Dressing disruption is a major risk factor for catheter-related infections*

Jean-François Timsit, MD, PhD; Lila Bouadma, MD, PhD; Stéphane Ruckly, MSc; Carole Schwebel, MD, PhD; Maïté Garrouste-Orgeas, MD; Régis Bronchard, MD; Silvia Calvino-Gunther, RN; Kevin Laupland, MD; Christophe Adrie, MD, PhD; Marie Thuong, MD; Marie-Christine Herault, MD; Sebastian Pease, MD; Xavier Arrault, PharmD; Jean-Christophe Lucet, MD, PhD

Objective: Major catheter-related infection includes catheter-related bloodstream infections and clinical sepsis without bloodstream infection resolving after catheter removal with a positive quantitative tip culture. Insertion site dressings are a major mean to reduce catheter infections by the extraluminal route. However, the importance of dressing disruptions in the occurrence of major catheter-related infection has never been studied in a large cohort of patients.

Design: A secondary analysis of a randomized multicenter trial was performed in order to determine the importance of dressing disruption on the risk for development of catheter-related bloodstream infection.

Measurements and Main Results: Among 1,419 patients (3,275 arterial or central-vein catheters) included, we identified 296 colonized catheters, 29 major catheter-related infections, and 23 catheter-related bloodstream infections. Of the 11,036 dressings changes, 7,347 (67%) were performed before the planned date because of soiling or undressing. Dressing disruption occurred more frequently in patients with higher Sequential Organ Failure

Assessment scores and in patients receiving renal replacement therapies; it was less frequent in males and patients admitted for coma. Subclavian access protected from dressing disruption. Dressing cost (especially staff cost) was inversely related to the rate of disruption. The number of dressing disruptions was related to increased risk for colonization of the skin around the catheter at removal (p < .0001). The risk of major catheter-related infection and catheter-related bloodstream infection increased by more than three-fold after the second dressing disruption and by more than ten-fold if the final dressing was disrupted, independently of other risk factors of infection.

Conclusion: Disruption of catheter dressings was common and was an important risk factor for catheter-related infections. These data support the preferential use of the subclavian insertion site and enhanced efforts to reduce dressing disruption in postinsertion bundles of care. (Crit Care Med 2012; 40:1707–1714)

KEY WORDS: bloodstream infection; care bundles; catheter; dressing; prevention

B loodstream infection is a common complication among patients admitted to intensive care units (ICUs) and increases cost, length of ICU stay, and mortality

(1–5). Because bloodstream infections interrupt the integrity of the skin and serve as a gateway for bacteria to enter the systemic circulation, percutaneously inserted intravascular catheters are the major risk factor for development of nosocomial bloodstream infections in patients with short-term catheters (6). Dressings are routinely used to cover and protect the insertion site in an attempt to reduce

*See also p. 1962.

From the University Joseph Fourrier (J-FT, SR, SC-G, KL), Albert Bonniot Institute, La Tronche Cedex, France; Medical Intensive Care Unit (J-FT, CS, SC-G), University hospital A Michallon, Grenoble, France; Medical Intensive Care Unit (LB), Bichat-Claude Bernard University Hospital, Paris, France; Medical-Surgical Intensive Care Unit (MG-0), Saint Joseph Hospital Network, Paris, France; Surgical Intensive Care Unit (RB), Bichat-Claude Bernard University Hospital, Paris, France; Critical Care Medicine (KL), Peter Lougheed Centre and University of Calgary, Calgary, Alberta, Canada; Delafontaine Hospital (CA), Saint Denis, France; National Biomedecine Agency (MT), Saint Denis la Plaine, France; Department of Physiology (CA, MT), University of René Descartes, Cochin University Hospital, Assistance-Publique Hôpitaux de Paris, Paris, France; Mixed Surgical Intensive Care Unit (M-CH), University hospital A Michallon, Grenoble, France; Surgical Intensive Care Unit (SP), Beaujon University Hospital, Clichy, France; Department of Pharmacy (XA), Bichat Claude Bernard Hospital, Paris, France: and Infection Control Unit (J-CL), Bichat—Claude Bernard University Hospital, Assistance-Publique Hôpitaux de Paris, and University Paris VII Denis Diderot, Paris, France

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (http://journals.lww. com/ccmjournal).

The dressing study was entirely funded by the French Ministry of Health (Projet Hospitalier de Recherche Clinique 2005-PHN01).

Currently listed as clinicaltrials.gov NCT 00417235. Ethicon provided all the chlorhexidine-impregnated sponges free of cost. Neither the French Ministry of Health nor Ethicon had any role in designing the study, collecting or analyzing the data, or deciding to publish the results.

Dr. Timsit received research grants from 3-M company and Johnson & Johnson. Dr. Timsit received lecture fees from 3-M and Carefusion companies.

Dr. Timsit conceived the study design and coordinated the data-capture, the data-cleaning, the statisti-

cal analysis, and the revision of the final manuscript. Drs. Bouadma, Orgeas, Bronchard, Herault, and Pease enrolled patients into the study. Dr. Laupland contributed to the study design and to the revision of the final manuscript. Drs. Thuong and Adrie participated to the advisory board and contributed to the manuscript revision. Mr. Arrault coordinated the safety monitoring committee. Mr. Ruckly performed the statistical analysis. Miss Gunther coordinated the research monitors activities, data cleaning, and participated in manuscript revision. Mr. Lucet conceived the study design and contributed to final manuscript revision. All the authors read and approved the final manuscript.

