Incidence of non-tunnelled central venous catheter-related infections in oncologic patients receiving chemotherapy in an outpatient setting

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INTRODUCTION Central venous catheters (CVCs) are becoming more popular for delivery of outpatient courses of intravenous therapy such as chemotherapy and long-term antibiotics. The incidence of non-tunnelled type CVC-related infections in patients with solid tumours receiving chemotherapy in an ambulatory setting has not been well studied. We aimed to determine the baseline data on CVC-related infections in this retrospective study conducted from January 2005 to December 2007.

METHODS Data on cancer patients with CVCs inserted as outpatients at National Cancer Centre Singapore over a three-year period were collected and analysed retrospectively. Data retrieved from medical records included patients' demographics, the number of catheter days, cancer type and other medical illnesses. Definitions from the Centre for Disease Control and Prevention for CVC-related infections were used. For data analysis, graphical and quantitative techniques were employed.

RESULTS A total of 88 CVCs were inserted during the study period, with a total of 11,541 catheter days (median 114; range 2–510 days). Infection rate was 0.87 per 1,000 catheter days. The risk of infection was higher when catheters were left *in situ* for longer periods of time and in patients with solid tumours.

CONCLUSION The infection rate for non-tunnelled type CVCs is low in our centre. Hence, its use for chemotherapy on an outpatient basis is relatively safe and convenient in oncologic patients.

Keywords: ambulatory care, central venous catheter, chemotherapy, infection
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INTRODUCTION

Outpatient therapy has become more common in recent years, as it helps to shorten hospital stay. Ambulatory patients may need venous access for long-term intravenous medications, total parenteral nutrition and infusional chemotherapy. Central vascular access devices, namely central venous catheter (CVC), peripherally inserted central catheter and implanted ports, often provide such access. CVCs provide cancer patients with consistent and convenient intravenous access for infusional chemotherapy. They reduce the discomfort associated with repeated venepuncture, decrease the incidence of thrombophlebitis from vesicant medications and allow for early hospital discharge.[1] The most common complication associated with these devices is catheter-related infection. The Centre for Disease Control and Prevention (CDC) has listed specific criteria for CVC-associated infections.[2] The most common organisms associated with CVC infections are Gram-positive cocci.[3-9]

The CVC is implanted via a surgical procedure under strict sterile environment. The two most commonly used catheters are Hickman line and Port-a-cath. No difference has been found between two study groups with respect to the incidence of infection and mechanical complication between Hickman line and Port-a-cath.[10] Subclavian access of CVCs has the advantage of easier maintenance and lower risk of infection compared to the internal jugular approach.[11,12] Moreover, subclavian venous catheterisation carries a lower risk of catheter-related thrombosis compared to the internal jugular route.[13] It has been observed that the incidence of CVC-related infections was higher in CVCs that were kept in place for more than seven days.[12] In patients with AIDS, non-tunnelled catheters have been reported to result in a lower infection rate than central venous access devices; however, this has not been reported in oncologic patients.[14] The objective of this three-year retrospective study was to determine the baseline data on CVC-related infections in oncologic patients according to the definitions proposed by the CDC.

METHODS

We retrospectively identified and analysed all cancer patients who had a CVC successfully inserted at National Cancer Centre Singapore (NCCS) during a three-year period from January 2005 to December 2007. During the study period, a total of 84 patients had one CVC inserted, while two patients had more than one CVC inserted. For the analysis, we considered each CVC placement as a new event. Hence, including the demographic description of the patient group, we used the number

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Table I. Demographic and disease characteristics of patients in the study (n = 88).

Characteristic	No. (%)
Median age (yrs)	56
Age by quartile (yrs)	
≤ 60	61 (69.32)
> 60	27 (30.68)
Gender	
Male	55 (62.50)
Female	33 (37.50)
Underlying cancer	
Gastrointestinal tumour	68 (77.27)
Sarcoma	7 (7.95)
Breast carcinoma	8 (9.09)
Others	5 (5.68)

Table II. Outcome of catheters inserted during the study period (n = 88).

