

# The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population\*

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**Objective:** The objective was to assess the risk of central venous catheter infection with respect to the site of insertion in an intensive care unit population. The subclavian, internal jugular, and femoral sites were studied.

**Design:** An epidemiologic, prospective, observational study.

**Setting:** The setting is a well-functioning intensive care unit under a unified critical care medicine division in a university teaching hospital. Critical care medicine attendings and fellows covered on site 17 and 24 hrs per day, respectively.

**Patients:** Patients were critically ill. All patients were triaged into the intensive care unit by on-site critical care medicine fellows.

**Interventions:** None.

**Measurements and Main Results:** In an intensive care unit population, we prospectively studied the incidence of central venous catheter infection and colonization at the subclavian, internal jugular, and femoral sites. The optimal insertion site for each individual patient was selected by experienced intensive care physicians (critical care medicine attendings and fellows). All of the operators were proficient in inserting catheters at all three sites. Confounding factors were eliminated; there were a limited number of experienced operators inserting the catheters, a uniform protocol stressing strict sterile insertion was enforced, and standardized continuous catheter care was provided by dedicated intensive care nurses proficient in all aspects of central venous catheter care.

Two groups of patients were analyzed. Group 1 was patients

with one catheter at one site, and group 2 was patients with catheters at multiple sites. Group 1 was the primary analysis, whereas group 2 was supporting.

A total of 831 central venous catheters and 4,735 catheter days in 657 patients were studied. The incidence of catheter infection (4.01/1,000 catheter days, 2.29% catheters) and colonization (5.07/1,000 catheter days, 2.89% catheters) was low overall.

In group 1, the incidence of infection was subclavian: 0.881 infections/1,000 catheter days (0.45%), internal jugular: 0/1,000 (0%), and femoral: 2.98/1,000 (1.44%;  $p = .2635$ ). The incidence of colonization was subclavian: 0.881 colonization/1,000 catheter days (0.45%), internal jugular: 2.00/1,000 (1.05%), and femoral: 5.96/1,000 (2.88%,  $p = .1338$ ). There was no statistically significant difference in the incidence of infection and colonization or duration of catheters ( $p = .8907$ ) among the insertion sites.

In group 2, there was also no statistically significant difference in the incidence of infection and colonization among the three insertion sites.

**Conclusion:** In an intensive care unit population, the incidence of central venous catheter infection and colonization is low overall and, clinically and statistically, is not different at all three sites when optimal insertion sites are selected, experienced operators insert the catheters, strict sterile technique is present, and trained intensive care unit nursing staff perform catheter care. (*Crit Care Med* 2005; 33:13–20)

**KEY WORDS:** central venous catheters; infection; subclavian; internal jugular; femoral; experienced operators

The impact of central venous catheter (CVC) infection is far reaching. Pittet and Wenzel (1) reported that catheter infection carries an odds ratio for death as high as 20.45 (95% confidence interval, 18.9–22.1); others have reported similar findings (2). Some estimate 500–4,000

deaths annually (3, 4) at a cost per infection of 3,124 Euros in Europe (5) and \$3,700–\$29,000 in the United States (3). CVC infection not only increases patient mortality but also greatly burdens the entire health care system.

The actual risk of infection at the three most commonly used insertion sites—subclavian (SC), internal jugular (IJ) and femoral (FEM)—remains controversial. Merrer et al. (6) showed an increase at the FEM site, whereas others reported no increased risk (7–9), even when used in immunocompromised patients (10). Some have even reported a higher risk at the IJ site (7, 11–13).

Sometimes an otherwise optimal insertion site is actively avoided because, traditionally, some sites are assumed to have a higher risk of infection; this is especially true with the FEM site. Great importance is given to avoid possible infection, whereas minimal importance is given to avoid mechanical complications. Often, critically ill patients have tenuous cardiopulmonary and hemodynamic status. The consequences of iatrogenic mechanical complications in patients with high positive pressure ventilation, coagulopathy, and chronic lung disease with bullae are potentially catastrophic; delirium can further increase the risk because

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patients are unable to cooperate with CVC insertion. Avoiding devastating complications from tension pneumothorax and vascular accidents with subsequent loss of airway is vital to patient safety.

Pneumothorax and vascular injury are well described complications of SC and IJ catheter insertion. Although the FEM catheter insertion can also result in vascular accidents, the consequences are less devastating. Pneumothorax, non-compressible bleeding, and potential loss of airway secondary to bleeding from the carotid artery injury are not issues. Having the option to use all three sites avoids many unnecessary iatrogenic complications and increases patient safety.

Aside from the potential risks, each insertion site provides unique information for goal-directed therapy (14). For example, SC and IJ catheters provide central venous pressure monitoring for proper fluid management in septic shock, whereas FEM catheters provide intra-abdominal pressure monitoring (15) for timely surgical decompression to prevent shock and multiple-organ failure in trauma situations. Thus, when selected appropriately, each insertion site provides unique and useful information at the bedside.

The goal of the study was to compare the risk of CVC infection at the three commonly used insertion sites. We show that in a well-functioning intensive care unit (ICU), all three insertion sites are safe to use with regard to infection when optimal insertion sites are selected, experienced operators insert the catheters, strict sterile technique is present, and trained ICU nursing staff perform catheter care.

