Infectious risk associated with arterial catheters compared with central venous catheters*

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LEARNING OBJECTIVES

After participating in this activity, the participant should be better able to:

1. Illustrate factors associated with arterial catheter-related colonization.
2. Explain risk factors associated with central venous catheter-associated colonization.
3. Use this information in a clinical setting.

Unless otherwise noted below, each faculty or staff's spouse/life partner (if any) has nothing to disclose.

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Background: **Scheduled replacement of central venous catheters and, by extension, arterial catheters, is not recommended because the daily risk of catheter-related infection is considered constant over time after the first catheter days. Arterial catheters are considered at lower risk for catheter-related infection than central venous catheters in the absence of conclusive evidence.**

Objectives: **To compare the daily risk and risk factors for colonization and catheter-related infection between arterial catheters and central venous catheters.**

Methods: **We used data from a trial of seven intensive care units evaluating different dressing change intervals and a chlorhexidine-impregnated sponge. We determined the daily hazard rate and identified risk factors for colonization using a marginal Cox model for clustered data.**

Results: **We included 3532 catheters and 27,541 catheter-days. Colonization rates did not differ between arterial catheters and central venous catheters (7.9% [11.4/1000 catheter-days] and 9.6% [11.1/1000 catheter-days], respectively). Arterial catheter and central venous catheter catheter-related infection rates were 0.68% (1.0/1000 catheter-days) and 0.94% (1.09/1000 catheter-days), respectively. The daily hazard rate for colonization increased steadily over time for arterial catheters ($p = .008$) but remained stable for central venous catheters. Independent risk factors for arterial catheter colonization were respiratory failure and femoral insertion. Independent risk factors for central venous catheter colonization were trauma or absence of septic shock at intensive care unit admission, femoral or jugular insertion, and absence of antibiotic treatment at central venous catheter insertion.**

Conclusions: **The risks of colonization and catheter-related infection did not differ between arterial catheters and central venous catheters, indicating that arterial catheter use should receive the same precautions as central venous catheter use. The daily risk was constant over time for central venous catheter after the fifth catheter day but increased significantly over time after the seventh day for arterial catheters. Randomized studies are needed to investigate the impact of scheduled arterial catheter replacement. (Crit Care Med 2010; 38:1030–1035)**

KEY WORDS: intensive care units; statistics; data; bacteremia; epidemiology; etiology; microbiology; catheterization; adverse effects; aged; incidence; catheter-related infections; prevention; prospective studies; risk; time factors

***See also p. 1208.**

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Central venous catheters (CVCs) are usually required in patients admitted to the intensive care unit (ICU). In Europe, the incidence density of CVC-related bloodstream infection (BSI) ranges from 1 to 3.1 per 1000 patient-days (1). In the United States, 15 million CVC-days are estimated to occur each year in ICU patients, as well as approximately 80,000 cases of CVC-related BSI (CVC-BSI) (2).

Arterial catheters (ACs) are frequently used for continuous hemodynamic monitoring and repeated blood sampling in critically ill patients. BSI prevention strategies in the ICU have focused on CVCs rather than ACs, and few studies have addressed the infection risk associated with ACs. This limited interest for AC-related BSI (AC-BSI) may be related to the shorter duration of AC use compared to CVCs and to a perceived lower risk of infection with ACs (3), based perhaps on statements in the 2002 recommendations issued by the Centers for Disease Control (4). Recently, however, small, single-center studies suggested a higher AC-BSI rate than previously thought (5–7).

Several studies indicate that the daily risk of CVC-BSI remains constant over time. Furthermore, several randomized trials and one meta-analysis found no evidence that scheduled CVC replacement decreased the BSI rate compared to continued use of the same CVC (8–10). Therefore, current guidelines state that scheduled CVC replacement is inappropriate (11). The same recommendation is made for ACs, despite the absence of data from clinical studies.

The incidence density rate of CVC-BSI has been proposed as a healthcare quality indicator, and its reporting is now mandatory in several countries (12). If incidence rates of a device-related infection are to serve as a quality indicator, then they must satisfy several criteria, including stability of the infection risk over time to enable valid comparisons of departments with different hospitalization durations; nonmodifiable risk factors should be accounted for as well (13, 14).

To compare the risks of infection associated with CVCs and ACs, we examined a large database on prevention strategies for catheter-related infections (CRIs). We evaluated the incidence, daily risk, and risk factors of colonization and infection associated with CVCs and ACs.

