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Factors associated with unscheduled venous access port removal in cancer patients

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ABSTRACT

Aims: Implantable venous access ports (IVAP) are used in cancer patients to provide central venous circulation access. This study investigated the prognostic factors for IVAP removal among cancer patients.

Methods: A retrospective cohort study was conducted on cancer patients implanted with IVAP in the Hospital Universiti Sains Malaysia and followed up with at least one cycle of chemotherapy. The primary endpoint was unscheduled IVAP removal due to complications. Kaplan-Meier curves were used to estimate removal probability, and the log-rank test and Cox proportional hazards regression model were used to explore independent predictors.

Results: A total of 205 patients were included [mean, standard deviation (SD) age: 31.55 (22.45)]. More than half of the patients were male (53.2%) and of Malay ethnicity (91.2%). During the observation period, 222 IVAPs were implanted in 205 patients with predominantly solid cancers. During the mean follow-up of 15.03 (SD: 18.45) months, 28 complications were recorded. Prognostic factors for unscheduled IVAP removal were kidney disease [hazard ratio (HR): 8.33; 95% confidence interval (CI): 2.78, 24.90; p<0.001] and receiving no radiotherapy (HR: 5.25; 95% CI: 1.44, 19.11; p<0.012).

Conclusions: Cancer patients with kidney disease records or those who were not planned for radiotherapy were at higher risk of unscheduled IVAP removal.

Introduction

Due to the frequent infusions and the medication's severe vasculature irritancy, cancer patients taking chemotherapy require a central vascular device. The most popular option is implanted venous access ports (IVAP). In cancer settings, the use of IVAPs has recently increased, allowing easier repeated injections, infusions, and, optionally, blood collection (1). It is placed beneath the dermis where a catheter extends to the central vein and a needle is used to reach the subdermal reservoir (2).

IVAP was initially introduced by Niederhuber et al. (3) at the MD Anderson Cancer Center in Houston in 1982. Since then, it has been used for treating oncology diseases. The single BardPort with Grosong catheter has been used in the Hospital Universiti Sains Malaysia (USM), Kelantan, in cancer patients requiring long-term venous access to administer chemotherapy. Its port is made of plastic and titanium with single and dual lumens (power-injectable). An 8-F Grosong catheter is connected to single-lumen ports (4). The distal tip of the Grosong catheter, which was invented in 1978, featured a pressure-sensitive valve

with three positions. The valve opens under positive or negative pressure, effectively preventing unintended air embolism and spontaneous blood reflux. Because of its distinctive characteristics, it is more expensive.

Although IVAP allows convenient prolonged access to central veins with minimal disruption of lifestyle and discomfort (5), it is also associated with several complications, albeit less frequent than other venous access routes (6). IVAP-related complications not only prolong the length of hospital stay and reduce the life of infusion ports but also increase costs (6).

Several authors have reported that 46.2% of patients had their infusion port removed because of catheter-associated infections (7,8). Although infusion ports reduce the chance of bacterial infections, 3-10% of infusion ports are removed because of port-associated infections (9).

Various factors have been linked to IVAP complications, including age, gender, surgical technique, choice of puncture route, type of tumor (solid or hematologic), physical condition, chemotherapy type and care level (10,11). Hematologic malignancies are the most significant risk factors for catheter-associated infections (10), particularly in younger patients, which are linked to intense chemotherapy and neutropenia (12). In the current study, we explored the prognostic factors for IVAP removal due to complications among cancer patients.

Methods

Study design and sample size

This retrospective cohort study was conducted among cancer patients with IVAP at Hospital USM, Kelantan, Malaysia, between 1st January 2008 and 31st December 2014. Ethical approval was obtained from the Human Research and Ethics Committee of USM (USM/JEPeM/15090289 on 4th January 2016). Personal details, disease status, clinical characteristics, and other retrieved information were secured by identification number instead of patient name, registration number, and identification card number in the data collection form.

Inclusion and exclusion criteria

The inclusion criteria were a cancer diagnosis, an IVAP implant, and receipt of at least one cycle of chemotherapy. IVAP implantations in non-malignant diseases were excluded. In the case of IVAP renewal due to a complication, only the first procedure was recorded in the analyses. Patients transferred to other hospitals without a single chemotherapy cycle were excluded.

