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A needleless closed system device (CLAVE) protects from intravascular catheter tip and hub colonization: a prospective randomized study☆

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Catheter-related infection; Catheter-related bloodstream infection; Hub colonization; Tip colonization; CLAVE; Needleless catheter; Needlesticks; Cardiac surgery; Cardiothoracic intensive care unit

Summary Hub colonization and subsequent intraluminal progression due to frequent opening and manipulation of intravenous systems is the cause of many catheter-related infections (CRI). A prospective, comparative, randomized study was performed to assess a new closed-needleless hub device (CLAVE®) compared with conventional open systems (COS). End-points were hub and skin colonization, catheter tip colonization, catheter-related bloodstream infection (CRBSI) and number of accidental needlesticks. All cultures were processed following standard semiquantitative microbiological techniques. The study involved patients who underwent heart surgery over an 11-month period in a post-surgical ICU. During the study period, 352 patients underwent major heart surgery and 1774 catheters were inserted. Overall, 865 catheters in 178 patients were allocated to the CLAVE system and 909 catheters in 174 patients to COS. The groups were similar regarding underlying conditions and risk factors for infection. Comparison of endpoint results in CLAVE and COS groups was as follows: incidence density per 1000 catheter-days of tip colonization: 59.2 versus 83.6 ($P = 0.003$); of hub colonization: 7.56 versus 24.66 ($P = 0.0017$); of skin colonization: 41.5 versus 58.9 ($P = 0.038$); and of CRBSI 3.78 versus 5.89 ($P = 0.4$). There was one accidental needlestick and one catheter-related prosthetic endocarditis in the COS group. Multivariate analysis showed that CLAVE use was an independent protective factor for tip colonization. CLAVE offered significant protection from catheter-tip and hub colonization.

☆ CLAVE systems for the study were provided free of charge by the manufacturer who did not take part in the design, development or analysis of the results. A travelling grant for the presentation of the preliminary results in the 41st ICAAC Meeting (Abs 2048) was also provided.

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Introduction

Patients undergoing cardiac surgery are at high risk of developing catheter-related colonization (CRC) due to the need for multiple invasive intravascular devices (e.g. circulatory assistance devices, pulmonary artery catheters, etc.) and frequent jugular insertion.[1-3] Patients with valvular prosthesis are also at special risk for nosocomial endocarditis when suffering catheter-related bloodstream infections (CRBSI).[4,5] Strict application of new educational guidelines[6-9] and the design of innovative and more infection-resistant devices[10-13] are among the most important tools to reduce CRBSI.

In a previous study, we observed that educational strategies improved catheter care and significantly reduced skin colonization around the skin insertion site. However, the educational programme did not affect of hub colonization.[14]

Although extraluminal progression of microorganisms is the most common cause of catheter tip colonization, hub colonization due to frequent opening and manipulation of intravenous systems in intensive care units is the cause of 29–38% of catheter infections[15,16] and of 60% of CRBSI.[16,17] Strategies aimed at reducing hub colonization have an impact on reducing the rate of CRBSI.[18,19]

The CLAVE® closed system consists of different types of swabable one-piece devices that allow the connection of syringes and luers to peripheral and central vascular catheters (Figure 1). These connectors reduce needlestick injuries but are also claimed to lower the likelihood of contamination of the catheters by the internal route. It does not permit the use of needles, thereby forcing compliance with needle-free policies. Following the manufacturer's recommendations it has to be swabbed with a disinfectant substance before and after each manipulation and CLAVE systems have to be changed only every seven days. However, it has never been evaluated in a properly designed prospective clinical study.

We performed a prospective, randomized, comparative study to assess the efficacy in the prevention of CRC of a new closed-needless hub device (CLAVE) as compared with conventional open systems (COS) in a heart surgery intensive care unit (HSICU).

Material and methods

Patients and catheter care

Our hospital is a 1750-bed tertiary referral general teaching institution serving a population of approximately 650000 inhabitants, with about 50000 admissions per year. The HSICU of our hospital is an 11-bed post-surgical unit for all adult patients who have undergone a major cardiac surgical procedure.

Heart surgery patients admitted to the HSICU during the 11-month study period (1 June, 2000 to 30 April, 2001) were included in the study. Nurse to patient ratio in this unit is 1:2. Patients arrive from the operating room with intravascular preanaesthetic lines in place. These include an arterial line (radial or femoral), Swan-Ganz catheter (jugular or subclavian), central line (jugular or subclavian), a peripheral catheter, and sometimes others. Jugular lines are preferred during surgery and subclavian lines are mostly used with chronic patients who require secondary catheter placements. Experienced anaesthesiologists or heart surgeons insert all catheters following aseptic standards. Surgical prophylaxis consisted of three doses of cefazolin, or a single dose of vancomycin in penicillin-allergic patients. All patients were followed-up by an infectious diseases physician to determine the presence of catheter-related infection.

