



Online article and related content
current as of June 10, 2008.

Femoral vs Jugular Venous Catheterization and Risk of Nosocomial Events in Adults Requiring Acute Renal Replacement Therapy: A Randomized Controlled Trial

Jean-Jacques Parienti; Marina Thirion; Bruno Mégarbane; et al.

JAMA. 2008;299(20):2413-2422 (doi:10.1001/jama.299.20.2413)

<http://jama.ama-assn.org/cgi/content/full/299/20/2413>

Correction

[Contact me if this article is corrected.](#)

Citations

[Contact me when this article is cited.](#)

Topic collections

Obesity; Quality of Care; Patient Safety/ Medical Error; Renal Diseases; Dialysis; Infectious Diseases; Infectious Diseases, Other; Randomized Controlled Trial; Critical Care/ Intensive Care Medicine; Adult Critical Care; Public Health
[Contact me when new articles are published in these topic areas.](#)

Subscribe

<http://jama.com/subscribe>

Permissions

permissions@ama-assn.org

<http://pubs.ama-assn.org/misc/permissions.dtl>

Email Alerts

<http://jamaarchives.com/alerts>

Reprints/E-prints

reprints@ama-assn.org

Femoral vs Jugular Venous Catheterization and Risk of Nosocomial Events in Adults Requiring Acute Renal Replacement Therapy

A Randomized Controlled Trial

Jean-Jacques Parienti, MD, DTM&H

Marina Thirion, MD

Bruno Mégarbane, MD, PhD

Bertrand Souweine, MD, PhD

Abdelali Ouchikhe, MD

Andrea Polito, MD

Jean-Marie Forel, MD

Sophie Marqué, MD

Benoît Misset, MD

Norair Airapetian, MD

Claire Daurel, MD

Jean-Paul Mira, MD, PhD

Michel Ramakers, MD

Damien du Cheyron, MD, PhD

Xavier Le Coutour, MD

Cédric Daubin, MD

Pierre Charbonneau, MD

for Members of the Cathedia Study Group

FEMORAL, JUGULAR, AND SUBCLAVIAN venous catheterizations are routinely performed during critically ill patient care. These invasive procedures contribute to additional morbidity, mortality, and costs derived from the interactions between mechanical, infectious, and thrombotic complications.^{1,2} Femoral venous catheterization, which is rapid to perform, is considered an emergency procedure to gain vascular access, but which should be avoided to limit nosocomial complications.^{1,3-7} The subclavian site, although often a first choice,⁸ is less suit-

Context Based on concerns about the risk of infection, the jugular site is often preferred over the femoral site for short-term dialysis vascular access.

Objective To determine whether jugular catheterization decreases the risk of nosocomial complications compared with femoral catheterization.

Design, Setting, and Patients A concealed, randomized, multicenter, evaluator-blinded, parallel-group trial (the Cathedia Study) of 750 patients from a network of 9 tertiary care university medical centers and 3 general hospitals in France conducted between May 2004 and May 2007. The severely ill, bed-bound adults had a body mass index (BMI) of less than 45 and required a first catheter insertion for renal replacement therapy.

Intervention Patients were randomized to receive jugular or femoral vein catheterization by operators experienced in placement at both sites.

Main Outcome Measures Rates of infectious complications, defined as catheter colonization on removal (primary end point), and catheter-related bloodstream infection.

Results Patient and catheter characteristics, including duration of catheterization, were similar in both groups. More hematomas occurred in the jugular group than in the femoral group (13/366 patients [3.6%] vs 4/370 patients [1.1%], respectively; $P = .03$). The risk of catheter colonization at removal did not differ significantly between the femoral and jugular groups (incidence of 40.8 vs 35.7 per 1000 catheter-days; hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.62-1.16; $P = .31$). A prespecified subgroup analysis demonstrated significant qualitative heterogeneity by BMI (P for the interaction term $< .001$). Jugular catheterization significantly increased incidence of catheter colonization vs femoral catheterization (45.4 vs 23.7 per 1000 catheter-days; HR, 2.10; 95% CI, 1.13-3.91; $P = .017$) in the lowest tercile (BMI < 24.2), whereas jugular catheterization significantly decreased this incidence (24.5 vs 50.9 per 1000 catheter-days; HR, 0.40; 95% CI, 0.23-0.69; $P < .001$) in the highest tercile (BMI > 28.4). The rate of catheter-related bloodstream infection was similar in both groups (2.3 vs 1.5 per 1000 catheter-days, respectively; $P = .42$).

Conclusion Jugular venous catheterization access does not appear to reduce the risk of infection compared with femoral access, except among adults with a high BMI, and may have a higher risk of hematoma.

Trial Registration clinicaltrials.gov Identifier: NCT00277888

JAMA. 2008;299(20):2413-2422

www.jama.com

Author Affiliations and the Cathedia Study Group are listed at the end of this article.

Corresponding Author: Jean-Jacques Parienti, MD, DTM&H, Department of Biostatistics and Clinical Research, Côte de Nacre University Hospital Center, Ave

de la Côte de Nacre, 14033 Caen CEDEX, France (parienti-jj@chu-caen.fr).

Caring for the Critically Ill Patient Section Editor: Derek C. Angus, MD, MPH, Contributing Editor, JAMA (angusdc@upmc.edu).

able for larger catheters, such as noncuffed temporary dialysis catheters. The US Centers for Disease Control and Prevention states: "Place catheters used for hemodialysis in a jugular or femoral vein rather than a subclavian vein to avoid venous stenosis if catheter access is needed."⁸

Some studies reported a higher incidence of complications associated with femoral vs jugular catheterizations,⁹⁻¹² while other studies reported lower or similar incidences with femoral catheterizations¹³⁻¹⁶; however, all of these studies were observational. Consequently, the choice between femoral and jugular sites remains a subject of debate and is dictated by preference rather than evidence-based decision in the setting of severely ill, bed-bound patients. Most studies on acute dialysis catheters are performed in ambulatory patients with end-stage renal disease starting chronic dialysis.¹⁷ In this context, the National Foundation of Kidney Disease Outcome and Quality Initiative guideline¹⁸ suggests noncuffed, nontunneled dialysis catheter not to exceed 3 weeks for jugular and 5 days for femoral accesses, because the risk of catheter-related bloodstream infection increases after these points. Patients with chronic dialysis, however, differ in many respects from critically ill patients, raising the question of whether these recommendations can be extrapolated to critically ill patients.

Because a higher load of microorganisms cultured from the catheter tip on removal are predictive of catheter-related bloodstream infection,^{19,20} we compared the rates of catheter colonization on removal (primary end point) between internal jugular and femoral catheterization among patients in the intensive care unit (ICU) requiring renal replacement therapy (RRT). We hypothesized that using the jugular site would decrease the rate of catheter colonization on removal and, therefore, catheter-related bloodstream infection (secondary end point) compared with the femoral site catheterization. This assumption is based on the fact that catheter-tip colonization on removal and

catheter-related bloodstream infection are both highly correlated clinically and statistically ($r=0.69$, $P=.001$).²¹ Other end points included insertion complication rates and thrombotic events.