Drs. Timsit and Lucet consulted for 3-M and Carefusion, and received honoraria from 3-M and Ethicon. The remaining authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: jftimsit@chu-grenoble.fr

Copyright C 2012 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins

DOI: 10.1097/CCM.0b013e31824e0d46

the risk of infection. Extraluminal catheter colonization is the major pathophysiologic route for catheter colonization and infection in short-term catheters. Therefore, dressing management is one cornerstone of preventive measures for catheter-related bloodstream infection (CR-BSI) (7.8). However, dressings may become disrupted for a number of reasons and thus fail in their attempt to protect from skin colonization, catheter colonization, and subsequent infection. Surprisingly, the impact of dressing disruption on the risk for developing central-vein or arterial catheterrelated infections has not been previously systematically studied.

The objectives of this study were to define factors associated with disruption (undressed and/or soiled) of catheter dressings and to quantify the relationship between dressing disruption and the risk for catheter colonization and infection.

PATIENTS AND METHODS

This study was an ancillary study based on the previously reported Dressing study (9) involving seven ICUs (two medical, two surgical, and three medical–surgical). This was a patient- and assessor-blind factorial randomized multicenter trial comparing two dressing change intervals (3 days vs. 7 days) and two types of dressings (chlorhexidine-impregnated sponges (Biopatch, Ethicon Inc., Somerville, NJ) vs. standard) on major catheter-related infection (M-CRI) in intensive care.

All study centers followed French recommendations for catheter insertion and care, which are similar to Centers for Disease Control and Prevention recommendations (7-9). The insertion sites were the radial artery and subclavian vein whenever possible, unless using these sites carried an increased risk of noninfectious complications (10). Maximal sterile barrier precautions (using a large sterile drape; using a surgical hand antisepsis; and wearing a mask, a cap, sterile gloves, and a gown) were used at catheter insertion (11-14). The insertion site was scrubbed with 4% aqueous povidone-iodine solution (Betadine Scrub; Viatris Pharmaceuticals, Merignac, France), rinsed with sterile water, and dried with sterile gauze: an alcohol-based antiseptic solution (5% povidone-iodine in 70% ethanol, Betadine Alcoholic Solution; Viatris Pharmaceuticals, Merignac, France) was then applied for at least 1 min, and sterile drapes were placed around the site. Antiseptic- or antibiotic-impregnated centralvein catheters were not used in any of the study ICUs. The same semipermeable transparent dressings (Tegaderm, 3M, Saint Paul, MN) were used in all four treatment groups (15).

The time of dressings changes was planned 24 hrs after catheter insertion (Day 1), then every 3 days (Day 4, Day 7, etc.) in the 3-day group, and every 7 days (Day 8, Day 15, etc.) in the

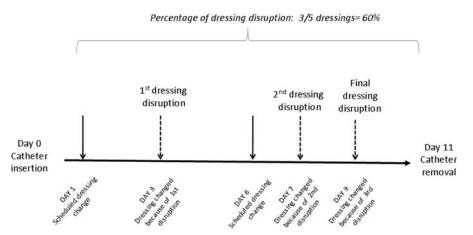


Figure 1. Example of a catheter in a patient enrolled in the 3-day scheduled dressing group. In this group the scheduled dressing changes are planned at day 1, day 4, etc. and every 3 days. Three dressing were done before the planned date because of disruption and represent the first, second, and final (third) disruption. For this catheter, three of five dressings were performed because of disruption, indicating a 60% rate of dressing disruption.

7-day group. Dressing disruption was defined by a leakage or soiling and led to an immediate dressing change. After an unscheduled dressing change for disruption, a new planned time was scheduled 3 days or 7 days later according to the group of randomization (Fig. 1).

For semiquantitative insertion-site cultures, the insertion site was sampled before catheter removal by pressing a nutritive trypticase-soy agar (Count-tact, Biomerieux, Crapone, France) for 10 secs on the skin, centering the plate on the insertion site. The plate was sent to the local microbiology laboratory and cultured for 48 hrs. The number of microorganisms recovered from the surface area corresponding to that of the chlorhexidine-impregnated sponges was counted.

Catheter colonization was defined as a quantitative catheter-tip culture yielding at least 1,000 colony-forming units/mL. CR-BSI was defined as a combination of one or more positive peripheral blood cultures sampled immediately before or within 48 hrs after catheter removal, a quantitative catheter-tip culture testing positive for the same microorganisms or a differential time to positivity of blood culture ≥ 2 hrs and no other infectious focus explaining the positive blood culture result. If a patient's blood culture tested positive for coagulase-negative staphylococci, the same pulsotype from the strains recovered from the catheter and blood culture was required for a diagnosis of CR-BSI. Catheter sepsis without BSI was defined as a combination of fever or hypothermia, a catheter-tip culture yielding at least 103 colony-forming units/mL, pus at the insertion site or resolution of clinical sepsis after catheter removal, and absence of any other infectious focus or the presence of a CR-BSI. Major catheter-related infection (M-CRI) was defined by either CR-BSI or catheter sepsis without BSI.

First and second dressing disruptions were recorded when they occurred. Final disruption occurred when the last dressing before catheter removal was replaced because of disruption (Fig. 1).

The cost per dressing was estimated during the study using a microcosting analysis of data from an audit of 146 randomly selected dressing procedures. In each center, we measured the time needed per dressing, the number of nurses involved, and the material used. The cost of the chlorhexidine-impregnated sponge was not included in the cost calculation (see reference [1] for details).

