Multilumen Central Venous Catheters Increase Risk for Catheter-Related Bloodstream Infection: Prospective Surveillance Study

A. Templeton, M. Schlegel, F. Fleisch, G. Rettenmund, B. Schöbi, S. Henz, G. Eich

Abstract

Background: Catheter-related bloodstream infections (CRBSI) are a leading cause of nosocomial infections associated with significant mortality and costs. The objective of this study was to determine the rate of CRBSI in two large Swiss hospitals and to identify risk factors for this condition.

Patients and Methods: During 1 year all central venous catheter (CVC)-inserted in patients admitted for visceral, orthopedic or urologic surgery at the cantonal hospital in St Gallen and cantonal hospital in Chur were included in the study. Catheters were followed for the duration of their insertion. Blood cultures and semiquantitative cultures from catheters were drawn in the presence of local or systemic signs of infection. Primary endpoint was CRBSI defined as definite if (a) the same pathogen grew in at least one blood culture and from the distal segment of the catheter or (b) the same pathogen grew in at least one peripherally and centrally drawn blood culture and the differential time to positivity of central blood culture vs peripheral blood culture was > 120 min. CRBSI was defined as probable if at least one blood culture was positive with a recognized pathogen in the absence of another site of infection. Data were analyzed using univariate and multivariate time-to-event methods.

Results: During the study period, 1,396 CVCs were prospectively studied in 1,162 patients. Incidence density of all CRBSIs (definite n = 29, probable n = 7) was 2.5 (95% CI: 1.8–3.5) per 1,000 catheter-days. The lowest rate of CRBSI was found in subclavian catheters, the adjusted hazard ratio (HR) for jugular catheters was 2.2 (95% CI: 1.1–4.3; p = 0.03) and for femoral catheters 2.9 (95% CI: 0.6–14.4; p = 0.19). Each additional lumen increased the risk (HR = 4.4; 95% CI: 2.5–7.7; p < 0.001), whereas the permanent blocking of additional lumens was protective (HR = 0.3; 95% CI: 0.1–0.7; p = 0.006). The most commonly isolated organism were coagulase-negative staphylococci with a rate of 28%.

Conclusion: Number of lumens and site of access were independent risk factors for CRBSI. The use of catheters with multiple lumens should therefore be restricted as far as possible. If a catheter cannot be removed, the permanent closure of unneeded lumens may reduce the risk of CRBSI.

Infection 2008
DOI 10.1007/s15010-008-7314-x

Introduction

Central venous catheters (CVCs) are widely used in critically ill patients throughout the developed world. They permit hemodynamic monitoring and allow access for the administration of fluids, blood products, medications, and total parenteral nutrition (TPN). Catheter-related bloodstream infections (CRBSIs) are among the four most frequent nosocomial infections and significantly increase mortality, length of stay and hospital costs [1–5]. Strategies for preventing CRBSI are most likely to be effective if guided by an understanding of the risk factors associated with these infections and surveillance activities have been considered of paramount importance for effective infection control programs. Intervention programs have been shown to reduce the risk of CRBSI [2, 6–8].

The aim of the study was to measure the incidence of CRBSIs and catheter-related local infections (CRLI) and to evaluate associated risk factors in patients of two Swiss tertiary-care hospitals in a 1-year prospective observational study.

Patients and Methods

Study Setting and Local Protocols of Catheter Insertion

The cantonal hospital of St Gallen has 745 beds and more than 30,000 admissions per year and serves as a primary hospital for

A. Templeton, M. Schlegel, B. Schöbi, G. Rettenmund, G. Eich (*corresponding author*)
Infectious Diseases and Hospital Hygiene, Stadtspital Triemli, Birmendorferstr. 497, 8063, Zürich, Switzerland;
Phone: (+41/44) 466-2101, Fax: -2602,
e-mail: gerhard.eich@triemli.stzh.ch
F. Fleisch
Hospital Hygiene, Kantonspital Chur, Chur, Switzerland
S. Henz
Dept. of Internal Medicine, Kantonspital St. Gallen, St. Gallen, Switzerland

Received: July 27, 2007 · Revision accepted: November 11, 2007
Published online: July 28, 2008

the local population and as a tertiary care center for a population of about half a million people. The cantonal hospital of Chur has 220 beds, 10,000 admissions per year and serves as referral center for a population of 200,000 people.

Case report forms were completed directly after insertion by a responsible physician, a follow up form by an attending nurse, and a final form after the removal of the CVC by members of the Department of Hospital Hygiene.