METHODS

Study Design, Setting, and Population

The Cathedia Study was a concealed, randomized, multicenter, prospective, evaluator-blinded, parallel-group trial comparing femoral and internal jugular access for RRT in critically ill patients within a network of 9 tertiary care university medical centers and 3 general hospitals in France between May 2004 and May 2007. The study was approved by the institutional review board at the Côte de Nacre University Hospital, Caen, France. Informed written consent was obtained from all participants or their proxies in cases of impaired decision-making capacity at the time of enrollment.

Eligible patients were critically ill adults (≥ 18 years) who were expected to require support with RRT. Only patients who were undergoing their first venous catheterization for acute RRT and without contraindications to attempt both jugular and femoral access were considered. Consequently, patients with coagulopathy (definition left at the operator's discretion), morbid obesity with a body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) of more than 45, local skin infection, profound volume overload that precluded Trendelenburg positioning, chronic renal failure with arteriovenous fistula, thoracic life-threatening condition, and patients with only 1 site available (femoral or jugular) were not included. Eligible operators were trained physicians with at least 50 successful catheter insertions in both sites. We chose this level of operator skill experience because it limited the risk of mechanical complications.²

Randomization

Patients fulfilling the inclusion criteria were randomized to 1 of 2 treatment groups, stratified by center and

type of RRT, before catheterization. Allocation concealment was obtained by a centralized 24-hour Internet or telephone service (EOL; MedSharing, Bondy, France), involving a dynamic semideterminist computed-generated algorithm, to ensure complete separation of the randomization process from those physicians providing care.

Catheter Insertion and Care Procedures

Insertions took place in the ICU. Surgical hand-scrubbing or hand-rubbing was performed by the operator before putting on sterile gloves.²² Operators wore sterile surgical long-sleeved gowns, caps, and mask. Skin disinfection and catheter care used the same alcohol-based povidone-iodine disinfectant, as previously described.²³ Large sterile drapes were placed over the insertion site, which was disinfected again by the operator. Physicians inserted all catheters by using the Seldinger technique. Vein puncture was achieved by using anatomical landmarks on the skin's surface. Ultrasound guidance and right-side positioning were recommended for jugular insertions, but these were left to the investigators' discretion. In cases of unsuccessful insertions, physicians were instructed to switch to the contralateral side, if possible, and then switch from one site to the other site. Catheter maintenance was performed according to local protocol and was similar between groups in each center. Catheters were not used for routine blood sampling or to administer drugs. None of the studied catheters was tunneled or antibiotic-impregnated. One center used antiseptics-impregnated catheters (ARROWg + ard Blue; Arrow International Inc, Reading, Pennsylvania). Unfractionated heparin or low-molecular-weight heparin was used for anticoagulation, when indicated. During the interdialytic period, catheters were filled with heparinized saline or saline fluids only, according to each center protocol. No alcoholic or antibiotic locks were used.

Decisions to remove catheters were made independently by the physicians in charge of each patient when the

catheters were no longer needed (renal function recovery or death) or new access was required (suspicion of catheter-related infection, catheter dysfunction, or thrombosis). Patients were followed up until death or ICU discharge.

End Points Definition

Catheter Insertion and Mechanical Complications. Time required for catheter insertion, number of skin punctures, number of failures, and occurrence of mechanical complications were recorded from insertion to removal.

Catheter-Related Infections. According to the simplified Brun-Buisson quantitative technique,²⁰ catheter colonization was defined as cultures with at least 10^3 colony-forming units (CFUs) per milliliter from the catheter tip. The microbiologist technicians in charge of the bacterial counting required to define catheter-tip colonization were blinded to the study group.

A blood sample was drawn from a peripheral vein at the time of the removal if there was any suspicion of catheter-related infection. As previously described,² catheter-related bloodstream infection was defined as catheter-tip colonization plus at least 1 peripheral blood culture yielding the same species with the same antimicrobial susceptibility as the catheter tip within 48 hours of catheter removal, with no other apparent source of sepsis. Two different peripheral blood cultures were used to define catheter-related bloodstream infection with potential skin contaminants.

Catheter-Related Thrombosis. The presence of thrombotic complications (partial or complete) of the vein was assessed systematically by ultrasonography performed within 4 days of catheter removal in 2 participating centers only, because a smaller sample size was desired to demonstrate the absolute 25% difference in deep venous thrombosis expected between the upper and lower extremity sites.²⁴ These 2 centers were able to perform an onsite permanent ultrasonography.

Power and Statistical Analysis

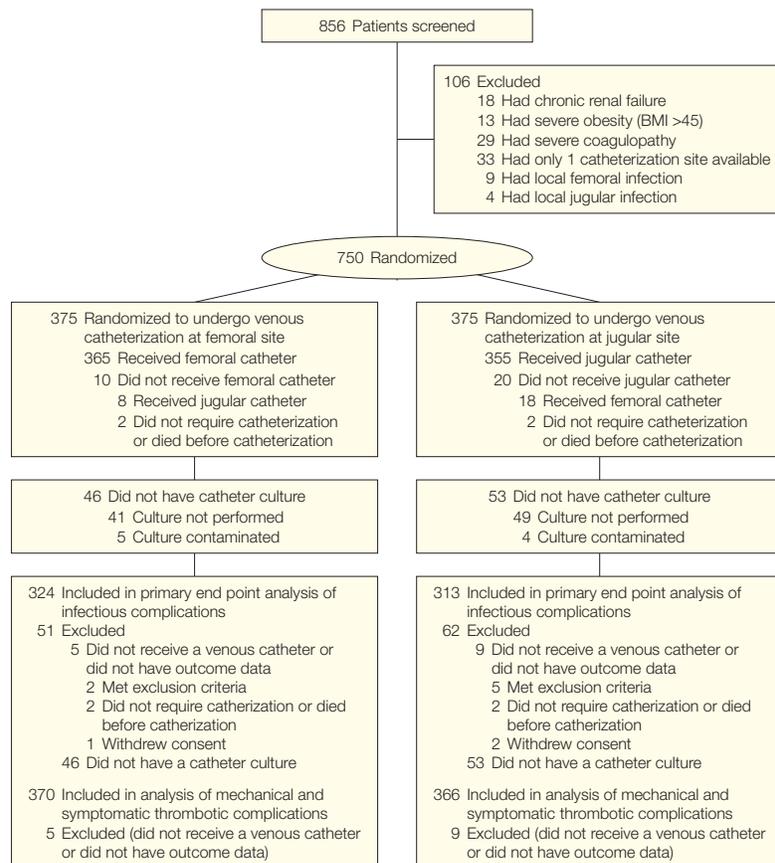
Estimation of the study sample size was based on the expected difference in the time to colonization on removal of jugular vs femoral catheters (primary end point). With 650 patients, the study had 90% power to detect a treatment difference at a 2-sided 5% significance level, if the true hazard ratio (HR) is 0.77. This is based on the assumption that the true median times to colonization on removal for the femoral and jugular sites are 14.0 and 18.2 days or more, respectively.²³ Assuming that 15% of the catheters would not be inserted, removed outside the ICU, or not sent to culture, we planned to include 750 patients.

