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Complications After Implantation of Subcutaneous Central Venous Ports: Focus on Infection and Catheter Pinch-off

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Objective: The objective of this study was to determine the causes of postoperative complications associated with subcutaneous central venous ports.

Summary of Background Data: Central venous ports were subcutaneously implanted in 523 patients between January 2005 and December 2013.

Methods: The purpose of port implantation was administration of chemotherapy in 439 patients and home central venous nutrition in 84 patients. The underlying disease was malignant in 481 patients and benign in 42.

Results: The median follow-up was 12 months (range, 1–99 months), and postoperative complications developed in 69 patients (13%). Infection occurred in 40 patients (7.6%) and catheter pinch-off in 11 patients (3%). Significant risk factors for infection were nutritional port placement ($P < 0.001$) and use of a femoral vein approach ($P = 0.001$). A left subclavian approach was a significant risk factor for catheter pinch-off ($P = 0.003$).

Conclusions: Postoperative complications, mainly infections and catheter pinch-off, developed in 13% of the patients. As for measures against complications, a femoral vein approach should be avoided to prevent infection. Moreover, because ports for parenteral nutrition require multiple punctures, methods to reduce the number of punctures and techniques for disinfection and management should be reevaluated. To prevent catheter pinch-off, an internal jugular vein approach should be used instead of a left subclavian approach.

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Subcutaneously implanted central venous ports (ports) are used to deliver anticancer chemotherapy and home parenteral nutrition. Recently, the use of ports has increased annually because of increased numbers of patients who are receiving long-term treatment because of progress made in chemotherapy, as well as patients in whom it is difficult to place a catheter in a peripheral vein to allow repeated intravenous infusion therapy.[1] In patients with conditions such as terminal cancer and short bowel syndrome who require long-term central venous nutrition because oral and parenteral nutrition is not feasible, parenteral nutrition can be initiated easily at home without the need for hospitalization, thereby enabling early resumption of work and other routine activities. Moreover, in patients in whom it is difficult to access a peripheral vein, the use of a central venous port decreases the risk of extravascular leakage and allows infusions to be intravenously administered safely and reliably. However, the placement of an indwelling catheter has been reported to potentially cause complications, such as infection, pinch-off, and thrombosis.[2–15] The present study was designed to identify risk factors for complications occurring after port implantation in a series of patients who were treated in the same institution.

Patients and Methods

The study group comprised 523 patients [203 male patients (39%) and 320 female patients (61%)] in whom ports were implanted in our hospital from January 2005 through December 2013 (Table 1). The mean age was 61 years (range, 2–91 years). The mean body mass index (BMI) was 20 kg/m^2 (range, 12–46 kg/m^2). A total of 481 patients had malignant tumors (3 lung cancers, 96 breast cancers, 23 malignant lymphomas, 1 thyroid cancer, 5 pancreatic cancers, 7 esophageal cancers, 22 stomach cancers, 140 colon cancers, 96 rectal cancers, 36 ovarian cancers, 27 uterine cancers, 8 renal cancers, 8 bladder cancers, 6 leukemia, and 3 prostate cancers), and 42 had benign diseases (4 systemic lupus erythematosus, 4 scleroderma, 6 metabolic disorders, 4 aplastic anemia, 6 chronic ulcerative colitis, 7 short bowel syndrome, 1 pulmonary arterial hypertension, and 1 cerebral hemorrhage). The purpose of port implantation was the administration of anticancer chemotherapy in 439 patients (84%) and home central-venous nutrition in 84 (16%).

The mean operation time was 60 minutes (range, 19–170 minutes). The median postoperative follow-up was 12 months (range, 1–99 minutes). Ports were placed under local anesthesia in all patients. Ports were placed only into the internal jugular vein. The external jugular vein was not used for port placement. A subclavian vein approach was mainly used from 2005 through 2010. From 2011 onward the use of an internal jugular vein approach under ultrasonic guidance increased. In patients in whom a subclavian or internal jugular vein approach was precluded by poor general condition or lesion location, a femoral vein approach was used. A subclavian vein approach was used in 362 patients (69%), an internal jugular vein approach in 127 patients (24%), and a femoral vein approach in 34 patients (7%). Bard X-Port *isp* (Medicon Inc, Osaka, Japan) implantable ports were used. As risk factors for postoperative complications after the implantation of central venous ports for home use, the following 6 variables were studied: sex, age, BMI, purpose for placement, approach site, and operation time. Port infection was evaluated on the basis of the detection of pathogens on blood cultures and port or catheter cultures and the results of other detailed examinations performed to exclude other diagnoses. Catheter pinch-off was graded on the basis of frontal chest X-rays as follows: grade 0, no catheter-induced compression; grade 1, compression evident, but no narrowing of the catheter lumen; grade 2, narrowing of the catheter lumen; and grade 3, cross-sectional breakage or snapping of the catheter.[2] Pinch-off was evaluated in 362 patients in whom a subclavian vein approach was used and postoperative complications developed (right subclavian vein, 131 patients; left subclavian vein, 231 patients). Univariate analysis was performed using the χ^2 test and Mann-Whitney *U* test, and cumulative usage rates were analyzed using the log-rank test. *P* values of less than 0.05 were considered to indicate statistical significance.