The catheters used were nonantimicrobially coated, radiopaque polyurethane catheters (Certofix® Mono/Duo/Trio/Quattro; B. Braun, Melsungen, Germany).

Placement and maintenance of catheters were performed according to local protocols and included strict sterile techniques and the use of masks and gloves.

After insertion of the line, the site was covered with a sterile, transparent, semipermeable dressing (Tegaderm 3M™, St Paul, USA or OpSite IV 3000, Smith & Nephew, GB) or with a sterile gauze (Salzmann AG, Switzerland) and Fixomull stretch (Smith & Nephew, GB).

Catheters were followed for the duration of their insertion and entry sites were examined daily for the presence of local inflammation. Catheters were removed if they were no longer needed or if a catheter-related complication was suspected. In case of clinically suspected CRBSI, recommended procedure was to collect blood culture by puncture of a peripheral vein and via the CVC and to culture the distal segment of the catheter.

Selection of Study Patients and Data Collection

During 1 year all CVC-inserted patients, who were admitted to visceral, orthopedic, or urologic departments in St Gallen and all adult patients in Chur were included in the study. Catheters, that where removed within 2 days after insertion, were excluded from analysis.

No formal informed consent was obtained because the study was strictly observational and part of the institutional quality control activities.

The following variables were collected: hospital, age, gender, body mass index (BMI), total parenteral nutrition (TPN), days in intensive care unit (ICU), date and site of insertion, guidewire technique if applied, number of lumens, antiseptics used for insertion and maintenance, type of dressing, sterile technique (including long sleeved sterile coat), date and reason for catheter removal, presence of local infection signs, and culture results of blood and from the catheter tip.

Endpoints and Definitions

Endpoints were CRBSI and CRLI. CRBSI was defined as definite if (a) the same pathogen grew in at least one blood culture and from the distal segment of the catheter or (b) the same pathogen grew in at least one peripherally and centrally drawn blood culture and the differential time to positivity of central blood culture vs peripheral blood culture was > 120 min [9]. CRBSI was defined as probable if at least one blood culture was positive with a recognized pathogen in the absence of another site of infection and the patient had clinical signs of infection not attributable to another infection site.

Catheter-related local infections were defined as any sign of local infection (erythema, induration, pain, purulent drainage) and colonization of the catheter tip but criteria for CRBSI were not fulfilled. Catheter tip colonization was defined as equal or more than 15 colony forming units (CFU) of a pathogenic organism on the intradermal part of the catheter, as indicated by the semiquantitative roll-plate technique [10].

Statistical Analysis

Continuous variables are reported as means and standard deviation (SD) and categoric variables as number and percentages. Differences between means were evaluated by the Student's t-test or the Mann-Whitney U-test according to normality assumptions, and proportions were compared with the χ^2 or Fisher's exact test, as appropriate. A cut-off p-value of < 0.05, two-tailed, was regarded as significant.

Catheter-related bloodstream infections and CRLI rates are reported as number of CRBSIs and CRLIs per 1,000 catheter-days (incidence density) as recommended by the Center of Disease Control (CDC) [11]. Kaplan–Meier survival curves and log–rank tests were used univariately to assess the time to the occurrence of CRBSI and CRLI. In order to adjust for potentially confounding variables and to assess the independent contribution of each univariate risk factor, a Cox proportional hazards model was used. All calculations were perfomed by using SAS version 8.2 (SAS Institute, Cary, NC, USA) and Stata version 7.0 (Stata Corp, TX, USA).

Results

During the study period (from January 2005 until January 2006 in St Gallen and from March 2005 until May 2006 in Chur), 1,559 CVCs were inserted in 1,297 patients. After exclusion of 163 CVCs which were removed within 2 days, 1,396 catheters in 1,162 patients could be analyzed (14,312 catheter-days). The baseline-characteristics are shown in Table 1. Mean age was similar at the two study sites, however, in St Gallen patients tended to be more severely ill (e.g. higher rates of TPN, longer ICU-stays). Additionally, in St Gallen most CVCs were in the subclavian position (59% vs 29%). The average number of lumens was higher in St Gallen (2.0 vs 1.2). Disinfectants used differed according to local practice. Most catheters were removed as they were no longer needed (n = 830, 59%) or because of suspected catheter-related infection (n = 200, 15%). Other causes included death, malfunction or removal by the patient. When catheter-related infection was suspected, the correct diagnostic procedure was performed in 80.2% (culture of the distal catheter segment plus blood cultures).