Study protocol

During the 11-month study period, patients were randomly allocated to receive care with either COS or CLAVE (ICU Medical, Inc., San Clemente, CA, USA) before surgery. Patients were not switched from one group to another so each patient always received the same type of catheters during their hospital stay. When new catheters had to be inserted, the same type was always used.

CLAVE was used according to the manufacturer's instructions, which include disinfecting the connector with 2% chlorhexidine before and after each use. CLAVE systems for the study were provided

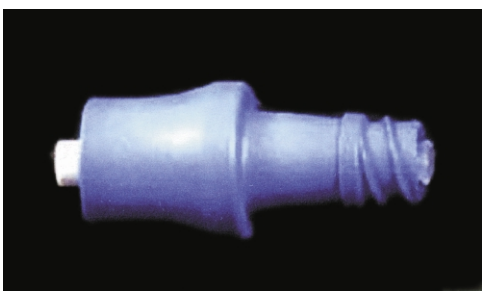

Figure 1 The CLAVE system consists of a one-piece device that allows the needlefree connection of syringes and luers to peripheral and central vascular catheters.

free of charge by the manufacturer. Chlorhexidine was also used to disinfect COS systems hubs.

Catheters in place for more than five days were surveyed by taking cultures of the skin insertion site and all hubs according to a methodology previously described by our group.[15] In summary, hub culture was performed by introducing an alginate swab able to fit within the hub. All cultures were processed following standard semi-quantitative microbiological techniques.

Following the manufacturer's instructions, CLAVE systems were changed every seven days, whereas COS systems were changed every three days following our current Nosocomial Infection Prevention Committee Guidelines. Site dressing consisted of sterile gauze and tape, which was replaced every 72 h or more frequently if required.

The end-points of our study were: catheter hub, skin and tip colonization, CRBSI and accidental needlesticks. Catheters were changed or withdrawn depending on patient outcome or needs at different points during their post-surgical period according to their physician's decision. All catheter tips were sent to the clinical microbiology department and were processed using Maki's semi-quantitative culture method.[20] Peripheral blood cultures and other samples were obtained when clinically indicated. Cultures were interpreted in a blinded fashion by clinical microbiologists.

The research and ethical committees of the hospital endorsed the study.

The manufacturers of CLAVE did not take part in the design of the protocol, its development or in the analysis of the data.

Protocol data

Patient and catheter data were recorded in a pre-established protocol.

Recorded data included: age, sex, admission date, underlying disease, ASA index, NNIS index and severity of the heart disease by means of the EuroSCORE[21] Canadian Cardiac Society (severity of angina) and New York Heart Association (NYHA) scores.

Surgical data recorded included: date of surgery, elective or urgent indication, type of surgery, extracorporeal circulation time, aortic clamping time, total surgical time, reintervention, surgical incidents, surgical prophylaxis and number and location of drainages.

Post-surgery recorded data included: HSICU admission and discharge date, hospital discharge date, APACHE II score at ICU admission, need for reintervention for bleeding, inotropic drug support, mechanical adjunctive cardiocirculatory support (ventricular assistance or intra-aortic balloon counterpulsation), duration of ventilatory support, drains, bladder catheterization, and intravascular lines, nosocomial infections not related to intravascular catheters, catheter-tip colonizations, CRBSI, the daily defined doses of antimicrobials required and the clinical cause of the patient.

For each intravascular line the following data were recorded: type of system (COS or CLAVE), type of catheter, insertion site, date of insertion and withdrawal, main use of the catheter, cause of removal, number of dressing changes, result of tip, skin and hub cultures, and presence or absence of related bloodstream infection.

The satisfaction of the nurses with one or other system, and the number of accidental needlesticks were also recorded.

Definitions

Catheter colonization was defined as the presence of $\geq$15 cfu in the semiquantitative culture of the catheter tip according to Maki's technique. CRBSI was defined as the isolation of the same organism (i.e. identical species, antibiogram) from a semi-quantitative culture of a catheter segment and from the blood drawn from a peripheral vein of a patient with accompanying clinical symptoms of BSI and no other apparent source of infection. Centers for Disease Control and Prevention definitions of other nosocomial infections were used. Micro-organisms were identified according to standard microbiological procedures.

Statistical analysis

The significance of the differences between the two study groups was determined by means of Student's *t*-test for continuous variables and chi-square or Fisher's exact test for categorical variables. Risk factors for catheter-related infections were determined by including variables that were significant in the univariate analysis into a stepwise logistic regression with adjustment for length of hospital stay, device use, and patient comorbidities. The receiver operator characteristic (ROC) curve analysis was employed to evaluate each model (risk factors for catheter tip colonization and for CRBSI). All *P*-values were based on a two-tailed test of significance. Statistical analysis was performed with SPSS version 9.0.

