Title: Influence of insertion site on central venous catheter (CVC) colonization and bloodstream infection rates.

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ABSTRACT

Objective: To compare colonization and catheter related bloodstream infection (CR-BSI) rates amongst three insertion sites (SC, IJ, FEM) used for central venous catheter (CVC) placement.

Design: 24 month prospective study, with relative effects analyzed by Cox proportional hazards regression.

Setting: 8-bed ICU/HDU.

Patients: 410 critically ill patients requiring CVC placement.

Measurements and results: All short term multi-lumen CVCs, including antimicrobial coated (AM) were studied. CVC management was standardized. Six hundred and five CVCs (4,040 catheter days) were analyzed. Colonization and CR-BSI incidence was 15.1 (95% CI 13.5; 21.0) and 1.8 (95% CI 1.2; 4.2) per 1,000 catheter-days. Colonization was higher at the IJ (HR 3.64; 95% CI 1.32; 10.00; p= 0.01) and FEM (HR 5.15; 95% CI 1.82; 14.51, p=0.004) sites compared with the SC. IJ v FEM sites were not different, p= 0.34.The FEM site carried a greater risk of being colonized by non S.epidermidis species compared with the SC and IJ sites combined (HR 4.15; 95% CI 1.79; 9.61, p=0.001). CVCs inserted in Department of Emergency Medicine (DEM) were more colonized than those inserted in the ICU or operating theatre (OT) (HR 2.66; 95% CI 1.27; 5.56; p= 0.01) and CVCs were less colonized in females

compared to males (HR 0.49; 95% CI 0.26; 0.89; p=0.02). No difference in CR-BSI rates was noted between the three sites.

Conclusions:

Colonization was lowest at the SC site. Regional differences exist with respect to type of pathogen isolated. Colonization was influenced by insertion location and gender. The incidence of CR -BSI was not different.

Descriptor: 45

Key Words:

Catheterization, CVC, Central Venous Catheter, Intensive Care, Sepsis, Colonization.

Introduction

Complications of intravascular access devices (IAD) in particular central venous catheters (CVCs) can be classified as mechanical and infective [1, 2]. Increasing awareness of factors that influence CVC related infection has resulted in evidence based practice guidelines which have been shown to be effective in reducing rates of CVC related sepsis [3]. Despite this, CVCs continue to remain one of the leading causes of nosocomial sepsis in the critically ill.

The anatomical insertion sites commonly used for CVC placement are the Internal Jugular (IJ), Subclavian (SC) and Femoral (FEM) veins. In terms of complications, several studies have compared one site with another [2, 4, 5] and others the three sites concurrently [6, 7, 8, 9, 10]. The Hospital Infection Control Advisory Committee (HICPAC) [11] has consistently given selection of the SC site an IA recommendation for preventing infection. A number of publications however have suggested the FEM site is on par with upper body sites in terms of both sepsis and mechanical complication rate [12, 13, 14, 15]. Some of these studies however were in particular subgroups of patients such as children and burns injury [15, 16] and in others the conclusions controversial [14, 17].

In our ICU all 3 vascular access sites were routinely used additionally accurate data on IAD infection rates was prospectively collected. Due to the conflicting reports in the literature we sought to investigate the use of CVCs in relation to placement site and to compare infective outcomes and risk factors between CVCs placed at all three sites.

Materials & Methods

This prospective observational study was carried out over 24 months in an 8-bed combined general intensive care unit (ICU) and co-located high dependency unit (HDU) of a 350-bed regional Australian teaching hospital. The ICU treated all forms of acute illnesses with the exception of post cardiothoracic surgical and acute neurosurgical cases. Admission and treatment rights in the ICU were limited to attending intensivists and the unit staffed by critical care registered nurses.

All short term non-tunneled CVCs (including peripherally inserted central lines), both regular and antimicrobial coated (AM) that presented to, or were inserted in, the ICU were included in the study. Neither pulmonary artery catheters, their introducer sheaths nor long term access devices (e.g. Hickman's catheters) were studied. The study was conducted without clinical interference amongst the physicians inserting CVCs and was intended to be a true reflection of clinical practice at that time. Institutional ethics committee approval was obtained for using the non-identified data.

