

OUTCOME RÉA

Programme de la Journée de Formation Médicale Continue

Jeudi 27 mai 2010

Infections liées aux cathéters à l'hôpital

14h30-14h50 : Infection sur cathéters d'hémodialyse B Souweine, (Clermont Ferrand)

Objectifs :

**spécificités épidémiologiques des infections
de CD en réanimation**

moyens de prévention

**place des verrous anti-infectieux dans la
stratégie de prévention et de traitement**

Cible : public déjà expert

	CD Dialyse	CVC Réa	CD Réa
Matériel	Tunnel / SL	DL	DL
Intraveineux / seldinger	+	+	+
patients	comorbidités	défaillances +	défaillances ++
Personnels : protocoles	centre	ICU	ICU
usage / manipulation	+	-	+++
durée	> 21j	7-14j	7-14j
autres équipements	-	++	+++
Infection / exoluminale	++	+++	+++
Infection / endoluminale	+++	+	?
Dysfonction	+	+/-	++

Device–utilization ratio of dialysis catheters

99 patients with both CVCs and DCs¹

ICU LOS = 1584 days

1177 days of CVCs, DUR=0.74

877 days of DCs, DUR=0.54

The mean number of DC /AKI patients on RRT averages 1.5²

The rates of DC-related BSI range between 2 and 3 per 1000 catheter-days³

Morbidity and mortality attributable to DC infection?

1, Souweine et al, *Am J Kidney Dis* 2006

2, Personal data

3, Parienti JJ, *Jama* 2008

Microbiological identification of the etiologic agent of dialysis catheter infection is demanded for diagnosing DC infection

Whether DC is left in place or removed

Diagnostic tools

Quantitative catheter tip culture

Blood cultures

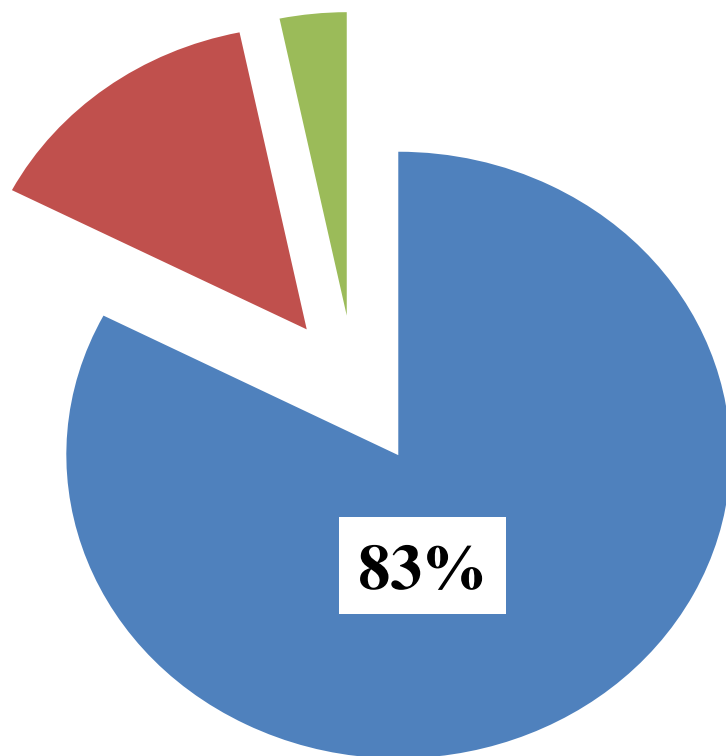
Exit site culture

Reference	Design	Type of DCs	N of DC
Crit Care med 1999	observational	2 PU single lumen DCs	151
Am J Med 2003 ^{a,b}	RCT (minocycline-rifampin-coated DCs vs non-)	PU double lumen DC	130 (66 vs 64)
Intensive Care Med 2005 ^b	observational	PU double lumen DC	79
Am J Kidney Dis 2006	observational	PU double lumen DC	130
Jama 2008	RCT (femoral site vs jugular)	PU double lumen DC	637 (324 vs 313)

a, cancer / hémopathies; b, 20% de patients hors réanimation

DC, dialysis catheters; PU, polyurethane; RCT, randomized control trial

Site of insertion of DCs (N=339)