Anonymous survey of nurses

An anonymous questionnaire was given to all nurses in the unit asking for their preferences

(conventional or CLAVE systems) and the problems they found with each system.

Results

During the study period, 352 patients who underwent a major heart surgical procedure were randomized to CLAVE (178) or COS (174). An additional group of seven patients could not be included in the study because of deficient randomization. Overall, 1774 catheters were inserted (a median of five catheters per patient): 865 were allocated to CLAVE and 909 to COS. We were able to evaluate complete data from 1708 catheters (96.3%), 838 CLAVE and 870 COS. The main reason for these losses was that the catheter was not sent to the microbiology laboratory for culture. These catheters were equally distributed in both groups.

The two groups of patients had similar characteristics before the surgical procedure (Table I). The following variables, which were also similar among both study groups, were not included in the table due to space restrictions and because they are part of more global scores: malnutrition, smoking, alcohol abuse, hypertension, hyperlipidaemia, Canadian Cardiac Society Score, left ventricular ejection fraction and pulmonary hypertension.

Type and length of surgery and post-surgical complications were also similar for both populations (Table I). Variables shown in the table, which were also similar in both groups, include: need for inotropic support, time on mechanical ventilation, duration of drains, duration of bladder catheterization, patients with open sternum, need for intra-aortic balloon or ventricular assistance device, need for haemodialysis or tracheostomy.

The type and main use of the catheters is shown in Table II. Overall accumulated catheter-days were 8.9 ± 11.1 in COS patients and 10.7 ± 15.9 in CLAVE patients ($P = 0.22$). No significant differences were found with regard to removal reasons.

CRC rates are shown in Table II. Compared with standard systems, CLAVE patients were less likely to have a catheter tip colonization (10.9 versus 17.2%, $P < 0.0001$). Incidence density of tip colonization per 1000 catheter-days [59.2 versus 83.6, relative risk 0.58 (OR 0.4–0.8) $P = 0.003$] and incidence density of tip colonizations per 100 days of ICU stay [92.8 versus 123, relative risk 0.58 (CI 0.4–0.7); $P = 0.0002$] were also significantly reduced in the CLAVE group. When type of catheter was analysed, CLAVE significantly reduced the incidence of colonization in Swan-Ganz catheters, central lines and peripheral lines (data not shown).

Despite a reduction of 46% in the incidence of CRBSI in the CLAVE group (3.4 versus 6.3%), this difference did not reach statistical significance ($P = 0.22$). When expressed as incidence density per 1000 catheter-days (3.78 versus 5.89; $P =$ nonsignificant) and as cumulative incidence/100 catheters (0.7 versus 1.3; $P =$ nonsignificant), CLAVE patients again had a lower rate of CRBSI, although not statistically significant (Table II). No peripheral catheter was considered the origin of a CRBSI.

Surveillance skin and hub cultures were obtained from 279 (32.3%) CLAVE and from 324 (35.6%) COS catheters in place for more than five days. CLAVE patients had a significantly lower rate of colonized hub cultures [4.3 versus 14.2%, $P < 0.0001$; density per 1000 catheter-days 7.5 versus 24.6, relative risk 0.28 (CI 0.12–0.63); $P = 0.0017$]. The incidence of skin colonization was also lower for CLAVE patients (34%; 41.5 per 1000 catheter days) than for COS patients (23.7%; 58.9 per 1000 catheter days). This difference was significant (Table II).

With regard to aetiology, Gram-positive microorganisms clearly predominated in all types of cultures (catheter tip, skin site and hub). *Staphylococcus epidermidis* was the most commonly isolated agent and accounted for 82% of tip colonizations in both groups.

The incidence of other nosocomial infections in both groups was not significantly different (COS 27.6% and CLAVE 22.5%; $P = 0.27$). It is worth mentioning that the only episode of prosthetic endocarditis was detected in the COS group in a patient who had had a CRBSI.

Despite a trend towards a higher use of daily defined doses (DDDs) of antimicrobial agents in the COS group (8.04 ± 23.6 in the CLAVE group and 13.2 ± 31.9 in the COS group; $P = 0.08$), neither DDDs nor global antimicrobial costs were significantly different between both groups.

Mean post-surgical stay in hospital (COS 18.5 ± 22.7 and CLAVE 18.6 ± 31.2; $P = 0.85$) and in the ICU (COS 7.3 ± 16.2 and CLAVE 5.7 ± 10.6; $P = 0.27$) was similar for both groups. Overall, mortality was higher in the COS group [20 patients (11.5%)] than in the CLAVE group [10 patients (5.6%); $P = 0.05$], however there were no differences in infection-related mortalities. Infection accounted for five (COS) and two (CLAVE) deaths, respectivey (NS).