Statistical Analysis. A per-protocol analysis including only patients with catheters inserted for more than one calendar-day, and including only catheters with culture performed, was conducted. For descriptive statistics, medians with interquartile ranges were used to describe skewed continuous variables. Medians were compared using the Mann–Whitney test. Categorical data were reported as percentages, and compared using the Fisher's exact test.

To study the risk factors of disruption, we used a hierarchical mixed logistic regression model with patient and center level as random effect to take into account a possible clustering effect of multiple catheters per patients and multiple patients per ICUs (Proc GLIMMIX, SAS 9.1.2). Firstly, we selected variables to be included in the model with univariate hierarchical mixed logistic regression models keeping significant variables at p < .2. Secondly, we used the same model at each level (center, patient, and catheter) with significant variables, and we applied a backward selection. Finally, we used the same model with all significant variables at each of the three levels.

In order to estimate the degree of risk of catheter infection associated with disruption, we used a marginal Cox model. This model takes into account the censored nature of the data and possible intracluster dependence using a robust sandwich covariate estimate (Proc TPHREG, SAS option cov=aggregate, SAS 9.1; SAS Institute Inc., Cary, NC). Three censored events were studied: catheter colonization, CR-BSI, and M-CRI. Risk factors for events were selected by a univariate marginal Cox model keeping significant variables at 20%. A multivariate marginal Cox model for clustered data with backward selection was then used to select risk factors of events. Analyses were stratified by ICU and adjusted on the random allocation groups. First-degree interaction terms were tested. The first, second, and final dressing disruptions were successively tested as risk factors of events as time-dependent covariates in the final model.

Statistical analyses were performed using SAS version 9.1 software. p values <.05 were considered statistically significant.

Ethical Issues. The study was approved by the ethics committee of the Grenoble University Hospital, France. Written informed consent was obtained from patients whose decision-making capacity was intact. The ethics committee approved delayed consent from patients who were unable to make decisions at the time of catheter insertion, according to French law.

RESULTS

Of the 1,636 patients in the original study, 1,419 with at least one dressing change were included in the present dressing disruption analysis. A total of 11,036 dressings were studied, and 3,275 catheters representing a total of 24,127 catheter-days were cultured and analyzed. Of the 11,036 dressings changes, 7,347 (67%) were performed before the planned date because of soiling or undressing as shown in Table 1. The median (interquartile range) time between catheter insertion and the first, second, and final disruptions were 35 (21–67), 71 (47–115), and 106 (56–189) hrs, respectively. During the study, 296 colonizations, 29 M-CRI, and 23 CR-BSI were identified.

The estimated cost of a standard dressing was calculated using microcosting techniques as detailed elsewhere (1). It cost \$9.08 per dressing (year 2008) and varied from \$5.00 to \$9.50 across study ICUs. The percentage of disrupted dressings varied from 25% to 77%, with a significant correlation with estimated global (p = .046) and staff costs (p = .008) (Supplemental Figure E1; [Supplemental Digital Content 1, http://links.lww.com/ CCM/A444]). Most of the cost variation was explained by staff.

As the percentage of dressing disruptions per catheter followed a bimodal distribution (Fig. 2), we created a binary

Table 1. Dressing characteristic	Table 1.	Dressing	characteristics
----------------------------------	----------	----------	-----------------

	No. (%)
Characteristic	All Dressing $(N = 11,036)$
Time in place, median (interquartile range), days	1 (0-3)
Dressing soiled or unstuck, n (%)	7347 (66.6)
Local signs at dressing removal ^{<i>a</i>} , n (%)	
Normal	9789 (88.7)
Redness	711 (6.4)
Pain	22 (0.2)
Nonpurulent discharge	588 (5.3)
Purulent discharge	22 (0.2)
3 days/7 days allocation ^b , n (%)	5729 (51.9)/5307 (48.1)
Chlorhexidine-impregnated sponges/standard allocation ^b , n (%)	5760 (52.2)/5276 (47.8)

^{*a*}One or more local sign per dressing; ^{*b*}in the original study, patients were randomly allocated to either a 3-day or 7-day planned time between dressings and to either a standard or a chlorhexidine-impregnated sponge dressing using a two-way factorial design.

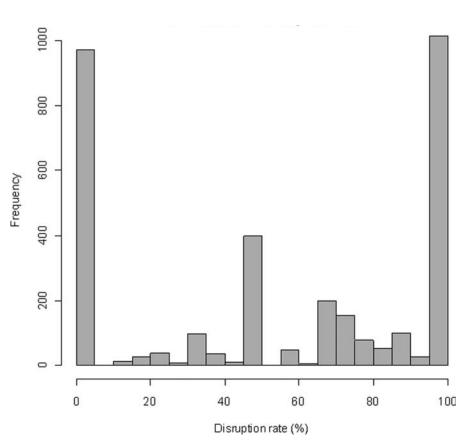


Figure 2. Distribution of disruption rate in the final cohort (The number of dressing disrupted divided by the number of dressings performed \times 100).

variable <50% or $\ge50\%$. Patients and catheters risk factors for >50% dressing disruption are presented in Tables 2 and 3, respectively.