- Femoral
- internal jugular
- subclavian

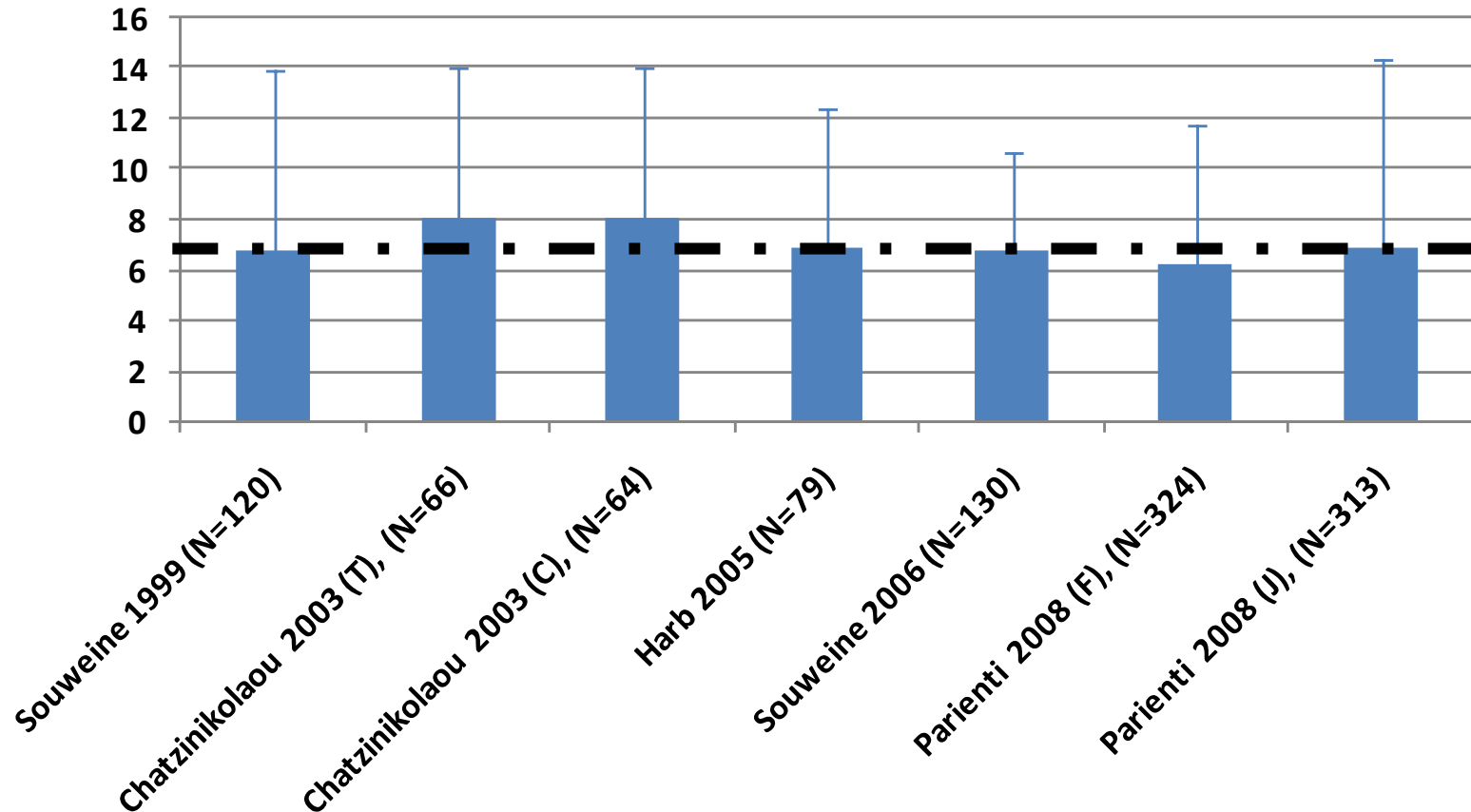
Chatzinikolaou I, *Am J Med* 2003
 Harb, A *Intensive Care Med* 2005
 Souweine B, *Am J Kidney Dis* 2006

Site of insertion of CVCs

Venous catheter	2051 (54.3)
Jugular	560 (27.3)
Subclavian	819 (39.9)
Femoral	672 (32.8)
Guidewire exchange	85 (4.1)