Only one nurse suffered an accidental needle puncture during the study period and this happened with a COS catheter. No adverse events were related to the use of the CLAVE connectors. The opinion of the nurses was requested before disclosing the results of the study. We gave nurses an

Table I Epidemiological, surgical and post-surgical characteristics of the patients

	CLAVE ($N = 178$)	COS ($N = 174$)	P
Age (years) (mean ± SD)	63.94 ± 13.18	64.89 ± 11.60	0.473
Sex (male; female)	102(57%); 76(43%)	116(67%); 58(33%)	0.070
APACHE II score	8.29 ± 3.22(8)	8.66 ± 3.40(8)	0.290
ASA score			0.200
II	2 (1.1%)	2 (1.1%)	
III	144 (80.9%)	126 (72.4%)	
IV	29 (16.3%)	38 (21.8%)	
V	3 (1.7%)	8 (4.6%)	
NNIS score			0.238
C	154 (86.5%)	140 (80.5%)	
D	19 (10.7%)	24 (13.8%)	
E	5 (2.8%)	10 (5.7%)	
Obesity	26 (14.6%)	19 (10.9%)	0.300
Diabetes mellitus	42 (23.5)	44 (25.2%)	0.873
EuroScore (median ± SD)	6.60 ± 2.96	6.36 ± 2.97	0.450
NYHA score			0.716
I	55 (30.9%)	62 (35.6%)	
II	37 (20.8%)	35 (20.1%)	
III	68 (38.2%)	64 (36.8%)	
IV	18 (10.1%)	13 (8.0%)	
Type of surgery			0.919
Valvular	92 (51.7%)	87 (50%)	
Coronary bypass	58 (32%)	53 (30.5%)	
Valvular and bypass	16 (9%)	19 (10.9%)	
Transplant	6 (3.4%)	7 (4%)	
Others	6 (3.4%)	8 (4.6%)	
Duration of surgery (median ± SD)			
Extracorporeal circulation (minutes)	120.74 ± 49.93	116.65 ± 53.04	0.457
Aortic clamp (minutes)	76.90 ± 32.67	71.12 ± 32.50	0.097
Surgical time (hours)	4.13 ± 1.19	4.10 ± 1.21	0.931
Urgent surgery	16 (8.9%)	22 (12.6%)	0.269
Reintervention	21 (11.8%)	21 (12.1%)	0.937
Reintervention due to bleeding	10 (5.6%)	17 (9.8%)	0.143
Need for inotropic support	90 (50.6%)	94 (54.0%)	0.192
Time on mechanical ventilation (hours)	42.94 ± 103.90	58.62 ± 131.63	0.215
Duration of drains (days) (median ± SD)	2.15 ± 0.77	2.25 ± 1.08	0.310
Days of bladder catheterization	5.15 ± 11.72	7.40 ± 15.83	0.130
Intra-aortic balloon counterpulsation	15 (8.4%)	20 (11.5%)	0.336
Ventricular assistance device (ABIOMED)	3 (1.7%)	1 (0.6%)	0.326
Haemodialysis	6 (3.4%)	8 (4.6%)	0.556
Post-surgical stay in the ICU median ± SD	5.7 ± 10.6	7.3 ± 16.2	0.274
Post-surgical stay in the hospital	18.6 ± 31.2 (10)	18.5 ± 227 (10)	0.850

ASA: American Society of Anesthesiology; NNIS: National Nosocomial Infections Surveillance; NYHA: New York Heart Association.

anonymous survey asking which system they preferred and what problems they encountered. Thirty-three nurses completed the survey (95%). In summary, 82% preferred CLAVE, although most suggested reserving this system for patients who require a prolonged stay in the ICU. This was because CLAVE connectors were more difficult to use in critical situations (common in the immediate postoperative period) when very rapid infusion was required and many urgent accesses had to be made. Although the protocol was not violated in any case, CLAVE management was found more difficult under such circumstances.

Finally, in order to assess whether the use of CLAVE connectors had an independent protective effect, we performed a stepwise multivariable analysis of risk factors for catheter tip colonization.

Factors that increased the risk of CRC in the univariate analysis included: a high Euroscore ($P = 0.002$), a high APACHE II score (9.3 versus 7.9; $P < 0.0001$), a high ASA score (ASA IV 31.4 versus 10.8%, $P < 0.0001$), a high NNIS score ($P < 0.0001$), poor ventricular fraction before surgery ($P < 0.0001$), prolonged extracorporeal circulation ($P < 0.0001$), urgent indication for surgery ($P < 0.0001$), reintervention for bleeding