Catheter-Related Bloodstream Infections and Risk Factors

Over all, 36 CRBSIs (definite n = 29, probable n = 7) and 27 CRLIs were observed and analyzed (Table 2). In 19 cases CRBSI and CRLI occurred during the same observation period. The overall incidence density (ID) of CRBSIs was 2.5 (95% CI: 1.8–3.5) per 1,000 catheter-days and differed significantly according to the site of insertion ($p = 0.02$). ID was lowest in subclavian (2.0; 95% CI: 1.2–3.3), higher in the jugular position (2.9; 95% CI: 1.8–4.5), and highest in femoral catheters (12.7; 95% CI: 3.2–51), respectively, although the latter did not reach statistical significance due to the small sample volume.

Univariate risk factors for CRBSI are shown in Table 3. Significant risk factors were the number of lumens (HR 1.9 per each additional lumen; 95% CI: 1.3–2.8), and

Table 1
Baseline characteristics of central venous catheters in 1,162 patients (St Gallen n = 736, Chur n = 426).

	Total	St Gallen	Chur	p
Number of CVCs	1,396 (100)	912 (65.3)	484 (34.7)	
Catheter-days	14,312 (100)	10,094 (70.5)	4,218 (29.5)	
Days of single CVC	10.3 ± 7.5	11.1 ± 7.8	8.7 ± 6.6	< 0.001
Male	802 (57.5)	499 (54.7)	303 (62.6)	0.005
BMI (kg/m^2)	26.4 ± 6.21	26.2 ± 6.26	26.8 ± 6.10	ns
Patients with more than one CVC	245 (17.6)	187 (20.5)	58 (12.0)	< 0.001
Age (years)	63.3 ± 15.5	62.8 ± 16.2	64.1 ± 13.9	ns
Patients in ICU	864 (61.9)	623 (68.3)	241 (49.9)	< 0.001
Average of stay in ICU (days)	4.56 ± 4.23	4.95 ± 4.53	3.56 ± 3.14	< 0.001
Patients died	69 (4.95)	57 (6.25)	12 (2.48)	0.002
Access vein				
Subclavian	676 (48.4)	535 (58.7)	141 (29.1)	< 0.001
Internal jugular	706 (50.6)	363 (39.8)	343 (70.9)	< 0.001
Femoral	14 (1.00)	14 (1.54)	0 (0)	0.003
Number of lumens	1.70 ± 0.75	1.96 ± 0.73	1.20 ± 0.47	< 0.001
1	647 (46.4)	249 (27.3)	398 (82.2)	< 0.001
2	529 (37.9)	456 (50.1)	73 (15.1)	< 0.001
3	208 (14.9)	195 (21.4)	13 (2.7)	< 0.001
4	11 (0.79)	11 (1.2)	0 (0)	0.011
Lumen disused	358 (25.6)	357 (39.1)	1 (0.21)	< 0.001
Guidewire technique	141 (10.1)	101 (11.1)	40 (8.3)	ns
Total parenteral nutrition	423 (30.3)	393 (43.1)	30 (6.2)	< 0.001

Continuous variables means ± SD, categoric variables number (%); CVC: central venous catheter; BMI: body mass index; ICU: intensive care unit; SD: standard deviation

femoral access (HR 5.8; 1.3–25.6). A trend towards more CRBSIs was found for TPN (HR 1.8; 95% CI: 0.9–3.6) and guidewire technique (HR 1.9; 95% CI: 0.9–4.2) whereas gender, age, BMI, type of dressing, and disinfectant did not show any association. Except for pain, signs of local infection were predictive for CRBSI (erythema, HR 2.7; 95% CI: 1.3–5.3; pus, HR 3.9; 95% CI: 1.2–13; induration, HR 2.5; 95% CI: 0.9–7.2).

After adjustment for age, gender, total parenteral nutrition, and ICU-stay only the site of venipuncture, the number of lumens and the presence or absence of inactivated lumens were significant predictors of CRBSI in a multivariate analysis (Table 4). The lowest rate of CRBSI was found in subclavian catheters (reference); the adjusted hazard ratio (HR) was 2.2 (95% CI: 1.1–4.3; p = 0.03) for jugular catheters and 2.9 (95% CI: 0.6–14.4; p = 0.19) for femoral catheters (Figure 1). Each additional lumen increased the risk (HR = 4.4, 95% CI: 2.5–7.7; p < 0.001), whereas the permanent closure by a sterile stopcock (=screw-on cap) and a knot to the line (blocking) of unneeded lumens was protective (HR = 0.3; 95% CI: 0.1–0.7; p = 0.006). The results essentially remained unchanged when the hospital was included as a variable in the model or only the first catheter in patients with more than one catheter was analyzed (data not shown).

Table 2
Catheter-related bloodstream infections and catheter-related local infections.