The statistical unit was the patient because only the first inserted catheter was analyzed, in keeping with the independence of observations criteria. Pa-

tients were analyzed according to a modified intention-to-treat strategy, in which catheters with missing data for the primary end point were excluded. In addition, we complemented this analysis with a per-protocol strategy, in which patients with crossover (insertion failure to the allocated group) were analyzed in the group the catheter was inserted rather than randomized.

Rates of catheter insertion failure and mechanical complications were compared between study groups by Fisher exact tests. Comparisons of the incidences of colonization on removal, catheter-related bloodstream infections, and thrombosis per 1000 catheter-days between groups were analyzed by Poisson regression, in which the incidence was used as the numerator and the number of catheter-days for patients was used as the denominator

Figure 1. Flow Diagram of the Cathedia Trial



BMI indicates body mass index, calculated as weight in kilograms divided by height in meters squared.

to form a ratio. Exact Poisson 95% confidence intervals (CIs) were computed.

The proportions of catheters that were free of colonization on removal (primary end point) were compared between groups using time-to-event methods with log-rank tests. After checking for the proportionality assumption, we fitted a Cox proportional hazards regression model to

estimate HRs, with values of less than 1 favoring the jugular over the femoral group. Subgroups analysis for the primary end point according to the catheter insertion time (≤ 5 days vs > 5 days), BMI (cutoffs according to the population tercile), sex, and type of RRT were prespecified by the study group. The a priori hypothesis was that the effect of jugular site catheter-

ization in preventing colonization was stronger in patients with longer catheterization times^{11,18} and higher BMIs.²⁵ Interactions were assessed in a Cox proportional hazards regression model that included the group, the subgroup variable, and the interaction between group and subgroup variables. In case of significant interaction with a continuous factor and because the use of tercile is very dependent of the sample studied, we explored the relationship between the continuous variable and the occurrence of the primary end point by plotting a logistic model curve, separately for jugular and femoral catheters. We also computed multivariate Cox proportional hazard regression models including the group and adjusting for potential confounding variables significantly associated with primary end point. Overall and each subgroup adjusted HRs were similar to unadjusted HRs and thus were not reported.

All tests were 2-sided; $P < .05$ denoted statistical significance. In cases of multiple testing regarding the primary end point, Bonferroni adjustment was applied, resulting in a significance level of $P < .05$ divided by 2 ($P < .025$) or 3 ($P < .017$), depending on the number of subgroups. We used SAS version 9.1 (SAS Institute Inc, Cary, North Carolina) for statistical analysis.

RESULTS

Patient Population

FIGURE 1 shows the patient inclusion process for the Cathedia Study. Characteristics of the patients and catheters, including duration of catheterization, were similar in both groups (TABLE 1).

Mechanical Complications

Jugular catheters were more difficult to insert than femoral catheters and required longer insertion times, had more failures on 1 side, and more crossovers (Table 1). Rates of arterial puncture between jugular and femoral groups did not differ significantly (19/366 patients [5.1%] vs 13/370 pa-

Table 1. Characteristics of the Cathedia Intention-to-Treat Patients and Catheters^a

Characteristics	Femoral (n = 370)	Jugular (n = 366)
Patients		
Age, mean (SD), y	64.5 (14.9)	65.3 (14.8)
Male sex	247 (66.8)	247 (67.5)
Body mass index, mean (SD)	26.7 (6.0)	26.7 (5.8)
APACHE II score, mean (SD)	27.7 (9.6)	27.8 (9.7)
No. of organ failures, mean (SD)	2.4 (1.2)	2.5 (1.2)
Ventilated	262 (70.8)	274 (74.9)
Days from admission to inclusion, median (IQR)	1 (0-2)	1 (0-2)
Body temperature, mean (SD), °C	36.8 (2.1)	36.8 (2.2)
White blood cell count, median (IQR), cells/ μ L	12 750 (7485-19 450)	12 500 (7720-20 100)
Platelet count, median (IQR), cells/mL	163 000 (86 000-243 000)	163 000 (80 000-233 000)
Received systemic antibiotics	219 (59.2)	233 (63.7)
Received catecholamines	136 (36.8)	152 (41.5)
Immunosuppression	62 (16.8)	65 (17.8)
Diabetes	97 (26.2)	95 (26.0)
Primary bacteremia	70 (18.9)	80 (21.8)
Catheter insertion		
Antiseptic-impregnated catheter	79 (21.4)	82 (22.4)
Ultrasound-guided insertion	0	7 (1.9)
No. of attempts, median (IQR)	1 (1-2)	1 (1-2)
Time required for insertion, min		
Mean (SD)	13.3 (9.7)	15.0 (12.7)
Median (IQR)	10 (8-15)	11 (8-20)
First attempt of the right side	211 (57.0)	258 (70.5)
Failure on 1 side	18 (4.9) ^b	34 (9.3) ^b
Crossover	8 (2.2) ^b	18 (4.9) ^b
Catheter follow-up		
Days of insertion		
Mean (SD)	6.2 (5.5)	6.9 (7.5)
Median (IQR)	5 (2-9)	5 (2-9)
Reason for catheter ablation		
No more required	144 (38.9)	125 (34.2)
Catheter dysfunction	36 (9.7)	38 (10.4)
Suspicion of catheter infection	34 (9.2)	45 (12.3)
Systematic	31 (8.4)	21 (5.7)
Death	98 (26.5)	109 (29.8)
Spontaneous catheter withdrawal	5 (1.4)	4 (1.1)
Unknown or not inserted	22 (5.9)	24 (6.6)

Abbreviations: APACHE II score, Acute Physiology and Chronic Health Evaluation II score, where higher values imply a more severe disease and a higher risk of death (range, 0-71 points); IQR, interquartile range.

^aData are presented as No. (%) unless otherwise specified. Body mass index was calculated as weight in kilograms divided by height in meters squared.

^b $P = .02$ for failure on 1 side, and $P = .05$ for crossover.

tients [3.6%], respectively), although the rate of hematoma formation was significantly higher for the jugular group (13/366 patients [3.6%]) compared with the femoral group (4/370 patients [1.1%]; $P=.03$).

In the jugular group, 2 patients had severe respiratory distress due to compressive hematoma and required intubation. Another patient in the jugular group, admitted for cardiogenic shock following cardiac arrest, experienced catheter insertion in the carotid artery and required vascular surgery for removal. One patient in the femoral group, admitted for septic shock, had arterial occlusion with acute leg ischemia and required amputation. Surgical examination revealed an arteriovenous fistula related to catheter insertion in the femoral vein, which occluded the femoral artery. None of these 4 patients had ultrasound guidance for catheter insertion.

Infectious Complications

The results of catheter-related infections are shown in TABLE 2. The rate of randomized participants with missing data and not included in this analysis did not differ significantly between jugular and femoral groups (62/375 patients [16.5%] vs 51/375 patients [13.6%]; $P=.31$). FIGURE 2 shows a Kaplan-Meier curve of overall catheters free of colonization on removal. Colonization occurred in 84 of 324 patients (25.9%) with femoral catheters (incidence of 40.8 per 1000 catheter-days) and in 78 of 313 patients (24.9%) with jugular catheters (incidence of 35.7 per 1000 catheter-days). The corresponding HRs were 0.85 (95% CI, 0.62-1.16; $P=.31$) in the modified intention-to-treat analysis and 0.83 (95% CI, 0.61-1.13; $P=.24$) in the per-protocol analysis.