Many variables were found to be associated with dressing disruption in multivariable analyses as shown in Table 4. The mean dressing cost per ICU was inversely and significantly associated with dressing disruption (adjusted odds ratio [aOR] 0.58, 95% confidence interval [CI] 0.41–0.80; Supplemental Figure E1; [Supplemental Digital Content 1, http:// links.lww.com/CCM/A444]). After breaking down the global cost into personnel cost and material cost, only the personnel

			No. (%)	
		Defiled	d or Unstuck >50)%
Characteristic	All Patients (N = 1419)	No (n = 690)	Yes (n = 729)	р
Age, median (interquartile range), years Men	62 (49–74) 921 (64.9)	63 (50–74) 461 (66.8)	61 (48–72) 460 (63.1)	.029 .15
Group 3 days ^a	696 (49.1)	362 (52.5)	334 (45.8)	.013
Group chlorhexidine-impregnated sponge ^{<i>a</i>} Main reason for intensive care unit admission	718 (50.6)	355 (51.4)	363 (49.8)	.56
Coma	188 (13.3)	107 (15.5)	81 (11.1)	.015
Trauma	168 (11.8)	88 (12.8)	80 (11)	.32
De novo respiratory failure	315 (22.2)	136 (19.7)	179 (24.6)	.03
Renal failure	37 (2.6)	14 (2)	23 (3.2)	.24
Metastatic cancer	57 (4)	35 (5.1)	22 (3)	.058
Immune deficiency	79 (5.6)	37 (5.4)	42 (5.8)	.82
Sequential Organ Failure Assessment, median (interquartile range) ^b	12 (9–15)	11 (9–14)	12 (10-15)	.0004
Simplified Acute Physiology Score II, median (interquartile range) ^c	51 (40-64)	49 (37–61)	54 (42-66)	<.0001
Admission category				
Medical	963 (67.9)	447 (64.8)	516 (70.8)	.017
Scheduled surgery	98 (6.9)	53 (7.7)	45 (6.2)	.30
Emergency surgery	358 (25.2)	190 (27.5)	168 (23)	.058
Diabetes mellitus	107 (7.5)	54 (7.8)	53 (7.3)	.76
Chronic respiratory failure Admission for respiratory problems	109 (7.7) 315 (22.2)	45 (6.5) 136 (19.7)	64 (8.8) 179 (24.6)	.11 .03
······································	/		(/	

^{*a*}In the original study, patients were randomly allocated to either a 3-day or 7-day planned time between dressings and to either a standard or a chlorhexidine-impregnated sponge dressing using a two-way factorial design; ^{*b*}range of possible scores, 0–24; ^{*c*}range of possible scores, 0.162.

cost remained significantly associated with dressing integrity (aOR 0.72, 95% CI 0.57-0.92).

At the patient level, the rate of dressing disruption was lower in males and in comatose patients. It was higher in patients with high severity of illness scores at ICU admission and in patients receiving antimicrobials at catheter insertion.

At the catheter level, the subclavian insertion site was protective (aOR as shown in Supplemental Table E1; [Supplemental Digital Content 1, http://links.lww.com/ CCM/A444] and Supplemental Table E2; [Supplemental Digital Content 1, http:// links.lww.com/CCM/A444]). When computing the risk of disruption on venous catheter only, the use of accesses other than subclavian increased the disruption risk (aOR 1.58, 95% CI 1.24–2.01, p = .0003; Supplemental Table E2; [Supplemental Digital Content 1, http:// links.lww.com/CCM/A444]). A separate analysis for arterial catheter showed that the insertion site was no longer associated with the risk of dressing disruption (Supplemental Table E2; [Supplemental Digital Content 1, http:// links.lww.com/CCM/A444]).

The percentage of dressing disruption increased with the duration of catheter maintenance. It also increased if the patient was treated by extra-renal replacement when the catheter was in place (Table 4).

The rate of catheter-tip colonization increased after the first disruption, from 8.6 to 13.1/1,000 catheter-days, and remained stable for further disruption. The occurrence rate of infection increased after the second disruption, from 0.5 to 1.7/1,000 catheter-days for M-CRI, and from 0.5 to 1.4/1,000 catheter-days for CR-BSI. Major catheter-related infections and CR-BSI rates remained stable after further disruption (Supplemental Table E3; [Supplemental Digital Content 1, http://links.lww.com/ CCM/A444]).

The final dressing was disrupted in 221/296 (75%), 22/29 (76%), and 17/23 (74%) of the colonized, M-CRI, and CR-BSI cases, respectively (p < .001 as compared to the final dressings of not colonized, uninfected catheters) (Supplemental Table E4; [Supplemental Digital Content 1, http://links.lww.com/CCM/A444]).

In univariate marginal Cox's model, first, second, and final dressing disruptions were associated with catheter colonization (Table 5). However, only final disruption was significantly associated with catheter colonization on multivariate marginal Cox's model. The second and the final dressing disruptions (but not the first) were associated with M-CRI and CR-BSI in univariate and multivariate analyses. The second dressing disruption was associated with a higher than three-fold increase in the risk for M-CRI (Table 5). The final dressing disruption increased by >12-fold the risk of M-CRI (adjusted hazard ratio 12.51, 95% CI 3.95-39.62, p < .0001) and CR-BSI (adjusted hazard ratio 18.11, 95% CI 5.66–57.88, p < .0001) (Table 5).

The rate of dressing disruption and the level of cutaneous colonization were not different for femoral and radial arterial catheters (Supplemental Table E1; [Supplemental Digital Content 1, http:// links.lww.com/CCM/A444]). The rate of dressing disruptions and the cutaneous colonization at catheter removal were significantly lower for subclavian catheters as compared to other venous catheters. When analyzing separately subclavian catheters (n = 547), both percentage of disruption (p = .0043) and disruption of the final dressing (p = .0004) increased the cutaneous colonization at catheter removal even when adjusted for the time the catheter was in place (two-way analysis of variance by rank).