## MATERIALS AND METHODS

**Study.** This is an epidemiologic, prospective, observational study approved by the institutional review board. Data were collected continuously over 21 months in the institution's 30 general medical/surgical ICU beds served by a unified critical care medicine (CCM) division. Triple lumen, nonantibiotic impregnated catheters (Arrow model) were used.

Formal consent was not required for CVC insertion by ICU policy. We did not obtain consent for the study because the study was observational. The institutional review board approved our consent policy.

Only catheters in the ICU were studied. Comparing catheter infection rates among catheters in non-ICU areas with catheters in ICU areas adds a serious confounding factor in

the study because the reported incidence of CVC infection is higher in non-ICU areas (16).

**Institution.** Montefiore Medical Center is the university teaching hospital for the Albert Einstein College of Medicine, a tertiary care facility, in Bronx, New York.

**Setting.** The ICU beds were staffed by experienced physicians on site 24 hrs per day. The nursing staff was an experienced group dedicated to the ICU.

**Patients.** Patients were triaged from general wards, the emergency department, the operating room, and the recovery room. CCM fellows evaluated patients for admission and discharge based on criteria set by the Society of Critical Care Medicine (17, 18).

**Selection of Insertion Sites.** Catheters were inserted at optimal sites. The optimal site was determined by the clinical situation including anatomy. The insertion site selections were made by CCM attendings and fellows. The operators were proficient in accessing all three sites. The study did not dictate selection of insertion site.

**Operators.** The operators were senior physicians. The CCM fellows were board eligible or certified subspecialists in pulmonary disease; a few were board eligible or certified internists. The institution had on-site CCM attendings and fellows 17 and 24 hrs per day, respectively. During a given 24 hrs, multiple CCM attendings and fellows rounded on the same patient.

**Insertion Technique.** All CVCs were inserted using strict sterile precautions consistent with Healthcare Infection Control Practices Advisory Committee guidelines. The patient's skin was cleaned with 2% iodine tincture applicator sticks containing a saturating solution of 47% alcohol and 2% iodine. Sterile drapes were placed over the insertion site. Operators wore sterile surgical gowns, sterile gloves, and masks (19). Iodine ointment was placed at the insertion site (not part of HICPAC guidelines). Transparent dressing was used to maximally visualize the insertion site.

**Catheter Care.** Standardized CVC care was achieved by a highly trained ICU nursing staff proficient in all aspects of CVC care. All insertion sites were maximally visualized for potential dressing contamination (including the FEM site). Every 3 days or earlier if clinically indicated, the nursing staff changed the dressing, cleaned the skin site and the catheter hub with iodine solution, and changed the intravenous accessory tubing. There was effective removal of urine and feces. Furthermore, the nursing staff independently enforced sterile insertion technique.

**Data Collection.** After insertion, catheters were tracked with a form containing the patient's diagnosis, operator's name, site chosen and reason why, date placed and removed, date of ICU discharge or death, mechanical ventilation, arterial catheters, parenteral nutrition, vasopressor support, and daily clinical assessment (e.g., induration, discharge, erythema, and tenderness) of possible catheter infection.

The operator inserting the catheter entered the data; study personnel monitored data collection three to four times per week.

**Indications for Catheter Removal.** CVCs were removed when there was a suspicion of infection, when the catheter was no longer required, and after 14 days at all three sites. Fourteen days duration is an institutional policy to avoid catheter infection from excess catheter duration (11, 12, 20, 21); the duration is based on the incidence of CVC infection from the institution's infection control program. Occasionally, CVCs remained >14 days if the risk of obtaining new venous access was higher than leaving the current CVC in place.

**Evaluation of CVC Infection.** The definitions of catheter infection and colonization (Table 1A) are based on the Centers for Disease Control bloodstream infection guidelines and the semiquantitative culture technique by Maki et al. (22). Infectious complications were determined by both bacterial culture information and strong clinical input (23).

The clinical status of the patients was assessed multiple times daily by on-site attendings and fellows. There was strong surveillance for any new infection (Table 1B). The insertion sites were examined as a routine part of the clinical assessment. We were able to have strong clinical input and surveillance by having multiple CCM attendings and fellows evaluate patients several times daily. Potential CVC infection was considered any time an infection occurred. This technique has been shown to have a sensitivity of 92.8% and specificity of 100% (23).

Once CVC infection was suspected, the catheter was removed and a detailed infection workup was performed. The infection workup included analysis of the CVC tip by semiquantitative culture technique, peripheral blood cultures, a chest film, and urine analysis with culture and sensitivity. Other studies including hepatic sonogram and head computed tomography with lumbar puncture performed as clinically indicated. In general, since there was an abundance of experienced operators for catheter insertion, there was a low threshold to initiate catheter removal and analysis.

**Culture Techniques.** Blood cultures were grown in Becton Dickinson Bactec (BD Biosciences, San Jose, CA) broth aerobic and anaerobic media. The intradermal and intravascular portion of the catheter was analyzed by the semiquantitative culture technique described by Maki et al. (22).