MATERIALS AND METHODS

Study Design

The study design has been described elsewhere (15). Briefly, we used a multicenter randomized two-by-two factorial design to compare dressing changes every 3 days (standard practice) or every 7 days, with or without chlorhexidine-impregnated sponge (CHGIS; BioPatch; Ethicon, Somerville, NJ). The study was conducted from December 20, 2006 to May 20, 2008, in seven ICUs in five hospitals. Adults requiring a CVC or AC for >48 hrs were randomly assigned to one of the four study groups, with stratification on the ICU. The study was approved by the ethics committee of the Grenoble University Hospital, France.

All ACs and CVCs in a given patient were managed in the same way. The study did not include pulmonary arterial catheters, hemodialysis catheters, or peripherally inserted CVCs. All study centers followed French recommendations for catheter insertion and care, which are similar to CDC recommendations, as follows: 1) maximal sterile barrier precautions were used for all AC and CVC insertions; 2) the preferred insertion sites were the radial artery or subclavian vein; 3) the insertion site was scrubbed with 4% aqueous povidone iodine scrub, rinsed with sterile water, and dried with sterile gauze, after which an alcohol-based antiseptic solution (5% povidone-iodine in 70% ethanol; Betadine scrub; Viatris Pharmaceuticals, Merignac, France) was applied for at least 1 min; and 4) a semipermeable transparent dressing (Tegaderm; 3M, Saint Paul, MN) was used at all insertion sites and for all treatment groups. The dressing was changed (together with the CHGIS in the CHGIS groups) 24 hrs after catheter insertion, and then every 3 days or every 7 days, according to the treatment group. Povidone-iodine alcoholic solution was used for skin antisepsis during dressing changes.

Catheters were removed if no longer needed, usually before ICU discharge, or when a CRI was suspected. Catheter tips were cultured using a simplified quantitative broth dilution technique (16). When CRI was suspected, one or more peripheral blood cultures were collected. If the catheter tip culture revealed colonization, or if a blood culture sampled at the time of removal was positive, an investigator blinded to the study group reviewed the case report form and medical chart to prepare an independent blinded review.

Definitions and Evaluation Criteria

The following definitions were used, according to French and American guidelines (17, 18). Catheter colonization was defined as a quantitative catheter tip culture yielding at least $\geq 10^3$ colony-forming units/mL. Catheter-related clinical sepsis without BSI was defined as a fever (body temperature $\geq$38.5°C) or hypothermia (body temperature $\leq$36.5°C), a catheter tip culture yielding at least 10^3 colony-forming units/mL, pus at the insertion site or resolution of clinical sepsis after catheter removal, and absence of any other infectious site. Catheter-related BSI was defined as one or more positive peripheral blood cultures sampled immediately before or during the 48 hrs after catheter removal, a positive quantitative catheter-tip culture, with the same microorganisms (same species and same susceptibility pattern) or a differential time to positivity of blood cultures $\geq$2 hrs (19), and no other infectious site explaining the positive blood culture(s). If a patient had blood culture(s) positive with coagulase-negative staphylococci, then the same pulsotype from the strains recovered from the catheter and blood culture(s) was required for a diagnosis of catheter-related BSI. We defined major CRI as either catheter-related clinical sepsis without BSI or catheter-related BSI.

The catheter colonization rate was the primary evaluation criterion. Therefore, only catheters subjected to bacteriologic cultures were included. The secondary evaluation criterion was the rate of major CRI.

Statistical Analysis

We used a per-protocol analysis including only the cultured catheters. Characteristics of patients, catheters, and dressings were described as number (percent) or median (interquartile range) for qualitative and quantitative variables, respectively. ACs and CVCs were analyzed separately. We first determined the incidence rates of catheter colonization and major CRI and the daily hazard rate for catheter colonization using the hazard function in the Cox model to estimate the event rate per day.

To identify variables associated with catheter colonization, we used a marginal Cox model for clustered data (PROC PHREG of SAS version 9.1; SAS, Cary, NC) to take into account a possible clustering effect of multiple catheters per patient. This model takes into account the censored nature of the data and possible intracluster dependence using a robust sandwich covariate estimate. Analyses were stratified by ICU and allocation groups under the assumption of no interaction between the two study interventions (20). Risk factors for catheter colonization were evaluated by univariate and multivariate analysis, and first-degree interaction terms were tested. The proportionality of the colonization and CRI hazard risks was checked using graphical method and the introduction of a time-dependent covariate (21). Comparison of incidence densities between arterial and venous