In cases of colonization (Table 2), significantly more Gram-positive bacteria were found in the jugular site ($P=.04$) and significantly more Gram-negative bacteria ($P=.03$) were found in the femoral site. The mean (standard deviation) load of microorgan-

Table 2. Microorganisms Recovered From Colonized Catheters and Bloodstream Infections

	Femoral (n = 324)	Jugular (n = 313)	P Value ^a
No. of catheter colonizations	84	78	.79
Incidence per 1000 catheter-days (95% CI)	40.8 (29.3-55.4)	35.7 (25.0-49.5)	.54 ^b
Log ₁₀ CFU per mL, mean (95% CI)	3.77 (3.58-3.96)	3.59 (3.38-3.80)	.20 ^c
No. of microorganisms			
Gram-positive	41	51	.04
<i>Staphylococcus epidermidis</i>	28	43	.007
<i>Staphylococcus aureus</i>	5	5	>.99
<i>Enterococcus</i> species	4	2	.69
Other	4	1	.37
Gram-negative	30	15	.03
<i>Escherichia coli</i>	10	1	.01
<i>Proteus</i> species	5	0	.06
<i>Pseudomonas aeruginosa</i>	7	6	>.99
<i>Enterobacter</i> species	5	3	.73
Other	3	5	.49
Fungi	11	5	.20
Polymicrobial	2	8	.06
No. of catheter-related bloodstream infections	3	5	.50
Incidence per 1000 catheter-days (95% CI)	1.5 (0.1-6.4)	2.3 (0.3-7.7)	.42 ^b
No. of microorganisms			
<i>Staphylococcus epidermidis</i>	2	2	>.99
<i>Staphylococcus aureus</i>	1	3	.36

Abbreviations: CFU, colony-forming unit; CI, confidence interval.

^aAll P values are derived from Fisher exact χ^2 test unless otherwise specified.

^bBy Poisson regression.

^cBy t test.

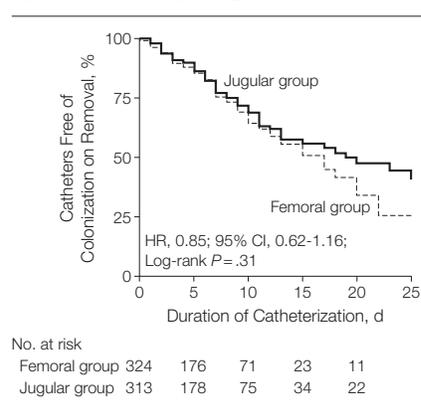
isms cultured from the catheter tip did not differ significantly between jugular and femoral catheter-tip culture (3.59 [0.93] vs 3.77 [0.90] for log₁₀ CFU/mL; $P=.20$ by t test).

Catheter-related bloodstream infection occurred in 3 of 324 patients (0.9%) with femoral catheters (incidence per 1000 catheter-days, 1.5; 95% CI, 0.1-6.4) and in 5 of 313 patients (1.6%) with jugular catheters (incidence per 1000 catheter-days, 2.3; 95% CI, 0.3-7.7). This difference was not significant by Poisson regression ($P=.42$).

Thrombotic Complications

Overall, 2 of 370 patients (0.5%) in the femoral group and 2 of 366 patients (0.5%) in the jugular group had symptomatic deep venous thrombosis. In 2 participating centers, systematic ultrasound evaluation of thrombotic events was performed. The mean duration of catheterization with ultrasound evaluation was 6.2 days (95% CI, 5.3-7.1) and 7.3 days (95% CI, 6.2-8.4) in the

Figure 2. Overall Kaplan-Meier Curve of Time to Catheter Colonization on Removal



HR indicates hazard ratio; CI, confidence interval. Colonization occurred in 84 of 324 patients (25.9%) with femoral catheters and in 78 of 313 patients (24.9%) with jugular catheters.

femoral and jugular groups, respectively ($P=.15$). Rates of thrombosis were found in 8 of 76 patients (10.5%) in the femoral site vs 17 of 75 patients (22.7%) in the jugular site. This difference was

Table 3. Subgroup Analyses of Time to Catheter Colonization on Removal^a

	Incidence per 1000 Catheter-Days (95% CI) ^b		Hazard Ratio (95% CI)	P Value
	Femoral	Jugular		
Overall	40.8 (29.3-55.4)	35.7 (25.0-49.5)	0.85 (0.62-1.16)	.31
Sex				
Male	37.8 (26.7-51.9)	32.2 (22.1-45.4)	0.75 (0.45-1.25)	.54
Female	40.7 (29.2-55.3)	39.0 (27.7-53.3)	0.98 (0.58-1.66)	
Body mass index				
Lowest tertile (<24.2)	23.7 (15.1-35.4)	45.4 (33.2-60.7)	2.10 (1.13-3.91)	<.001
Middle tertile (24.2-28.4)	43.0 (26.5-51.6)	37.5 (31.1-57.9)	0.94 (0.54-1.62)	
Highest tertile (>28.4)	50.9 (37.9-66.9)	24.5 (15.8-36.3)	0.40 (0.23-0.69)	
Catheter duration, d				
≤5	79.8 (63.3-99.3)	78.8 (62.4-98.2)	0.99 (0.62-1.58)	.52
>5	27.3 (18.0-39.6)	24.1 (15.5-35.8)	0.80 (0.53-1.22)	
Initial renal replacement therapy				
Intermittent	46.7 (34.3-62.2)	38.3 (27.1-52.5)	0.80 (0.55-1.16)	.41
Continuous	25.9 (16.9-38.8)	28.2 (18.8-40.7)	1.05 (0.58-1.87)	

Abbreviation: CI, confidence interval.

^aHazard ratio of less than 1 favors the jugular group. Body mass index was calculated as weight in kilograms divided by height in meters squared.^bExact Poisson confidence limits.

not significant by Poisson regression ($P = .16$).

Subgroup Analysis

The results of the predefined subgroup analyses are shown in TABLE 3. A significant interaction ($P < .001$) was found for the effect of BMI on the relationship between catheter site and colonization-free catheter on removal survival, suggesting risk stratification. Patients with a lower BMI had a higher incidence of colonization in the jugular vs femoral group (45.4 vs 23.7 per 1000 catheter-days, respectively), and those patients with a higher BMI had a significantly lower incidence of colonization in the jugular vs femoral group (24.5 vs 50.9 per 1000 catheter-days, respectively). The corresponding Kaplan-Meier curves are shown in FIGURE 3. The effect of BMI on the a priori (ie, when the catheter is inserted) probability of catheter colonization on removal is shown in FIGURE 4.

