position of the guidewire and aid in the prevention of malposition. In addition, imaging guidance enables optimal positioning for increasing the efficiency of the catheter.

In the present study the most common complication during the procedure was temporary cardiac arrhythmia. Cardiac arrhythmias can be seen with a frequency of up to 40% during the central vein catheterization [11]. Most of these dysrhythmias do not disturb the hemodynamic status of the patient and are temporary. Serious outcomes can be easily prevented by cardiac monitoring and avoidance of overinsertion of the guidewire. Another common operative complication was accidental arterial puncture. Most of these cases occurred during the time when no ultrasonography guidance was used. The frequency of unintentional arterial puncture during subclavian vein catheterization is 6-8% [12]. Pneumothorax is a relatively common complication during central vein catheterization procedure with a reported incidence of 1-4% [13]. It depends on the level of experience of the performing surgeon and is seen more commonly in subclavian vein catheterization. Close observation is sufficient in most cases, however in more serious cases tube thoracostomy is needed. We did not come across any hemothorax cases in our series, however it can happen after accidental puncture of subclavian, intercostal or internal mammary arteries during subclavian vein canulization [14]. Inadvertent carotid artery puncture can also manifest as hemothorax. The use of ultrasonographic guidance substantially decreases the rate of these complications. In addition, ultrasonographic guidance provides the surgeon rapid access to veins and thereby help decrease the operation time [15].

Local inflammation, pocket hematoma, wound dehiscence are among the common early complications. In our series the most common early complication was local inflammation with a frequency of 4.62%. All the cases resolved with antibiotic and anti inflammatory treatment without necessitating wound debridement or any other invasive procedure. The lack of serious wound infections during the early period can be attributed to the use of operation room under sterile conditions for invasive procedures and prohibition of catheter usage before unstiching. Pocket hematoma is more commonly seen in patients receiving anticoagulant or antiplatelet therapies and patients with hematological malignancies. In these cases it is advised that the catheters should not be accessed before the resolution of the hematoma. In our series the frequency of hematoma formation was found to be similar to the rates reported in literature [16]. Wound dehiscence was not observed in our series, however it is reported that early

usage of port catheter and bevacizumab therapy is associated with this complication [17].

Thrombosis related to catheter, infection, "pinch off" syndrome, catheter rupture and embolisation, extravasation and large vein thrombosis are listed as late complications. In our series the most common late complications were catheter thrombosis and infection. Thrombosis can occur at the tip of the catheter, around it or inside the vein where it is placed [18]. The incidence of thrombosis is not accurately known because of its asymptomatic course, however it is the most common reason for catheter dysfunction. In a post mortem analysis, the thrombotic complication rate in catheterized veins was 38%, whereas this rate was 1.4% in uncatheterized veins [19]. Therefore, it is advised that after infusions and also during periods where catheter is not in use regular maintenance with saline and heparin flushes should be done. In a study where standard heparin treatment was compared with every 2- week urokinase administration, urokinase treament was found to be significantly associated with lower rates of thrombosis and infection in long-term catheters [20,21].

Catheter-related infections are defined as bacteremia or fungemia in a patient with intravascular catheter and at least one positive blood culture from the blood sample taken from a peripheral vein. Port-related infection rates vary between 1-6% in various reports from the literature [4,5,7,18]. The performance of surgical procedures by an experienced surgical team, strict regulation of aseptic technique rules by the oncology nurses, allowance of the use of catheter after unsticthing and education of the patients may have played a role in the lower rates of infections observed in our series. It is reported that delayed usage of catheter (4-7 days rather than 0-3 days) leads to two-fold decrease in the risk of infection and a 8-day interval between TIVAD placement and its use is advised [22]. In our series, 1 gram of cephazoline iv. was given as prophylactic antibiotic treatment before the procedure, however it should be noted that periprocedural antibiotic use was not shown to be associated with decreased long-term infection rates [23].

"Pinch- off" syndrome is defined as long-term compression of the subclavian venous catheter between the clavicle and the first costa [24]. It can be a sign of serious catheter wall damage thus its recognition is important. It can manifest itself as inability to aspirate blood from the catheter or impairment of drug delivery by infusion. It is often reported as intermittent catheter occlusion which is relieved by changing the position of the shoulder and the arm. Repetitive compressions damage and weaken the catheter wall, and this condition can lead to fragmentation of the catheter and embolization into the central veins, right atrium, right ventricle or pulmonary artery [25].

In our series a case of pulmonary embolism was successfully treated with removal of the emboli by percutaneous transvenous snare. The risk of catheter tip migration (sometimes referred as "secondary malposition") is high when the catheter is short, and it is also associated with shallow tip location (relative to the carina), increased intrathoracic pressure and subclavian vein puncture. The catheter can migrate towards the internal jugular vein or the contralateral brachiocephalic vein [26].

Extravasation is still a problem even in the presence of most sophisticated surgical techniques and equipment. Improper needle placement, improper puncture, leak from port catheter junction and catheter rupture are the main reasons [27]. Extravasation of vesicant drugs (anthracyclines and vinblastine) can lead to progressive tissue necrosis. Prompt aspiration of the vesicant drug and taking appropriate measures is necessary for prevention of further damage to the patient.

Catheter removal is done at the end of the treatment protocol or when catheter infection, rupture or migration occurs. In our series catheter was removed in 11.23% of the patients. In long-term catheters, the catheter may become fixed to the surrounding tissue, therefore careful use of force should be applied during removal process to avoid catheter tip rupture [28]. After the removal of the catheter the length of the catheter and its tip should be checked in order to be sure that no part of the catheter remains in the body.

Conclusion

TIVADs provide a viable option for chemotherapy administration to cancer patients who need long-term and frequent venous access for their treatment. They have low complication rates and are reliable for durability with proper maintenance. As our results clearly demonstrate, usage imaging techniques are strongly advised during placement of central venous catheters for reducing procedural complications which can sometimes lead to life-threatening situations. Early complications mostly do not generate serious problems and

can be managed without catheter removal. High level of expertise by the perform ing surgeons, close teamwork between patients, oncology nurses, oncologists and the surgeons, and adherence to hygiene techniques play an important role in reduction of long-term complications.

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