Outcome	No. (%)
Complications requiring CVC removal (n = 14)*	
Catheter-related infection†	10 (11.36)
Catheter occlusion	3 (3.41)
Gapping of wound	1 (1.14)
CVC removal for uncomplicated catheters (n = 74)‡	
Completion of therapy	56 (63.64)
Death	5 (5.68)
Change in drug	1 (1.14)
Patient request	11 (10.23)
Others	3 (3.41)

*All outcomes that resulted in CVC removal were considered as complications. †The infection rate per 1,000 catheter days was 0.87. ‡Two cases were multifactorial.
CVC: central venous catheter

of CVC placements rather than individual patients as the unit. Data collected from the patients' medical records included the number of catheters inserted, the duration of catheter usage, episodes of catheter-related infections according to the CVC-related bloodstream infection (CRBSI) definitions, catheter occlusion, patient age and gender, other coexistent diseases such as diabetes mellitus and renal failure, and the type of tumour. We also reviewed the microbiological reports to ensure data accuracy. This study was approved by the NCCS Institutional Review Board as part of the quality improvement programme for the Infection Control Unit.

CVC disposition was assigned after the completion of therapy or during the removal of CVCs (included CVCs without complications and those with complications such as catheter occlusion or infection). Reasons for premature removal of the CVC were determined, and data on patient characteristics and infection rates were analysed. All patients with positive blood culture without any other sources of infection were considered to have CVC-related infection.

The definitions from the CDC for CRBSI[2] were used for our analysis. CRBSI must meet one of the following criteria: (1) The patient must have a recognised pathogen cultured from one or more blood cultures, with the organism cultured from blood not related to an infection at another site; (2) The patient must have at least one of the following signs or symptoms: fever (> 38°C), chills or hypotension; signs and symptoms of infection and positive laboratory results not related to an infection at another site; and common skin contaminant (i.e. diphtheroids [*Corynebacterium* spp.], *Bacillus* spp. [not *B. anthracis*], *Propionibacterium* spp., coagulase-negative *Staphylococci* [including *S. epidermidis*], *Streptococcus viridans*, *Aerococcus* spp. and *Micrococcus* spp.) cultured from two or more blood cultures drawn on separate occasions.

All CVCs were inserted at NCCS. The surgical team members followed infection control policies such as wearing of mask, cap, sterile gown and sterile gloves.[15] Povidone iodine was used as antiseptic for skin preparation before the insertion. The position for the catheter tip was confirmed by chest radiograph. All catheters, which were non-tunnelled Hickman lines, were inserted into the subclavian vein and used for the purpose of chemotherapy treatment. Patients or their caregivers were given educational booklets and health education training on care of the line. Dressings were changed 24 hours after catheter insertion, once every week or more frequently if the dressing was wet, loose or when redness was observed at the site. It was changed by the patients themselves or their caregivers as well as by the nurses in NCCS when the patients attended the centre for chemotherapy.

For statistical analysis, exploratory analyses that comprised graphical and quantitative techniques were used to investigate the data. Graphical techniques such as bar charts or pie charts were adopted to describe the distribution of interesting variables. Quantitative techniques such as median with range and frequency with percentage were used to describe demographic and disease characteristics. Two individuals had repeat CVC insertions over time, which resulted in data that were correlated; this correlation was modelled using the generalised estimating equations method, and the model was used to investigate the association between the variables and CRBSI. All analyses were conducted using S-PLUS 6.0 (Insightful Corporation, Seattle, WA, USA), and a p-value ≤ 0.05 was considered to be statistically significant.

RESULTS

A total of 88 CVCs were inserted into 86 patients during the study period. Two patients had more than one catheter inserted. The demographic profiles of all the patients and their primary indications for CVC placement are listed in Table I. The patient population included 55 male and 33 female patients, with a median age of 56 (range 14–80) years. All patients presented with solid tumours. The main primary malignancies were gastrointestinal cancers (n = 68), sarcoma (n = 7), breast cancer (n = 8) and others, including lung cancer and renal cell carcinoma (n = 5).