Data collection

For study entry the CVC must have been inserted within the departments of emergency medicine (DEM), operating theatre (OT) or the ICU. CVCs inserted in other hospitals were not included. During the study, CVCs were excluded if their removal, and microbiological sampling, was not according to the study protocol. On admission to the ICU, CVCs were identified with a unique identifier label which was attached to an external lumen. Data collected and entered included: CVC insertion details (time, place, and operator level of experience), CVC type (regular or AM, lumen number), anatomical insertion site (FEM, SC, IJ, cubital) and CVC removal details (date, time, reason and location).These data were completed for each CVC inserted. The clinical nurse followed up the patient and completed the data entry in cases where discharge from the ICU occurred prior to CVC removal. Other data collected included 24 hour APACHE and SAPS II scores, APACHE II diagnostic codes, age, and sex. Data on patient co morbidity or thrombotic events was not recorded. Microbiological details including all catheter tip culture, blood culture and microorganisms isolated were collected concurrently.

CVC management

Insertion of CVCs was performed by ICU personnel (intensivist, registrar, senior resident). CVCs inserted in the OT or DEM were likewise inserted by trained operators ideally under the same conditions. All regular (non AM) CVCs used were multi-lumen 20cm polyurethane (Arrow® International, Reading, PA,USA) inserted using a standard

Seldinger approach under maximum sterile barrier precautions (sterile gloves, gown, large drapes, mask and cap). Chlorhexidine 0.5% in ethanol was used as skin antisepsis. AM catheters were ARROWg$^+$ard Blue®, (Arrow® International, Reading, PA, USA). These were also 20cm multi-lumen devices inserted under identical conditions. No *antibiotic* coated CVCs were used. AM CVCs were used at the discretion of the medical team. In general these CVCs were placed if the clinician expected the CVC in- situ duration to exceed 7days or if the patient was clinically judged at high risk for developing CR-BSI however insertion was not subject to protocol. All patients had optimal CVC tip placement confirmed by plain CXR. For both types of CVC (regular and AM) no specific anatomical insertion site was mandated by policy rather, insertion into the IJ, SC, or FEM veins was based on patient variables such as risk of pneumothorax and level of operator experience.

The CVC insertion site was inspected daily as part of the multidisciplinary ICU ward round however superficial skin cultures were not taken. All line manipulations including pressure transducers, giving sets, and site dressings were performed by ICU nursing staff. All site dressings and giving sets were changed according to current guidelines [11]. CVCs were not used routinely for blood sampling and guide-wire exchange was not performed. The CVC was not changed on a scheduled basis but removed for clinical suspicion of sepsis (with culture of the catheter tip and peripheral blood), mechanical failure, or when no longer required. All patients if possible had their CVC removed prior to discharge to the general wards and peripheral IV access inserted if intravenous therapy was still deemed necessary [18].

Microbiological Sampling

CVCs were removed by the bedside ICU nurse.. The distal 3 to 5cm end of the CVC tip was removed using a sterile dressing pack which included sterile forceps and scissors, taking care not to contaminate the tip on removal. The tip was then immediately transferred to a sterile container and transported to the microbiology department for analysis [19].

Microbiological Definitions

The following definitions of CVC infection were applied [11]; Catheter Colonization: tip culture > 15 CFU in the absence of BSI and CR-BSI: Catheter tip culture >15 CFU plus a positive blood culture taken before or within 48 hours of CVC removal with the same micro-organism and antibiogram with no other obvious source of infection apparent.

Statistical analysis

The reported rates per 1,000 catheter days of colonization and CR-BSI were calculated using Poisson regression. These were reported after adjustment for age, gender, APACHE and SAPSII scores, insertion location (ICU, OT, DEM) and CVC type (regular or AM) in order to remove these sources of confounding when assessing these rates within the study. Poisson regression and simpler comparable methods for calculation of incidence rates assume that these events were occurring at random throughout the period each CVC is in-situ. However, colonization and CR-BSI are

terminating events, either because they are recorded only at the time of CVC removal or because the CR-BSI provokes the removal of the catheter. The relative rates were therefore compared using Cox proportional hazards regression, which is based on the variable time of occurrence of each terminating event. A multivariate Cox proportional hazards regression model was constructed by stepwise removal of insignificant ($p>0.2$) variables (anatomical site of insertion, regular and or AM CVC, ICU/OT/DEM location of insertion, specialist/registrar/RMO operator, diagnostic category, age, gender, APACHEII and SAPSII scores). The same variables were then analyzed separately in multivariate Cox proportional hazards regression models for the three sites of insertion. All analyses were adjusted where required for multiple comparisons by the Holm method. Time-to-event graphs were drawn to illustrate the occurrence of these events over time. Statistical analyses were performed using *STATA™* Statistics/Data Analysis Version 9.2 (Stata Corp, College Station, Texas USA).