COMMENT

In this large, multicenter randomized trial, we did not detect any clinically relevant benefit of the jugular site catheterization compared with femoral site catheterization for reducing the risk of nosocomial complications in critically

ill adults requiring venous access for acute RRT. This result is inconsistent with the widely accepted convention to avoid femoral catheterization to prevent the risk of catheter-related infection. Interestingly, in the subgroup analysis, there was qualitative heterogeneity of the effect of insertion site on the risk of catheter colonization on removal according to BMI. This probability regularly increased with the BMI for the femoral group, but not for the jugular group.

To our knowledge, our study is one of the largest randomized trials of the prevention of catheter complications in adult patients in the ICU. Consequently, we consider that the absence of an overall statistical effect in our population precludes any clinically important effect size.

Random allocation avoided channeling bias commonly associated with observational studies. Patient factors or therapeutic interventions that could increase or decrease the risk of catheter colonization were prospectively monitored and were similar between groups.

Assessment of the catheter-tip colonization on removal was evaluator-blinded and objective. Catheter colonization, however, is a dynamic process

and it is unlikely to occur exactly at the time of removal. A bias would occur if the delay between intravascular colonization and colonization on catheter removal differed between jugular and femoral groups. In this case, it is likely that one catheter group would have been more heavily colonized than the other and consequently more prone to lead to bacteremia, which is not what we observed.

Our study involved severely ill, bed-bound patients who required RRT with poor outcomes and high-illness acuity.²⁶ Consequently, our primary end point results may not be applicable to ambulatory patients with end-stage renal disease admitted to hemodialysis units. In addition, data concerning infectious complications of hemodialysis catheters may not necessarily be applied to catheters used to administer drugs. Conversely, the epidemiological characteristics of colonization were similar between temporary catheters used for hemodialysis and those used for drug administration in the intensive care setting.²⁷⁻²⁹ In addition, patients with acute renal failure represent a subset of critical patients with higher risk of nosocomial bacteremia.³⁰ Consequently, we believe the findings can be extended to the larger population of critically ill patients in general.

The catheter duration observed in our study are consistent with those results reported in other randomized studies that demonstrated significant reductions in catheter colonization^{31,32} and with those results of other studies that investigated temporary dialysis catheters.^{28,29} However, our incidence of colonization is higher than previously reported.^{28,29} Several factors inherent to the study population or study design may explain these discrepancies. For example, Harb et al²⁸ reported a low colonization incidence of 5.4 per 1000 catheter-days for the 79 dialysis catheters inserted in 47 critically ill patients with cancer. A total of 82% were inserted at the femoral site. Although not reported, it is likely that this population had a very low BMI, which would correspond to a low risk

of femoral colonization (Figure 4). Souweine et al²⁹ excluded dialysis catheters inserted for less than 48 hours, while we found a high incidence of colonization among catheters inserted for 5 days or less (Table 3), in accordance with 1 prospective study of catheter replacement every 5 days in consecutive patients in the ICU who were treated by hemodiafiltration.³³ In addition, the incidence of catheters colo-

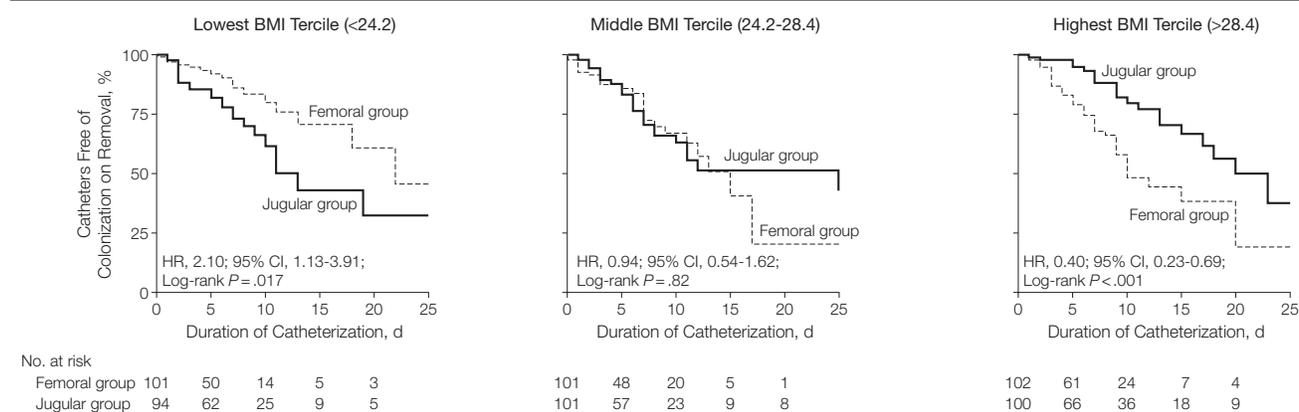
nized from consecutive patients included by this center²⁹ in our study was homogeneous with other centers.

The predominance of Gram-negative bacteria and fungi cultured from femoral catheters was also described for catheter-related bloodstream infection,³⁴ confirming the extraluminal pathogenesis of short-term, catheter-related infection³⁵ and the validity of using colonization as a

surrogate for catheter-related bloodstream infection.²¹

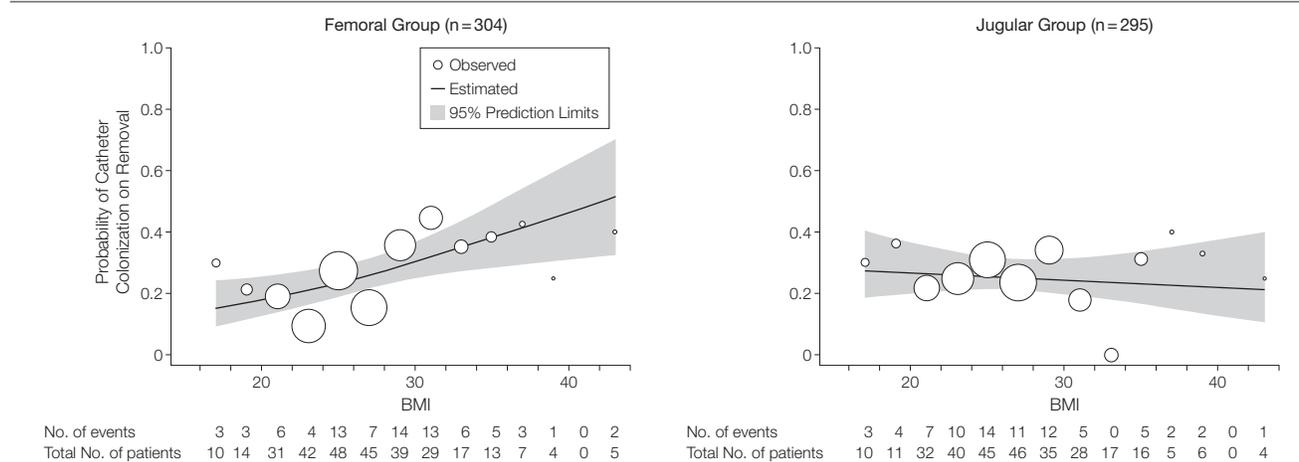
Despite our relatively large sample size, we did not reach statistical significance for detecting a higher incidence of colonization between the 2 groups, except among patients stratified according to BMI (with opposite effects). Inadequate dressings were previously associated with increased BMI in a study that included 66% femoral

Figure 3. Kaplan-Meier Curves of Time to Catheter Colonization on Removal Stratified According to BMI Terciles



BMI indicates body mass index, calculated as weight in kilograms divided by height in meters squared; HR, hazard ratio; CI, confidence interval. For the lowest BMI tercile, colonization occurred in 18 of 101 patients (17.8%) with femoral catheters and in 25 of 94 patients with (26.6%) jugular catheters; for the middle BMI tercile, colonization occurred in 25 of 101 patients (24.8%) with femoral catheters and in 28 of 101 patients (27.7%) with jugular catheters; and for the highest BMI tercile, colonization occurred in 38 of 102 patients (37.2%) with femoral catheters and in 22 of 100 patients (22.0%) with jugular catheters.

