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Complication rates in the clinical practice of long-term use central venous catheters in cancer patients

Esperienza clinica riguardante il tasso di complicanze nell'utilizzo di cateteri venosi centrali a lunga permanenza in pazienti neoplastici

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Summary

Background. **The use of indwelling long term central venous catheters (CVC) has improved the management of cancer patients. However, this device might cause morbidity and lead to a great number of central venous catheter-related thrombosis (CRT). Medical consequences include catheter dysfunction and pulmonary embolism. Vessel injury caused by the procedure of CVC insertion is the most important risk factor for development of CRT. In this retrospective study, we analyzed the incidence and complications of long term use of CVC in adult patients with cancer.** ***Methods*****. We examined the data about the CVC inserted in our institution during an 8-year period. A single type of port-a-cath was used: BardPort (Bard Access System, Salt Lake City, USA). Two-hundred and ten CVC were placed in 197 consecutive unselected patients; 12 pts received a second device, 1 pt a third one (mean age 63 yrs, range 37-83; Male: Female ratio 123: 74). The follow-up continued until CVC was removed or the patient died.** ***Results*****. 92 CVC were removed, 79 pts died with CVC** ***in***

Riassunto

Introduzione**. L'uso di cateteri venosi centrali a lunga permanenza (CVC) ha migliorato la gestione dei pazienti neoplastici. Comunque, questi dispositivi sono gravati da morbilità e possono causare un elevato numero di trombosi venose catetere correlate (CRT). Le conseguenze mediche comprendono disfunzione del catetere ed embolie polmonari. Il danno vasale causato dalla procedura di inserimento del CVC è il più importante fattore di rischio per lo sviluppo di CRT. Alla luce di questi dati, in uno studio retrospettivo, abbiamo analizzato l'incidenza e le complicazioni dell'uso dei CVC a lunga permanenza in adulti con cancro.** ***Metodi.*** **Abbiamo analizzato i dati riguardanti i CVC inseriti presso la nostra divisione durante un periodo di 8 anni. Un solo tipo di CVC è stato utilizzato: BardPort (Bard Access System, Salt Lake City, USA). 210 CVC sono stati posizionati in 197 consecutivi e non selezionati pazienti; 12 pazienti hanno ricevuto un secondo posizionamento, 1 paziente un terzo, l'età mediana era 63 anni, range 37-83; Maschi: Femmine rapporto 123: 74. Il follow-up è proseguito fino a che il**

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***situ*; 39 pts are still alive carrying CVC. Over 60978 pt-days of follow-up (mean 310±329, range 1-1752) 37 out of 197 pts (18.8%) showed complications in 37 of 210 CVC (17.6% and 0.61 episodes per 1000 catheter days of use). 12 pts (6%) removed CVC for complications, 2 for sepsis and the other ones for catheter-related thrombosis; 9 pts (4.5%) changed the treatment plan, 1 for sepsis and 8 for CRT. The mean time of CRT was 125±158 days (range 14-746 days). All pts with CRT were treated with anticoagulants, 4 pts underwent thrombolisis treatment, 8 pts needed removal of CVC. 4 port-a-caths reported bacteraemia (1.9% of devices) (0.06 episodes per 1000 catheter days of use). Furthermore only 1 complication (0.5%) life-threatening was reported. *Conclusions*. We observed that the incidence of CRT is the most frequent complication and it may change the treatment plan in few cases (4%). The efficacy and safety of pharmacologic prophylaxis for CVC related thrombosis is not established and the last recommendations suggest that clinicians do not routinely use prophylaxis to try to prevent thrombosis related to long-term indwelling CVCs in cancer patients. Additional studies performed in high risk populations with appropriate dosage and timing will help to define which patients could benefit from this prophylaxis. Eur. J. Oncol., 14 (1), 27-31, 2009**