	Total	St Gallen	Chur	p
Catheter-related bloodstream infections				
All (%)	36 (2.63)	31 (3.40)	5 (1.03)	
Definite (%)	29 (2.12)	24 (2.63)	5 (1.03)	
Probable (%)	7 (0.51)	7 (0.77)	0 (0)	
Rate per 1,000 catheter-days (95% CI)	2.51 (1.2–3.5)	3.07 (2.2–4.4)	1.19 (0.1–2.9)	0.14
Catheter-related local infections				
All (%)	27 (1.97)	21 (2.30)	6 (1.24)	
Rate per 1,000 catheter-days (95% CI)	1.89 (1.3–2.8)	2.08 (1.4–3.2)	1.42 (0.6–3.2)	0.72

CI: confidence interval

Table 3
Univariate analysis of risk factors for catheter-related bloodstream infetions.

	HR	95% CI	p
Male	1.01	0.52–1.94	ns
BMI (per 10 kg/m^2)	0.91	0.51–1.63	ns
Age (per decade)	0.92	0.75–1.12	ns
Access vein			
Subclavian (Ref)	1.00		
Internal jugular	1.70	0.86–3.35	ns
Femoral	5.82	1.32–25.6	0.020
Number of lumen (per each additional lumen)	1.88	1.27–2.78	0.002
Lumen disused	0.96	0.47–1.96	ns
Guidewire technique	1.92	0.87–4.24	0.107
Total parenteral nutrition	1.80	0.91–3.57	0.093
Local signs of infection			
Erythema	2.65	1.33–5.28	0.006
Induration	2.48	0.86–7.15	0.092
Pain	1.31	0.31–5.48	ns
Pus	3.87	1.18–12.7	0.025

HR: hazard ratio; CI: confidence interval; BMI: body mass index; Ref: reference

Catheter-Related Local Infections

The incidence density of CRLIs was 1.89 (95% CI: 1.3–2.8) per 1,000 catheter-days (Table 2). In the multivariate model after adjustment for age, BMI, and ICU-stay only guidewire technique to change an existing catheter at the same insertion site was associated with a significantly higher rate of catheter-related local infections (HR 2.9; 95% CI: 1.2–7.0; p = 0.015).

Isolated Microorganisms

The aetiology of CRBSIs was predominantly gram-positive cocci: coagulase-negative staphylococci (n = 10, 28%), *Staphylococcus aureus* (n = 7, 19%), *Streptococcus* spp. (n = 2, 6%), and *Enterococcus* spp. (n = 1, 3%). Gram-negative rods found were *Klebsiella* spp. (n = 6, 16.7%), *Pseudomonas aeruginosa* (n = 2, 6%), *Escherichia coli* and *Enterobacter cloacae* (both n = 1, 3%). *Candida* spp. was the causative microorganism in 17% (n = 6).

Discussion

We prospectively studied CRBSIs and associated risk factors in two Swiss hospitals. Although some patient characteristics differed at the two study sites (in St Gallen only surgical patients, higher rates of TPN, ICU-stay, catheters with more lumens) the overall rates of infections did not differ significantly. However, the site of venipuncture, the number of lumens and the inactivation of unneeded lumens were identified as major determinants of risk for CRBSIs. In a multivariate analysis subclavian catheters were associated with the lowest risk, whereas the hazard ratio was 2.2 in jugular catheters and even 2.9 in femoral catheters. The finding of higher rates with catheters in jugular and femoral position than in the subclavian position in our study is consistent with published data [12–16].

Catheters with multiple lumens have long been accused to be associated with a higher rate of infection [17].

Table 4
Multivariate analysis of risk factors for catheter-related bloodstream infections (adjusted for age, gender, total parenteral nutrition, and ICU-stay [data not shown]).

	HR	95% CI	p
Access vein			
Subclavian (Ref)	1.00		
Jugular	2.16	1.08–4.31	0.030
Femoral	2.90	0.59–14.4	0.192
Every additional lumen	4.36	2.48–7.67	< 0.001
Lumen disused	0.32	0.14–0.72	0.006

CRBSI: catheter-related bloodstream infection; HR: hazard ratio; CI: confidence interval; Ref: reference; ICU: intensive care unit

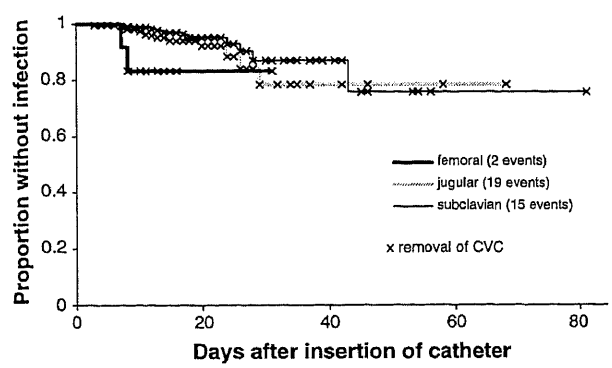

Figure 1. Catheters without infection by access vein.