Table 1. Patient characteristics

Variable	Arterial Catheter			Central Venous Catheter		
	No Colonization, n = 1096	Colonization, n = 116	*p*	No Colonization, n = 1232	Colonization, n = 171	*p*
Age, median (IQR), yr	62 (50–74)	62 (48–71)	.30	62 (50–74)	62 (47–74)	.06
Male, n (%)	725 (66.1)	72 (62.1)	.09	797 (64.7)	109 (63.7)	.61
≥1 chronic disease[a]	347 (31.7)	45 (38.8)	.11	417 (33.8)	49 (28.7)	.14
Immune deficiency	62 (5.7)	5 (4.3)	.90	75 (6.1)	4 (2.3)	.16
Metastatic cancer	44 (4)	3 (2.6)	.78	54 (4.4)	2 (1.2)	.07
Chronic renal failure[a]	43 (3.9)	2 (1.7)	.29	54 (4.4)	5 (2.9)	.32
Chronic cardiac failure[a]	48 (4.4)	9 (7.8)	.004	56 (4.5)	12 (7)	.031
Chronic respiratory failure[a]	76 (6.9)	16 (13.8)	.08	93 (7.5)	11 (6.4)	.09
Rapidly or ultimately fatal disease (McCabe score)	396 (36.1)	52 (44.8)	.09	446 (36.2)	69 (40.4)	.37
Simplified Acute Physiology Score II, median (IQR)	53 (41–67)	54 (44–67.5)	.34	53 (41–66)	54 (40–66)	.27
Sequential Organ Failure Assessment, median (IQR)	12 (9–15)	11 (8–15)	.026	12 (9–15)	12 (10–15)	.85
Admission category, n (%)						
Medical	769 (70.2)	79 (68.1)		870 (70.6)	110 (64.3)	
Scheduled surgery	66 (6)	7 (6)	.95	82 (6.7)	11 (6.4)	.38
Emergency surgery	261 (23.8)	30 (25.9)		280 (22.7)	50 (29.2)	
Main reason for ICU admission						
Septic shock	245 (22.4)	21 (18.1)	.11	285 (23.1)	29 (17)	.002
Cardiogenic shock	109 (9.9)	12 (10.3)	.13	117 (9.5)	18 (10.5)	.01
De novo respiratory failure	230 (21)	31 (26.7)	.32	254 (20.6)	31 (18.1)	.14
Coma	139 (12.7)	14 (12.1)	.90	170 (13.8)	14 (8.2)	.08
Trauma	129 (11.8)	16 (13.8)	.77	117 (9.5)	37 (21.6)	.006
Length of ICU stay	990 (90.3)	109 (94)	.80	1069 (86.8)	159 (93)	.84
Mechanical ventilation n (%)	11 (5–22)	22.5 (12–36.5)		11 (5–22)	19 (10–36)	
ICU death	392 (35.8)	49 (42.2)		419 (34)	66 (38.6)	
Hospital death	447 (40.8)	59 (50.9)		492 (39.9)	75 (43.9)	

IQR, interquartile range; ICU, intensive care unit.

[a]According to Knaus WA, Zimmerman JE, Wagner DP, et al: APACHE-acute physiology and chronic health evaluation: A physiologically based classification system. *Crit Care Med* 1981; 9:591–597.

catheters (in place for at least 7 days or for <7 days) was performed using a comparison of Poisson rates.

Tests were two-tailed, with $p < .05$ being considered significant. Analyses were performed using SAS (version 9.1; SAS Institute, Cary, NC) and R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of 2095 patients with at least one intravascular catheter in the seven ICUs, 1636 could be enrolled, of whom 1525 had at least one assessable catheter; 1212 patients had at least one AC and 1403 had at least one CVC, and 1090 patients had at least one AC plus at least one CVC (Table 1).

A total of 3532 catheters, for a total of 27,541 catheter-days, were cultured and analyzed. There were 1617 ACs and 1915 CVCs (Table 2). The incidence density per 1000 AC-days was 11.4 (n = 127) for AC colonization and 0.9 (n = 11) for major colonization and 0.99 (n = 11) for major CRI. The same figure was 17.8 (n = 90) and 1.6 (n = 8), respectively, in the control group and was 6.1 (n = 37) and 0.5 (n = 3), respectively, in the CHGIS group.

The incidence density per 1000 CVC-days was 11.1 (n = 183) for CVC colonization and 1.09 (n = 18) for major CRI. The difference between ACs and CVCs was not statistically significant ($p = .80$). The same figure was 16.2 (n = 123) and 1.5 (n = 11), respectively, in the control group, and was 6.8 (n = 60) and 0.8 (n = 7), respectively, in the CHGIS group.