**End Points.** The primary end point for the study was CVC infection at the SC, IJ, and FEM sites; the secondary end point was CVC colonization. Once patients were discharged from the ICU or died, the catheter was no longer studied; the former is to avoid the addition of a confounding factor as explained previously. Mechanical complications such as pneumothorax and vascular accidents were tracked. Deep vein thrombosis was not tracked.

Table 1. Definition of infection, colonization, and contamination

A. Definitions	
1. Catheter infection	
A.	>15 CFU on catheter tip with the same bacteria and sensitivities (one different sensitivity included) in one or more blood cultures.
B.	Resolution of clinical signs and symptoms of infection, as noted by the CCM attending, in 24–48 hrs after catheter removal regardless of bacterial growth either in blood or on catheter tip.
C.	>15 CFU on catheter tip with local signs of infection regardless of blood culture bacterial growth (37).
2. Catheter colonization	
A.	Catheter tip with >15 CFU without growth in blood cultures and another source of infection found.
B.	Catheter tip with >15 CFU and bacteria in peripheral blood cultures from another source of infection.
3. Contamination: <15 CFU on catheter tip without bacterial growth in blood cultures or bacteria in blood cultures from another source of infection.	
B. Clinical signs raising suspicion for catheter infection	
1.	Temperature >38°C <sup>a</sup>
2.	Hypotension <sup>a</sup>
3.	Chills <sup>a</sup>
4.	Hypothermia (<36°C)
5.	Pulse >100
6.	Respiratory rate >20
7.	Sudden increase or decrease in white blood cell count
8.	Metabolic acidosis
9.	Respiratory alkalosis
10.	Acute renal failure
11.	Disseminated intravascular coagulation
12.	Local signs such as induration, discharge, erythema, and tenderness
13.	Multiple attempts during CVC insertion
14.	Presence of a hematoma
15.	Organism in the blood suspicious for catheter infection (e.g., <i>Staphylococcus epidermidis</i> )

CFU, colony-forming units; CCM, critical care medicine; CVC, central venous catheter.

<sup>a</sup>From the Centers for Disease Control bloodstream infection guidelines. The remaining outlined by the study.

**Data Analysis.** We analyzed the two groups of patients separately. Group 1 was the primary analysis whereas group 2 was supporting. Group 2 has the unique advantage of automatically ruling out selection bias; the patients themselves acted as the control.

**Inclusion/Exclusion Criteria.** Only newly inserted CVCs placed by the ICU fellows and attendings were studied. No catheters changed over a guide wire were studied. No patients were excluded.

In the final analysis we excluded CVCs when data were missing such that cultures could not be tracked, catheters in the contamination category, and all pulmonary artery catheters. We excluded the contaminated catheters because Maki et al. (22) did not find contaminated catheters to cause deleterious infectious outcomes; rather than clouding the definition of infectious end points, we uniformly excluded these catheters. The catheters with missing data and contaminated catheters were small in number and did not affect the study. Pulmonary artery catheters were excluded because the use of these catheters is very different from CVCs.

**Statistical Analysis.** An independent statistician did a power analysis before the study and then analyzed the final data. The study was designed such that we would have required 336 patients in each group if it were assumed that the infection rate for the SC and IJ group was

0.5% and that for the FEM group was 4.0% for 80% power for a two-tailed test with alpha = .05. These presumptive rates were based on the hospital's infection control program data for catheter infection rates. We halted the study early because the incidence of clinical infection was smaller than predicted at all three sites, especially at the FEM site. Rather than continuing the study to have a sample size large enough to achieve a statistical conclusion, we found the clinical difference among all three insertion sites to be small and not clinically important.

In group 1, the Fisher's exact test was used to determine the existence of statistical significance ( $p < .05$ ) in infection and colonization rates, whereas the chi-square test was used to determine the existence of statistical significance in catheter duration at the three insertion sites. In group 2, the Student's *t*-test was used. A power analysis was performed on group 1.

To ensure further accuracy, the analysis of the data was reviewed. A CCM attending only allowed to view the culture data and clinical comments reviewed the analysis of the data. There was 99.68% correlation by the separate evaluation and the data presented.

## RESULTS

A total of 4,735 catheter days and 831 catheters in 657 patients were analyzed.

The overall incidence of catheter infection (4.01 per 1,000 catheter days, 2.29% of catheters) and colonization (5.07 per 1,000 catheter days, 2.89% of catheters) was low. We halted the study early because, at all three sites, the rates were much lower than presumed in the preliminary analysis. In fact, the rates were so much lower than predicted that we found all three sites safe with regard to risk of infection.

In group 1, the incidence of infection was SC: 0.881 infections per 1,000 catheter days (0.45%), IJ: 0 per 1,000 (0%), and FEM: 2.98 per 1,000 (1.44%;  $p = .2635$ ). The incidence of colonization was SC: 0.881 colonization per 1,000 catheter days (0.45%), IJ: 2.00 per 1,000 (1.05%), and FEM: 5.96 per 1,000 (2.88%;  $p = .1338$ ) (Table 2). There was no statistically significant difference in the incidence of infection and colonization or of duration of catheters ( $p = .8907$ ) among the insertion sites. A power analysis found that given the difference in infection rates among the three catheter sites and the sample size, we would have needed a difference of 5.1% between the sites to achieve a  $p = .05$ .