In the Hospital USM, orthopedic surgeons use the operating room to implant IVAP in cancer patients under aseptic conditions and general anesthesia. Depending on the patient's condition, a single type of IVAP (Bardport) made up of titanium and silicon rubber and connected with a 6-8 F silastic Grosong catheter in the cephalic vein, internal jugular vein, or femoral vein was placed in the enrolled patients. The position of the catheter tip was examined by fluoroscopy.

Data collection

Between January 2008 and December 2014, 420 cancer patients were implanted with an IVAP. From this pool, 220 patients were identified using a simple random selection procedure (Simple Random Sampling Generator in Microsoft Excel). After further exclusions, 205 patients formed the final study sample.

The endpoint was the removal of IVAP in patients with cancer due to complications. The observation was censored when the IVAP was not removed until study completion, or when the patient died, refused chemotherapy, was lost to follow-up, or was still under follow-up at the time of study completion.

Complications were classified as early and late. Early complications were those that occurred within 30 days of the procedure, including infections, malposition, and malfunction. Late complications were defined as complications that occurred after 30 days of the procedure, including infections, malposition, malfunction, and thrombosis.

Statistical Analysis

Data were evaluated using Stata SE version 11 (Stata Corp, 2009). Descriptive analysis was used to report sociodemographics, comorbidities, clinical characteristics, surgery type, and complications. Results are presented as frequency [percentage (%)] for categorical variables and mean [standard deviation (SD)] for numerical variables.

Kaplan-Meier curves were used to estimate the removal probability, and the log-rank test and Cox proportional hazard regression model were used to explore independent predictors. The results are shown as the hazard ratio (HR), 95% confidence interval (CI), and p-value. The cut-off for statistical significance was $p<0.05$.

Results

The mean age was 31.55 years (SD 22.45), with male (53.2%) and Malay predominance (91.2%) (Table 1). The majority of cases were lung cancer (22.9%). Of the 205 patients, 9.8% had diabetes mellitus, 17.6% had hypertension, 12.7% had liver disease, and 4.4% had heart disease.

Table 2 shows the clinical characteristics of cancer patients treated with IVAP. The insertion site of the catheter was the cephalic vein in most patients (97.6%). The majority of insertions were on the right side (92.7%). The oncology ward was the primary care site after implantation (61.9%), followed by the general ward.

Approximately two-thirds of the patients had solid cancer (68.3%), of which 36.6% were carcinoma type and 31.7% were sarcoma type. Hematologic malignancies were recorded

by 31.7%, of which 18.0% were lymphoma and 13.7% were leukemia. The most common cancer types were bone cancer (31.7%), lymphoma (18.0%), leukemia (13.7%), and gastrointestinal tract (17.6%). Other cancer types (19.0%) were hepatobiliary, gynecologic, nasopharyngeal, breast, genitourinary, and neuroblastoma. Most cancers were in the advanced stage (68.3%). Metastases were recorded by 42.9%. Relapse was 5.9%. Chemotherapy was completed in 56.6% of the patients. A history of surgery was recorded by 10.7% and radiotherapy was recorded by 49.8%.

Table 1. Socio-demographic characteristics of cancer patients with IVAP in Hospital Universiti Sains Malaysia (n=205)

Variables	n (%)
Age (years)*	31.55 (22.45)
Gender, male	109 (53.2)
Ethnicity	
Malay	187 (91.2)
Non-Malay	18 (8.8)
Educational level	
Tertiary	29 (14.1)
Secondary	79 (38.5)
Primary	59 (28.8)

IVAP: Implantable venous access ports

Table 2. Clinical characteristics of cancer patients with IVAP (n=205)

Variables	n (%)
Insertion site	
Cephalic vein	200 (97.6)
Others	5 (2.4)
Insertion side	
Right	190 (92.7)
Left	15 (7.3)
Ward of care	
General	80 (39.0)
Oncology	125 (61.0)
Types of cancer	
Solid	140 (68.3)
Hematologic	65 (31.7)
Stage of cancer	
I-II	65 (31.7)
III-IV	140 (68.3)
Metastases of cancer	88 (42.9)
Relapsed of cancer	12 (5.9)
Chemotherapy regime, complete	116 (56.6)
Surgery	
Yes	22 (10.7)
Not applicable	183 (89.3)
Radiotherapy	
Yes	102 (49.8)
Not applicable	103 (50.2)

IVAP: Implantable venous access ports

During the observation period, 222 IVAPs were implanted in 205 patients with predominantly solid cancers. During the mean follow-up of 15.03 (SD: 18.45) months, 28 complications were recorded. IVAP removal was recorded in 17 of these complications, and a second port was implanted. All patients received at least one cycle of chemotherapy through the device after insertion.