Table II Characteristics of the catheters and catheter-related infections

	CLAVE ($N = 865$)	COS ($N = 909$)	P
Type of catheter			0.164
Swan-Ganz	187 (21.6%)	192 (21.1%)	
Jugular central line	186 (21.5%)	187 (20.6%)	
Subclavian central line	20 (2.3%)	31 (3.4%)	
Femoral central line	9 (1.0%)	11 (1.2%)	
Radial-humeral arterial line	209 (24.2%)	203 (22.3%)	
Femoral arterial line	5 (0.6%)	11 (1.2%)	
Peripheral	249 (28.8%)	274 (30.1%)	
Use of the catheters			0.621
Medication (fluid or drug therapy)	436 (50.4%)	466 (51.3%)	
Parenteral nutrition	18 (2.1%)	27 (3%)	
Haemodynamic monitoring	400 (46.2%)	404 (44.4%)	
Haemofiltration	11 (1.3%)	12 (1.3%)	
Mean days of catheter exposure (catheter-days)	8.9 ± 11.1	10.7 ± 15.9	0.22
Number of dressing changes (median ± SD)	2.36 ± 3.3	2.67 ± 3.7	0.061
Cause of withdrawal			0.273
End of therapy	681 (78.7%)	685 (75.4%)	
Suspicion of infection	53 (6.1%)	75 (8.3%)	
Dysfunction	56 (6.5%)	62 (6.8%)	
Others	75 (8.7%)	87 (9.6%)	
Tip colonization	94 (10.9%)	156 (17.2%)	0.0001
Density per 1000 catheter-days	59.2	83.6	0.003
Density per 100 days of ICU stay	92.8	123	0.0002
Episodes of CRBSI	6 (3.4%)	11[a] (6.3%)	0.22
Cumulative incidence/100 catheters	0.72	1.21	1
Density per 1000 catheter-days	3.78	5.89	0.4
Catheters with surveillance cultures	279 (32.3%)	324 (35.6%)	0.133
Skin colonization	66 (23.7%)	110 (33,9%)	0.002
Density per 1000 catheter-days	41.5	58.9	0.038
Hub colonization	12 (4.3%)	46 (14.2%)	0.0001
Density per 1000 catheter-days	7.5	24.6	0.0017

[a] In nine patients.

(13.6 versus 3.8%, $P < 0.002$), transfusional needs ($P < 0.0001$), need for inotropic support (68 versus 41%, $P < 0.001$), duration of mechanical ventilation (98 versus 19 h, $P < 0.0001$), duration of bladder catheterization (11.3 versus 2.9 days, $P < 0.0001$), intra-aortic balloon counterpulsation (18.6 versus 4.2%, $P < 0.0001$), haemodialysis (8.6 versus 0.9%, $P < 0.0001$), tracheostomy (10 versus 0.9%, $P < 0.0001$), use of the catheter ($P < 0.0001$), type of connectors (CLAVE 37 versus 51%, $P < 0.0001$), hub colonization (10.8 versus 2%, $P < 0.0001$) and skin colonization (39.6 versus 5%, $P < 0.0001$).

Multivariate analysis identified the following as independent risk factors for colonization: the need for urgent surgery (OR 3), jugular central line (OR 2.2), hub colonization (OR 2.4) and skin colonization (OR 8.2; Table III). The use of CLAVE was found to be an independent protective factor (OR −0.63; 95% CI 0.46-0.85) and this effect persisted over time as shown in the Kaplan-Meier analysis (Figure 2; $P < 0.05$).

Independent risk factors for CRBSI were hub colonization (OR 11.4), urgent surgery (OR 4.4), prolonged extracorporeal circulation (minutes) (OR 1.01), and prolonged exposure to the catheter (days) (OR 1.08) (Table IV). No CRBSI was caused by peripheral catheters. The ROC curves analysis showed that both multivariate models were accurate. (Areas under the curve of 0.90 for prediction of BSI and 0.81 for prediction of catheter tip colonization.)

Discussion

Patients undergoing heart surgery are exposed to a high risk of infectious complications due to their age and underlying diseases, the high number of central lines required and the perisurgical need for a jugular insertion site.[3-11,22-25] Catheter-related infections cause significant morbidity and resource use,[26-28] so maximum effort must be made to prevent them.[29] In this study, 6.3% of the patients with conventional catheters suffered a CRBSI and 17% a catheter tip colonization. These figures are

consistent with other studies in cardiac surgery patients (5.9% of CRBSI and 23.8% of tip colonizations, respectively)[11] and in other groups of intensive care patients (8.7 and 21%, respectively).[16] Our figures of CRBSI are higher than those provided by the NNIS report from cardiothoracic units in the USA (median value 2.4 per 1000 catheter-days).[30] Our hospital is a referral centre for cardiovascular surgery, taking care of complicated cases and elderly populations. We believe that this may account, in part, of our results and was one of the reasons we initiated this study.