Group 2 also had no statistically significant difference in the incidence of infection and colonization (Table 3) among the insertion sites. Group 2 analysis supports that there is no selection bias; patients themselves acted as controls. The duration of catheters was not significant between sites except for a small subgroup (SC and IJ catheter group,  $p = .03$ ).

We excluded 838 catheter days and 122 catheters. Missing data accounted for 6 days and 2 catheters (SC group). The contamination category accounted for 205 days and 21 catheters: SC, 45 days ( $n = 4$  catheters); IJ, 127 days ( $n = 13$ ); and FEM, 33 days ( $n = 4$ ). The missing data and contamination category were small; the exclusion of these groups did not change the final outcome. The pulmonary artery catheter category accounted for 627 catheter days and 99 catheters: SC, 282 days ( $n = 45$  catheters); IJ, 281 days ( $n = 43$ ); and FEM, 64 days ( $n = 11$ ). Eighty catheters were further excluded in patients with more than one catheter because catheters were placed subsequently at the same anatomical location on the opposite side (SC,  $n = 38$  catheters; IJ,  $n = 16$ ; FEM,  $n = 26$ ); in such cases, the first catheter inserted was analyzed.

The three insertion sites had equally distributed demographics for diagnoses (including medical and surgical) and se-

Table 2. Group 1: Patients with one catheter: Infection, colonization, and duration of catheter

	Subclavian (n = 221)	Internal Jugular (n = 191)	Femoral (n = 139)	<i>p</i>
Infection				
%	0.45	0	1.44	.2635 NS (Fisher's exact)
Per 1,000 catheter days	0.88	0	2.98	
Colonization				
%	0.45	1.05	2.88	.1338 NS
Per 1,000 catheter days	0.88	2.00	5.96	
Line days	1134	998	671	.8907 NS (chi-square)
Mean	5.13	5.22	4.83	
SD	3.70	3.71	2.95	
Median	4	4	4	
Range	1–19	1–19	1–16	

n, number of catheters; NS, not significant.

Table 3. Group 2: Patients with multiple catheters: Infection, colonization, and duration of catheter

	Subclavian	Internal Jugular	Femoral	<i>p</i>
Patients with three catheters (n = 8)				
Infections	0	25.00	13.88	.3927 NS
Colonization	0	0	45.83	.1361 NS
Line days	11.37	7.37	5.87	.1397 NS
Patients with two catheters				
IJ/FEM (n = 24)				
Infections	—	22.22	0	.50 NS
Colonization	—	47.85	8.33	.0625 NS
Line days	—	5.41	6.54	.0987 NS
SC/FEM (n = 22)				
Infections	0	—	0	NS
Colonization	0	—	0	NS
Line days	6.86	—	5.45	.2033 NS
SC/IJ (n = 42)				
Infections	5.38	12.54	—	.5625 NS
Colonization	16.70	4.54	—	.6250 NS
Line days	8.30	7.1	—	.0290

SC, subclavian; IJ, internal jugular; FEM, femoral; n, number of catheters; NS, not significant. Values are infection and colonization events per 1,000 catheter days.

verity of illness (as defined by level of illness, requirement for mechanical ventilation, arterial catheters, and vasopressor support; Tables 4 and 5). The only difference found was that FEM catheters were more often placed in less ideal situations—uncooperative patients (agitation), failed attempt at another site, or when the risk of pneumothorax and bleeding was high (Table 6). Even here, the senior operators used the same sterile protocol for insertion. Although parenteral nutrition use was not equally distributed, the incidence of infection did not reflect parenteral nutrition use (Table 5).

Organisms involved with catheter infection/colonization (Table 7) have no particular predisposition per site. Most organisms were consistent from having originated from the skin.

Mechanical complications recorded during the study included six pneumothoraxes and one SC vein laceration.

## DISCUSSION

All three insertion sites have the same risk of catheter infection in the setting of optimal site selection, catheter insertion by senior operators, strict sterile insertion technique, and standardized continuous catheter care by trained ICU nurses. There was not a statistically significant or, more important, clinically significant difference in the incidence of catheter infection/colonization with respect to insertion site in this setting. The actual inherent risk of infection with respect to insertion site is greatly overstated.

Although we can say that all three insertion sites are safe with regard to risk of infection, we do not state that statistically all three sites have the same risk of infection; our sample size, although larger than any previous study, was not large enough to justify this conclusion. Regardless, given the overall low infec-

tion rates, any actual biological difference would not have been substantially higher than 1%. Proving or disproving such a small statistical difference is not clinically important. With regard to patient safety, having the option to use all three insertion sites and avoiding devastating mechanical complications is far more important than a small theoretically increased risk of infection. The conclusion of our data is that all three insertion sites are safe with regard to risk of infection.