Four of the 28 complications were classified as early, and one was infection leading to IVAP renewal. Three were due to the malposition of the port. Two malpositions did not require port removal but required intervention for readjustment. One malposition resulted in IVAP renewal.

Delayed or late complications were recorded in 24 (11.7%) patients. Eleven (45.8%) were infected, 6 (25.0%) were malfunctioned, 4 (16.7%) were thrombosed, 2 (8.3%) were malpositioned, and 1 (4.2%) was dislodged (Table 3). Five (45.5%) of infected ports required IVAP removal, while the remaining cases were successfully treated with antibiotics. All four thrombosed catheters required removal because anticoagulants were ineffective. Only one (16.7%) malfunctioning port did not require removal. There was only one case of a dislodged port necessitating removal.

Up to 1 month, the probability of IVAP removal was 0.98 due to complications, whereas it was 0.92 up to 6 months, 0.91 up to 12 months, and 0.88 up to 24 and 36 months (Table 4). The removal probabilities decreased over time. The maximum time for IVAP removal was 27 months.

Table 5 shows the prognostic factors associated with IVAP removal due to complications. Kidney disease (adjusted HR: 8.33; 95% CI: 2.78, 24.90; p<0.001) and receiving radiotherapy (adjusted HR: 5.25; 95% CI: 1.44, 19.11; p=0.012) were the two independent factors.

Table 3. Complications of cancer patients with IVAP (n=205)

Complications, n (%)	177 (86.3)
Early complications	4 (2.0)
Infected port	1 (25.0)
Malposition	3 (75.0)
Late complications	24 (11.7)
Catheter dislodge	1 (4.2)
Malposition	2 (8.3)
Malfunction	6 (25.0)
Thrombosed-catheter	4 (16.7)
Infected port	11 (45.8)

IVAP: Implantable venous access ports

Discussion

IVAP is used more frequently than in the past, mostly in cancer patients for its benefits in preventing repetitive punctures and irritation and safety in long-lasting treatment schedules (13). It is suitable for high-concentration medications, reduces the discomfort caused by frequent venipuncture, prevents damage to peripheral superficial veins, and reduces restrictions in daily activities, ultimately improving quality of life (13). Its maintenance is also easier after wound healing. Such benefits encourage IVAP placements, particularly for cancer patients requiring long-term, ambulatory chemotherapy.

The introduction of IVAP has resolved many challenges in venous access in patients with cancer (14). However, IVAPs may also cause harm through infections, wound gaping and thrombosis (15), requiring their removal before the completion of chemotherapy. Numerous studies have shown that 10% of patients may require IVAP removal because of catheter-related infections and thrombotic events (16-19). Catheter removal may also be necessary because of thrombotic occlusion. In case of potential recurrence, the port is sometimes maintained during follow-up (20-22).

The overall complication rate in our study was 13.7%, similar to previous studies, which reported rates between 6.9% and 17.7% (23). In the worst case, IVAP-associated complications lead to IVAP removal. Nevertheless, every single removal puts the patient at additional risk by delaying ongoing chemotherapy and making parenteral nutrition difficult, ultimately resulting in increased morbidity, mortality, and costs (24).

With the progress in the types of equipment and surgical techniques, the most frequent complications became catheter-associated infections and thrombosis (17,25). In the current study, infections occurred in 12 patients, and it as the most common complication and reason for IVAP removal. A total of 17 catheters were removed and required renewal. These results align with those of earlier studies that indicated IVAP-related infections as the most frequent reason for port removal (26-28). The other complications included port malfunction, malposition, thrombosed catheter, and catheter dislodging from the port.

No immediate or procedural complications were recorded in the current study. This finding may be related to the improved surgical practices in the Hospital USM. The cut-down surgical technique was reported as the only approach to prevent possible fatal complications compared with other techniques (29).