The 88 CVCs were in place for a total of 11,541 catheter-days (median 114 days; range 2–510 days, mean 131.15 days). The median time between catheter insertion and diagnosis of infection was 75 (range 13–180) days. Table II shows the CVCs

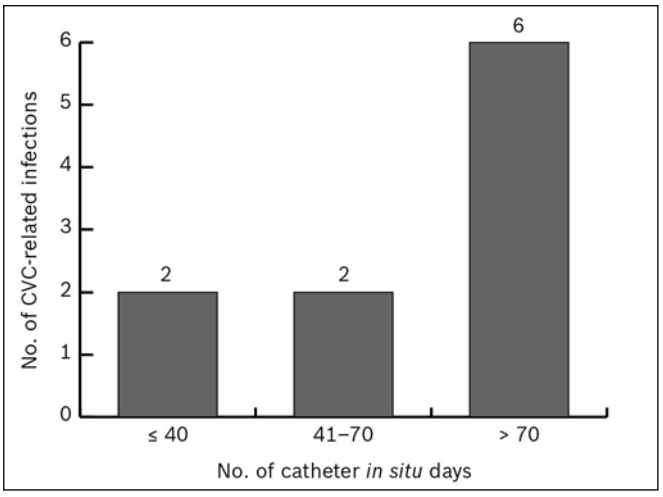

Fig. 1 Frequency distribution of infection requiring central venous catheter removal. 80% of central venous catheter-related infections occurred after 40 catheter days.

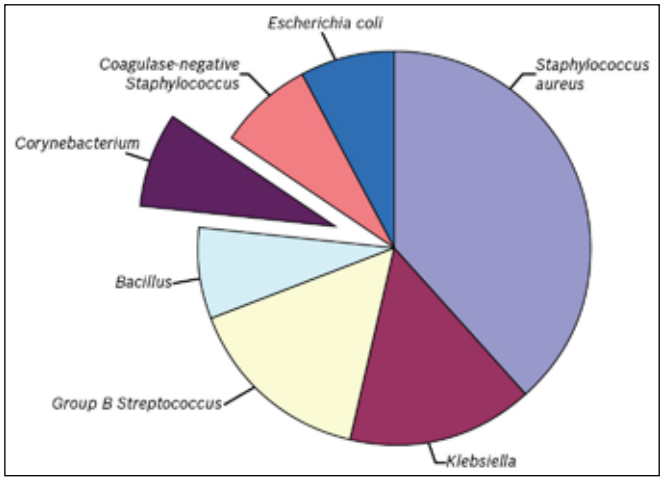

Fig. 2 Breakdown of microorganisms infecting the central venous catheters.

that were removed either prematurely due to complications or in uncomplicated cases. Ten catheters (11.36%) were removed due to infection at a rate of 0.87 per 1,000 catheter days, and three were removed due to catheter occlusion. The reason for CVC removal in the majority of uncomplicated patients was completion of chemotherapy or at the patient's request. Of the 11 patients who requested for removal of the CVC line, seven were not keen to continue chemotherapy in spite of the physician's advice, two had travel plans and the remaining two had persistent fever and proteinuria. Of the 74 cases with uncomplicated catheters, two were multifactorial, i.e. patient request with other compounding factors such as persistent fever and proteinuria. Of the ten CVCs removed for CVC-related infections, only one catheter was removed within one month of insertion. There was a higher incidence of infection when the catheters remained *in situ* for a longer period of time (Fig. 1).

The influence of demographic and disease characteristics on the risk of infection is summarised in Table III. Seven out of 61 catheters inserted into patients aged ≤ 60 years developed CVC-related infections in contrast to three out of 27 catheters inserted into patients aged > 60 years. Out of the ten CVC-related

Table III. Relationship between demographic/disease characteristics and risk of infection resulting in catheter removal (n = 10).