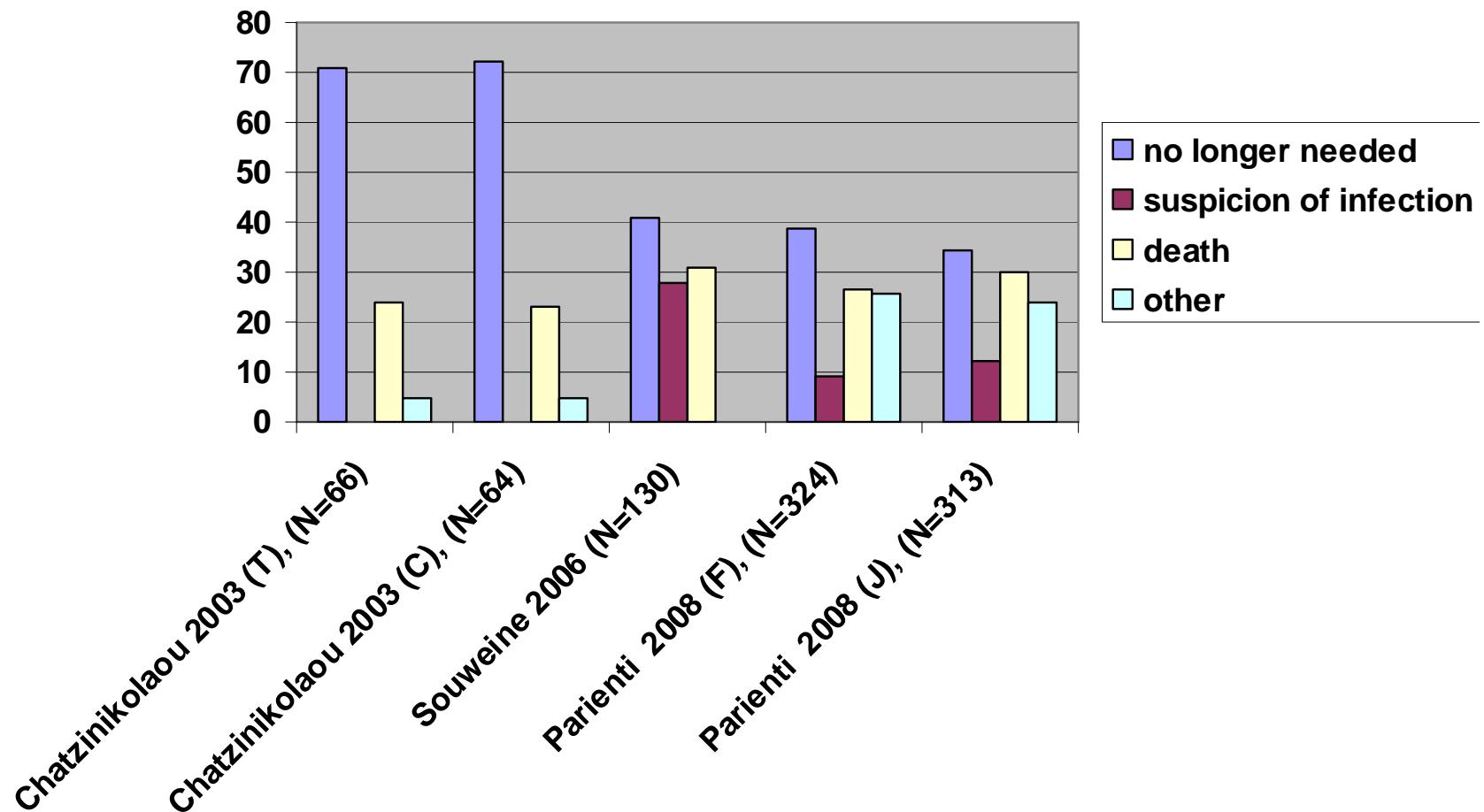
Timsit JF, *Jama* 2009

Duration of dialysis catheter insertion (7 days)

