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A Comparison of Outcomes and Complications of Totally Implantable Access Port Through the Internal Jugular Vein Versus the Subclavian Vein

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Totally implantable access ports (TIAPs) are generally used in oncology. Few studies have addressed complications associated with the insertion site. A total of 233 consecutive oncology patients were enrolled to receive TIAP inserts via internal jugular vein (IJV) or subclavian vein (SV). Data on clinicopathologic parameters and early/late complications were retrospectively collected. No differences were found early and late complication rates. Catheter injury was observed more frequently in the IJV group (2.9%) than in the SV group (1.0%) without statistical significance. Multivariate logistic regression analysis showed that age, switch to palliative use of TIAP, and the distribution of diseases (low risk in patients with colorectal cancer) were independent risk factors for determining complications. In conclusion, TIAP insertion site showed no impact on the early and late complication rates. Catheter injury appears to occur at the same frequency with both approaches. Therefore, medical doctors may choose their preferred puncture site when performing TIAP insertion.

Key words: TIAP – Internal jugular vein – Central venous port – Totally implantable venous access devices – TIVAD

Totally implantable access ports (TIAPs) have been widely used for the safe delivery of chemotherapy or parenteral nutrition in patients with malignant disease and other debilitating diseases.[1–3] Early complications of TIAP placement have been reported to be pneumothorax, hemothorax, and arterial rupture. Late complications include infection and obstruction or fracture of the cathe-

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ter.[4,5] The pinch-off syndrome has been thought to reflect the occlusion or fracture of catheters inserted through the subclavian vein (SV).[1] To avoid the occurrence of this syndrome, some researchers recommended that the TIAP catheter should be inserted through the right internal jugular vein (IJV)[6–8] or infraclavicular axillary vein under ultrasound guidance.[9] However, we have reported 2 rare cases of TIAP catheter fracture when introduced through the right IJV.[10,11] Accordingly, we wished to evaluate whether TIAPs inserted via the IJV would present fewer catheter injury and complications than those inserted via the SV. To clarify this issue, we retrospectively compared early and late complications following TIAP insertion in our institute.

Methods

Patients

A total of 233 consecutive oncology patients were planned to receive TIAP inserts for systemic intravenous chemotherapy from January 2007 to July 2012 at the Department of Surgery, Shiga University of Medical Science in Shiga, Japan, and the associated hospital. The deadline for data acquisition was April 30, 2013. We retrospectively collected data on patient clinicopathologic parameters by reviewing medical records. We compared early and late complications between 2 different routes, the IJV and SV. We defined early complications as those observed peri-operatively and those related to the surgical procedure. We defined late complications as those reported at least 24 h after the surgical procedure, such as TIAP infection (including TIAP-related sepsis confirmed by microbiologic blood cultures), venous thrombosis, catheter injury, and catheter malfunctioning (allowing perfusion but not aspiration or total catheter obstruction), as previously reported in the other study.[12] The early complications were compared between the planned IJV approach group and the planned SV approach group. Late complications were compared between the implanted via the IJV group and the implanted via the SV group. Patients received chest radiography or chest computed tomography for routine follow-up of malignant diseases care at least every 6 months or less. The catheter tip position and late complications such as port dislocation, catheter injury, and vein thrombosis were reviewed using these follow-up chest radiography or chest computed tomography compared to the initial tip position, catheter route, and port position.

Surgical procedure

The surgeons selected the first puncture position and placement site of the TIAPs. The TIAPs were implanted in the surgical room, using maximal barrier precautions under local anesthesia and electrocardiography, heart rate, blood pressure, and pulse oximetry monitoring. BARD X-port isp (Medicon Inc., Osaka, Japan) was used in all patients. We inserted the guide wire and catheter using the Seldinger technique under fluoroscopy to confirm placement in the superior vena cava. We checked the incidence of early complications using chest radiography after the surgical procedure. On puncturing the SV, the central vein was cannulated using the Seldinger technique according to an anatomical landmark. If the catheter could not be placed in the first planned SV, a different puncture site was selected. Ultrasound-guided puncture was employed to mark the position of the IJV. If venous puncture could not be completed, a different puncture site was selected.