Catheter colonization may occur as a consequence of contamination during insertion, skin colonization and extraluminal progression or hub contamination and endoluminal progression. Colonization of the hub and intraluminal progression is, however, more frequently associated with severe infections, such as CRBSI (52–70%).[16,30–39] Moreover, hub colonization was found as an independent risk factor for CRC (OR, 17.9; CI95, 2.4–132) and for symptomatic infection (OR, 36.6; CI95, 7–190).[31]

Several devices for reducing hub colonization have demonstrated their utility. A commercially available (not in Europe) chlorhexidine-impregnated sponge dressing placed around the catheter hub of short-term arterial and uncuffed CVCs led to a threefold reduction in CRBSIs in a recent prospective, multi-centre randomized study.[18]

A catheter hub containing an antiseptic chamber filled with 3% iodinated alcohol led to a fourfold reduction (RR 0.2, CI 0.1–0.7) in the incidence of infections in a prospective, randomized trial of catheters in place for approximately two weeks.[17–19] The device has recently been modified to avoid intravenous spillage of iodine that was a cause of concern with the first design.[12] However, this new hub device was no more effective in preventing CRC than standard good clinical procedures in a recent study.[32]

Previous studies with needleless devices suggested the potential risk of microbial contamination of the device and associated infection, especially in a home-care setting.[33–36] Recent data suggest that when the device is properly disinfected before each puncture according to the manufacturer's recommendations, there was no increased rate of contamination.[34,37–40] Their effectiveness in reducing percutaneous injuries to staff is well established, although strong data evaluating the clinical impact of these devices in patients is lacking.[41]

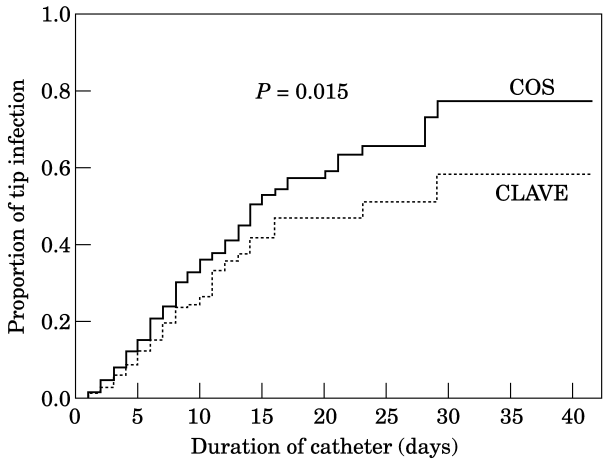

Figure 2 Analysis of the Kaplan–Meier estimates of the risk of catheter tip colonization according to the length of time the catheters were in place in each group showed that CLAVE group catheters were less likely to be colonized over time (log-rank test $P = 0.015$).

The CLAVE Connector is a one piece, swabable intravenous connection system designed to eliminate intravenous-related needlesticks without the use of additional cannulas or caps.

The study shows that when CLAVE was used, there was a significant reduction in hub colonization (4.3 versus 14.2%, $P < 0.0001$) and catheter tip colonization (10.9 versus 17.2%, $P < 0.0001$). It has recently been published that catheter-tip colonization is a good surrogate endpoint for CRBSI[42] and in our study we found that hub colonization is an independent risk factor for CRBSI. However,

Table III Independent risk factors for CRI

	Odds ratio	β	*P*-value	95% CI
Patient characteristics				
Urgent surgery	3.0289	1.1082	0.096	1.31–7.01
Catheter characteristics				
Jugular central line	2.2195	0.7973	<0.0001	1.58–3.11
Hub colonization	2.4253	0.8860	0.0097	1.24–4.74
Skin colonization	8.1557	2.0987	<0.0001	5.64–11.79
Radial–humeral arterial line	0.2009	−1.6049	<0.0001	0.10–0.41
CLAVE connectors	0.6285	−0.4644	0.0033	0.46–0.86

Multivariate logistic regression analysis.

Table IV Independent risk factors for catheter-related bloodstream infection

	Odds ratio	β	*P*-value	95% CI
Patient characteristics				
Urgent surgery	4.3988	1.4813	0.0199	1.26-15.31
Extracorporeal circulation (minutes)	1.0122	0.0121	0.0073	1.00-1.02
Catheter characteristics				
Hub colonization	11.3869	2.4325	<0.0001	4.17-31.11
Duration of catheter	1.0759	0.0731	0.0019	1.03-1.13
Radial-humeral arterial line	0.0935	−2.3699	0.0350	0.01-0.85

Multivariate logistic regression analysis.

although patients who received CLAVE connectors showed a 46% reduction in the rate of CRBSI (3.4 versus 6.3%), probably due to the low number of BSI in our population, it did not reach statistical significance (850 patients would be needed in each arm of the study, with an α error of 0.05 and a power of 85%). Other authors demonstrated that an intensive intervention reduced central venous catheter colonization but did not achieve a significant reduction in the rate of bacteraemia.[43]

The study also showed that hub colonization (OR 11.4), urgent surgery (OR 4.4), prolonged extracorporeal circulation, and prolonged exposure to the catheter were independent risk factors for developing a CRBSI (Table IV).

