Randomized Controlled Trial of Chlorhexidine Dressing and Highly Adhesive Dressing for Preventing Catheter-related Infections in Critically III Adults

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Category Name	Total Journals in Category	Journal Rank in Category	Quartile in Category
CRITICAL CARE MEDICINE	26	1	Q1
RESPIRATORY SYSTEM	48	1	Q1



A - CRITICAL CARE MEDICINE

B - RESPIRATORY SYSTEM

Introduction

- Central venous catheter (CVC)-related bloodstream infections (BSIs) are associated with attributable mortality rates of up to 11.5% and excess ICU stay lengths of up to 12 days.
- Combining this catheter-care bundle with continuous quality improvement programs can decrease the CR-BSI rate below 2 per 1,000 CVC days .
- Most organisms responsible for short-term CR-BSIs originate from the insertion site.

Decreasing bacterial skin colonization at the insertion site by improving dressing adhesion or using antisepticimpregnated dressings may decrease the CR-BSI risk.

步驟 I:研究探討的問題為何?

研究族群 / 問題 (Population/ Problem):

- 1. The patient in the ICU
- 2. (18 yr) admitted to <u>12 ICUs</u> in <u>seven university</u> and <u>four general</u> <u>hospitals.</u>
- 3. Expected to require intravascular catheterization for 48 hours

介入措施 (Intervention):

highly adhesive Dressing



Chlorhexidine Dressing



比較 (Comparison):

- 1. A highly adhesive Dressing (Tegaderm HP Transparent Film Dressing)
- 2. A standard breathable, hypoallergenic dressing (Tegaderm Transparent Film Dressing).
- 3. Standard Dressing

結果: Catheter-related Infections, catheter colonization, Skin reactions

招募(Recruitment) - 受試者是否具有代表性?



- 1. We recruited adults (18 yr) admitted to <u>12 ICUs</u> in <u>seven</u> <u>university</u> and <u>four general hospitals.</u>
- 2. Expected to require intravascular catheterization for 48 hours(Inclusion).
- 3. Patients with known allergies to chlorhexidine or transparent dressings were excluded.
- 4. The study was approved by the Rhône-Alpes-4 ethics committee, France. Informed consent was obtained from patients or surrogates.(有接受IRB及受試者同意)



the permutation procedure.



1,879 were assessable for the intent-to-treat analysis, for a total of 4,163 catheters and 34,339 catheter-days. Patient and catheter characteristics are reported in Tables 1 and 2.

每個組別,在研究開始時的情況是否相同?

TABLE 1. PATIENT CHARACTERISTICS

Characteristic	All Patients ($n = 1,879$)	Standard ($n = 476$)	Highly Adhesive ($n = 465$)	Chlorhexidine ($n = 938$)
Age, yr, median (IQR)	64 (53-75)	64 (53-74)	64 (52-76)	63.5 (53-74)
Male, n (%)	1,255 (66.8)	313 (65.8)	305 (65.6)	637 (67.9)
At least one chronic disease, n (%)	587 (31.2)	154 (32.4)	135 (29)	298 (31.8)
Immune deficiency, n (%)	91 (4.8)	28 (5.9)	16 (3.4)	47 (5)
Hematologic malignancy, n (%)	53 (2.8)	14 (2.9)	8 (1.7)	31 (3.3)
Metastatic cancer, n (%)	118 (6.3)	28 (5.9)	28 (6)	62 (6.6)
AIDS, n (%)	44 (2.3)	13 (2.7)	7 (1.5)	24 (2.6)
SAPS II, median (IQR)*	51 (37-67)	49 (36-66.5)	51 (36-67)	52 (39-68)
SOFA, median (IQR) [†]	8 (5-11)	8 (5-11)	8 (5-11)	8 (5-11)
Admission category, n (%)				
Medical	1,386 (73.8)	335 (70.4)	342 (73.5)	709 (75.6)
Scheduled surgery	150 (8)	35 (7.4)	45 (9.7)	70 (7.5)
Emergency surgery	343 (18.3)	106 (22.3)	78 (16.8)	159 (17)
Main reason for ICU admission, n (%)				
Septic shock	334 (17.8)	92 (19.3)	89 (19.1)	153 (16.3)
Cardiogenic shock	128 (6.8)	29 (6.1)	37 (8)	62 (6.6)
De novo respiratory failure	488 (26)	129 (27.1)	114 (24.5)	245 (26.1)
Coma	167 (8.9)	41 (8.6)	39 (8.4)	87 (9.3)
Trauma	114 (6.1)	35 (7.4)	23 (4.9)	56 (6)
Mechanical ventilation, n (%)	1,336 (71.1)	333 (70)	333 (71.6)	670 (71.4)
Length of ICU stay, d, median (IQR)	9 (5-20)	10 (5-20)	9 (5-18)	9 (5-20)
ICU death, n (%)	586 (31.2)	141 (29.6)	152 (32.7)	293 (31.2)