This study suggests that IVAPs implanted on the left side may be particularly vulnerable to catheter thrombosis. Additionally, IVAPs implanted on the right side were associated with fewer complications and lasted longer than IVAPs implanted on the left. This finding may be explained by the fact that the left brachiocephalic vein forms a wider angle with the superior vena cava. When the catheter is positioned on the left side, downward pressing of the catheter may harm the endothelium. However, in this study, out of four patients with the thrombosed catheter, only one patient had a catheter inserted on the left side, and only one of 15 left-sided catheters was related to a complication.

Complications of IVAP often result in removal, prolonged hospital stay, intensive care unit admission, and death (30). Infection is the most common complication associated with IVAP (31). In particular, IVAP infection has a high morbidity rate and can result in early removal of IVAP (30). In addition, infections increase the length of hospital stay, morbidity, mortality, long-term antibiotic use, and costs (31,32).

Kidney disease was a prognostic factor for IVAP removal in the present study. This observation suggests that cancer patients with kidney disease had a higher risk of IVAP removal

Table 4. The overall removal probabilities of IVAP due to complications among cancer patients (n=205)

Time	Overall removal probabilities (95% CI)
1 month	0.98 (0.95, 0.99)
6 months	0.92 (0.87, 0.95)
12 months	0.91 (0.86, 0.95)
24 months	0.88 (0.81, 0.93)
36 months	0.88 (0.81, 0.93)

IVAP: Implantable venous access ports, CI: Confidence interval

Table 5. Prognostic factors of IVAP removal due to complications among cancer patients (n=205)

	Simple Cox regression			Multiple Cox regression		
	B	Crude HR (95% CI)	p	B	Adjusted HR (95% CI)	p
Kidney disease						
No	-	1.00	-	-	1.00	-
Yes	1.85	6.33 (2.16, 18.56)	**0.001**	2.12	8.33 (2.78, 24.90)	**<0.001**
Radiotherapy						
Yes	-	1.00	-	-	1.00	-
Not indicated	1.41	4.08 (1.15, 14.48)	**0.029**	1.66	5.25 (1.44, 19.11)	**0.012**

Backward log-rank Cox proportional hazard regression model applied.
Log-minus log plot, hazard function plot and partial residual were used to check the model assumptions.
IVAP: Implantable venous access ports, CI: Confidence interval, HR: Hazard ratio

due to complications. However, the explanation for this novel finding is difficult; because no previous study has reported a similar finding.

Another significant factor for IVAP removal was no radiotherapy treatment. Radiotherapy may not be suitable for patients with advanced cancer, cachexia, significant weight loss, severe dehydration, and inadequate nutrition. The current findings suggest that cancer patients with worse health conditions may be more prone to complications resulting from IVAP removal. In our dataset, some esophageal cancer patients had perforations precluding radiotherapy.

Some limitations of this study should be acknowledged. First, the retrospective cohort design may cause selection bias. Consistent with this, we identified up to 50% loss to follow-up in the registry. Improper follow-up may be related to late complications that can be prevented early. Second, the data retrieved from the medical records may cause information bias. Clinical records may not always be suitable for research. Finally, missing or unrecorded data (e.g., body mass index) reduces the number of critical variables in the adjusted analyses.

Conclusion

This study found that cancer patients with kidney disease and those who were not planned for radiotherapy had a higher risk of IVAP removal due to complications. Further studies with prospective enrollment and targeted follow-up are required to confirm these results and identify other predictors of unscheduled IVAP removal.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Human Research and Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/15090289 on 4th January 2016).

Informed Consent: Retrospective cohort study.

Authorship Contributions

Surgical and Medical Practices: N.N.N., A.H.S-A., S.Y., Concept: N.M.M., N.N.N., A.H.S-A., S.Y., Design: N.M.M., N.N.N., A.H.S-A., S.Y., Data Collection or Processing: N.M.M., A.H.S-A., Analysis or Interpretation: N.M.M., N.N.N., A.H.S-A., S.Y., W.N.A.W.A., Literature Search: N.M.M., N.N.N., A.H.S-A., S.Y., W.N.A.W.A., Writing: N.M.M., W.N.A.W.A.

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