We combined strong clinical input with culture data to diagnose infectious complications. This method is shown to have a sensitivity of 92.8% and a specificity of 100% (23). With our method, the threshold to diagnose infectious complications was very low; infection was diagnosed regardless of the culture results if clinically appropriate. We were able to have strong clinical input by having 17 and 24 hrs of on-site CCM attending and fellow coverage, respectively, to provide surveillance. Furthermore, in a given 24 hrs, multiple CCM attendings and fellows provided input for the same patients, further increasing surveillance.

The concepts for our study are well documented in the literature. First, Eggiman et al. (24) showed a decrease in bloodstream infection from 22.9 to 6.2 episodes per 1,000 catheter days (relative risk, 0.27 [0.13–0.56]) when an institutional protocol consisting of strict sterile technique, operator training, and specifically outlined catheter care was instituted (25). Our protocol is conceptually the same.

Moreover, Bernard and colleagues (26, 27) showed that experience is inversely proportional to risk of complications. They found the incidence of mechanical (26) and infectious (27) complications to be much lower with experienced operators. In their study, the rate of mechanical complications with experienced operators (i.e., >50 catheterizations) was 0% and inexperienced operators was 8.1% (26). In the complementary study, a large difference was also found with infectious complications (experienced operators 25% vs. inexperienced operators 56%) (27). Experienced operators insert catheters proficiently and are less likely to break sterile barriers. Operators with different levels of expertise have confounded infection end points in many of the catheter infection studies thus far conducted (6). Each of our operators had performed far greater than 50 catheterizations before their involvement in this study.

Table 4. Diagnoses of patients

Total no. of patient	Subclavian		Internal Jugular		Femoral	
	n = 293	%	n = 265	%	n = 193	%
ARDS	14	4.8	11	4.2	8	4.1
Respiratory failure	52	17.7	54	20.4	31	16.1
Pneumonia	53	18.1	55	20.6	29	15.0
Emphysema	17	5.8	21	7.9	12	6.2
Asthma	3	1.0	3	1.1	7	3.6
Pulmonary embolism	4	1.4	2	0.8	3	1.5
Fat embolism	0	0	1	0.4	0	0
Upper airway obstruction	3	1.0	1	0.4	3	1.5
Sarcoidosis	2	0.7	1	0.4	3	1.5
Lung collapse	1	0.3	1	0.4	0	0
Alveolar hemorrhage	2	0.7	0	0	0	0
Mediastinitis	1	0.3	2	0.8	1	0.5
Acute chest syndrome	0	0	2	0.8	3	1.5
Bronchiectasis	1	0.3	1	0.4	0	0
Interstitial lung disease	1	0.3	0	0	0	0
Septic shock	79	27.0	71	26.8	50	25.9
HIV/AIDS	22	7.5	17	6.4	11	5.7
Gangrene	2	0.7	2	0.8	1	0.5
Meningitis	9	3.1	6	2.3	2	1.0
Fungemia	2	0.7	1	0.4	1	0.5
Peritonitis	6	2.0	10	3.8	5	2.6
Urinary tract infection	8	2.7	10	3.8	10	5.2
Acute renal failure	4	1.4	4	1.5	2	1.0
End-stage renal failure	16	5.5	10	3.8	12	6.2
Renal transplant	2	0.7	2	0.8	1	0.5
Myocardial infarction/CHF	22	7.5	18	6.8	11	5.7
Arrhythmia	5	1.7	3	1.1	1	0.5
Hypertensive crisis	13	4.4	7	2.6	7	3.6
Cerebrovascular accident	28	9.6	12	4.5	14	7.3
Seizures	12	4.1	6	2.3	3	1.5
Gastrointestinal bleeding	32	10.9	26	9.8	36	18.7
Liver failure	9	3.1	13	4.9	16	8.3
Pancreatitis	4	1.4	8	3.0	2	1.0
Necrotic bowel	9	3.1	10	3.8	5	2.6
Systemic lupus	5	1.7	2	0.8	1	0.5
CNS vasculitis	1	0.3	1	0.4	2	1.0
Malignancy	19	6.5	14	5.3	15	7.8
DIC	1	0.3	3	1.1	3	1.5
Neutropenia	2	0.7	2	0.8	1	0.5
Sickle cell	2	0.7	4	1.5	5	2.6
Diabetes and ketosis	15	5.1	17	6.4	14	7.3
Endocrine/metabolic	28	9.6	15	5.7	14	7.3
Obesity	2	0.7	5	1.9	4	2.1
Overdose	16	5.5	3	1.1	4	2.1

n, number of patients; ARDS, acute respiratory distress syndrome; HIV, human immunodeficiency syndrome; AIDS, acquired immune deficiency syndrome; CHF, congestive heart failure; CNS, central nervous system; DIC, disseminated intravascular coagulation.

Thus, it is not surprising that our infectious and mechanical complication rates are much lower than those of Bernard and colleagues' experienced group (26, 27).