Definition of abbreviations: ICU = intensive care unit; IQR = interquartile range; SAPS II = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment.

* Range of possible scores, 0-162.

[†] Range of possible scores, 0–24.

每個組別,在研究開始時的情況是否相同?

TABLE 2. CATHETER CHARACTERISTICS

			Highly	
	All Catheters	Standard	Adhesive	Chlorhexidine
Variable	(n = 4, 163)	(n = 1,067)	(n = 988)	(n = 2, 108)
Data for all vascular catheters				
Time in place, d, median (IQR)	6 (4–11)	7 (4–12)	6 (3–10)	6 (4–11)
Experience of the operator <50 procedures, n (%)	1,530 (36.8)	380 (35.6)	391 (39.6)	759 (36)
Antimicrobials at catheter insertion, n (%)	2,303 (55.3)	592 (55.5)	528 (53.4)	1,183 (56.1)
Transport to operating room with catheter in place, n (%)				
No	3,436 (82.5)	877 (82.2)	812 (82.2)	1,747 (82.9)
Once	587 (14.1)	148 (13.9)	140 (14.2)	299 (14.2)
Twice	94 (2.3)	24 (2.2)	25 (2.5)	45 (2.1)
More than twice	46 (1.1)	18 (1.7)	11 (1.1)	17 (0.8)
Transport out of ICU with catheter in place, n (%)				
No	2,638 (63.4)	675 (63.3)	632 (64)	1,331 (63.1)
Once	1,109 (26.6)	272 (25.5)	284 (28.7)	553 (26.2)
Twice	294 (7.1)	86 (8.1)	45 (4.6)	163 (7.7)
More than twice	122 (2.9)	34 (3.2)	27 (2.7)	61 (2.9)
Number of dressing changes per catheter, median (IQR)	2 (1-4)	3 (1-5)	2 (1-4)	2 (1-4)
Catheter removal for suspected infection, n (%)	563 (13.5)	155 (14.5)	130 (13.2)	278 (13.2)
Data for arterial catheters only				
Arterial catheter, n (%)	2,201 (52.9)	558 (52.3)	515 (52.1)	1,128 (53.5)
Femoral	773 (35.1)	207 (37.1)	173 (33.6)	393 (34.8)
Radial	1,428 (64.9)	351 (62.9)	342 (66.4)	735 (65.2)
Data for CVCs only				
All CVCs, n (%)	1,962 (47.1)	509 (47.7)	473 (47.9)	980 (46.5)
Jugular CVCs	728 (37.1)	180 (35.4)	175 (37)	373 (38.1)
Subclavian CVCs	567 (28.9)	152 (29.9)	140 (29.6)	275 (28.1)
Femoral CVCs	667 (34)	177 (34.8)	158 (33.4)	332 (33.9)
Guidewire exchange, n (%)	76 (3.9)	23 (4.5)	20 (4.2)	33 (3.4)
Tunneled catheters, n (%)	5 (0.3)	1 (0.2)	2 (0.4)	2 (0.2)
Venous catheter lumens, n (%)				
One	17 (0.9)	6 (1.2)	3 (0.6)	8 (0.8)
Two	201 (10.2)	50 (9.8)	42 (8.9)	109 (11.1)
Three	1,458 (74.3)	375 (73.7)	358 (75.7)	725 (74)
Greater than three	286 (14.6)	78 (15.3)	70 (14.8)	138 (14.1)
Use of lipids, n (%)	938 (47.8)	247 (48.5)	219 (46.3)	472 (48.2)
Use of heparin, n (%)	615 (31.3)	159 (31.2)	146 (30.9)	310 (31.6)
Red-blood-cell pack transfused, n (%)	766 (39)	201 (39.5)	182 (38.5)	383 (39.1)

Definition of abbreviations: CVC = central venous catheter; ICU = intensive care unit; IQR = interquartile range.