Results

General:

During the entire study period 618 CVCs were sited in 410 patients (226 (55.1%) males). These patients had a mean age of $61.5 \pm$ (SD) 16.5 years and APACHE II score 21.4 ± 17.9. Mean duration of catheterization was 6.5 ± 5.5 days. Ninety-five (23.2%) patients died in hospital. Primary admission diagnoses were: 69 (15.3%) sepsis or other major infection; 121 (26.9%) Post GI surgery; 55 (12.2%) multi-organ failure and multiple trauma; 47 (10.4%) non-septic respiratory failure; 11 (2.4%) non-surgical GI

disease; 37 (8.2%) neurological disease; 31 (6.9%) cardiac failure or instability; 43 (9.6%) non-surgical malignancy; 36 (8.0%) other major surgery. Forty patients were readmitted at later dates with alternate diagnoses.

In 13 CVC records the site was not recorded, leaving 605 CVCs (413 regular, 176 AM and 16 cubital) in 410 patients for further analysis. No CVCs were excluded for missing microbiological data. In total, these 605 CVCs were observed for 4,040 CVC days. Detail of these 605 CVCs with rates of colonization and CR-BSI and total CVC in situ time at each site is seen in table1. The overall incidence of microbial colonization and CR-BSI was 15.1 (95% CI 13.5-21.0) and 1.8 (95% CI 1.2-4.2) per 1,000 catheter-days. Inspection of fig 1 demonstrates the cumulative incidence of CVC colonization at the time of catheter removal increased over time.

CR-BSI and Colonization at each anatomical insertion site:
Further analysis of colonization and CR-BSI incidence was performed only on the 589 CVCs that were sited at the IJ (regular 204, AM 75), SC (regular 59, AM 43) and FEM (regular 150, AM 58) sites. Mean duration of catheterization at IJ, SC and FEM sites for regular and AM catheters respectively was 5.5, 7.4 and 5.4 days and 8.5, 9.2, and 5.7 days with a significant difference noted in dwell time between IJ sites only (p=0.001). There were 9 episodes of CR-BSI. Number of CR-BSI events by CVC type can be seen in table1. When using the SC as a reference CR-BSI rate between the three sites was not significantly different (table2). Of all CVCs studied, IJ AM CVCs were associated with the greatest CR-BSI rate (HR 7.02; 95% CI 0.35; 1.43, p=0.205).

Table 3a reports colonization rates and multivariate estimates of the simultaneous

effects of differing risk factors for CVC colonization at all sites combined and table 3b

at individual sites, after stepwise removal of insignificant (p>0.2) variables. The final

model found the only factors significantly associated with colonization were non SC

insertion site, DEM insertion location, male gender and use of regular CVCs.

Colonization at the IJ (HR 3.64; 95% CI 1.32; 10.00, p=0.01) and FEM (HR 5.15; 95%

CI 1.82; 14.51, p=0.004) sites was significantly greater than that at the SC (fig 2).

Colonization at the FEM site was not different from that at the IJ site (HR 1.31; 95% CI

0.54-3.21; p=0.34). CVCs inserted in the DEM were significantly more colonized than

those inserted in the ICU or OT (p= 0.01). CVCs were significantly less colonized in

females compared to males (p=0.02) an effect was most marked at the IJ site (p= 0.003).

There was a significant reduction in colonization when AB CVCs were used compared

with regular CVCs (p= 0.02). At individual sites this effect was greatest at the IJ site

(p=0.03) but not significant at FEM site (p=0.50). Colonization of CVCs was not

significantly different if inserted by registrars and residents (HR 1.22, 95% CI 0.31;

3.59 p=0.723) compared to specialists. Table 4 displays colonization and admitting

diagnosis. Colonization was lower in those patients with a primary diagnosis of sepsis

or other major infection (p=0.05).