The risk of infection with FEM catheters remains controversial (6–10, 28, 29). Thus far, Merrer and colleagues (6) have published the most definitive study. They

reported a significantly higher rate of infection with FEM compared with SC catheters (19.8% vs. 4.5%,  $p < .001$ ). At first glance, our study appears to contradict Merrer et al.'s (6). However, when both studies are analyzed, our study is on a continuum with Merrer et al.'s. First, the definitions used for catheter infection are different. Merrer and colleagues (6)

**C**linically, the incidence of catheter infection is low and not different at the subclavian, internal jugular, and femoral sites in an optimum intensive care unit setting.

included both minor and major catheter infections. We excluded "minor infections" because there was no deleterious clinical end point. When they compared only major catheter infections (which have the same deleterious clinical end points as our definitions of CVC infection), the difference was not statistically insignificant (FEM 4.4% vs. SC 1.5%,  $p = .07$ ). Thus, both studies have the most important conclusion in common; the risk of major catheter infection is not statistically different among the insertion sites.

There are several important discussion points when comparing the two studies. To begin, although the rates of major infections were not statistically different among SC and FEM sites in Merrer et al.'s (6) study, overall, the absolute rates were much higher compared with our study. This difference is a result from their initial hypothesis and methods. In the initial power analysis, they assumed much higher rates of infection (SC 7.5% and FEM 20%). Based on our traditionally low infection rates, we assumed much lower rates. Crucially, in their study, junior operators placed more FEM catheters than SC catheters. We uniformly had senior operators. As discussed earlier (25), this is fact alone likely accounts for Merrer and colleagues' (6) higher infection rate at the FEM site. Other important differences include that their study was multiple-centered (four university-affiliated and four general hospitals) with different protocols for reporting data. Ours was a single-center study with one division and the same protocol for reporting data. Also, they performed a randomized study to prove the inherent risk of infection between two insertion sites. In contrast, we performed an epide-

miologic study and compared the actual infection rates at all three insertion sites in an optimum ICU setting. Finally, they compared two insertion sites whereas we compared three. On careful analysis, the conclusions between the studies are not contradictory. Our study added other dimensions on the issue of catheter infections and removed many of the confound-

ing factors clouding previous catheter infection studies. We now show, in an optimum ICU setting, that the actual clinical difference in risk of infection among CVC insertion sites is so small that there is no biological significance.

We identified several potential flaws in our study design and methods. The most important is that our study was epidemi-

ologic rather than randomized. However, there is no evidence of selection bias among the catheter groups. The sample size was large enough in the three catheter groups such that the demographics including critical illness and diagnoses were equally proportioned (Tables 4 and 5). No patients were excluded. Most important, the analysis from group 2 convincingly shows there was no selection bias with regard to severity of illness and diagnoses. Here, insertion sites were compared in the same patient; severity of illness and diagnoses cannot be different. The patient in essence acted as the control.

We decided to perform an epidemiologic study rather than a randomized study for ethical reasons and clinical applicability. Randomly choosing insertion sites for individual patients increases the risk of devastating mechanical complications. Such a study cannot be performed because of patient safety. Furthermore, the conclusions from randomized CVC studies are difficult to apply in daily ICU practice. For example, analyzing data from a randomized study where SC catheters are placed in patients with a sternal chest wound and an open chest, vs. FEM catheters placed in patients with a lower extremity infection, vs. any catheter placed in ambulatory patients is clinically not meaningful in daily ICU practice. Thus, we constructed an epidemiologic study to answer meaningfully the risk of CVC infection in daily ICU practice. In our methodology, no comparison is made of suboptimal insertion sites as described previously.

Catheter duration is a risk factor for infection (11, 12, 20, 21, 30). Catheter duration did not bias our data because statistically all three sites had the same catheter duration—except for one small

Table 5. Severity of illness

	Subclavian	Internal Jugular	Femoral
Age, mean (range)	62.87 (19–98)	64.68 (22–94)	60.2 (21–98)
Gender, % (n)			
Male	42.32 (124)	43.40 (115)	49.22 (95)
Female	57.68 (169)	56.60 (150)	50.78 (98)
Level of illness, % (n) <sup>a</sup>			
1	75.09 (220)	70.20 (186)	79.95 (135)
2	24.57 (72)	29.05 (77)	29.53 (57)
3	0.34 (1)	0.75 (2)	0.52 (1)
Ventilator support requirement, % (n)	66.55 (195)	60.00 (159)	61.66 (119)
Invasive blood pressure monitoring, % (n)	60.07 (176)	53.58 (142)	61.14 (118)
Vasopressor support requirement, % (n)	27.65 (81)	25.28 (67)	31.09 (60)
TPN, % (n)	10.92 (32)	6.79 (18)	3.11 (6)
Death (only in ICU), % (n)	12.63 (37)	10.57 (28)	12.95 (25)

TPN, total parenteral nutrition; ICU, intensive care unit.

<sup>a</sup>Level 1: critically ill patient with active ICU intervention. Example: Septic shock requiring mechanical ventilation and vasopressor support. Level 2: Patient requiring observational type care. Example: Patient requiring chronic mechanical ventilation awaiting tracheostomy. Level 3: Patient awaiting general hospital floor bed.