維持(Maintenance) - 各組是否給予相同的治療? 評讀結果:■是 □否 □不清楚 說明:

- 1. All used as part of standard care.
- Pulmonary arterial, hemodialysis, peripherally inserted venous catheters, and catheters inserted before ICU admission were not included.
- 3. Followed "French recommendations" for catheter insertion and care.
- The insertion sites were the radial artery and subclavian vein.
- Maximal sterile barrier precautions (large sterile drape; surgical hand antisepsis; and wearing a mask, cap, gown, and sterile gloves) were used at catheter insertion.

各組是否給予相同的治療(續)?

- Antiseptic skin preparation was with alcoholic povidoneiodine (PVI) or alcoholic chlorhexidine solution.
 - ♦ The insertion site was scrubbed with a detergent or 4% chlorhexidine solution.
 - \diamond Rinsed with sterile water; and dried with sterile gauze.
 - ♦ An alcohol-based antiseptic solution (5% PVI in 70% ethanol or 0.5% chlorhexidine, ..etc.) was then applied for at <u>least 1 minute</u>, and sterile drapes were placed around the site.
- Antiseptic- or antibiotic-impregnated catheters were not used in any of the study ICUs.
- Dressings were changed 24 hours after catheter insertion (Day 1) then every 3 or 7 days. Alcoholic PVI solution or alcoholic chlorhexidine was used for skin antisepsis during dressing changes.

各組是否給予相同的治療(續)?

- Suspected contact dermatitis or skin allergy was confirmed by a dermatologist.
- The investigator could decide to stop using the allocated dressing inpatients with suspected skin reactions.
- > Patients were followed until 48 hours after ICU discharge.
- Catheters were immediately removed if no longer needed (usually before ICU discharge) or if a CRI was suspected.
- Catheter tips were cultured using a simplified quantitative broth dilution technique with vortexing in 11 ICUs and sonication in one ICU.
- In patients who needed to keep the CVC beyond ICU discharge, paired blood samples were drawn simultaneously from the catheter hub and a peripheral vein before ICU discharge for determination of the differential time-to-positivity.

各組是否給予相同的治療(續)?

- Skin colonization was assessed using semiquantitative insertion-site cultures; the insertion site was sampled as previously reported before catheter removal by pressing a sterilized nutritive trypticase soy agar plate containing antiseptic-neutralizing agents for 10 seconds on the skin, centering the plate on the insertion site.
 - ♦ This agar plate contains chlorhexidine neutralizers that avoid in vitro artificial sterilization of cutaneous culture by inhibiting residual chlorhexidine effect.
 - ♦ The plate was sent to the local microbiology laboratory and cultured for 48 hours. The number of colony-forming units (CFU) was counted.
- When major-CRI was suspected, one or more peripheral blood samples for culturing were collected.

…是否有足夠的追蹤(Follow up)? 評讀結果:■是 □否 □不清楚 說明:

Of 2,054 patients with at least one catheter, 1,898 could be enrolled and 1,879 were assessable for the intent-to-treat analysis (Figure 1), for a total of 4,163 catheters and 34,339 catheter-days.



Figure 1. Flow chart of the study. CR-BSI = catheter-related bloodstream infection; CRI = catheter-related infections; ITT = intention to treat.

changes per catheter-days was significantly lower in the highly adhesive group (0.33 [0.20-0.50] per catheter-day; P < 0.0001; Mann-Whitney test) than in the standard group (0.36 [0.25-0.56] per catheter-day). The catheter colonization rate was significantly higher in the highly adhesive group compared with the standard group (Table 3 and Figure 2) (HR, 1.651; 95% CI, 1.208-2.256; P = 0.0016). The major-CRI and CR-BSI rates were not significantly

different between these two groups (Table 3; see Figure E1). Also, CLA-BSI rate was not different between groups (HR, 1.284; 95% CI, 0.674–2.446; P = 0.45).

The incidence of colonization, major-CRI, and CR-BSI was not different between arterial catheters and CVCs. There was no heterogeneity of the chlorhexidine-impregnated effect and catheter types (see Table E2).

評估(Measurement) - 受試者與評估者是否對治療方式 及(或)評估目的維持盲法(blind)? 評讀結果:■是 □否 □不清楚 說明:

The study was not masked to the investigators or ICU staff but was masked to the microbiologists processing the skin and catheter cultures and to the adjudication committee.