DISCUSSION

This large multicenter study demonstrated that catheter dressing disruption was a common event in ICU patients with central-vein or arterial catheters. More than two dressing changes for disruption were associated with a higher than threefold increase in the risk of M-CRI and CR-BSI. When the final dressing is disrupted, the risk of catheter colonization or infection is increased by more than 12-fold.

Occlusive dressings decrease skin colonization (15) and the subsequent

		No. (%) Defiled or Unstuck >50%			
Characteristic	All Catheters (N = 3275)	No (n = 1594)	Yes (n = 1681)	р	
Time in place, median (IQR), days	6 (3–10)	5 (3–9)	7 (4–11)	<.0001	
Experience of the operator ≥ 50 procedures	973 (29.7)	623 (19)	350 (11)	<.0001	
Site					
Radial artery	887 (27.1)	407 (12.4)	480 (14.7)	.054	
Femoral artery	585 (17.9)	250 (7.6)	335 (10.2)	.0016	
Femoral or jugular venous insertion site	1051 (32.1)	472 (14.4)	579 (17.7)	.0031	
Subclavian insertion site	752 (23)	465 (14.2)	287 (8.8)	<.0001	
Dialysis at catheter removal	402 (12.3)	158 (9.9)	244 (14.5)	<.0001	
Antibiotic at catheter insertion	2237 (68.3)	1020 (64)	1217 (72.4)	<.0001	
No. of dressing changes per catheter, median (IQR)	3 (1-4)	2 (1–3)	4 (2-6)	<.0001	
Local signs at catheter removal					
Normal	2914 (89)	1433 (89.9)	1483 (88.2)	.13	
Redness	318 (9.7)	145 (9.1)	173 (10.3)	.26	
Pain	10 (0.3)	4 (0.3)	6 (0.4)	.75	
Nonpurulent discharge	42 (1.3)	14 (0.9)	28 (1.7)	.06	
Purulent discharge	15 (0.5)	4 (0.3)	11 (0.7)	.12	
Catheter removal for suspected infection	592 (18.1)	264 (16.6)	328 (19.5)	.03	
Group 3 days ^a	1576 (48.1)	806 (50.6)	770 (45.8)	.007	
Group chlorhexidine-impregnated sponge ^a	1729 (52.8)	860 (54)	869 (51.7)	.21	
		Final Dressing Defiled or Unstuck			
		No	Yes		
		(n = 1246)	(n = 2029)	р	
Time in place, median (IQR), days		4 (2–9)	6 (4–10)	<.0001	

IQR, interquartile range.

^{*a*}In the original study, patients were randomly allocated to either a 3-day or 7-day planned time between dressings and to either a standard or a chlorhexidine-impregnated sponge dressing using a two-way factorial design.

risk for extraluminal route of infection (11), and are therefore widely and strongly recommended (7, 8). However, this recommendation is only based on one study that found that moisture of the peripheral catheter dressing was associated with a 2.5-fold increase of exit site infection (16). We provide a confirmation in a large cohort that dressing disruption is significantly associated with skin colonization at catheter removal.

Little is known about the rate of catheter dressing disruption in ICU patients (17) and its role in catheter-related infection. The reported rate of dressing disruption or moistening is limited to non-ICU patients, and usual reported rate is <15% (18). One study performed on hematological patients reported a rate of unscheduled dressings up to 40% and confirmed the difficulties of keeping dressing occlusive (19). In another study, Maki et al (20) found that the rate of totally adherent dressing of pulmonary artery catheters was 34%, 38%, and 24% in gauze, conventional polyurethane, and highly permeable polyurethane dressings, respectively. In this study, there was no difference in the rate of catheter colonization between dressing types. Two crosssectional surveys also emphasized the importance of the problem: the number of nonadherent dressings was as high as 57% and 11% in previously reported audits performed outside and inside the ICU, respectively (21). In another study, the number of intact dressing on daily inspection was <90%, even in the ICUs despite a complete agreement of almost all the staff members to this recommendation (22).

This study is important because we identify risk factors for dressing disruption,

and that these may justify enhanced preventive efforts. The rate of disruption was higher for the sickest patients who need extra-renal replacement. The cause of significant association between disruption and extra-renal replacement remained speculative because we did not measure the importance of weight gain, edema, or skin disorders. This may reflect the fact that dressings are frequently nonocclusive in diaphoretic patients. However, severity of illness is not a readily modifiable factor. On the other hand, we found that the subclavian vein access led to a dramatic decrease in dressing disruption, possibly explaining the significant and constant decreased risk of catheter colonization and CR-BSI, as compared with femoral or jugular insertion sites (9, 23, 24). Our data support the preferential use of the subclavian insertion site.

We found that the mean cost dedicated to dressings (in particular the personnel cost) per ICU was inversely related to the rate of dressing disruption. This unexpected association may have several explanations. First, meticulously performing a dressing takes time and can be a protective factor for dressing integrity over time. Alternatively, nursing staff reduction below a critical level has been shown to contribute to an increase in CR-BSI rates in the surgical intensive care unit by making adequate catheter care difficult (25, 26). It has also been shown that inexperienced nursing care might increase the rate of CR-BSI (27). Finally, as dressing cost was evaluated at the ICU level, variations in dressing cost and dressing disruption may be explained by other ICU-related confounding factors. During the study period, nine fulltime, dedicated research nurses and study monitors followed the studies. Formal procedures of catheter postinsertion cares were similarly discussed and taught to the staff members in all centers. All the centers were familiar with the prevention of CR-BSI. Because of these stringent study conditions, we believe that the delay between dressing disruption and dressing replacement was minimized. Despite this, the number of dressing disruptions was associated with an important and significant increase of M-CRI and CR-BSI after controlling for other risk factors, random allocation groups, and duration of catheters in place.