Statistical analysis

Data for continuous variables are expressed as median values (range, minimum–maximum). Data for categorical variables are expressed as cases (percentages). We used JMP Version 9 (SAS Institute Inc., Cary, NC, USA) for statistical analysis. Wilcoxon and Kruskal-Wallis rank order tests were performed for ordinal variables. Comparison between 2 groups was performed using Fisher's exact test or the chi-square test. Reverse Kaplan-Meier plots were used to illustrate the risk of late complications after implantation of totally implantable access ports in the IJV and SV groups. To identify the prognostic risk factors for determining the late complications after the implantation of TIAPs, univariate and multivariate logistic regression analyses were performed. A P value of < 0.05 was considered to indicate statistical significance.

Results

Patients and backgrounds

The first puncture site was the IJV in 133 patients (IJV approach group) and the SV in 100 patients (SV approach group). In the SV approach group, the insertion site was changed to the opposite side of the SV in 4 patients and to the IJV in 4 patients. In the IJV approach group, the puncture site was changed to the opposite side of the IJV in 1 patient and to the

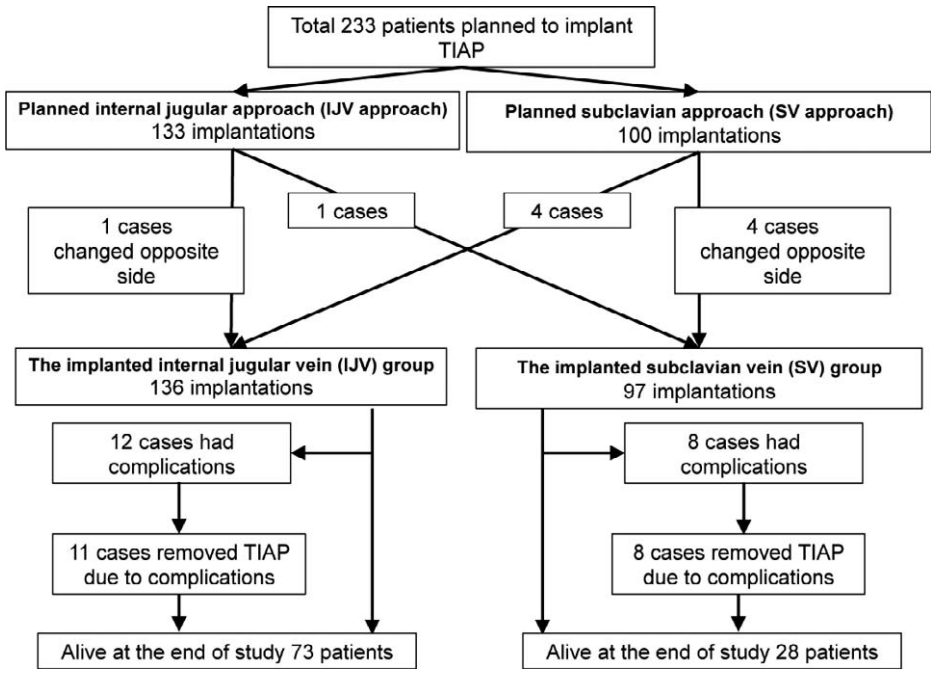

Fig. 1 The study flow chart.

SV in 1 patient (Fig. 1). Gender distribution differed between the 2 groups: the number of female patients was higher in the IJV approach group than in the SV approach group. Patients in the SV approach group were older. Body mass index (BMI) was higher in the IJV approach group ($P = 0.0285$). The distribution of diseases was statistically different ($P < 0.0001$), particularly with regard to gastric cancer and breast cancer (Table 1). The completion rate of TIAP implantation was 100% in each group. The success rate for the first planned puncture site was significantly higher in the IJV approach group (98.5%) than in the SV approach group (92.0%; $P = 0.0201$). The duration of surgery was shorter in the SV approach group than in the IJV approach group (44 min vs. 51 min, $P = 0.0033$; Table 1).