The daily hazard rates of AC and CVC colonization are reported in the Figure 1. For ACs, the daily hazard rate increased from 1.3% on day 5 to 2.4% on day 10 and 3.0% on day 15. The difference was significant between ACs used for <8 days and ACs used for ≥8 days ($p = .008$). The daily hazard rates of AC colonization were 1.9%, 3.8%, and 5.5% at days 5, 10, and 15, respectively, in the control group. They were 0.8%, 1.3%, and 0.9% at days 5, 10, and 15, respectively, in the CHGIS group. The difference was significant in the control group only. For CVC colonization, the daily hazard rate was 1.2% on day 5, 1.6% on day 10, and 1.4% on day 15. The differences were not statistically significant.

The hazard of colonization was not different between AC and CVC during the first 7 days of catheter maintenance but it was higher for AC after the seventh day ($p = .0078$). The incidence density ratio for colonization of catheters used for <8 days was similar for ACs and CVCs (6.8 and 8.8 per 1000 catheter-days, respectively; rate ratio, 1.28; 0.93–1.79; $p = .09$). In contrast, the incidence density ratio for colonization of catheters used for ≥8 days (excluding the first 7 days) was significantly higher for ACs than for CVCs (24.5 and 15.4 per 1000 catheter-days, respectively; rate ratio, 1.59; 1.17–2.17; $p = .0001$). For CRI, there was no difference in hazard rate between AC and CVC, probably because of the low number of events.

The distribution of microorganisms associated with colonization or CRI was not different between ACs and CVCs (Table 3). No differences were found in the distribution of microorganisms associated with colonization of catheters at different insertion sites (data not shown). By univariate analysis, variables associated with AC colonization were chronic heart failure ($p = .004$), Sequential Organ Failure Assessment score at ICU admission ($p = .026$), and site of insertion

Table 2. Catheter characteristics

Variable	Arterial Catheters, n = 1617			Central Venous Catheters, n = 1915		
	No Colonization, n = 1490	Colonization, n = 127	*p*	No Colonization, n = 1732	Colonization, n = 183	*p*
Time in place, median (interquartile range), days	5 (3–8)	5 (9–12)		4 (7–11)	7 (5–12)	
Catheter insertion at intensive care unit admission, n (%)	701 (47)	33 (26)	.48	723 (41.7)	70 (38.3)	.003
Experience of the operator, n (%)						
<50 procedures	1037 (69.6)	92 (72.4)		1146 (66.2)	136 (74.3)	
≥50 procedures	437 (29.3)	33 (26)	.73	550 (31.8)	46 (25.1)	.29
Junior operator with help from a senior	16 (1.1)	2 (1.6)		36 (2.1)	1 (0.5)	
Site of catheter insertion, n (%)						
Jugular				451 (26)	67 (36.6)	
Subclavian				735 (42.4)	36 (19.7)	<.0001
Femoral	599 (40.2)	64 (50.4)		546 (31.5)	80 (43.7)	
Radial	891 (59.8)	63 (49.6)	<.0001			
N of lumens of venous catheters, n (%)						
One				33 (1.9)	2 (1.1)	
Two				166 (9.6)	28 (15.3)	.059
Three				1533 (88.5)	153 (83.6)	
Guidewire exchange	0	0		76 (4.4)	5 (2.7)	.23
Antimicrobials at catheter insertion, n (%)	1025 (68.8)	85 (66.9)	.08	1182 (68.2)	111 (60.7)	.0016
Mechanical ventilation at insertion	1316 (88.3)	116 (91.3)	.23	1419 (81.9)	157 (85.8)	.099
Vasopressors at insertion	1008 (67.7)	83 (65.4)	.28	984 (56.8)	113 (61.7)	.43
Use of lipids, n (%)	0	0		675 (39)	60 (32.8)	.11
Use of heparin, n (%)	14 (0.9)	1 (0.8)	.77	606 (35)	68 (37.2)	.61
Packed red blood transfused, n (%)	0	0		509 (29.4)	58 (31.7)	.53
Number of dressing changes per catheter	3.3 (3), 2	5.1 (3.7), 4	<.0001	3.5 (2.8), 3	4.3 (3.4), 3	<.0001

(mean [SD], median).