The use of the CLAVE system was found to be an independent protective factor for catheter tip colonization (OR 0.63; 95% CI 0.46-0.85), probably because it reduces hub colonization. Finally, it is worth mentioning that the only episodes of accidental needlestick and valvular prosthesis-associated endocarditis occurred in patients with conventional connectors. The explanation for these findings may be related to the fact that the CLAVE system avoids the need for disconnection and significantly reduces the number of system changes (every seven days instead of every three days), which could account, at least partially, for the beneficial effects on catheter infection rates.[17,44]

In the study, we found that the reduction of hub colonization associated with a needleless connector also led to reduced insertion site colonization. The reason for the relation between these variables is not clear cut, but it has also been demonstrated by other authors such as Moro et al. who found that total parenteral nutrition and skin colonization were independently associated with an increased risk of hub colonization.[31]

Limitations of our study include the fact that we have only studied one type of critically ill patient. The selection of a subgroup of patients in whom the CLAVE system could prove especially efficacious (e.g., cardiac surgery patients with complicated postoperative course) is an interesting issue which deserves further study. Finally, a comparison with other preventive procedures and a detailed cost-effectiveness study should be carried out.

The CLAVE connector is well tolerated, reduces the incidence of hub and tip colonization and the number of needlesticks injures. Further studies are needed to clarify their influence over long-term catheters and on BSI episodes, hospital stay, and mortality.

References

1. Henar M, Bernal JM, Llorca J, Rabasa JM, Revuelta JM. Nosocomial infections in patients having cardiovascular operations: a multivariate analysis of risk factors. *J Thorac Cardiovasc Surg* 1996;**112**:908—913.
2. Kollef MH, Sharpless L, Vlasnik J, Pasque C, Murphy D, Fraser VJ. The impact of nosocomial infections on patient outcomes following cardiac surgery. *Chest* 1997;**112**:666—675.
3. Erez E, Sharoni E, Ovadia B, Vidne BA, Dagan O. Septic emboli caused by vascular catheters after surgery for congenital heart disease. *Crit Care Med* 2000;**28**:845—847.
4. Gordon S, Keys T. Bloodstream infections in patients with implanted prosthetic cardiac valves. *Semin Thoracic Cardiovasc Surg* 1995;**7**:2—6.
5. Fang G, Keys T, Gentry L, et al. Prosthetic valve endocarditis resulting from nosocomial bacteremia. *Ann Intern Med* 1993; **119**:560—567.
6. Mermel LA. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000;**132**:391—402.
7. Raad II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994;**15**:231—238.
8. Sherertz RJ, Ely EW, Westbrook DM, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med* 2000;**132**:641—648.
9. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000;**355**:1864—1868.
10. Maki DG, Stolz SM, Wheeler S, Mermel LA. Prevention of central venous catheter-related bloodstream infection by