Figure 4. BMI Effect on the Risk Probability of Catheter Colonization on Removal by Study Group



BMI indicates body mass index, calculated as weight in kilograms divided by height in meters squared. Each circle is proportional to the size of the subsample and represents the observed proportion of catheter colonization on removal every 2 points of BMI. The solid line displays the estimated probability curve with bounding 95% prediction limits. The a priori modeled probability of catheter colonization on removal increased significantly as BMI increases for the femoral site (odds ratio [OR] for 2-points increase, 1.15; 95% confidence interval [CI], 1.04-1.26; $P=.006$). In contrast, this risk was not predicted by BMI for catheters inserted in the jugular site (OR, 0.98; 95% CI, 0.87-1.07; $P=.52$).

catheters.²⁵ In contrast, BMI does not seem to influence dressing integrity in jugular catheters.

The cumulative hazards of colonization on removal in femoral and jugular catheters are quite linear with an instantaneous risk relatively constant over time (Figure 2). This result suggests that catheter colonization and subsequent infection is a random event and that a threshold duration at which the probability of catheter-related bloodstream infection sharply increases does not exist within the range of catheter durations examined in our study. The implication for clinical practice is to avoid systematic catheter change after a predetermined length of time in ICUs, in accordance with current Centers for Disease Control and Prevention guideline.⁸ However, the National Foundation of Kidney Disease Outcome and Quality Initiative recommendation¹⁸ to change femoral acute dialysis catheters every 5 days to prevent infectious complications does not appear appropriate in critically ill adults.

The rate of mechanical complications in the jugular group is similar to previously reported rates of complication.^{2,36} In contrast, the low rate of mechanical complications in the femoral group is noteworthy and could be explained by several factors. First, the operators were similarly experienced for both sites. Second, the femoral route was selected by chance, not by choice. Deshpande et al¹⁵ found that the reasons for selecting a site for central catheterization differed between jugular and femoral regarding operator preference (higher for jugular) and patients risk factor (bleeding, emergency, and agitation, all higher for femoral). Third, patients were excluded from our study if the operators had no choice (eg, coagulopathy making jugular site hazardous). In those situations, the risk of complications might be higher in femoral as well.

Three randomized studies have already compared the risk of thrombosis according to site of insertion.^{24,37,38} A significantly higher risk in the femoral group was found by Trotter et al²⁴

(25% for femoral vs 0% for jugular and subclavian sites) and by Merrer et al³⁷ (21% for femoral vs 2% for subclavian site). It is difficult to compare the results of these 2 studies with our study because within upper extremity sites, rates of thrombosis may be higher in jugular site than in subclavian site (42% vs 10%, respectively).³⁹ In addition, all of our patients received routine anticoagulation for RRT, which might have contributed to lower rates of thrombosis in both groups.³⁹ Karakitsos et al³⁸ compared the “low-approach” vs “standard approach” for femoral catheterization in patients in the ICU requiring RRT. Their rate of deep venous thrombosis using the standard approach (4/40 patients [10.0%]) is very similar to our estimate in the femoral group (8/76 patients [10.5%]), increasing the external validity of our finding.

Subgroup analysis should always be conducted and interpreted with extreme caution. However, several factors inherent to our study need to be acknowledged. First, a formal interaction test identified a highly statistically significant heterogeneity in our overall population.⁴⁰ Second, the occurrence of a qualitative interaction with opposite effects is unlikely to occur by chance.⁴⁰ Third, although subgroup analysis generally implies lower statistical power, the tests comparing femoral vs jugular groups reached statistical significance in one subgroup and was significant in the other subgroup. Finally, the differential effect is anatomically plausible, at least for the higher BMI subgroup.²⁵ However, the unexpected protective effect of femoral vs jugular in the lower BMI subgroup probably needs to be interpreted as hypothesis-generating rather than hypothesis-supporting until replicated in a different population. A second possible limitation is the absence of systematic ultrasound guidance during catheter insertion in the jugular group. The mechanical complication rate reported for the jugular group might be overestimated because ultrasound guidance decreases this risk sig-

nificantly.^{2,36} Conversely, the use of ultrasound guidance is not currently routine practice. Third, catheter survival was rather short, with only 9% of the catheters inserted for more than 15 days. The conclusions can therefore not be extrapolated to dialysis catheters with longer stay. Similarly, the dialysis catheters were inserted early in the ICU stay and the conclusions can therefore not be extrapolated to catheters that are inserted at a later stage of ICU stay.

In conclusion, the decision for the best site of insertion to prevent complications might be more complex than previously suggested.¹² Our results support the current guideline for preventing catheter complications regarding the optimal site for catheter insertion in the ICU.⁸ If a subclavian approach is not available^{37,41} and the a priori individual risk of complications between the jugular and femoral sites is equal, the jugular site should be strongly considered for patients with higher BMI. We suggest that first-choice careful femoral catheterization by an experienced operator with full sterile precautions and appropriate postinsertion site care in nonobese, bed-bound, severely ill patients is acceptable and could reduce catheter-related morbidity compared with jugular catheterization.

Author Affiliations: Departments of Biostatistics and Clinical Research (Drs Parienti and Le Coutour), Medical Intensive Care (Drs Parienti, Ramakers, du Cheyron, Daubin, and Charbonneau), Surgical Intensive Care (Dr Ouchikhe), and Microbiology (Dr Dauriel), Côte de Nacre University Hospital Center, Caen; Department of Medical Intensive Care, Cochin University Hospital Center, Paris (Drs Thirion, Marqué, and Mira); INSERM U567, Cochin Institute, University of Paris Descartes, Faculty of Medicine, Paris (Dr Mira); Department of Medical Intensive Care, Lariboisière University Hospital Center, Paris, and University of Paris VII (Dr Mégarbane); Departments of Medical Intensive Care and Nephrology, University Hospital Center, Clermont-Ferrand (Dr Souweine); Department of Medical Intensive Care, University Hospital Center, Garches (Dr Polito); Department of Medical Intensive Care, University Hospital Center, Marseille (Dr Forel); Department of Medical-Surgical Intensive Care, Saint-Joseph Hospital, and Faculty of Medicine, University of Paris Descartes, Paris (Dr Misset); and Departments of Medical Intensive Care and Nephrology, University Hospital Center, Amiens (Dr Airapetian), France. Dr Thirion is now with the Department of Medical-Surgical Intensive Care, Argenteuil, France; Dr Ouchikhe is now with the Department of Anaesthesiology, General Hospital, Saintes, France; Dr Marqué is now with the Department of Medical Intensive Care, University Hospital, Rennes, France; and Dr Airapetian is now with the Department of Surgical Intensive Care, Amiens, France.