Table 1 Patient characteristic among IJV and SV approach

	IJV approach (n = 133)	SV approach (n = 100)	*P* value
Gender, male/female	67/66	63/37	0.0227[a]
Age (y.o.)[b]	62 (25–84)	66 (28–85)	0.0148[c]
Body mass index[b]	21.2 (15.3–32.1)	20.0 (13.7–37.6)	0.0285[c]
Diseases[e]			
Colorectal cancer	63 (47.4%)	48 (48%)	< 0.0001[d]
Gastric cancer	12 (9.0%)	30 (30%)	
Brest cancer	37 (27.8%)	1 (1%)	
Hepato-biliary-pancreatic cancer	6 (4.5%)	8 (8%)	
Esophageal cancer	3 (2.3%)	10 (10%)	
Others	12 (9.0%)	3 (3%)	
Success at the 1st planned vein[e]	131 (98.5%)	92 (92%)	0.0201[a]
Completion rate of TIAP[e]	133 (100%)	100 (100%)	1.0000[a]
Duration of surgery (min)[b]	51 (11–162)	44 (15–230)	0.0033[c]

[a]Fisher's exact test.

[b]Median (range).

[c]Wilcoxon and Kruskal-Wallis rank order tests.

[d]Chi-square test.

[e]Cases (%).

IJV, internal jugular vein; SV, subclavian vein; TIAP, totally implantable access port.

Table 2 Early complications following TIAP implantation via the IJV and SV

	IJV approach (n = 133)	SV approach (n = 100)	*P* value
Pneumothorax[a]	1 (0.8%)	3 (3.0%)	
Arterial puncture[a]	2 (1.5%)	1 (1.0%)	
Hematoma[a]	1 (0.8%)	1 (1.0%)	
Total[a]	5 (3.8%)	5 (5.0%)	0.5931[b]

[a]Cases (%).

[b]Chi-square test.

IJV, internal jugular vein; SV, subclavian vein; TIAP, totally implantable access port.

Early complications

Five patients in the IJV approach group (3.8%) and 5 patients in the SV approach group (5.0%) experienced early complications, and this difference was not statistically significant ($P = 0.5931$; Table 2).

Late complications

The implanted via the IJV group included 136 cases, and the implanted via the SV group, 97 cases. The background characteristics of these 2 groups showed the same trends as those of the IJV approach group and the SV approach group (data not shown). The duration of the observation period differed significantly between the implanted via the IJV group (556 days) and the implanted via the SV group (402 days). More patients were alive at the end of the study in the implanted via the IJV group than in the implanted via the SV group. The frequency of switching to palliative use of TIAP was significantly higher in the implanted via the SV group than in the implanted via the IJV group (Table 3).

We observed late complications in 8 cases (8.2%) in the implanted via the SV group and in 12 cases (8.1%) in the implanted via the IJV group ($P = 1.000$). The characteristics of late complications associated with TIAPs did not differ significantly between TIAPs placed in the IJV and in the SV. The incidence of catheter injury (3 cases of catheter fracture and 1 case of pin hole leakage) was rather higher in the IJV group (2.9%) than that (1 case of catheter fracture) in the SV group (1.0%), but this difference was not statistically significant (Table 4). The cumulative risk of late complications after implantation of TIAPs did not differ significantly between the IJV group and the SV group (Fig. 2). Univariate analysis demonstrated statistical significance for age, BMI, access vein (IJV or SV), switch to palliative use, and the distribution of diseases. Multivariate logistic regression analysis showed that age, switch to palliative use, and the distribution of diseases were independent prognostic factors for determining late complications after implantation of TIAPs. In particular, patients with colorectal cancer presented the lowest risk for TIAP removal due to complications (Table 5).

Table 3 Patient outcomes after TIAP implantation via the IJV and SV

	IJV group (n = 136)	SV group (n = 97)	*P* value
Duration of observation[a]	566 (3−2013)	402 (7−2220)	0.0058[b]
Duration of implantation[a]	468 (3−1940)	326 (7−1894)	0.0051[b]
Alive at the end of study[c]	73 (53.7%)	28 (28.8%)	0.0002[d]
Switch to palliative use[c]	65 (47.8%)	69 (71.1%)	0.0005[d]
TIAP removal due to the complication[c]	11 (8%)	8 (8.2%)	0.9651[d]

[a]Days.

[b]Wilcoxon and Kruskal-Wallis rank order tests.

[c]Cases (%).

[d]Fisher's exact test.

IJV, internal jugular vein; SV, subclavian vein; TIAP, totally implantable access port.