Catheter bundling is increasingly recommended and used in many ICUs. It has been proven to be effective in reducing central line–associated bloodstream

Table 4. Final hierarchical mixed logistic regression model for dressin	ng disruption with patient and center level as random effect
---	--

Fixed Effects	Estimate	Standard Error	Odds Ratio	95% Confidenc Interval	e Degree of Freedom	$\Pr > t $
Intercept	2.2198	1.2136			7505	.1072
Global cost	-0.5512	0.1680	0.58	0.39-0.86	7012	.0135
3 days group	-0.1647	0.09969	0.85	0.70 - 1.03	1126	.0988
Chlorhexidine-impregnated sponge group	-0.1756	0.09968	0.84	0.69 - 1.02	1140	.0784
Male	-0.2920	0.1065	0.75	0.61 - 0.92	1144	.0062
Metastatic cancer	-0.5645	0.2654	0.57	0.34-0.96	1106	.0337
Intensive care unit admission: coma	-0.3972	0.1502	0.67	0.50-0.90	1169	.0083
Sequential Organ Failure Assessment admission	0.03235	0.01210	1.03	1.01 - 1.06	1267	.0076
Antibiotic	0.2311	0.1007	1.26	1.03 - 1.54	3263	.0218
Site: femoral artery	0.7812	0.1479	2.18	1.63 - 2.92	3263	<.0001
Site: radial artery	0.7263	0.1282	2.07	1.61 - 2.66	3263	<.0001
Site: femoral or jugular vein	0.5707	0.1273	1.77	1.38-2.27	3263	<.0001
Site: subclavian vein	0		1			
Time in place: <4 days	0		1			
Time in place: 4–6 days	0.7487	0.1194	2.11	1.67 - 2.67	3263	<.0001
Time in place: 7–10 days	1.2265	0.1338	3.41	2.62-4.43	3263	<.0001
Time in place: >10 days	1.5981	0.1408	4.94	3.75-6.52	3263	<.0001
Dialysis at catheter removal	0.2600	0.1540	1.30	0.96 - 1.75	2491	.0915
Random Effects	Estimate	Standard Error	Pr Wald			
Center	0.4170	0.2352	.0762			
Patient	0.7882	0.1203	<.0001			

infections (28). However, most measures in these bundles include preventive measures at catheter insertion. Only the daily check for the need of catheter maintenance is usually included in catheter bundles. Although postinsertion bundles of care are included in educational programs and appear effective in reducing catheter-related infections (29, 30), they are insufficiently implemented.

Whereas the use of barrier precautions is largely present in written procedures and correctly implemented, the daily check for local signs of infection is only present in 82% of written policies (31). The daily inspection check was monitored for implementation in only 47%, and reported as correctly implemented and applied at any time in only 25% of National Healthcare Safety Network ICUs in 2010 (31).

In the Pronovost and colleagues' cornerstone study, the intervention failed to control infection 60% of the time (32). This result may suggest that other preventive measures have not been implemented. One before–after study suggested that if compliance to

insertion bundles is almost perfect. postinsertion bundles of care including, in particular, daily inspection of the insertion site, immediate replacement of dressing if necessary, proper application of chlorhexidine-impregnated sponges at the insertion site was associated with a dramatic decrease in central lineassociated bloodstream infection (33). Our study results reinforce the need for postinsertion bundle of care. We also found that efforts to reduce dressing disruption act independently of the use of chlorhexidine-impregnated sponges in preventing major catheter-related infection and CR-BSI.

As the main outcome measure of the Dressing study (9) was not dressing disruption, one might question the accuracy of measuring dressing disruption. Furthermore, the report form did not allow distinctions between dressing moistening and secondary disruption and dressing disruption due to other causes. Despite these methodological flaws, our study clearly underlines the importance of dressing disruption in the mechanism of short-term catheterrelated infections.

Finally, one might question the absence of significant association between the first dressing disruption and infection. We hypothesized that the impact of dressing disruption was less pronounced because the median delay between the first dressing disruption and catheter removal was 107 hrs. Indeed, either catheter removal occurred early with a minimal risk of catheter infection or catheters were maintained for a long period of time with a minimal effect of the first disruption on the infectious status at catheter removal.