Characteristic	No. (%)		p-value
	CRBSI	No CRBSI	
Age (yrs)			
≤ 60	7 (11.48)	54 (88.53)	0.96
> 60	3 (11.11)	24 (88.89)	
Gender			
Male	9 (16.36)	46 (83.64)	0.089
Female	1 (3.03)	32 (96.97)	
Underlying cancer			
Gastrointestinal tumour	6 (8.82)	62 (91.18)	0.06
Sarcoma	3 (42.86)	4 (57.14)	
Breast carcinoma	0 (0.0)	8 (100.0)	
Others	1 (20.0)	4 (80.0)	
Comorbidity			
Diabetes mellitus	0 (0.00)	6 (100.0)	< 0.001
Renal failure	0 (0.00)	2 (100.0)	
None	10 (14.3)	70 (85.7)	
Median catheter days	98	125	0.23

CRBSI: catheter-related bloodstream infections

Table IV. Clinical presentation of central venous catheter-related infections (n = 10).

Presentation	No. (%)
Fever	7 (70.0)
Fluctuant mass around catheter exit site	2 (20.0)
Inflammation around catheter exit site	1 (10.0)

infections, six occured in patients with gastrointestinal tumour, three in patients with sarcoma and one in a patient with lung carcinoma. Patients with sarcoma were found to be at increased risk for CVC-related infections, whereas those with breast carcinoma were the least vulnerable, although this was not statistically significant (p = 0.06). None of the ten patients with CVC-related infections had diabetes mellitus or renal failure, nor were they in an immunocompromised state, except for cancer and chemotherapy. The median number of catheter days was 98 in the ten patients with CVC-related infections and 125 in the 78 non-infected ones; however, this did not show any statistical significance for CVC-related infection.

Aetiological organism was cultured in at least one specimen from the blood, catheter tip or exit wound. A total of 13 isolates were identified from the ten patients with CVC-related infections. *Staphylococcus aureus* predominated, accounting for 38.5% of the infections (three out of five isolates were methicillin-resistant), while 23.08% of infections were attributable to Gram-negative rods. The frequency of pathogens recovered from 13 consecutive CVCs is summarised in Fig. 2. The most common clinical presentation of CVC-related infections was fever, accounting for 70% of cases (Table IV).

DISCUSSION

The infection rate due to CVCs in this study was 0.87 per 1,000 catheter days. This is lower than the rates reported in other

studies for inpatient settings (1.0–5.8 per 1,000 catheter days).[16-20] Our low rate of infection may be attributed to the careful aseptic techniques employed by the hospital staff during insertion and maintenance of catheters, as well as a high compliance to hand hygiene and infection control practices in our centre. Moreover, oncologic patients are generally highly motivated to learn about their diseases, participate in treatment and take extra precautions in order to improve their quality of life and survival, which may also explain the low infection rate among our patients. Nevertheless, a systemic infection in oncologic patients can be catastrophic due to the degree of physiologic impairment and reduced immune response. As reported in previous studies, Gram-positive cocci represented a majority of the bacterial isolates in all study groups. There were no statistically significant risk factors such as age, gender or comorbidities identified for CVC-related infections in our study. The incidence of infection was found to be higher when the catheter was left *in situ* for a longer period.

There are some limitations in the current study. First, the patients were treated in a single ambulatory cancer centre, and thus, our results may not be applicable to other centres, as infection control policies may differ significantly in different hospitals. For example, recent recommendations favoured chlorhexidine rather than povidone iodine, the antiseptic that was used in our current study. Moreover, the lack of a definite control group with CVCs placed for other reasons prevents definitive conclusions about the catheter infection rate seen in our study. We were also unable to determine the cause of death in some patients; this missing information could yield additional information about catheter-related complications leading to death, since some of the patient deaths could have been related to bacteraemia and/or sepsis due to central line infection. Finally, the size of the study sample was small. Therefore, this study will be followed prospectively to determine the risk factors, complications and preventive factors for CVC-related infections in oncologic patients in an ambulatory setting.

In conclusion, the incidence of CVC-related infections at NCCS is low. Subclavian access of non-tunnelled type CVCs is relatively safe and convenient for long-term venous access in an ambulatory cancer centre. CVC-related infections occur most commonly in patients with sarcoma, and the incidence is higher when the catheters are kept *in situ* for a longer period of time.