A recent meta-analysis of 15 studies has found that multilumen CVC were associated with a slightly higher risk of infections when compared with single-lumen catheters (OR 2.15), though this relation diminished when only high-qualitiy studies were considered. However, correction for other possible risk factors are not reported in this meta-analysis [18]. In this study we found a hazard ratio of 4.4 for each additional lumen used. Our data give evidence that catheters with multiple lumens should be used restrictively or these catheters should be removed as early as possible.

If the removal of a catheter seems not feasible, unneeded lumens are sometimes permanently inactivated. In our study this was done by a simple knot to the lumen. There is an ongoing clinical debate if this inactivation increases the risk or if it is even protective. Our data strongly favors the latter hypothesis: the blocking of lumens was associated with a significantly lower hazard ratio of only 0.3.

Placement of a new catheter at the site of a previous catheter by guidewire exchange has also been described as independent risk factor for CRBSI [16]. in this study this technique was only associated with an increased rate of CRLIs, presumably reflecting persisting skin lesion with a foreign body predisposing for infection.

The finding of coagulase-negative staphylococci as the most common causative organisms for CRBSI is consistent with the literature [11, 15, 19].

In our univariate analysis there was a trend for more infections associated with TPN. The hazard ratio of TPN was reduced to 1.6 and no longer statistically significant after multivariate adjustment (data not shown), but the power of our study was insufficient to rule out a clinically relevant effect. The literature on this topic is controversial: *Dimick* et al. [14] found a significant lower risk of infection for catheters used solely for total parenteral nutrition, whereas, e.g., *Tokars* et al. [17] describe higher rates with TPN.

In general, the use of either sterile gauze or sterile transparent semipermeable dressing to cover the catheter site is recommended [11]. In one French study semipermeable transparent dressing was found to be an independent risk factor for colonisation of central catheters [15]. According to published guidelines tincture of iodine or 70% alcohol can be used as disinfectant, although 2% chlorhexidine-based preparations are preferred [11, 20]. Experimental and clinical data suggest the use of maximal sterile barriers with catheter insertion [16, 21]. In our study we have collected data about sterile technique, the disinfectants used with insertion and for maintenance, and the type of dressing used and found no relevant differences. However, our study was strictly observational and not powered for subgroup analysis.

Descriptive epidemiology, pathophysiology, risk factors and best means of diagnosing CRBSI have not yet been fully defined [19, 22, 23]. Diagnostic criteria for CRBSI differ for surveillance and clinical purpose [11]. The criteria used in our study were adapted from guidelines published in 2001 [24]. According to the National Nosocomial Infection Surveillance (NNIS) our rate of 2.51 CRBSIs per 1,000 catheter-days is between percentile 25 and 50 [25]. The rate of 1.89 CRLIs per 1,000 catheter days in this study is very low compared with other studies [12]. Indeed the rate may have been somewhat underestimated due to a detection bias: although the study was conducted prospectively, catheter tips were not routinely cultivated in the absence of suspicion of infection. Since we did not assess the use of antibiotics, some true infections may not have been detectable due to concomitant use of antibiotics. On the other hand, we excluded 163 catheters from analysis which were removed within 2 days in order not to inflate the denominator, as it was assumed unlikely that bloodstream infections would occur in such a short time after insertion – in fact 94% of CRBSIs occurred more than 4 days after insertion – and published guidelines state that CRBSI is only considered to be associated with a central line if the line was in use during the 48-h period before development of the bloodstream infection [11].

A limitation of our study was the lack of information on the primary diagnoses. Thus, correction for health conditions associated with an increased risk of catheter-related infection could not be done. At least *Öncü* et al. [22] found an association of catheter-related infections with primary diagnosis in intensive care unit patients.

We conclude that the use of catheters with multiple lumens should be restricted as far as possible. If a catheter cannot be removed, the permanent closure of unneeded lumens may reduce the risk of CRBSI.

Acknowledgment

We thank Katharina Diethelm and Corina Weber for their meticulous assistance with data collection and all participating staff members whose motivation made this study possible. We also gratefully acknowledge Pietro Vernazza and Philippe Rafeiner for careful review of the manuscript.

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