Discussion

Some researchers have recommended that TIAPs be inserted through the IJV to avoid the pinch-off syndrome[6,13], thrombosis, and stenosis[14], but a few reports have compared SV and IJV. In the present study, we retrospectively compared early and late complications following the introduction of TIAPs via the IJV and SV in our institute. We hypothesized that TIAPs inserted via the IJV would present fewer catheter injuries and complications than those inserted via the SV. In particular, we expected a

Table 4 Late complications of TIAP indwelling in the IJV and SV

	IJV group (n = 136)	SV group (n = 97)	*P* value
Infection[a]	4 (2.9%)	6 (6.2%)	
Thrombosis[a]	2 (1.5%)	0 (0%)	
Catheter injury[a]	4 (2.9%)	1 (1%)	
Catheter dislocation[a]	1 (0.7%)	0 (0%)	
Fibrin sheath[a]	1 (0.7%)	0 (0%)	
Vasculitis[a]	0 (0%)	1 (1%)	
Total[a]	12 (8.1%)	8 (8.3%)	0.2741[b]

[a]Cases (%).

[b]Chi-square test.

IJV, internal jugular vein; SV, subclavian vein; TIAP, totally implantable access port.

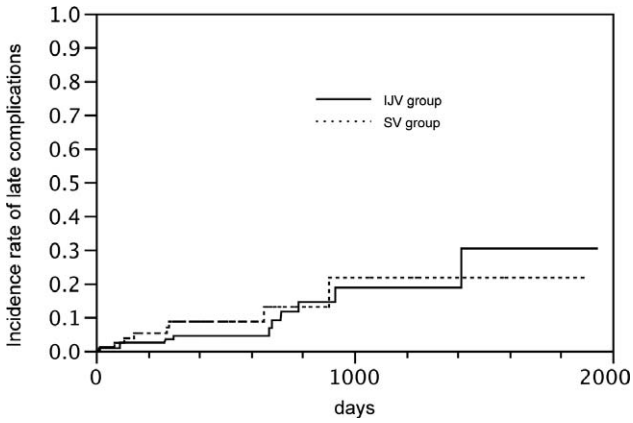

Fig. 2 Reverse Kaplan-Meier plot showing the cumulative risk of late complications after implantation of TIAPs in the internal jugular vein (IJV) group and the subclavian vein (SV) group. There was no significant difference between the 2 groups. Log-rank test: $P = 0.4935$.

lower frequency of catheter injury in the IJV group than in the SV group; however, there was no difference in the incidence of early and late complications between TIAP insertion via the IJV and SV. A randomized control study also demonstrated that central venous insertion modality and sites (IJV, SV, and cephalic access) had no impact on either early or late complication rates.[15] Charvat *et al* showed that late complications requiring removal of TIAPs were found in 6.2% of patients receiving an implant via the right IJV.[6] Plumhans *et al* found no differences in late complications between indwelling in the IJV and SV.[14] Our results were almost similar to those presented in these reports regarding early and late complications.

Our results showed that the incidence of catheter injury was 2.9% with IJV placement. The cause of catheter fracture in the SV group was pin-off syndrome. Catheter injury due to TIAPs inserted via the IJV is believed to be very rare. Growing evidence indicates that TIAPs inserted via the IJV cause catheter injury more frequently than expected.[6,7,14,15] A recent large-scale retrospective study also showed that the incidence of catheter fracture in patients who had a TIAP catheter introduced via the right internal jugular vein was 1.69%.[16] The incidence of catheter rupture because of the pinch-off syndrome is reported to range from 1.1% to 5.0%.[1,17] It is possible that the risk of catheter injury on placing the catheter in the IJV is similar to that on placing the catheter in the SV. The causes of catheter fracture and pinhole leakage in the IJV group were suggested chronic stress against catheter. For example, we experienced the catheter fracture of the TIAP at the level of the clavicle. In this case, the strap of the patient's backpack appeared to come in contact with the catheter and compress it against the clavicle, resulting in catheter injury.[10] The other case suggested the catheter fatigue and fracture were

Table 5 Univariate and multivariate logistic regression analyses of prognostic factors for determining the late complications of TIAP