The investigators were unaware of the block size and of the permutation procedure.



步驟 3:研究結果的意義為何?

TABLE 3. HAZARD RATIOS IN THE INTENTION-TO-TREAT ANALYSIS

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Variable	Nonchlorhexidine vs. Chlorhexidine Dressings (941 patients/2,055 catheters vs. 938 patients/2,108 catheters)	Standard vs. Highly Adhesive Dressings (476 patients/1,067 catheters vs. 465 patients/988 catheters)
Catheter colonization		
Incidence (n per 1,000 catheter-days)	10.9 vs. 4.3	9.6 vs. 12.5
Hazard ratio	0.412 (0.306-0.556), P < 0.0001	1.651 (1.208-2.256), P = 0.0016
Catheter-related bloodstream infection		
Incidence (n per 1,000 catheter-days)	1.3 vs. 0.5	1.3 vs. 1.3
Hazard ratio	0.402 (0.186-0.868), P = 0.02	1.215 (0.470-3.142), P = 0.689
Major catheter-related infections		
, Incidence (n per 1,000 catheter-days)	2.1 vs. 0.7	2.3 vs. 1.9
Hazard ratio	0.328 (0.174-0.619), P = 0.0006	1.052 (0.517-2.142), P = 0.888

With chlorhexidine, the major-CRI rate decreased from 2.11 per 1,000 to 0.69 per 1,000 catheter-days (hazard ratio [HR], 0.328; 95% confidence interval [CI], 0.174–0.619; P = 0.0006) (Figure 2). The

Overall data on dressing changes are given in the online supplement. Early dressing changes were significantly less common in the highly adhesive group (64.3%) than in the standard group (71.9%) (P < 0.001). The median (IQR) number of dressing



Figure 2. Cumulative risk of (A) major catheter-related infections (CRI) with chlorhexidine-gel (CHG) dressings and nonantiseptic dressings, and (B) catheter colonization with highly adhesive nonchlorhexidine dressings versus standard dressings.



步驟 3:研究結果

- A total of 1,879 patients (4,163 catheters and 34,339 catheter-days) were evaluated.
- With chlorhexidine dressings, the major-CRI rate was 67% <u>lower (0.7 per 1,000 vs. 2.1 per 1,000catheter-days;HR 0.328;95%</u> CI 0.174–0.619; P < 0.0006) and the CR-BSI rate 60% <u>lower</u> (0.5 per 1,000 vs. 1.3 per 1,000 catheter-days; HR, 0.402; 95% CI, 0.186– 0.868; P < 0.02) than with nonchlorhexidine dressings; decreases were noted in catheter colonization and skin colonization rates at catheter removal.
- The contact dermatitis rate was 1.1% with and 0.29% without chlorhexidine.
- Highly adhesive dressings decreased the detachment rate to 64.3% versus 71.9% (P,0.0001) and the number of dressings per catheter to two (one to four) versus three (one to five) (P,0.0001) but increased skin colonization (P,0.0001) and catheter colonization (HR, 1.650;95%CI, 1.21–2.26; P¹/₄0.0016) without influencing CRI or CR-BSI rates.







 Chlorhexidinegel-impregnated dressings decreased the CRI rate in patients in the ICU with intravascular catheters.



 Highly adhesive dressings decreased dressing detachment but increased skin and catheter colonization.









Highly adhesive dressings 45元

Chlorhexidinegel-impregnated dressings 200元

***是否建議醫院使用?** 1.使用highly adhesive敷料 贊成:2 // 考慮:4 // 不贊成:13 2.使用含Chlorhexidine 敷料 贊成:7 // 考慮:8 // 不贊成:5



討論-2

- Chlorhexidinegel-impregnated dressings目前台灣尚無法 取得,但有部分醫院 ICU 已全面使用 Highly adhesive dressings
- 插管當時的皮膚消毒方式、插管部位、插管時間...等
 ,是日後是否感染的主要因素,需一併納入考量,而
 非只是更換敷料
- 成本效益評估,除敷料本身的費用之外,也應包含因 感染造成的滞院天數延長、抗生素使用...所耗費的醫 療成本、照護人員工作負荷及是否減少照護時間等
- 本研究由3M公司出錢,須注意利益衝突議題