REFERENCES

1. Legha SS, Haq M, Rabinowits M, Lawson M, McCredie K. Evaluation of silicone elastomer catheters for long-term intravenous chemotherapy. Arch Intern Med 1985; 145:1208-11.
2. Division of Healthcare Quality Promotion, National Centre for Infectious Disease (2006). The National Healthcare Safety Network (NHSN). Patient safety component protocol. Centers For Disease Control and Prevention, 2006, Atlanta, Georgia.
3. Hickman RO, Buckner CD, Clift RA, et al. A modified right atrial catheter for access to the venous system in marrow transplant recipients. Surg Gynecol Obstet 1979; 148:871-5.
4. Press OW, Ramsey PG, Larson EB, Fefer A, Hickman RO. Hickman catheter infections in patients with malignancies. Medicine (Baltimore) 1984; 63:189-200.
5. Johnson PR, Decker MD, Edwards KM, Schaffner W, Wright PF. Frequency of broviac catheter infections in pediatric oncology patients. J Infect Dis 1986; 154:570-8.
6. Lazarus HM, Lowder JN, Herzig RH. Occlusion and infection in Broviac catheters during intensive cancer therapy. Cancer 1983; 52:2342-8.
7. Becton DL, Kletzel M, Golladay ES, Hathaway G, Berry DH. An experience with an implanted port system in 66 children with cancer. Cancer 1988; 61:376-8.
8. Bendig EA, Singh J, Butler TJ, Arrieta AC. The impact of the central venous catheter on the diagnosis of infectious endocarditis using Duke criteria in children with Staphylococcus aureus bacteremia. Pediatr Infect Dis J 2008; 27:636-9.
9. Ruhe JJ, Menon A. Clinical Significance of isolated Staphylococcus aureus central venous catheter tip cultures. Clin Microbiol Infect 2006; 12:933-6.
10. Mueller BU, Skelton J, Callender DP, et al. A prospective randomized trial comparing the infectious and noninfectious complications of an externalized catheter versus a subcutaneously implanted device in cancer patients. J Clin Oncol 1992; 10:1943-8.
11. Breschan C, Platzer M, Jost R, et al. Comparison of catheter-related infection and tip colonization between internal jugular and subclavian central venous catheters in surgical neonates. Anesthesiology 2007; 107:946-53.
12. Oncü S, Ozsüt H, Yildirim A, et al. Central venous catheter related infections: risk factors and the effect of glycopeptide antibiotics. Ann Clin Microbiol Antimicrob 2003; 2:3.
13. Timsit JF, Farkas JC, Boyer JM, et al. Central vein catheter-related thrombosis in intensive care patients: incidence, risk factors, and relationship with catheter-related sepsis. Chest 1998; 114:207-13.
14. Skiest DJ, Grant P, Keiser P. Nontunneled central venous catheters in patients with AIDS are associated with a low infection rate. J Acquir Immune Defic Syndr Hum Retrovirol 1998; 17:220-6.
15. Intravenous Therapy Systems, Infection Control Manual, NCCS.
16. van Hoff J, Berg AT, Seashore JH. The effect of right atrial catheters on infectious complications of chemotherapy in children. J Clin Oncol 1990; 8:1255-62.
17. Decker MD, Edwards KM. Central venous catheter infections. Pediatr Clin North Am 1988; 35:579-612.
18. Moureau N, Poole S, Murdock MA, Gray SM, Semba CP. Central venous catheters in home infusion care: outcomes analysis in 50,470 patients. J Vasc Interv Radiol 2002; 13:1009-16.
19. Penel N, Neu JC, Clisant S, et al. Risk factors for early catheter-related infections in cancer patients. Cancer 2007; 110:1586-92.
20. Howell PB, Walters PE, Donowitz GR, Farr BM. Risk factors for adult patients with cancer who have tunneled central venous catheters. Cancer 1995; 75:1367-75.