Author Contributions: Dr Parienti had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Parienti, Ramakers, du Cheyron, Daubin, Charbonneau.

Acquisition of data: Parienti, Thirion, Mégarbane, Souweine, Ouchikhe, Polito, Forel, Marqué, Misset, Airapetian, Daurel, Mira, Ramakers, du Cheyron, Daubin, Charbonneau.

Analysis and interpretation of data: Parienti, Thirion, Daurel, Ramakers, du Cheyron, Le Coutour, Daubin, Charbonneau.

Drafting of the manuscript: Parienti.

Critical revision of the manuscript for important intellectual content: Parienti, Thirion, Mégarbane, Souweine, Ouchikhe, Polito, Forel, Marqué, Misset, Airapetian, Daurel, Mira, Ramakers, du Cheyron, Le Coutour, Daubin, Charbonneau.

Statistical analysis: Parienti, Le Coutour.

Obtained funding: Parienti.

Administrative, technical, or material support: Thirion, Souweine, Daurel, Mira.

Study supervision: Parienti.

Financial Disclosures: None reported.

Funding/Support: This study was funded by the Centre Hospitalier Universitaire de Caen, Caen, France, and supported by an unrestricted academic grant from the French Health Ministry (Programme Hospitalier de Recherche Clinique National 2003). MEDA Pharma provided the antiseptics used in this study.

Role of the Sponsors: The funding agencies were not involved in the design and conduct of the study, in the collection, management, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Participating Centers in France and Cathedia Investigators: Centre Hospitalier Universitaire de Caen, *Réanimations Médicale*: J. J. Parienti (principal investigator), M. Ramakers, D. du Cheyron, C. Daubin, P. Charbonneau, N. Terzi, B. Bouchet, S. Chantepie, A. Seguin, S. Chevalier, D. Guillotin, X. Valette, T. Desieux, W. Grandin, S. Lammens, C. Buleon, V. Potier, C. Quentin, S. Thuaudet, C. Le Hello; *Réanimations Chirurgicales*: A. Ouchikhe (principal investigator), D. Samba, C. Jehan, G. Viquesnel, G. Leroy, E. Frostin, C. Eustratiades, M. O. Fischer, M. R. Clergeau, F. Michaux; Centre Hospitalier Universitaire Cochin-Port-Royal, *Assistance Publique-Hôpitaux de Paris, Réanimation Médicale*: J. P. Mira (principal investigator), S. Marqué, M. Thirion, S. Buysse, E. Clapson, J. D. Chiche, A. Soummer, B. Planquette, C. Baklini, D. Grimaldi, T. Braun, O. Huet, S. Perbet, J. Medrano, N. Verroust, A. Mathonnet, N. Joram, E. Lopez, D. Grimaldi, G. Colin; Centre Hospitalier Universitaire Lariboisière, *Assistance Publique-Hôpitaux de Paris, Réanimation Médicale*: B. Megarbane (principal investigator), F. J. Baud, N. Deye, D. Résière, G. Guerrier, J. Theodore, S. Rettab, P. Brun, S. Karyo, S. Delorme, A. Abdelwahab, J. M. Ekhérian, I. Malissin, A. Mohebbi-Amoli; Centre Hospitalier Universitaire de Clermont-Ferrand, *Réanimation Médicale et Néphrologie*: N. Gazui (principal investigator), B. Souweine, F. Thiollère, A. Lautrette, J. Liotier; Centre Hospitalier Universitaire Sainte Marguerite, *Assistance Publique-Hôpitaux de Marseille, Réanimation Médicale*: J. M. Forel (principal investigator), S. Gayet, N. Embriaco, D. Demory, J. Allardet-Servent, F. Michel; Centre Hospitalier Universitaire Garches, *Assistance Publique-Hôpitaux de Paris, Réanimation Médicale*: A. Polito (principal investigator), D. Annane, V. Maxime; Centre Hospitalier General, *Argentueil, Réanimation Médicale*: M. Thirion (principal investigator), E. Bourgeois, I. Rennuit, R. Hellmann, J. Beranger; *Fondation Hôpital Saint-Joseph, Paris, Réanimation Médicale*: B. Misset (principal investigator), V. Willems, F. Philippart, A. Tabah; Centre Hospitalier Universitaire d'Amiens, *Service de Néphro-*

logie Réanimation Médicale: B. de Cagny (principal investigator), M. Slama, N. Airapetian, J. Maizel, B. Gruson, A. Sarraj, F. Lengelle; Centre Hospitalier Universitaire Croix Rousse, *Hospices Civils de Lyon*: C. Guérin (principal investigator); Centre Hospitalier Général, *Pau*: P. Badia (principal investigator); Centre Hospitalier Général, *Saint-Malo*: L. Auvray (principal investigator).

Data Monitoring Task Force: A. Gauneau (clinical research assistant, CHU de Caen); J. J. Duthel (clinical research assistant, CHU de Caen); E. Vastel (clinical research assistant, CHU de Caen); F. Chaillot (administrator, CHU Caen); N. Marin (PharmD, CHU Cochin).

Previous Presentation: This work has been previously presented in part at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy (abstract K-1751); September 17-20, 2007; Chicago, Illinois.

Additional Contributions: Leonard Mermel, DO, ScM, FIDSA, FSHEA (Rhode Island Hospital and The Warren Albert Medical School of Brown University, Providence, Rhode Island), reviewed the protocol and a previous version of the manuscript. Gérard Nitenberg, MD (Institut Gustave Roussy, Villejuif, France), provided supporting comments during the early stage of this project. Gonzalo Bearman, MD, MPH (Virginia Commonwealth University, Richmond), Roland Leclercq, MD, PhD (University Hospital, Caen, France), and Christian Brun-Buisson, MD, PhD (Hôpital Henri Mondor, France), reviewed an earlier version of the manuscript. None of the aforementioned persons received compensation for their contribution.

We gratefully acknowledge the dedication of the nursing and medical staff members of all the participating centers and the generosity of the study participants or family members, without whom this study could not have been completed.