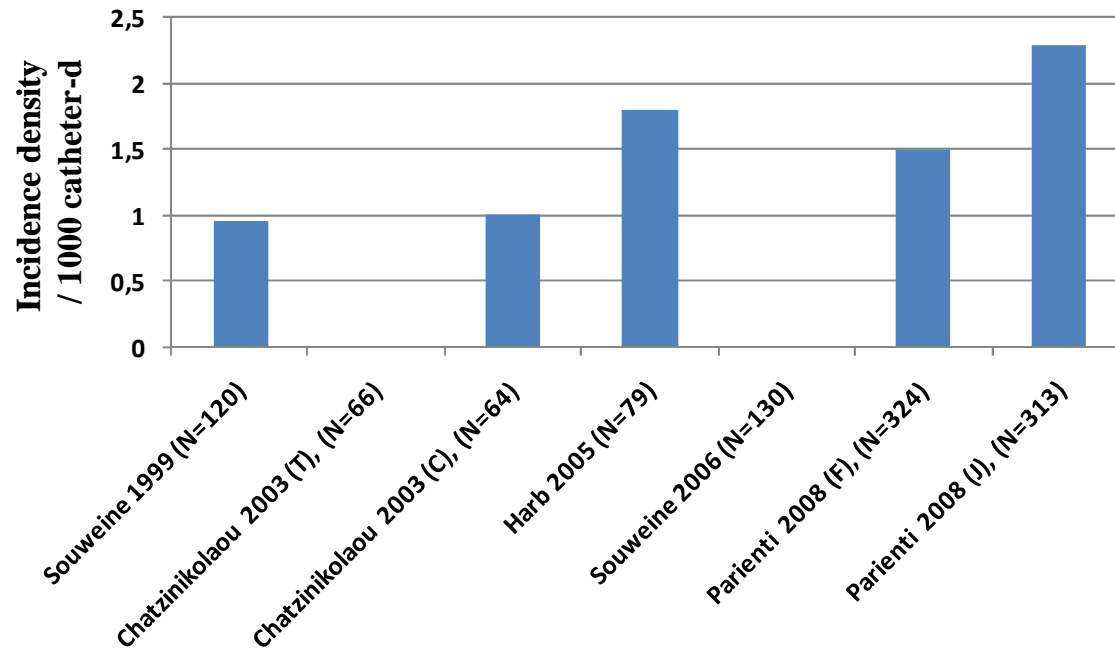
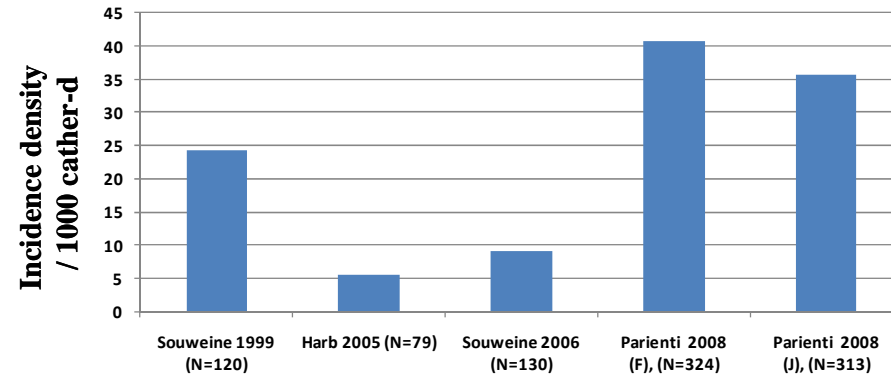
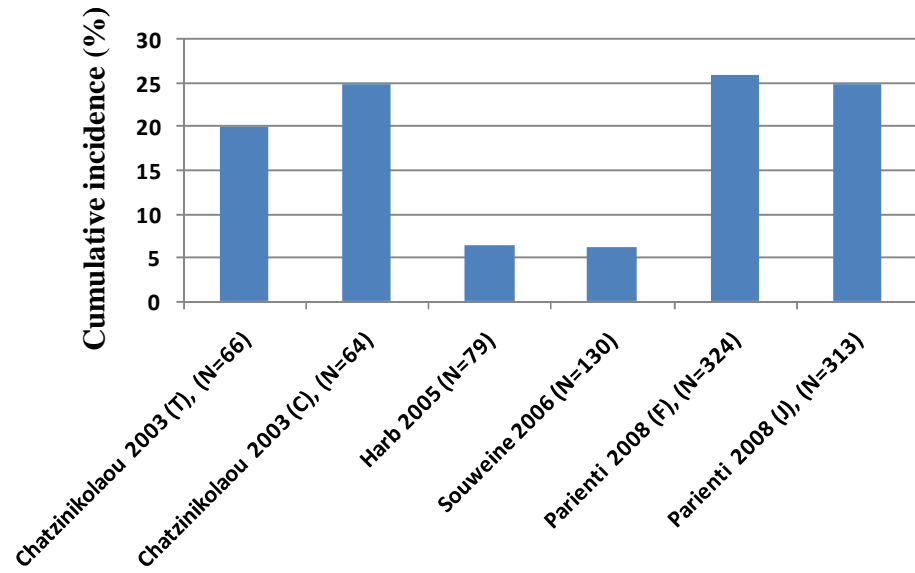


Median duration of CVC is about 6 days in most studies in critically ill patients