Results

After port implantation, 13% (69 of 523) of the patients had postoperative complications. Infection developed in 7.6% (40 of 523) of the patients, and

Table 1 Demographic characteristics of patients

	Value (n = 523)
Male-to-female ratio, n	203:320
Age, y, median (range)	61.2 (2–91)
BMI, kg/m^2, median (range)	20 (12–46)
Disease, malignancy-to-benign ratio, n	481:42
Purpose, chemotherapy-to-nutrition ratio, n	439:84
Approach, right-to-left ratio, n	
Subclavian	130:232
Jugular vein	100:27
Femoral vein	28:6

catheter pinch-off occurred in 3% (11 of 362). All cases of pinch-off were grade 3. Thrombosis developed in 2.3% (12 of 523) of the patients, port breakage in 3 patients, and postoperative bleeding in 1 patient. Ports were removed in 8% (42 of 523) of the patients because the objective of port placement had been completed. The rate of infection was 5% (23 of 439) in patients with ports for anticancer chemotherapy, compared with 20% (17 of 84) in patients with ports for home-based central venous nutrition. This difference was significant ($P < 0.0001$). The infection rate according to the approach used for catheter placement was 8.3% (30 of 362) for the subclavian vein, 1.6% (2 of 127) for the internal jugular vein, and 23.5% (8 of 34) for the femoral vein.

The respective cumulative usage rates at 1 year, 2 years, and 3 years were 87%, 80%, and 77% for ports placed via a subclavian vein approach; 97%, 95%, and 95% for ports placed via an internal jugular vein approach; and 66%, 56%, and 56% for ports placed via a femoral vein approach. These rates differed significantly among the 3 groups ($P < 0.0001$). The usage rates according to purpose were 95% at 1 year, 93% at 2 years, and 92% at 3 years for ports used to administer anticancer drug therapy compared with 81% at 1 year, 67% at 2 years, and 61% at 3 years for ports used to deliver home-based central venous nutrition. The cumulative usage rates were significantly lower for ports used for home-based central venous nutrition ($P < 0.001$; Fig. 1).

Two factors were found to be significant risk factors for infection: the use of ports for home-based central venous alimentation ($P < 0.001$) and the use of a femoral vein approach for port placement ($P = 0.001$; Table 2). The following causative organisms were identified on catheter or blood cultures: *Staphylococcus epidermidis* in 11 patients, methicillin-sensitive *Staphylococcus aureus* in 5 patients, methicillin-resistant *S aureus* in 2 patients, *Pseudomonas aeruginosa* in 2 patients, and *Acinetobacter* sp in

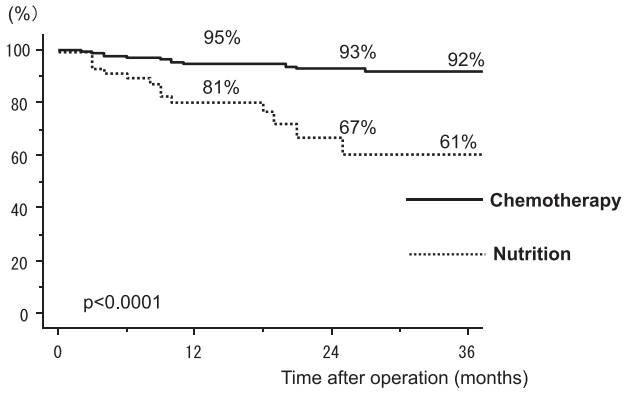

Fig. 1 Cumulative usage rate.

1 patient. Cultures were negative in 19 patients. The median time to the development of infection was 15.7 months (range, 2–68 months), and 68% (27 of 40) of infections developed within 1 year, which comprised the highest proportion. In years 2 and 3, the infection rate was 15% (6 of 40). Only 1 case of infection developed after year 3.

The infection rate associated with port placement for the administration of chemotherapy was 95% at 1 year, 92% at 2 years, and 93% at 3 years. The infection rate was significantly higher than that associated with ports used for home-based nutrition ($P < 0.0001$). The respective cumulative infection rates at 1 year, 2 years, and 3 years according to the approach used for port placement were 93%, 89%, and 87% for ports placed via the subclavian vein; 99%, 97%, and 97% for ports placed via the inner jugular vein; and 71%, 61%, and 61% for ports placed via the femoral vein. A femoral vein approach was associated with a significantly higher rate of infection ($P < 0.0001$; Fig. 2).