A total of 81 microorganisms were responsible for the 68 CVC colonization's (table5),

of which 62 (76.5%) were Gram-positive bacteria, 14 (17.3%) were Gram-negative

bacteria and 5 (6.2%) were yeasts. Isolated from the 81 microorganisms were: 50

(61.7%) Staphylococcus epidermidis; 12 (14.8%) Enterococcus faecalis; 9 (11.1%) S. aureus; 5 (6.2%) Candida albicans; 3 (3.7%) Corynebacterium sp; and 2 (2.5%) Klebsiella sp. The SC site was associated with the lowest level of isolates (3.7%).

At the IJ site 83% of isolates were S. epidermidis compared with 34% at the FEM site. The likelihood of heavy colonization with non S. epidermidis organisms was significantly greater at the FEM site v the SC and IJ sites combined (HR 4.15;95% CI 1.79;9.61,p=0.001) whereas the SC and IJ sites were similar (HR 2.01;95% CI 0.23;17.6, p=0.52).

 Discussion

We have shown that in an environment of consistent CVC care after adjusting for the effect of AM CVCs and CVC in situ time, that catheter tip colonization (CTC) was significantly different between the 3 commonly used CVC insertion sites in favor of the SC. IJ and FEM sites were not different. Differences in colonization were also observed with respect to insertion location, gender and type of pathogen isolated at individual and all sites combined. For all CVCs no significant difference was detected in CR-BSI rate between sites.

The HICPAC guidelines [11] for the prevention of intravascular catheter related infections recommend that the SC site be used preferentially for CVC catheterization to reduce the incidence of catheter related infection. This is based on 4 studies including Merrer's randomized controlled trial comparing FEM and SC access sites [2] and Goetz's prospective observational study [7]. The former study found that catheterization

at the FEM site was associated with a 5 fold increased incidence density in catheter related infection over the SC site. In particular when the endpoints of colonization plus CR-BSI were combined this difference was highly significant. Goetz [7] also found catheter contamination to be associated with FEM location (HR 4.2; p=0.0001) and a trend towards greater clinical infection at the same site (HR 4.7; p=0.08). Colonization rates in this study were comparable to our own at 28.8/1,000 and 5.8/1,000 CVC days for IJ and SC sites respectively but appeared lower than ours at the FEM site (12.6/1,000 CVC days). Other studies have produced conflicting results. Although Collignon [6] found a significantly higher colonization rate with catheters inserted at the FEM site compared with the SC site, Richet [8] found the IJ and not the FEM site to be independently associated with positive CVC tip culture. Despande [14] found that there was no significant difference in the rate of infection including BSI or colonization at three concurrently studied sites. These data led the authors to conclude all three sites were safe as regards risk of infection providing site selection was chosen carefully, trained personnel inserted the CVC and appropriate infection control measures were in place. One of the only other studies to examine infection rates at all 3 sites concurrently [10] found catheter related local infection (signs of local infection plus CTC) incidence density was statistically higher for FEM than for IJ (15.83 versus 7.65, $p < 0.001$) and SC (15.83 versus 1.57, $p < 0.001$) accesses, and higher for IJ than for SC access (7.65 versus 1.57, $p < 0.001$). CR-BSI incidence density was also statistically higher for FEM than for IJ (8.34 versus 2.99, $p = 0.002$) and SC (8.34 versus 0.97, $p < 0.001$) accesses.

A common theme thru all of these studies is that the SC site is remains the lowest risk in terms of both CTC and BSI rates. Our results support this assertion in that the SC site was significantly less colonized that either the IJ or FEM sites which appeared equivalent. CTC would appear to be a valid surrogate end point for BSI correlating powerfully with the subsequent development of CR-BSI [20]. The difference we observed at the IJ and FEM sites would support these two positions as second choice to the SC site for routine CVC insertion. The salient issues of patient and operator variables need consideration in this. In those at risk of complication with SC or IJ access the FEM approach may be safest. The perception that SC access is more prone to complication than the IJ may not be warranted with one study suggesting no difference in the incidence of haemopnuemothorax between the two. These results must be interpreted with caution however because they represent a meta analysis of non randomized studies and exclude certain high risk sub groups such as patients with COPD or ARDS [21]. Although our results suggest the SC is preferable in terms of colonization the clinical end point of CR- BSI was not different at each three sites. As suggested previously [14, 17] with optimal insertion and aftercare technique clinically meaningful outcomes such as BSI may be equivalent between the three sites, insertion site in this context being influenced by operator experience and risk of complication.