***Key words:* cancer patients, CRT**

CVC non veniva rimosso o il paziente non moriva. *Risultati*. 92 CVC sono stati rimossi, 79 pazienti sono deceduti con il CVC *in situ*; 39 pazienti sono ancora vivi e portatori di CVC. Oltre 60978 paziente-giorni di follow-up (media 310±329, range 1-1752) 37 su 197 pazienti (18,8%) hanno avuto complicanze in 37 di 210 CVC (17.6% e 0.61 episodi per 1000 catetere giorni di uso). 12 pazienti (6%) hanno rimosso CVC per complicanze, 2 per sepsi e gli altri per trombosi catetere correlata; 9 pazienti (4.5%) hanno cambiato il piano di trattamento, 1 per sepsi e 8 per CRT. Il tempo medio di CRT è stato 125±158 giorni (range 14-746 giorni). Tutti i pazienti con CRT sono stati trattati con anticoagulanti, 4 pazienti sono stati sottoposti a trattamento trombolitico, 8 pazienti hanno dovuto rimuovere il CVC. 4 port-a-cath hanno evidenziato batteriemia (1.9% dei dispositivi) (0.06 episodi per 1000 catetere giorni d'uso). Inoltre si è verificata solamente 1 complicanza (0.5%) a rischio di vita. *Conclusioni*. Abbiamo osservato che l'incidenza di CRT è stata la più frequente complicanza e questa può cambiare il piano di trattamento, ma solo in pochi casi (4%). L'efficacia e la sicurezza della profilassi farmacologica per trombosi catetere correlata non è stata dimostrata e le ultime raccomandazioni sconsigliano l'uso nella pratica clinica della profilassi per la trombosi correlata all'uso di catetere venoso a lunga permanenza in pazienti con cancro. Ulteriori studi effettuati in popolazioni ad alto rischio trombotico con valutazione dell'appropriato dosaggio e della tempistica aiuteranno a definire quali pazienti possono beneficiare di tale profilassi. Eur. J. Oncol., 14 (1), 27-31, 2009

***Parole chiave:* paziente affetto da cancro, CRT**

Introduction

Central venous catheters (CVC) are commonly used for delivering chemotherapy, parenteral nutrition, blood products, and other intravenous therapy in pts with cancer. The site of CVC insertion is either the subclavian vein or the internal or external jugular vein. In order to reduce the invasiveness of the insertion procedures, the majority of CVCs are positioned with fluoroscopic or ultrasonographic guidance. A surgical cutdown approach (1) or a bedside-blinded technique on the basis of the anatomic-landmark method is feasible.

The use of long-term CVC is associated with complications that could occur early, during the insertion procedure, or later, during the catheter

indwell. The early complications are catheter misplacement or breakage, pneumothorax and hemothorax, air embolism and injury to adjacent anatomic structures (2, 3). The late complications are catheter occlusion by catheter sleeve, local or systemic infection, and CVC-related deep venous thrombosis (CRT).

The risk of catheter-related infection is particularly high in neutropenic pts. Available data suggest that subclavian catheters are less likely to result in CVC-related infection than internal jugular catheters, although the two approaches have not been compared in randomized trials (4). The subcutaneous ports show a significantly lower incidence of CVC removal for sepsis than the partially implantable catheters (5). This lower rate of infection is probably due to the CVC protection from contamination by skin bacteria.

The incidence of CRT in retrospective studies widely varies from 2% to 67% (6-9). The reasons for this discrepancy are unknown but may include advances in catheter material and design, differences in patients populations, and methodologic limitations of some studies. The efficacy and safety of pharmacologic prophylaxis for CVC related thrombosis is not established and the last recommendations suggest that clinicians do not routinely use prophylaxis to try to prevent thrombosis related to long-term indwelling CVCs in cancer patients. We analyzed our data to evaluate the most frequent complication rates and the incidence of changing the treatment plan.

Materials and methods

We examined the data about the CVC inserted in our institution during an 8-year period (1 July 1998-31 March 2006). A single type of port-a-cath was used: BardPort (Bard Access System, Salt Lake City, USA).

All the venous ports were inserted using standard sterile techniques. Catheter tip placement at the junction of the superior vena cava and right atrium was confirmed by a chest X-ray examination and moreover all catheters were flushed with heparin solution 100 U/mL. All the patients were closely monitored for any signs of clinical malfunctioning of the venous infusion system as well as for any signs of CRT or pulmonary embolism (acute dispnea, pain, swelling, or alteration of the superficial venous circulation) or infections. No patients underwent systemic prophylaxis with low-molecular-weight heparin (LMWH) or low dose of warfarin. In patients with suspected CRT, a color Doppler US and/or angio-CT was performed to assess the presence of thrombosis or pulmonary embolism. Blood parameters including routine coagulation tests (PT, PTT and platelets) were monthly performed to monitor the chemotherapeutic toxicity. Follow-up continued until CVC was removed or the patients died. The patients' characteristics are reported in Table 1.