use of an antiseptic-impregnated catheter. A randomized, controlled trail. *Ann Intern Med* 1997;**127**:257—266.
11. Bach A, Eberhardt H, Frick A, Schmidt H, Böttiger BW, Martin E. Efficacy of silver-coating central venous catheters in reducing bacterial colonization. *Crit Care Med* 1999;**27**: 515—521.
12. Mermel LA. New technologies to prevent intravascular catheter-related bloodstream infections. *Emerg Infect Dis* 2001;**7**:197—199.
13. Veenstra DL, Saint S, Sullivan SD. Cost-effectiveness of antiseptic-impregnated central venous catheters for the prevention of catheter-related bloodstream infection. *JAMA* 1999;**282**:554—560.
14. Parras F, Ena J, Bouza E, et al. Impact of an educational program for the prevention of colonization of intravascular catheters. *Infect Control Hosp Epidemiol* 1994;**15**:239—242.
15. Cercenado E, Ena J, Rodriguez-Creixems M, Romero I, Bouza E. A conservative procedure for the diagnosis of catheter-related infections. *Arch Intern Med* 1990;**150**:1417—1420.
16. Diener JR, Coutinho MS, Zoccoli CM. Central venous catheter-related infections in critically ill patients. *Rev Assoc Med Bras* 1996;**42**:205—214.
17. Sitges-Serra A, Hernandez R, Maestro S, Pi-Suner T, Garces JM, Segura M. Prevention of catheter sepsis: the hub. *Nutrition* 1997;**4**(Suppl. 13):S30—S35.
18. Maki DG, Mermel LA, Kluger D, et al. The efficacy of a chlorhixidine impregnated sponge (Biopatch) for the prevention of intravascular catheter-related infection—a prospective randomized controlled multicenter study. Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, Ont., Canada, 2000; Washington: American Society for Microbiology; 17—20 September 2000.
19. Segura M, Alvarez-Lerma F, Tellado JM, et al. A clinical trial on the prevention of catheter-related sepsis using a new hub model. *Ann Surg* 1996;**223**:363—369.
20. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med* 1977;**296**:1305—1309.
21. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg* 1999;**16**: 9—13.
22. Damen J, Van der Tweel I. Positive tip cultures and related risk factors associated with intravascular catheterization in pediatric cardiac patients. *Crit Care Med* 1988;**16**:221—228.
23. Kriaras I, Michalopoulos A, Michalis A, et al. Antibiotic prophylaxis in cardiac surgery. *J Cardiovasc Surg (Torino)* 1997;**38**:605—610.
24. Zerr C, Levrot A, Fauchon G, et al. Pulmonary artery catheterization. advantages of internal jugular route. *Anesth analg (Paris)* 1981;**38**:15—19.
25. Kac G, Durain E, Amrein C, Herisson E, Fiemeyer A, Buu-Hoi A. Colonization and infection of pulmonary artery catheter in cardiac surgery patients: epidemiology and multivariate analysis of risk factors. *Crit Care Med* 2001;**29**:971—975.
26. Dimick JB, Pelz RK, Consunji R, Swoboda SM, Hendrix CW, Lipsett PA. Increased resource use associated with catheter-related bloodstream infection in the surgical intensive care unit. *Arch Surg* 2001;**136**:229—234.
27. Soufir L, Timsit JF, Mahe C, Carlet J, Regnier B, Chevret S. 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.
28. Rello J, Ochagavia A, Sabanes E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med* 2000;**162**:1027—1030.
29. Bach A. Prevention of infections caused by central venous catheters—established and novel measures. *Infection* 1999; **1**(Suppl. 27):S11—S15.
30. system. ArftN., National Nosocomial Infections Surveillance System Report. Data summary from January 1992—June 2001. *Am J Infect Control* 2000;**29**:404—421.
31. Moro ML, Vigano EF, Cozzi LA. 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**:253—264.
32. Luna J, Masdeu G, Perez M, et al. Clinical trial evaluating a new hub device designed to prevent catheter-related sepsis. *Eur J Clin Microbiol Infect Dis* 2000;**19**:655—662.
33. Danzig LE, Short LJ, Collins K, et al. Bloodstream infections associated with a needleless intravenous infusion system in patients receiving home infusion therapy. *JAMA* 1995;**273**: 1862—1864.
34. Cookson ST, Ihrig M, EM OM, et al. Increased bloodstream infection rates in surgical patients associated with variation from recommended use and care following implementation of a needleless device. *Infect Control Hosp Epidemiol* 1998; **19**:23—27.
35. McDonald LC, Banerjee SN, Jarvis WR. Line-associated bloodstream infections in pediatric intensive-care-unit patients associated with a needleless device and intermittent intravenous therapy. *Infect Control Hosp Epidemiol* 1998;**19**:772—777.
36. Do AN, Ray BJ, Banerjee SN, et al. Bloodstream infection associated with needleless device use and the importance of infection-control practices in the home health care setting. *J Infect Dis* 1999;**179**:442—448.
37. Brown JD, Moss HA, Elliott TS. The potential for catheter microbial contamination from a needleless connector. *J Hosp Infect* 1997;**36**:181—189.
38. Arduino MJ, Bland LA, Danzig LE, McAllister SK, Aguero SM. Microbiologic evaluation of needleless and needle-access devices. *Am J Infect Control* 1997;**25**:377—380.
39. Luebke MA, Arduino MJ, Duda DL, et al. Comparison of the microbial barrier properties of a needleless and a conventional needle-based intravenous access system. *Am J Infect Control* 1998;**26**:437—441.
40. Seymour VM, Dhallu TS, Moss HA, Tebbs SE, Elliot TS. A prospective clinical study to investigate the microbial contamination of a needleless connector. *J Hosp Infect* 2000;**45**:165—168.
41. Mendelson MH, Short LJ, Schechter CB, et al. Study of a needleless intermittent intravenous-access system for peripheral infusions: analysis of staff, patient, and institutional outcomes. *Infect Control Hosp Epidemiol* 1998;**19**:401—406.
42. Rijnders BJA, Van Wijngaerden EV, 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**:1053—1058.
43. Bijma R, Girbes AR, Kleijer DJ, Zwaveling JH. Preventing central venous catheter-related infection in a surgical intensive-care unit. *Infect Control Hosp Epidemiol* 1999; **20**:618—620.
44. Mahieu LM, De Dooy JJ, Lenaerts AE, Ieven MM, De Muynck AO. Catheter manipulations and the risk of catheter-associated bloodstream infection in neonatal intensive care unit patients. *J Hosp Infect* 2001;**48**:20—26.