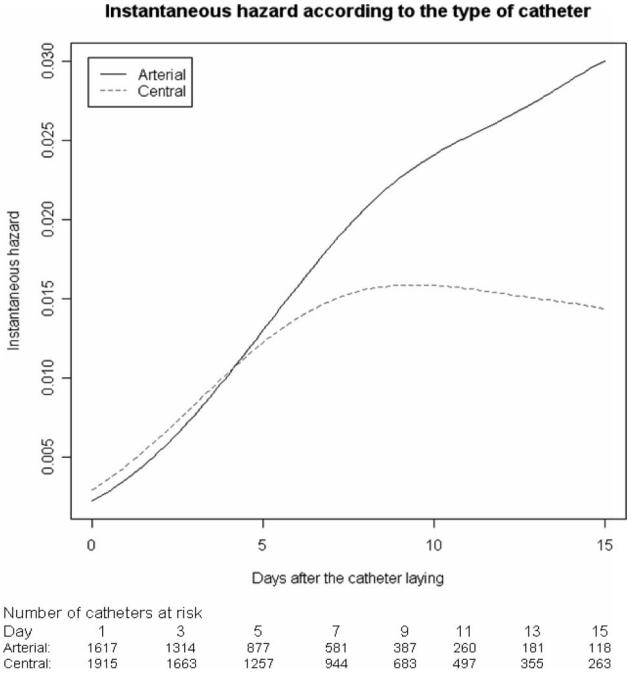

Figure 1. Daily hazard rate for catheter colonization.

($p = .0001$) (Tables 1 and 2). In the multivariate marginal Cox model, factors associated with AC colonization were femoral site of insertion (adjusted hazard ratio, 2.40; 95% confidence interval [CI], 1.66–3.49; $p = .0001$), chronic heart failure (2.37; 95% CI, 1.22–4.60; $p = .011$), and chronic respiratory failure (1.62; 95% CI, 0.99–2.63; $p = .053$). There were no significant interactions between variables.

By univariate analysis, variables associated with CVC colonization were: chronic heart failure ($p = .031$); septic shock ($p = .002$), cardiogenic shock ($p = .01$), or trauma ($p = .006$) as the main reason for ICU admission; CVC insertion at ICU admission ($p = .003$); site of insertion ($p < .0001$); and use of antimicrobials at CVC insertion ($p = .0016$). In the multivariate marginal Cox model, variables independently associated with CVC colonization were septic shock (0.63; 95% CI, 0.41–0.96; $p = 0.033$) or trauma (1.89; 95% CI, 1.11–3.21; $p = 0.018$); antibiotic treatment at CVC insertion (0.69; 95% CI, 0.50–0.95; $p = 0.021$); and insertion site ($p < .0001$) elsewhere than in the subclavian vein (jugular: 3.09; 95% CI, 1.96–4.88; and femoral: 7.05; 95% CI, 4.37–11.35). There were no significant interactions between variables.

DISCUSSION

This large, multicenter study produced two main findings regarding rates and risk factors for colonization: 1) rates of colonization and CRI were similar in the AC and CVC groups and 2) daily hazard rates of colonization differed between ACs and CVCs.

Our results confirm findings from recent single-center studies showing that infection rates with ACs were similar to those with CVCs (5, 6). Although ACs are

Table 3. Catheter colonization and catheter-related infections according to catheter type

Variable	Arterial Catheters, n = 1617	Central Venous Catheters, n = 1915
Catheter colonization $\geq 10^3$ colony-forming units,[a] n (%)	127 (7.8)	183 (9.6)
Staphylococcus aureus	6 (4.7)	10 (5.5)
Coagulase-negative staphylococci	63 (49.6)	90 (49.2)
Other Gram-positive cocci	16 (12.6)	18 (9.8)
Pseudomonas spp.	19 (15)	34 (18.6)
Enterobacter spp.	33 (26)	49 (26.8)
Escherichia coli	6 (4.7)	9 (4.9)
Acinetobacter baumannii	11 (8.7)	4 (2.2)
Fungi	3 (2.4)	10 (5.5)
Catheter-related bloodstream infection, n (%)	8 (0.5)	15 (0.8)
Major catheter-related infection,[a] n (%)	11 (0.7)	18 (0.9)
Staphylococcus aureus	1 (9.1)	4 (22.2)
Coagulase-negative staphylococci		4 (22.2)
Other Gram-positive cocci		1 (5.6)
Pseudomonas spp.	5 (45.5)	4 (22.2)
Enterobacter spp.	6 (54.5)	8 (44.4)
Escherichia coli	1 (9.1)	
Acinetobacter baumannii	1 (9.1)	
Fungi		1 (5.6)