Results

From July 1998 to March 2006, 210 CVC were placed at the S. Giovanni Bosco Hospital in 197

Table 1 - Baseline characteristics of patients

	No. of patients	%
Age, years		
Mean	63	
Range	37-83	
Central venous catheter *in situ*, days		
Mean	310 ± 319	
Range	1-1752	
Sex		
Male	123	63
Female	74	37
Disease		
Colorectal	113	57
Gastric cancer	31	16
Breast cancer	12	6
Ovarian cancer	8	4
Non Small Cell cancer	8	4
Others	25	13
Therapy		
Adjuvant	32	16
Metastatic	165	84
Central venous catheter		
Left insertion side	4	2
Right insertion side	206	98

consecutive oncological unselected pts; 12 pts received a second device and 1 pt a third one (mean age 63 yrs, range 37-83; Male: Female ratio 123: 74).

CVC was placed for chemotherapy continuous intravenous infusion (CIVI) treatment of 113 colorectal (32 adjuvant and 81 metastatic therapies), 31 metastatic gastric cancer, 12 metastatic breast cancer, 8 metastatic ovarian cancers, 8 metastatic non small cell lung cancers and 25 other cancers. Only 4 CVCs (2%) were inserted on left-side position, the other ones (98%) on right-side position.

We evaluated the CVCs for over 60978 pt-days of follow-up (mean 310±329, range 1-1752). 79 pts (40%) died with CVC *in situ*; 39 pts (20%) are still alive carrying CVC.

92 CVC were removed and 37 out of 197 pts (18.8%) showed complications in 37 out of 210 CVC (17.6% and 0.61 episodes per 1000 catheter days of use). The complications are reported in Table 2: 2 pneumothoraxes during insertion (0.9% of devices); 2 pocket infections (0.9% of devices); 4 CVC related bacteraemia (1.9% of devices) (0.06 episodes/1000 days of use), 9 catheter malfunction or decubitus (4.3% of devices) (0.15 episodes/1000 days of use), 20 venous thrombosis (10.5% of devices) (0.36 episodes/1000 days of use) and 1 of them showed pulmonary embolism. Only 12 out of 37 pts. (6%) had CVC removed for complications, 2 for sepsis and 10 (5%) for CRT; 9 pts (4.5%) changed the treatment plan, 1 for sepsis and 8 for CRT. The mean time of CRT was 125±158 days (range 14-746 days). All pts. with CRT were treated with anticoagulants, 4 pts underwent thrombolisis treatment and 8 pts needed CVC removal and changed the treatment plan. The 4 sepsis were caused by *Staphylococcus aureus* (1 pt), *Stenotrophomonas maltophila* (1 pt) *Acynetobacter* (1 pt) and *Staphylococcus epidermidis* (1 pt). The pts required admission to hospital and a target antibacterial agents. No sepsis related death was observed and only 1 patient changed the treatment plan.

Table 2 - Incidence of complications of CVCs

	No. of patients	%
Early		
Pneumothoraxes	2	0.9
Late		
Pocket infections	2	0.9
CVC related bacteraemia	4	1.9
Malfunction or decubitus	9	4.3
Venous thrombosis	20	10.5

Discussion

CIVIs are used in many standard cancer treatment and CVC have facilitated the problem of the vascular access. However important complications are associated with permanent CVC: mechanical complications after CVC insertion, such as haematoma and pneumothorax and long-term complications, such as infection and thrombosis. The patient's risk of complication may differ from different tumours and patients. Often the CVC complications lead to the change of the therapy plan.

Our data confirmed that the use of long-term CVC is associated with complications that may occur early, during the insertion procedure, or later, during the catheter indwell. We observed a low incidence of early complications (0.9% of all the complications) and a high incidence of late complications, causing sometimes the change of the treatment plan. 37 out of 197 pts (18.8%) showed complications in 37 of 210 CVC (17.6% and 0.61 episodes/1000 days of use). The most frequent complication is the symptomatic CRT (20 pts, 10%) with a case of pulmonary embolism (0.5%). So we decided to evaluated, with a retrospective study, the complication rates in the clinical practice of long term use CVC connected to port in cancer patients.

Cancer and its treatment are well-recognized risk factors for venous thromboembolism (10, 11). Up to 15% of patients with clinically overt cancer present venous thromboembolism in the course of their disease. Moreover, patients with cancer represent 20% of all patients in which deep venous thrombosis or pulmonary embolism are diagnosed (12). The malignancies most frequently associated with thrombosis are pancreas, breast, colon-rectum, and lung cancers (10). The risk of CRT is often underestimated and its diagnosis is often based on clinical criteria, such as ipsilateral pain and swelling, or superficial collateral venous circulation (13). The observed incidence of CRT considerably varies in

the literature between 12% and 66%, reflecting differences in examination procedures (14). The pathogenesis of CRT is multifactorial: irritation of the vessel wall due to chemotherapy, catheter tip position, side of insertion, thrombophilic abnormalities in cancer patients. CRT may be asymptomatic (15) and demonstrated only through screening diagnostic imaging. In our series we only examined symptomatic CRT.