Varying factors influenced the colonization rates at differing sites. Differences in colonization patterns of anatomical areas have been described previously [22]. We observed a clear colonization benefit in favor of females at the IJ site but not SC or FEM sites. The higher rate in males may in part be explained by the presence of facial

hair and beards which extends down to around the usual insertion sites of the IJ CVCs increasing the risk of contamination. Whilst the IJ site cannot be recommended above the SC for routine catheterization, our data suggests in females this site is likely to remain significantly less colonized and may pose less of an infective risk. Although the overall numbers of CVCs studied was small, devices inserted in the DEM, in particular FEM CVCs were significantly more colonized than those inserted in either the ICU or OT environments. This can be explained by the often emergent insertion in this environment where sterility may be suboptimal. CVCs inserted in these conditions should be replaced as soon as is practicable.

It has been suggested that anatomical insertion site may influence the type of bacteria isolated from catheter tip culture and as a cause of CR-BSI [22, 23] few studies however have compared three sites concurrently. Lorente [23] recently demonstrated that the FEM site is an independent risk factor for BSI due to yeasts and gram negative organisms. Our results also suggest that the FEM site carries a significantly greater risk of infection than either the IJ or SC sites for non S. epidermis organisms. This may have implications for treatment of suspected CR-BSI arising from the FEM site where organisms of significantly greater virulence may be responsible.

Our study has a number of limitations which need to be considered when interpreting the results. Despite the fact that clinical practice was uniform as regards insertion, use and maintenance of the CVCs studied this was not a randomized comparison, therefore

FEM site selection may be biased toward more junior operators and emergent insertions both of which will lead to higher colonization. Additionally despite the fact we controlled for severity of illness in our analysis it is possible that bias may have also occurred in patient selection with certain subgroups of patients more prone to FEM insertion (and avoidance of SC) e.g. severe respiratory failure .

Although CTC which is a valid surrogate of BSI [21] remains unequivocally different between the 3 sites, due to the very low rate of CR-BSI, our study was under powered to detect differences in this outcome measure. With quality improvement initiatives the use of CR-BSI may become problematic as the overall incidence of bloodstream infection continues to reduce. Unless the background incidence of BSI is high, CTC may therefore become a more valid and practically achievable end point in future studies

Overall, although AM CVCs have been associated with up to 50% reductions in both colonization rates and incidence of CR-BSI in multiple studies [24] controversy exists with regard to their role [25,26]. Our results are consistent with those previously reported with significant reductions in colonization compared with regular CVCS. Our study was however not designed to demonstrate an outcome benefit for the use of AB CVCs and analysis was limited by small numbers and confounded by microbiological technique used to analyze CVC tips in particular the impact of external antiseptic coating on colonization using the roll plate technique. We support the concept that AM

CVCs should be used selectively where the rates of CR-BSI remain unacceptably high despite adherence to standard infection control practices [27].

In conclusion when CTC is used as an end point our study suggests that the SC site remains the lowest risk of the three commonly used anatomical insertion sites for routine CVC catheterization with no difference being found between the IJ and FEM sites. Our results also suggest regional differences may exist with respect to insertion location, gender and type of pathogen isolated.

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Table1. Total numbers of CVCs at different insertion sites; with associated rates of colonization and CR-BSI

Site	CVC (n)*	CVC Time (CVC days)	Colonization‡			CR-BSI		
			n	%	Rate	n	%	Rate
IJ	204	1,118	25	12.3%	22.0	1	0.49%	0.7
SC	59	439	4	6.8%	8.7	0	0.00%	0.0
FEM	150	802	17	11.3%	20.1	1	0.67%	1.3
Cubital	16	203	1	6.3%	4.4	0	0.00%	0.0
IJ AM§	75	635	11	14.7%	18.2	5	6.67%	6.9
SC AM§	43	395	3	7.0%	7.5	2	4.65%	4.5
FEM AM§	58	330	7	12.1%	19.1	0	0.00%	0.0
All sites	*605*	*4,040*	*68*	*11.0%*	*15.1*	*9*	*1.46%*	*1.8*

Legend table 1

*   Of the 618 CVCs, the site was not recorded in 13 catheter records

‡Colonization (> 15 CFU): n= number observed and as % of total CVCs colonized at time of CVC removal with associated rate,

calculated by Poisson regression adjusted for age, gender, APACHE and SAPSII scores.