[a]More than one microorganism was recovered in some cases.

generally believed to have less risk of CRI compared to CVCs (3), one study found an incidence density of colonization of 9.4 and 12.0 per 1000 catheter-days for ACs and CVCs, respectively (5). Another study obtained similar results, with an incidence density of colonization of 15.7 and 16.8 per 1000 catheter-days for ACs and CVCs, respectively (6). Furthermore, CRI rates were similar with ACs and CVCs in these two studies, as in our study. In a systematic review, the incidence density rate of AC-BSI was estimated at 1.7 per 1000 catheter-days, which was close to the 2.1 per 1000 catheter-days estimate for CVCs (3). In addition, microorganisms associated with colonization were similar with ACs and CVCs. In one of these studies (6), the similar colonization risk between ACs and CVCs may be ascribable to differences in preventive measures at catheter insertion, because maximum barrier sterile precautions were inconsistently used for AC insertion. In the other study (5) and in our study, however, the same precautions were used for the insertion and care of all catheters. Furthermore, most ACs and CVCs were inserted in the same patients in these three studies, thus decreasing the impact of any confounding factors. However, only one of the earlier studies (6) and our study included adjustment for multiple comparisons in a Cox proportional hazard model.

This higher risk of AC colonization than previously thought may be ascribable to a higher frequency of AC access for blood drawing and heavy manipulation in severely ill patients. In addition, the 2002 Centers for Disease Control guidelines for CRI prevention recommend that ACs not be replaced routinely. This recommendation rests on an extrapolation of data obtained for CVCs (8–10). However, our group and others (7) found an increase in the daily hazard rate over time for ACs but not for CVCs. For the infection prevention perspective, our results support scheduled replacement of ACs. Only a prospective comparative study could provide a definitive answer to the issue of scheduled AC replacement. In addition, routine AC replacement would raise other challenges, such as the limited number of arterial access sites and the risk of mechanical complications.

The daily hazard rate of CVC colonization was stable over time after the first catheter days, confirming previous data (22). Although one single-center study showed a higher infectious risk for CVCs in place for 16 to 30 days than in CVCs in place for <16 days (23), several randomized controlled studies demonstrated that the scheduled replacement of CVC after 3 to 7 days did not decrease CRI, there fore suggesting a stable infectious risk over time (8–10). Assuming a relationship between colonization and infection (24), our results suggest that the CVC-BSI incidence density could be used as a quality indicator and for benchmarking.

Our study has strengths and limitations. The main strengths are the multicenter design and large number of patients and catheters included, with identical measures during catheter insertion and care in all study centers. Our study is the largest multicenter study performed to date in a mix of medical and surgical ICUs with data collected at the patient and catheter levels. Furthermore, a large proportion of eligible patients were included, and few patients were lost to follow-up. Therefore, our results can reasonably be generalized to ICU patients who are expected to need short-term intravascular catheters. Among the limitations, we used catheter colonization as the study end point rather than CRI, because of the low CRI rate. However, colonization is an accepted surrogate for CRI (24). Furthermore, the colonization-to-CRI ratio was similar for ACs and CVCs, supporting our choice of colonization as the end point. Second, in a patient with AC and CVC, attributing a CRI to one or the other device may be difficult unless only one of the catheter tips is colonized. Because CVCs are widely believed to have a higher risk of infection than ACs, misclassification may occur, with AC-BSIs being mistakenly classified as CVC-BSIs. However, all suspected CRIs were assessed by independent investigators, which minimized uncertainty about the portal of entry. Third, we examined a large database designed to investigate the impact of CHGIS and of dressing change intervals in 7 ICUs. Therefore, interactions may have occurred among the four study groups. Furthermore, because many patients had AC and CVC and/or several successive ACs or CVCs, a clustering effect may have occurred. Out statistical analysis took into account these potential drawbacks. We used a marginal Cox model for clustered data, checked that no interactions existed between study groups, and stratified the randomization by ICU. The main limitation of our study, however, is its observational design. Only a sufficiently powered, randomized, controlled trial evaluating the impact of scheduled AC replacement on CRIs and mechanical complications could definitively determine whether the risk of AC-related infection increases over time. However, our study strongly suggests that scheduled AC replacement every 7 days may be beneficial.

In conclusion, the catheter colonization and CRI rates were similar for ACs and CVCs in critically ill patients, sug-

gesting that both AC-BSIs and CVC-BSIs should be monitored and prevented in the ICU. Contrary to CVCs, ACs were characterized by an increase over time in the daily risk of AC colonization.

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