This study adds major arguments to include dressing integrity in catheter bundles. Further investigation is warranted in order to better understand the particularities of different types of dressings and to optimize their uses to improve adhesiveness (34). A new area/ field in catheter-related infection prevention should also be opened for the development, validation, and use of more adherent dressings. Table 5. Association between dressing disruption and catheter colonization or infection (unadjusted and adjusted marginal Cox model)

	Catheter Colonization ≥10 ³ colony-forming units/mL		Catheter-Related Bloodstream Infection		Major Catheter-Related Infection	
	HR (95% CI)	р	HR (95% CI)	р	HR (95% CI)	р
Unadjusted						
First	1.64(1.13-2.39)	.01	3.15(0.67 - 14.79)	.15	2.66 (0.50-14.26)	.25
Second disruption	1.52(1.14 - 2.04)	.005	5.18(1.85 - 14.48)	.002	4.31 (1.39-13.41)	.012
Final disruption	13.54 (10.17-18.04)	<.0001	14.90 (6.40-34.64)	<.0001	13.41 (5.17-34.75)	<.0001
Adjusted ^a						
First disruption	1.30(0.90 - 1.87)	.16	2.65(0.67 - 10.56)	.17	1.94(0.50-7.48)	.33
Second disruption	1.16(0.87 - 1.55)	.33	4.49 (1.71–11.79)	.002	3.26 (1.18-9.02)	.023
Final disruption ^b	13.99 (9.88–19.82)	<.0001	18.11 (5.66–57.88)	<.0001	12.51 (3.95–39.62)	<.0001

HR, hazard ratio; CI, confidence interval.

^{*a*}Analysis adjusted on significant risk factors of events and random allocation groups: For catheter colonization: 3-day group, chlorhexidine-impregnated sponge (CHGIS) group, at least one blood pack during catheter maintenance, antibiotic within 48 hrs of catheter removal, catheter insertion site, trauma; for catheter-related bloodstream infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related bloodstream infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, CHGIS group, hematological malignancy; for major catheter-related infection: 3-day group, chematological m

ACKNOWLEDGMENTS

Investigators (in alphabetical order): Aboab Jerome (Paris, Bichat-Claude Bernard). Alvarez Antonio (Saint Denis). Ara-Somohano Claire (Grenoble), Aubron Cecile (Paris, Bichat-Claude Bernard), Barnoud Didier (Grenoble), Benayoun Laurent (Clichy, Beaujon), Benbara Abdel (Clichy, Beaujon), Bonadona Agnes (Grenoble), Bonneville Claire (Clichy, Beaujon), Bronchard Regis (Paris, Bichat-Claude Bernard), Broux Christophe (Grenoble), Carlet Jean (Paris, St Joseph), de Vaumas Cyrille (Paris, Bichat-Claude Bernard), Declety Philippe (Grenoble), Dessertaine Géraldine (Grenoble), Falcon Dominique (Grenoble), Ferreira Luis (Paris, Bichat-Claude Bernard), Francony Gilles (Grenoble), Frenea Stephane (Grenoble), Garrouste-Orgeas Maité (Paris, St Joseph), Gasciolli Stephanie (Clichy, Beaujon), Geffroy Arnaud (Paris, Bichat-Claude Bernard), Gna Mathieu (Clichy, Beaujon), Rebecca Hamidfar-Rov (Grenoble), Hammer Laure (Grenoble), Hamzaoui Olfa (Clichy, Beaujon), Haouache Hakim (Saint Denis), Hanna Jerome (Grenoble), Herrault Marie Christine (Grenoble), Jacquot Claude (Grenoble), Kermarrec Nathalie (Paris, Bichat-Claude Bernard), Lakhal Karim (Clichy, Beaujon), Lasocki Sigismond (Paris, Bichat-Claude Bernard), Lavagne Pierre (Grenoble), Leport Yves (Paris, Bichat-Claude Bernard), Misset Benoit (Paris, St Joseph), Montravers Philippe (Paris, Bichat-Claude Bernard), Mourvillier Bruno (Paris, Bichat-Claude Bernard), Paugam Catherine (Clichy, Beaujon), Pease Sebastian (Clichy, Beaujon), Philippard Francois (Paris, St Joseph), Restoux Avmeric (Clichy, Beaujon), Tabah Alexis (Grenoble), Trouiller Pierre (Clichy, Beaujon), Willems Vincent (Paris, St Joseph), and Wolff Michel (Paris, Bichat-Claude Bernard).

Study monitors, research nurses, and biohygiene technicians: Brousse Caroline, Calvino Silvia, Fahim Monia, Goyer Floriane, Khadour Nadira, Menuet Daria, Riviere Sylvie, and Sehil Karima.

Statistics: Francais Adrien (INSERM U823, Grenoble), Vesin Aurelien (INSERM U823, Grenoble), and Timsit Jean-Francois (INSERM U823, Grenoble).

Safety monitoring committee: Arrault Xavier (Pharm D, Bichat-Claude Bernard, Paris), Descamps Vincent (Dermatologist, Paris, Bichat-Claude Bernard), Mallaret Marie-Reine (Bio-Hygiene unit, Grenoble), and Schmitt Delphine (PharmD; Grenoble).

Independent blind assessors: Adrie Christophe (Paris, Cochin), Lucet Jean-Christophe (Paris Bichat-Claude Bernard), Thuong Marie (Paris Biomedicine agency), and Zahar Jean-Ralph (Paris, Necker).