All 11 cases of infection associated with catheter pinch-off occurred when the approach was made

Table 2 Risk factors for port infection: univariate analysis

	Yes (n = 40)	No (n = 483)	*P* value
Purpose, chemotherapy-to-nutrition ratio	23:17	416:67	<0.001
Approach (vein), n			
Subclavian, jugular–to-femoral ratio	31:9	457:26	0.001
Male-to-female ratio	20:20	184:299	0.189
Age, ratio of ≤65 y to >65 y	19:21	279:204	0.274
BMI, ratio of <25 kg/m^2 to ≥25 kg/m^2	36:4	399:84	0.326
Operation time, ratio of ≤60 min to >60 min	19:21	200:283	0.559

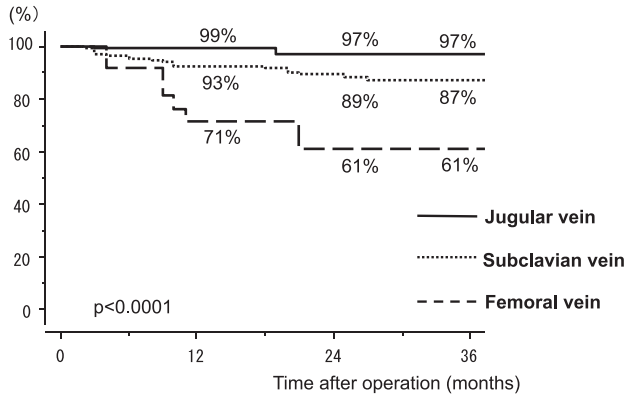

Fig. 2 Cumulative usage rate according to purpose for port placement.

Table 3 Risk factors for catheter pinch-off: univariate analysis

	Yes (n = 11)	No (n = 351)	*P* value
Approach part (subclavian), n			
Right-to-left ratio	0:11	130:221	0.027
Male-to-female ratio	6:5	133:218	0.422
Age, ratio of ≤65 y to >65 y	4:7	175:176	0.565
Operation time, ratio of ≤60 min to >60 min	6:5	147:204	0.598
BMI, ratio of <25 kg/m^2 to ≥25 kg/m^2	8:3	292:59	0.617
Purpose, chemotherapy-to-nutrition ratio, n	10:1	297:54	0.884

from the left subclavian vein (Table 3). The catheter snapped apart in 4 patients. Pinch-off occurred within 1 year in 69% (7 of 11) of the patients and between 1 and 2 years in 18% (2 of 11). A subclavian vein approach was made via the right subclavian vein in 130 patients (36%) and the left subclavian vein in 232 patients (64%). All cases of catheter pinch-off were associated with an approach from the left subclavian vein and were grade 3. The catheter was damaged in 7 patients and snapped apart in 4 patients. In the 7 patients with catheter damage, the catheter and port were removed on the same day as or within a few days. In the 4 patients in whom the catheter snapped apart, the broken catheter was removed under angiographic guidance. A left subclavian approach was the only significant risk factor for catheter pinch-off (P = 0.028).

Discussion

In our study, the incidence of port-related postoperative complications was 13%. Infection was the most common complication, followed by catheter pinch-off. Two variables were risk factors for infection: the use of a port to provide nutrition and port placement via a femoral vein approach. In contrast, the use of a left subclavian vein approach was clearly shown to be a risk factor for catheter pinch-off. Because our study was performed in a single institution and used a standard operation procedure and a standard protocol for perioperative care, our results are considered meaningful. Ports are now widely used as a route for the intravenous administration of anticancer agents on an outpatient basis as well as to provide home-based central venous nutrition in patients with poor oral intake. In particular, the increased use of FOLFOX and FOLFIRI regimens to treat colorectal cancer has led to a marked increase in the use of intravenous ports in recent years. Progress in chemotherapy and increased numbers of anticancer drugs as treatment options have also been associated with longer treatment periods and more frequent administration of chemotherapeutic agents. Consequently, the need to secure a reliable means of peripheral venous access has also led to an increase in port placement.[1] In addition, the gastrointestinal tract cannot be used as a nutritional route in increasing numbers of patients, such as those who have unresectable or recurrent cancer. The use of home-based central venous nutrition is thus also increasing to improve the quality of life of patients.