REFERENCE

- Mermel LA. Prevention of intravascular catheter-related infections [published correction appears in *Ann Intern Med*. 2000;133(5):5]. *Ann Intern Med*. 2000;132(5):391-402.
- McGee DC, Gould MK. Preventing complications of central venous catheterization. *N Engl J Med*. 2003;348(12):1123-1133.
- Moncrief JA. Femoral catheters. *Ann Surg*. 1958;147(2):166-172.
- Bearman GM, Munro C, Sessler CN, Wenzel RP. Infection control and the prevention of nosocomial infections in the intensive care unit. *Semin Respir Crit Care Med*. 2006;27(3):310-324.
- Timsit JF. What is the best site for central venous catheter insertion in critically ill patients? *Crit Care*. 2003;7(6):397-399.
- Canaud B, Formet C, Raynal N, et al. Vascular access for extracorporeal renal replacement therapy in the intensive care unit. *Contrib Nephrol*. 2004;144:291-307.
- Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;355(26):2725-2732.
- O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections: Centers for Disease Control and Prevention. *MMWR Recomm Rep*. 2002;51(RR-10):1-29.
- Harden JL, Kemp L, Mirtallo J. Femoral catheters increase risk of infection in total parenteral nutrition patients. *Nutr Clin Pract*. 1995;10(2):60-66.
- Goetz AM, Wagener MM, Miller JM, Muder RR. Risk of infection due to central venous catheters: effect of site of placement and catheter type. *Infect Control Hosp Epidemiol*. 1998;19(11):842-845.
- Oliver MJ, Callery SM, Thorpe KE, Schwab SJ, Churchill DN. Risk of bacteremia from temporary he-

modialysis catheters by site of insertion and duration of use: a prospective study. *Kidney Int*. 2000;58(6):2543-2545.

12. Lorente L, Henry C, Martin MM, Jimenez A, Mora ML. Central venous catheter-related infection in a prospective and observational study of 2,595 catheters. *Crit Care*. 2005;9(6):R631-R635.

13. Richet H, Hubert B, Nitenberg G, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. *J Clin Microbiol*. 1990;28(11):2520-2525.

14. Murr MM, Rosenquist MD, Lewis RW II, Heinle JA, Kealey GP. A prospective safety study of femoral vein versus nonfemoral vein catheterization in patients with burns. *J Burn Care Rehabil*. 1991;12(6):576-578.

15. Deshpande KS, Hatem C, Ulrich HL, et al. The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Crit Care Med*. 2005;33(1):13-20, 234-235.

16. Gowardman JR, Robertson IK, Parkes S, Richard CM. Influence of insertion site on central venous catheter colonization and bloodstream infection rates [published online ahead of print March 4, 2008]. *Intensive Care Med*. 2008.

17. Schetz M. Vascular access for HD and CRRT. *Contrib Nephrol*. 2007;156:275-286.

18. NKF-K/DOQI Clinical Practice Guidelines for Vascular Access: update 2000. *Am J Kidney Dis*. 2001;37(1)(suppl 1):S137-S181.

19. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med*. 1977;296(23):1305-1309.

20. Brun-Buisson C, Abrouk F, Legrand P, Huet Y, Larabi S, Rapin M. Diagnosis of central venous catheter-related sepsis: critical level of quantitative tip cultures. *Arch Intern Med*. 1987;147(5):873-877.

21. Rijnders BJ, Van Wijngaerden E, Peetermans WE. Catheter-tip colonization as a surrogate end point in clinical studies on catheter-related bloodstream infection: how strong is the evidence? *Clin Infect Dis*. 2002;35(9):1053-1058.

22. Parienti JJ, Thibon P, Heller R, et al. Hand-rubbing with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates: a randomized equivalence study [published correction appears in *JAMA*. 2002;288(21):2689]. *JAMA*. 2002;288(6):722-727.

23. Parienti JJ, du Cheyron D, Ramakers M, et al. Alcoholic povidone-iodine to prevent central venous catheter colonization: a randomized unit-cross-over study. *Crit Care Med*. 2004;32(3):708-713.

24. Trotter SJ, Veremakis C, O'Brien J, Auer AI. Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. *Crit Care Med*. 1995;23(1):52-59.

25. Trick WE, Miranda J, Evans AT, Charles-Damte M, Reilly BM, Clarke P. Prospective cohort study of central venous catheters among internal medicine ward patients. *Am J Infect Control*. 2006;34(10):636-641.

26. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005;294(7):813-818.

27. Souweine B, Traore O, Aublet-Cuvelier B, et al. Dialysis and central venous catheter infections in critically ill patients: results of a prospective study. *Crit Care Med*. 1999;27(11):2394-2398.

28. Harb A, Estphan G, Nitenberg G, Chachaty E, Raynard B, Blot F. Indwelling time and risk of infection of dialysis catheters in critically ill cancer patients. *Intensive Care Med*. 2005;31(6):812-817.

29. Souweine B, Liotier J, Heng AE, et al. Catheter colonization in acute renal failure patients: comparison of

central venous and dialysis catheters. *Am J Kidney Dis.* 2006;47(5):879-887.

30. Hoste EA, Blot SI, Lameire NH, Vanholder RC, De Bacquer D, Colardyn FA. Effect of nosocomial bloodstream infection on the outcome of critically ill patients with acute renal failure treated with renal replacement therapy. *J Am Soc Nephrol.* 2004;15(2):454-462.
31. Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet.* 1991;338(8763):339-343.
32. Rupp ME, Lisco SJ, Lipsett PA, et al. Effect of a second-generation venous catheter impregnated with chlorhexidine and silver sulfadiazine on central catheter-related infections: a randomized, controlled trial. *Ann Intern Med.* 2005;143(8):570-580.
33. Wester JP, de Koning EJ, Geers AB, et al. Catheter replacement in continuous arteriovenous hemo-

diafiltration: the balance between infectious and mechanical complications. *Crit Care Med.* 2002;30(6):1261-1266.

34. Lorente L, Jimenez A, Santana M, et al. Microorganisms responsible for intravascular catheter-related bloodstream infection according to the catheter site. *Crit Care Med.* 2007;35(10):2424-2427.
35. Crnich CJ, Maki DG. The promise of novel technology for the prevention of intravascular device-related bloodstream infection, I: pathogenesis and short-term devices. *Clin Infect Dis.* 2002;34(9):1232-1242.
36. Karakitsos D, Labropoulos N, De Groot E, et al. Real-time ultrasound-guided catheterisation of the internal jugular vein: a prospective comparison with the landmark technique in critical care patients. *Crit Care.* 2006;10(6):R162.
37. Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheter-

ization in critically ill patients: a randomized controlled trial. *JAMA.* 2001;286(6):700-707.

38. Karakitsos D, Saranteas T, Patrianakos AP, Labropoulos N, Karabinis A. Ultrasound-guided "low approach" femoral vein catheterization in critical care patients results in high incidence of deep vein thrombosis. *Anesthesiology.* 2007;107(1):181-182.
39. Timsit JF, Farkas JC, Boyer JM, et al. Central vein catheter-related thrombosis in intensive care patients: incidence, risks factors, and relationship with catheter-related sepsis. *Chest.* 1998;114(1):207-213.
40. Brookes ST, Whitley E, Peters TJ, Mulheran PA, Egger M, Davey Smith G. Subgroup analyses in randomised controlled trials: quantifying the risks of false-positives and false-negatives. *Health Technol Assess.* 2001;5(33):1-56.
41. O'Grady NP, Dezfulian C. The femoral site as first choice for central venous access? not so fast. *Crit Care Med.* 2005;33(1):234-235.

Every man is the builder of a temple, called his body, to the god he worships, after a style purely his own, nor can he get off by hammering marble instead. We are all sculptors and painters, and our material is our own flesh and blood and bones.

—Henry David Thoreau (1817-1862)