At present no sure indications about the need of routine anticoagulants prophylaxis are available (14). The aim of future studies will be to investigate prophylactic individualized strategies.

CVC-related infections may be particularly dangerous in neutropenic patients. Immunosuppressed patients with CVC have reported a mean of 0.2 infections per 1000 catheter-days (16). We observed 0.06 infections per 1000 catheter-days. The prevention of infections is essential using aseptic insertion technique and catheter care. Good training in catheter manipulations is the best preventive method (14, 17).

Comparison of our results with those reported in the international literature demonstrates similar risk of complication during CVC permanence. Furthermore our study suggests that maintaining long-term CVC in pts interrupting their chemotherapy may not be associated with improved risk.

We used only CVC port-a-cath. Probably this approach reduced the incidence of infective complication. In 12 pts (6%) the CVCs were removed for important complications and 9 pts (4.5%) changed their plan of treatment using oral treatment and bolus chemotherapy.

In conclusion, in this study, the infection morbidity associated with subcutaneous port CVCs is lower, even in pts undergoing standard chemotherapy and with related neutropenia, than that reported in the literature data. Furthermore we observed that the most frequent complication CVC related is CRT and that this complication may cause the change of the treatment plan but only in few cases (4%). These data do not justify the routine use of systemic prophylaxis with LMWH or with low dose of Warfarin. Additional studies performed in high risk populations with appropriate dosage and timing will help to define which cancer patients could benefit from this prophylaxis.

References

1. Povoski SP. A prospective analysis of the cephalic vein cutdown approach for chronic indwelling central venous access in 10 consecutive cancer patients. Ann Surg Oncol 2000; 7: 496-502.
2. Mansfield PF, Hohn DC, Fornage BD, *et al*. Complication and failure of subclavian-vein catheterization. N Engl J Med 1994; 331: 1735-8.
3. Taber SW, Bergamini TM. Long-term venous access: Indications and choice of site and catheter. Semin Vasc Surg 1997; 10: 130-4.
4. McGee DC, Gould MK. Preventing complications of central venous catheterization. N Engl J Med 2003; 348: 1123-33.
5. Groeger JS, Lucas AB, Thaler HT, *et al*. Infectious morbidity associated with long-term use of venous access devices in patients with cancer. Ann Intern Med 1993; 119: 1168-74.
6. Newman KA, Reed WP, Schimpff SC, *et al*. Hickman catheters in association with intensive cancer chemotherapy. Support Care Cancer 1993; 1: 92-7.
7. Fraschini G, Jadeja J, Lawson M, *et al*. Local infusion of Urokinase for the lysis of thrombosis associated with permanent central venous catheters in cancer patients. J Clin Oncol 1987; 5: 672-8.
8. Haire WD, Lieberman RP, Lund GB, *et al*. Thrombotic complications of silicone rubber catheters during autologous marrow and peripheral stem cell transplantation: prospective comparison of Hickman and Groshong catheters. Bone Marrow Transplant 1991; 7: 57-9.
9. Koksoy C, Kuzu A, Erden I, *et al*. The risk factors in central venous catheter-related thrombosis. Aust N Z J Surg 1995; 65: 796-8.
10. Lee AY, Levine MN. Venous thromboembolism and cancer: risk and outcomes. Circulation 2003; 107 (23 suppl 1): I 17-21.
11. Monreal M, Davant E. Thrombotic complications of central venous catheters in cancer patients. Acta Haematol 2001; 106: 69-72.
12. Cain GJ, Stonelake PS, Rea D, *et al*. Coagulopathic complications in breast cancer. Cancer 2003; 98: 1578-86.
13. Voog E, Lazard E, Juhel L. Prophylaxis of thrombosis induced by chemotherapy or central venous catheters. Presse Med 2007; 36: 225-34.
14. Vescia S, Baumgartner AK, Jacobs VR, *et al*. Management of venous port systems in oncology: a review of current evidence. Ann Oncol 2008; 19: 9-15.
15. Boersma RS, Jie KSG, Verbon A, *et al*. Thrombotic and infectious complications of central venous catheters in patients with hematological malignancies. Ann Oncol 2008; 19: 433-42.
16. Bouza E, Burillo A, Munoz P. Catheter-related infections: diagnosis and intravascular treatment. Clin Microbiol Infect 2002; 8: 265-74.
17. Mermel LA, Farr BM, Sheretz RJ, *et al*. Guidelines for the management of intravascular catheter-related infections. J Intraven Nurs 2001; 24: 180-205.