CR-BSI: n=number observed and as % of total CVCs inserted at each site

§   Anti-microbial CVC

Table 2: Adjusted rates of CR-BSI for each site for both regular and AM CVCs (n =589[§]) combined: the risks at the FEM and IJ sites are indexed to the risk at the SC site.

Site	Rate*	HR †	95% CI	P$^{\Omega}$
SC	1.26	1.00		
IJ	2.19	2.82	(0.50; 15.8)	0.47
FEM	0.75	1.39	(0.13; 15.2)	0.79

Legend table 2

*   CR-BSI rate per 1,000 catheter days, calculated by Poisson regression, † hazard ratio (HR) calculated by Cox proportional hazards regression, both adjusted to mean of age, gender, APACHE and SAPSII scores,, catheter insertion location, AM catheter, and presence of sepsis as a diagnosis.

$^{\Omega}$ p-values corrected for multiple comparisons by the Holm method.

§ CVCs sited at FEM, SC and IJ sites only

Table 3a. Comparison of colonization between IJ, FEM and SC sites

		N (colonized)	Rate*	HR†	95% CI	p‡
Site§	SC	102 (6)	8.1	1.00		
	IJ	279 (33)	19.7	3.64	(1.32 ; 10.03)	0.01
	FEM	208 (24)	26.4	5.15	(1.82 ; 14.51)	0.004
CVC type	Regular	413 (45)	18.3	1.00		
	AM	176 (18)	13.8	0.47	(0.25 ; 0.89)	0.02
Where inserted	ICU	443 (45)	16.0	1.00		
	OR	117 (13)	16.8	1.17	(0.60 ; 2.30)	0.63
	DEM	29 (5)	32.8	2.66	(1.27 ; 5.56)	0.01
Gender	Male	349 (41)	20.1	1.00		
	Female	240 (22)	12.9	0.49	(0.26 ; 0.89)	0.02
Sepsis	Absent	415 (51)	21.6	1.00		
	Present	120 (8)	13.4	0.60	(0.31 ; 1.19)	0.14

Table3b: Multivariate estimates of the simultaneous effects of different risk factors for CVC colonization at individual sites.

	SITE	SC			IJ			FEM		
		HR†	95% CI	p‡	HR†	95% CI	p‡	HR†	95% CI	p‡
CVC type	Regular	1.00			1.00			1.00		
	AM	0.29	(0.08; 1.03)	0.05	0.64	(0.42; 0.97)	0.03	0.66	(0.20 ; 2.23)	0.50
Where inserted	ICU	1.00			1.00			1.00		
	OR	0.57	(0.09 ; 3.82)	0.56	1.06	(0.40 ; 2.81)	0.91	0.11	(0.01; 1.02)	0.10
	DEM	0.00			3.56	(1.06; 12.0)	0.07	2.42	(0.83 ; 7.04)	0.10
Gender	Male	1.00			1.00			1.00		
	Female	1.40	(0.42 ; 4.64)	0.58	0.23	(0.09 ; 0.58)	0.002	1.03	(0.36; 2.92)	0.96
Sepsis	Absent	1.00			1.00			1.00		
	Present	7.75	(0.59 ; 103)	0.12	0.55	(0.20 ; 1.48)	0.23	0.29	(0.07; 1.24)	0.09

Legend table 3a and b

§   Colonization at the IJ and FEM sites was compared to colonization at the SC site
*   Colonization per 1,000 CVC days calculated by multivariate Poisson regression, † Hazard ratio and 95% confidence intervals estimated by multivariate Cox proportional hazards regression, The model included variables in the table adjusted to mean of age, and severity of illness.
‡   P-values corrected for multiple comparisons by the Holm method

Table 4: Absolute and relative rates of CVC colonization in patients with different reasons for admission: each disease is compared with the rates in all the remaining patients.