	Univariate			Multivariate		
	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Age (y)						
1-year increase	1.02	1.01–1.03	0.0048	1.01	1.00–1.03	0.0359
Body mass index						
1-point increase	0.92	0.89–0.96	<0.0001			
Gender						
Female	1					
Male	1.21	0.92–1.61	0.1496			
Access vein						
Internal jugular vein	1					
Subclavian vein	1.35	1.03–1.78	0.0323			
Switch to palliative use						
No	1			1		
Yes	1.91	1.45–2.53	<0.0001	2.09	1.52–2.88	<0.0001
Diseases						
Colorectal cancer	1			1		
Gastric cancer	4.50	2.98–6.66	<0.0001	3.62	2.33–5.55	<0.0001
Breast cancer	1.56	1.03–2.30	0.0355	2.69	1.67–4.27	<0.0001
Hepato-biliary-pancreatic cancer	2.59	1.41–4.40	0.0033	2.19	1.16–3.86	0.0177
Esophageal cancer	6.02	2.94–11.2	<0.0001	4.59	2.19–8.88	<0.0001
Others	2.87	1.59–4.85	0.0010	3.30	1.79–5.72	0.0003

caused by chronic stress at the flexure of the catheter induced by the motion of the neck.[11]

Park *et al* showed that the right high jugular vein approach is a feasible alternative to the right low jugular vein approach.[18] They reported that the right high jugular vein approach did not cause problems with catheter kinking, but could result in an acute angle between the subcutaneous portion and intravenous portion. We attempt to place TIAPs as low as possible in the IJV with ultrasound guidance in order to avoid catheter kinking and to shorten the subcutaneous tunnel. However, the catheter injury that we experienced during this observational period was suggested to be related to catheter kinking, in which we indicated right high jugular vein approach.[11] Park *et al* did not experience any catheter fracture during their observational period; however, their study included only 21 cases in the high puncture group.[18] Therefore, further studies are necessary to clarify whether the venous puncture position is related to catheter fatigue and fracture. Although the recommended venous puncture site in the IJV for TIAP remains unknown, we believe that lower puncture sites are safer when performing central venous insertion via the IJV for TIAP.

Moreover, multivariate logistic regression analysis to identify the prognostic factors for determining late complications of TIAPs showed that BMI (low risk in patients with a high BMI), switch to palliative use of TIAP, and the distribution of diseases (low risk in patients with colorectal cancer in particular) were selected as the independent risk factors. The patients' nutritional and immune status and disease progression appeared to be related to the occurrence of late complications, although we could not evaluate them in this study.[19] For example, we observed five late complications in patients with palliative use of TIAP. Three of 5 patients (60%) had infectious complication of TIAP. Furthermore, it is difficult to find the reason why the late complications of TIAP are fewer in colorectal cancer patients. In the subgroup analysis of this study, the frequency in palliative use of TIAP was significantly different among disease distribution (gastric cancer, 81%; hepato-biliary-pancreatic cancer, 86%; esophageal cancer, 77%; colorectal cancer, 55%; breast cancer, 22%). The incidence of removal due to completion of chemotherapy was also significantly different among disease distribution (colorectal cancer, 5.4%; breast cancer, 21%; other diseases, 0%). These kinds of bias may influence the results of multivariate logistic regression analysis.

We acknowledge several limitations of the current study. At first, this study was a retrospective, nonrandomized, study. Second, although we verified that the late complication after the implantation of TIAPs might be similar between SV and IJV group, the patients' backgrounds were quite different between the two groups. Therefore, multivariate logistic regression analysis to identify the prognostic factors for determining late complications of TIAPs was performed. Furthermore, there have been reported complications of TIAPs that we have not experienced in our study period, such as catheter migration, leakage from the port membrane, drug extravasation, port-site and pocket infection, port rotation, catheter malposition and kinking of catheter.[1] Additional prospective studies are needed to clarify the significant and proper risk factors for determining late complications of TIAPs.

In conclusion, TIAPs implanted through the IJV were associated with similar early and late complications to TIAPs implanted through the SV. The success rate for insertion via the IJV approach was higher than that via the SV approach. Age, switch to palliative use of TIAP, and distribution of diseases (low risk particularly in patients with colorectal cancer) were identified as independent prognostic factors for determining the late complications of TIAPs in this cohort. Therefore, medical doctors may choose their preferred puncture site when performing TIAP insertion.

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