REFERENCES

- 1. Schwebel C, Lucet JC, Vesin A, et al: Economic evaluation of chlorhexidine-impregnated sponges for preventing catheter-related infections in critically ill adults in the dressing study. *Crit Care Med* 2012; 40:11–17
- 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(3 Pt 1):1027–1030
- 3. Renaud B, Brun-Buisson C: ICU-Bacteremia Study Group: Outcomes of primary and catheter-related bacteremia. A cohort and case-control study in critically ill patients. *Am J Respir Crit Care Med* 2001; 163:1584–1590

- 4. Soufir L, Timsit JF, Mahe C, et al: Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: A matched, risk-adjusted, cohort study. *Infect Control Hosp Epidemiol* 1999; 20:396–401
- Warren DK, Quadir WW, Hollenbeak CS, et al: Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med* 2006; 34:2084–2089
- Mermel LA, Allon M, Bouza E, et al: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 49:1–45
- 7. O'Grady NP, Alexander M, Dellinger EP, et al: Healthcare Infection Control Practices Advisory Committee: Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002; 23:759–769
- Timsit JF: Updating of the 12th consensus conference of the Société de Réanimation de langue française (SRLF): Catheter related infections in the intensive care unit. *Ann Fr Anesth Reanim* 2005; 24:315–322
- Timsit JF, Schwebel C, Bouadma L, et al: Dressing Study Group: Chlorhexidineimpregnated sponges and less frequent dressing changes for prevention of catheterrelated infections in critically ill adults: A randomized controlled trial. JAMA 2009; 301:1231–1241
- Lucet JC, Bouadma L, Zahar JR, et al: Infectious risk associated with arterial catheters compared with central venous catheters. *Crit Care Med* 2010; 38:1030–1035
- 11. Mermel LA: What is the predominant source of intravascular catheter infections? *Clin Infect Dis* 2011; 52:211–212
- Timsit JF: Diagnosis and prevention of catheter-related infections. Curr Opin Crit Care 2007; 13:563–571

- Moro ML, Viganò EF, Cozzi Lepri A: Risk factors for central venous catheter-related infections in surgical and intensive care units. The Central Venous Catheter-Related Infections Study Group. *Infect Control Hosp Epidemiol* 1994; 15(4 Pt 1):253–264
- Safdar N, Maki DG: The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. *Intensive Care Med* 2004; 30:62–67
- Conly JM, Grieves K, Peters B: A prospective, randomized study comparing transparent and dry gauze dressings for central venous catheters. *J Infect Dis* 1989; 159:310–319
- Maki DG, Ringer M: Evaluation of dressing regimens for prevention of infection with peripheral intravenous catheters. Gauze, a transparent polyurethane dressing, and an iodophor-transparent dressing. *JAMA* 1987; 258:2396–2403
- 17. Gillies D, O'Riordan L, Carr D, et al: Gauze and tape and transparent polyurethane dressings for central venous catheters. *Cochrane Database Syst Rev* 2003; CD003827
- Rasero L, Degl'Innocenti M, Mocali M, et al: Comparison of two different protocols on change of medication in central venous catheterization in patients with bone marrow transplantation: Results of a randomized multicenter study. Assist Inferm Ric 2000; 19:112–119
- Vokurka S, Bystricka E, Visokaiova M, et al: Once- versus twice-weekly changing of central venous catheter occlusive dressing in intensive chemotherapy patients: Results

of a randomized multicenter study. *Med Sci Monit* 2009; 15:CR107–CR110

- Maki DG, Stolz SS, Wheeler S, et al: A prospective, randomized trial of gauze and two polyurethane dressings for site care of pulmonary artery catheters: Implications for catheter management. *Crit Care Med* 1994; 22:1729–1737
- Trick WE, Vernon MO, Welbel SF, et al: Unnecessary use of central venous catheters: The need to look outside the intensive care unit. *Infect Control Hosp Epidemiol* 2004; 25:266–268
- 22. Shapey IM, Foster MA, Whitehouse T, et al: Central venous catheter-related bloodstream infections: Improving post-insertion catheter care. J Hosp Infect 2009; 71:117–122
- Timsit JF: Central venous access in intensive care unit patients: Is the subclavian vein the royal route? *Intensive Care Med* 2002; 28:1006–1008
- 24. Merrer J, De Jonghe B, Golliot F, et al: French Catheter Study Group in Intensive Care: Complications of femoral and subclavian venous catheterization in critically ill patients: A randomized controlled trial. *JAMA* 2001; 286:700–707
- Fridkin SK, Pear SM, Williamson TH, et al: The role of understaffing in central venous catheter-associated bloodstream infections. *Infect Control Hosp Epidemiol* 1996; 17: 150–158
- Hugonnet S, Chevrolet JC, Pittet D: The effect of workload on infection risk in critically ill patients. *Crit Care Med* 2007; 35:76–81

- Robert J, Fridkin SK, Blumberg HM, et al: The influence of the composition of the nursing staff on primary bloodstream infection rates in a surgical intensive care unit. *Infect Control Hosp Epidemiol* 2000; 21:12–17
- Pronovost P, Needham D, Berenholtz S, et al: An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006; 355:2725–2732
- 29. Mermel LA: Prevention of central venous catheter-related infections: What works other than impregnated or coated catheters? *J Hosp Infect* 2007; 65 Suppl 2:30–33
- 30. Vandijck DM, Labeau SO, Secanell M, et al: The role of nurses working in emergency and critical care environments in the prevention of intravascular catheter-related bloodstream infections. *Int Emerg Nurs* 2009; 17:60–68
- Furuya EY, Dick A, Perencevich EN, et al: Central line bundle implementation in US intensive care units and impact on bloodstream infections. *PLoS ONE* 2011; 6:e15452
- Davidoff F: Heterogeneity is not always noise: Lessons from improvement. JAMA 2009; 302:2580–2586
- 33. Guerin K, Wagner J, Rains K, et al: Reduction in central line-associated bloodstream infections by implementation of a postinsertion care bundle. *Am J Infect Control* 2010; 38:430–433
- 34. Keene D, Hennessey I, Rakoczy G: Central venous line dressings: Can you stick it? *J Pediatr Surg* 2009; 44:432–435