	n*	N*	Rate	95% CI	HR†	95% CI	p
Organ failure	7	45	16.1	(7.31; 35.4)	2.84	(0.94 ; 8.58)	0.06
GI disease	2	10	31.2	(11.1; 88.0)	2.46	(0.13 ; 46.02)	0.54
Respiratory disease	6	44	17.6	(8.83 ; 35.2)	1.58	(0.45; 5.61)	0.47
Neurological disease	5	31	25.1	(10.3; 61.1)	1.54	(0.21 ; 11.35)	0.67
Cancer	8	38	17.7	(8.82 ; 35.3)	1.16	(0.25; 5.43)	0.85
GI surgery	16	102	21.7	(13.1;35.8)	0.88	(0.33; 2.36)	0.80
Sepsis	7	63	9.27	(4.57 ;18.8)	0.32	(0.10; 1.04)	0.05
Cardiovascular shock	3	24	16.8	(5.69; 49.7)	0.23	(0.01; 4.20)	0.32
Major surgery	0	18	8.7	(1.33; 57.7)	0.20	(0.03; 1.50)	0.11

Legend table 4

*   Number of colonization's (n) in patients (N) with the condition

†   Hazard Ratio (HR) or relative rate calculated by Cox proportional hazards regression, adjusted for age, gender, APACHE and SAPSII scores.

Table5. Types of organisms found at different CVC insertion sites for all CVCs

Organism Site	S.epidermidis	S.aureus	Enterococcus sp	Candida sp	Klebsiella sp	Other gram pos.	CVC (n)
SC	3	2	1	0	0	0	102
I J	35	1	3	3	0	0	279
FEM	11	6	8	2	2	3	208
Cubital	1	0	0	0	0	0	16
Total (n=81)	50	9	12	5	2	3	605

Legend table 5

The likelihood of heavy colonization with non S. epidermidis organisms was greater at the FEM site v the SC and IJ sites (HR 4.15; 95% CI 1.79; 9.61, p=0.001).

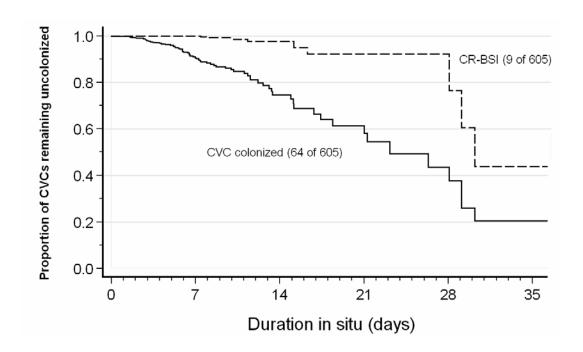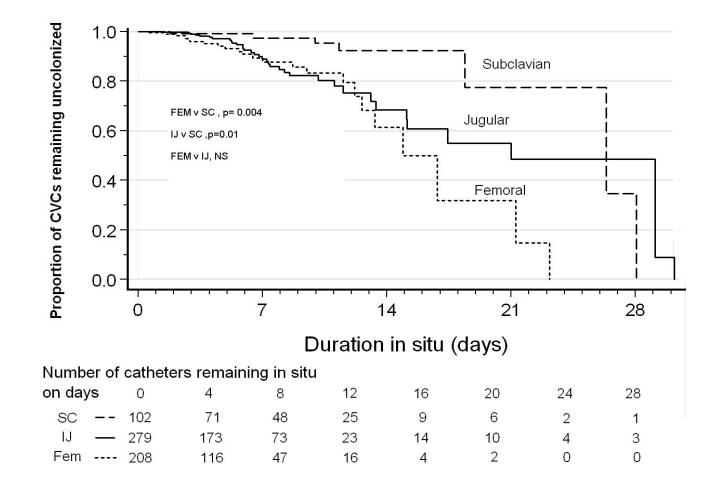Figure1. Proportion of CVCs remaining uncolonized and CR-BSI when removed at
different times

Figure 2. Proportion of CVCs remaining uncolonized versus duration in situ at three

sites.

Number of catheters remaining in situ									
on days		0	4	8	12	16	20	24	28
SC	--	102	71	48	25	9	6	2	1
IJ	—	279	173	73	23	14	10	4	3
Fem	----	208	116	47	16	4	2	0	0

Legend fig 2

Both plain and AM CVCs are represented. Colonization at the IJ (HR 3.64; 95% CI 1.32; 10.00, p=0.01) and FEM (HR 5.15; 95% CI 1.82; 14.51, p=0.004) sites was significantly greater than that at the SC. Colonization at the FEM site was not different from that at the IJ site (HR 1.31; 95% CI 0.54-3.21; p=0.34).