Table 6. Reason for selection of insertion site in individual patients

	SC (n = 293)	IJ (n = 265)	FEM (n = 193)
Operator preference	81.57 (239)	77.74 (206)	30.57 (59)
Risk of bleeding	0.34 (1)	4.91 (13)	17.6 (34)
Risk of pneumothorax	0.68 (2)	4.91 (13)	8.29 (16)
Only site available	5.46 (16)	4.15 (11)	9.32 (18)
Agitation	0 (0)	0.38 (1)	3.11 (6)
Emergent	20.5 (6)	0	19.69 (38)
Failed attempt at other site	5.12 (15)	4.15 (11)	7.25 (14)
Tenuous airway	0	0	0.52 (1)

n, number of patients; SC, subclavian; IJ, internal jugular; FEM, femoral. All values are % (n).

Table 7. Bacteria from infections and colonization

	Subclavian	Internal Jugular	Femoral
Infections			
Clinical infection	1	3	1
Blood cultures	<i>Staphylococcus aureus</i> (3) <i>Pseudomonas aeruginosa</i> <i>Enterococcus</i> <i>S. epidermidis</i>	<i>Staphylococcus epidermidis</i> <i>S. aureus</i> (2) <i>Staphylococcus</i> coagulase negative <i>A. calcoaceticus</i>	<i>Acinetobacter calcoaceticus</i> <i>Candida albicans</i> <i>S. epidermidis</i>
Colonization	<i>Enterococcus</i> (2) <i>A. calcoaceticus</i> (2) <i>S. aureus</i>	<i>Staphylococcus</i> coagulase negative (2) <i>Citrobacter koseri</i> <i>Enterococcus</i> <i>C. albicans</i> <i>P. aeruginosa</i> <i>S. epidermidis</i>	<i>A. calcoaceticus</i> <i>S. aureus</i> (3) <i>S. coagulase negative</i> (2) <i>S. epidermidis</i> (4) <i>P. aeruginosa</i> <i>C. albicans</i> (3)

n, number of infection and colonization events.

subgroup. Now that antimicrobial (21, 31) and antiseptic (32) impregnated catheters are shown to significantly decrease catheter infection and colonization, catheter duration can increase with further minimizing of the risk of infection.

Although we did not specifically track antibiotic use, our study design avoids antibiotics confounding the data. Since catheter infection is "cured" only with removal or a prolonged course of intravenous antibiotics, the relatively short courses of antibiotics used for ICU infections could not truly affect the catheter infection end point. However, antibiotic use can result in negative culture results even in the presence of catheter infection. Using strong clinical input with culture data ensures not missing catheter infection. With our method, if clinical infection resolved upon catheter removal, the end point was concluded as infection regardless of culture results. One example was an obvious case of an IJ infection. Although pus was found on the catheter and sepsis was resolved upon catheter removal, the peripheral and catheter tip cultures were negative because of broad-spectrum antibiotic coverage. If only culture data were used to determine catheter infection, this IJ infection would be missed. Our design avoids antibiotics clouding infectious end points. Furthermore, infectious disease diagnoses were equally proportioned in the three catheter groups.

Another potential bias is that a few study personnel were inserting catheters. However, all operators used the same sterile protocol for catheter insertion; the nurses who were not involved in the study independently enforced this protocol. Also, multiple attendings and fellows were involved with patient care in a given 24-hr period. Thus, given the infrastructure of patient care, the involvement of any personnel cannot affect end points.

Finally, although we did not prove or disprove a statistically significant difference in infection rates among the insertion sites, if such a biological difference exists, it is on the order of 1%. We did not find proving such a statistical fact clinically important. Furthermore, even with our statistically small sample size, a significantly larger difference in rates is required (5.1%) to achieve  $p = .05$ . Also to note, our study thus far has the largest sample size of all CVC studies conducted.

The FEM site does not have a significantly higher risk of infection in an ICU population when properly used. The

somewhat higher infection and colonization rates at the FEM site are likely due to greater frequency of FEM catheters placed in suboptimal situations (Table 6); however, to emphasize again, the difference in rates was not statistically significant among the sites. We certainly do not recommend the wide use of FEM catheters outside ICU settings. Without proper removal of urine and feces, we intuitively expect that FEM catheters will have a higher risk of infection.

SC and IJ catheter require less intense care compared to FEM catheters and are safer in general wards and less monitored settings. SC catheters are shown to have the least risk of infection (6, 12). IJ catheters are reported to have high rates of bacterial contamination (11, 12, 13). The latter finding stems from difficulty in dressing care.

## CONCLUSION

Clinically, the incidence of catheter infection is low and not different at the SC, IJ, and FEM sites in an optimum ICU setting. If there is an inherent risk of any catheter infection at a particular insertion site, it is biologically not significant. We conclude that all three sites can be used safely with respect to infection when optimum insertion sites are selected, experienced operators insert the catheters, strict sterile insertion technique is used and enforced, and standardized continuous catheter care is provided by dedicated ICU nurses.