Extravascular leakage of an anticancer drug causes adverse reactions, such as redness, swelling, pain, bubble formation, ulceration, and necrosis of perivenous soft tissue. A study performed by the Intravenous Nurses Society in the United States estimated that the incidence of extravasation of antineoplastic drugs that induce necrosis from peripheral veins ranges from 0.1% to 6.5%. Ports should therefore be used to secure venous access and decrease the risk of extravasation. Port placement is recommended in Europe and North America for the administration of antineoplastic drugs that potentially cause necrosis.[16]

Catheter-related infections are most often caused by contamination of the infusion solution due to bacterial invasion of the site of thrombus formation, site of port insertion, connectors, or 3-way stopcocks. Long-term catheter placement is associated with an increased frequency of thrombus formation, and the rate of thrombus formation has been reported to be 84% when the implantation period

is 10 months or longer.[14] The rate of thrombus formation in our hospital is 2%, and ports are removed within 1 year after placement in 67% of patients in whom related problems are detected on computed tomographic or ultrasonographic examinations. Sotir *et al*[12] reported that the overall rate of infection was 1.23 primary bloodstream infections per 1000 device days. Catheter-related infections were reported to be difficult to accurately diagnose because some patients have negative catheter cultures or blood cultures. Moreover, infections can cause serious complications, such as sepsis. Fungi are often the causative organism of infection in patients with long-term catheter placement or poor general condition. Scolapio *et al*[13] reported that timely appropriate action and prompt catheter removal are required when catheter infection is suspected because 11 of 225 patients (5%) with ports for home parenteral nutrition died of catheter sepsis. Port infection occurred at an incidence of 7.6% in our hospital, which is slightly higher than that reported by other studies. The most common causative organism was *S epidermidis*, and no patients had fungal infection. However, the diagnosis of port infection was often uncertain, and catheter or blood cultures were negative in 48% (19 of 40) of patients in whom ports were removed to eliminate the suspected cause of infection. The lower incidence of infection associated with ports used to administer chemotherapy is attributed to the fact that bags containing high-calorie infusion solutions have to be exchanged daily when ports are used to deliver nutrition. In contrast, ports used to administer anticancer therapy are most frequently used only once every 1 to 2 weeks. Ports used for anticancer therapy are thus associated with fewer opportunities for bacterial contamination, and the incidence of catheter infection arising from thrombus formation has probably also decreased. Moreover, the accumulation of sediment associated with fat emulsion preparations, electrolytes, and other substances on the inner surface of the reservoir might also contribute to frequent infections in patients with ports used to provide nutritional support. It is therefore necessary to reduce the number of punctures to prevent infection. In addition, because Isodine (povidone iodine) requires 30 to 60 seconds after application to produce its maximum disinfection effect because of its bactericidal properties, ethanol or chlorhexidine is recommended if puncture is performed immediately after disinfection.

Catheter pinch-off is a problem that occurs when a catheter placed in the subclavian vein gets caught between the clavicle and first rib. The port catheter snapping apart has been reported to occur at a rate of 1.1% to 2.1%.[3–5] In our study, the incidence of catheter breakage was 3%, which is slightly higher than that reported by other studies. Catheter breakage can lead to ventricular tachycardia, arrhythmias within 1 year, cardiac perforation, thrombosis, infection, and death. Early removal of a broken catheter by endovascular treatment is thus essential. Fisher and Ferreyro[6] reported that not removing catheter fragments is associated with about a 71% incidence of serious complications, such as arrhythmias, thrombosis, sepsis, and cardiac perforation. However, highly invasive procedures, such as thoracotomy and open-heart surgery, may be required in patients in whom catheter fragments cannot be successfully removed. If the catheter adheres to the vascular wall and becomes immobile, there is a high risk of vascular injury, and forced removal is not an option.[2] Therefore, a safe and highly reliable puncture technique performed under real-time sonographic guidance has been proposed to prevent pinch-off and avoid puncture-related complications.[17] When the puncture site is lateral to the midclavicular line and resistance is felt at the time of catheter insertion, the catheter should not be forcibly inserted, and other sites for catheter placement, such as the internal jugular vein or veins of the upper arm or forearm, should be used.[7,8] Moreover, chest X-rays should be obtained immediately after catheter insertion as well as every 3 months during the placement period to confirm the presence or absence of catheter pinch-off. As for the puncture site, if the approach is made via the internal jugular vein, there is no risk of pinch-off. However, because it is necessary to subcutaneously pass the catheter through a long tunnel to enable port placement, the procedure is somewhat more invasive, the length of the indwelling catheter must be extended, and patients may be very concerned about the esthetic problem associated with having a port placed in the neck. Future studies should focus on risk factors associated with port complications. Paying closer attention to such factors may reduce patient discomfort caused by port placement and management, and appropriate medical treatment might lead to maintaining a better quality of life for patients, as well as reducing health care costs.

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