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## REFERENCES

1. Pittet D, Wenzel RP: Nosocomial bloodstream infections. Secular trends in rates, mortality, and contribution to total hospital

deaths. *Arch Intern Med* 1995; 155: 1177-1184

2. Bryan CS, Hornung CA, Reynolds KL, et al: Endemic bacteremia in Columbia, South Carolina. *Am J Epidemiol* 1986; 123:113-127
3. Mermel LA: Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000; 132:391-402
4. Saint S, Savel R, Matthay M: Enhancing the safety of critically ill patients by reducing urinary and central venous catheter-related infections. *Am J Respir Crit Med* 2002; 165: 1475-1479
5. Rello J, Ochagavia A, Sabanes E, et al: Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med* 2000; 162: 1027-1030
6. Merrer J, De Jonghe B, Golliot F, et al: Complications of femoral and subclavian venous catheterization in critically ill patients. *JAMA* 2001; 286:700-707
7. Still JM, Law E, Thiruvaiyaru D, et al: Central line-related sepsis in acute burn patients. *Am Surg* 1998; 64:165-170
8. Stenzel JP, Green TP, Fuhrman BP, et al: Percutaneous femoral venous catheterizations: A prospective study of complications. *J Pediatr* 1989; 114:411-415
9. Montagnac R, Bernard C, Guillaumie J, et al: Indwelling silicone femoral catheters: Experience of three haemodialysis centres. *Nephrol Dial Transplant* 1997; 12:772-775
10. Lazarus HM, Creger RJ, Bloom AD, et al: Percutaneous placement of femoral central venous catheter in patients undergoing transplantation of bone marrow. *Surg Gynecol Obstet* 1990; 170:403-406
11. Richet H, Hubert B, Nitemberg G, et al: Prospective multicenter study of vascular-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. *J Clin Microbiol* 1990; 28:2520-2525
12. Norwood S, Wilkins HE, Vallina VL, et al: The safety of prolonging the use of central venous catheters: A prospective analysis of the effects of using antiseptic-bonded catheters with daily site care. *Crit Care Med* 2000; 28:1376-1382
13. Charalambous C, Swoboda SM, Dick J, et al: Risk factors and clinical impact of central line infections in the surgical intensive care unit. *Arch Surg* 1998; 133:1241-1246
14. Rivers E, Nguyen B, Havstad M, et al: Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368-1377
15. Gudmundsson FF, Viste A, Gislason H, et al: Comparison of different methods for measuring intra-abdominal pressure. *Intensive Care Med* 2002; 28:509-514
16. Climo M, Diekema D, Warren DK, et al: Prevalence of the use of central venous access devices within and outside of the intensive care unit: Results of a survey among hospitals in the prevention epicenter program of the Centers for Disease Control and Preven-

- tion. *Infect Control Hosp Epidemiol* 2003; 24:942–945
17. Society of Critical Care Medicine Ethics Committee: Consensus statement on triage of the critically ill patients. *JAMA* 1994; 271:1200–1203
  18. Nasraway SA, Cohen IL, Dennis RC, et al: Guidelines on admission and discharge for adult intermediate care units. American College of Critical Care Medicine and of the Society of Critical Care Medicine. *Crit Care Med* 1998; 26:607–610
  19. Raad II, Hohn DC, Gilbreath BJ, et al: Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994; 15:231–238
  20. Corona ML, Peters SG, Narr BJ, et al: Infections related to central venous catheters. *Mayo Clin Proc* 1990; 65:979–986
  21. Darouiche RO, Raad II, Heard SO, et al: A comparison of two antimicrobial-impregnated central venous catheters. *N Engl J Med* 1999; 340:1–8
  22. Maki DG, Weise CE, Sarafin HW: A semi-quantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med* 1977; 296:1305–1309
  23. Quilici N, Audibert G, Conroy MC, et al: Differential quantitative blood cultures in the diagnosis of catheter-related sepsis in intensive care units. *Clin Infect Dis* 1997; 25:1066–1070
  24. Eggimann P, Harbarth S, Constantin MN, et al: Impact of prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000; 355:1864–1868
  25. Coopersmith C, Rebmann T, Zack J, et al: Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med* 2002; 30:59–64
  26. Bernard RW, Stahl WM: Subclavian vein catheterizations: A prospective study. I. Non-infectious complications. *Ann Surg* 1971; 173:184–190
  27. Bernard RW, Stahl WM, Chase RM Jr: Subclavian vein catheterizations: A prospective study. II. Infectious complications. *Ann Surg*. 1971; 173:191–200
  28. Goetz AM, Wagener MM, Miller JM, et al: Risk of infection due to central venous catheters: Effect of site of placement and catheter type. *Infect Control Hosp Epidemiol* 1998; 19:842–845
  29. Oliver MJ, Callery SM, Thorpe KE, et al: Risk of bacteremia from temporary hemodialysis catheters by site of insertion and duration of use: A prospective study. *Kidney Int* 2000; 58:2543–2545
  30. Pawar M, Mehta Y, Kapoor P, et al: Central venous catheter-related blood stream infections: Incidence, risk factors, outcome, and associated pathogens. *J Cardiothorac Vasc Anesth* 2004; 18:304–308
  31. Hanna HA, Raad II, Hackett B, et al: Antibiotic-impregnated catheters associated with significant decrease in nosocomial and multidrug-resistant bacteremias in critically ill patients. *Chest* 2003; 124:1030–1038
  32. Maki DG, Stolz SM, Wheeler S, et al: Prevention of central venous catheter-related bloodstream infections by use of an antiseptic-impregnated catheter. A randomized, controlled trial. *Ann Intern Med* 1997; 127:257–266