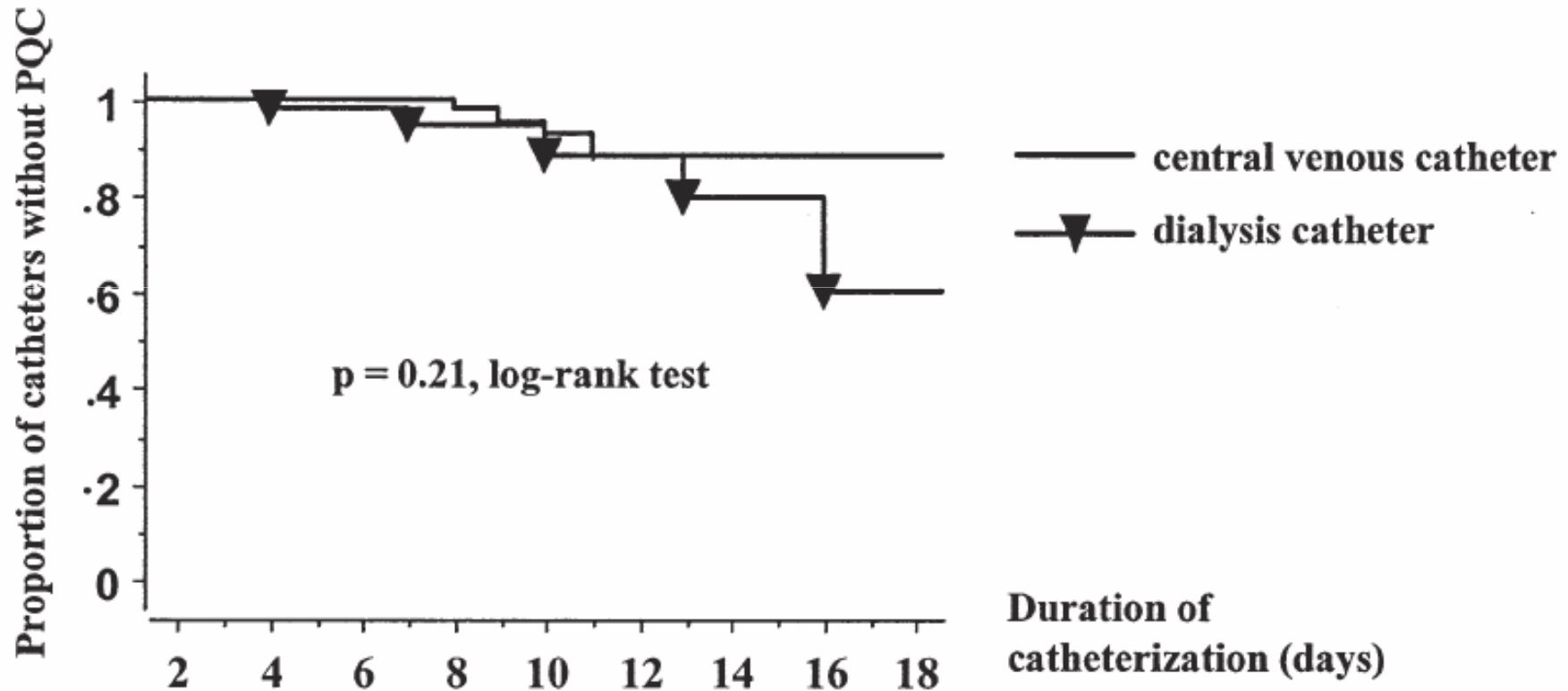
Causes of dialysis catheter removal in ICU patients



Rates of DC infections



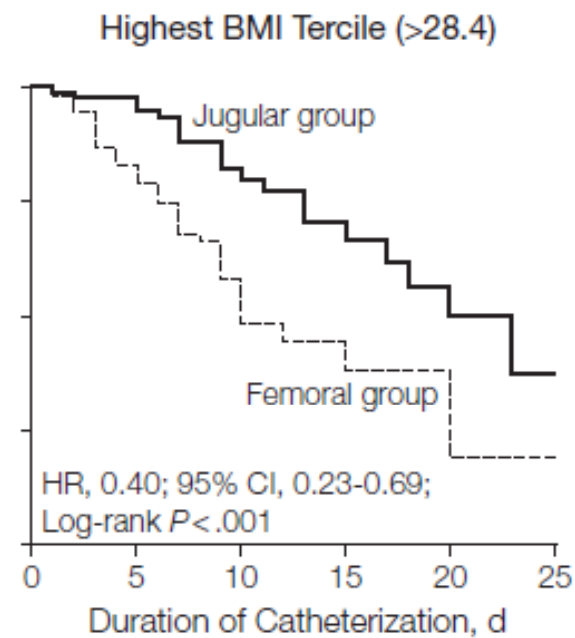
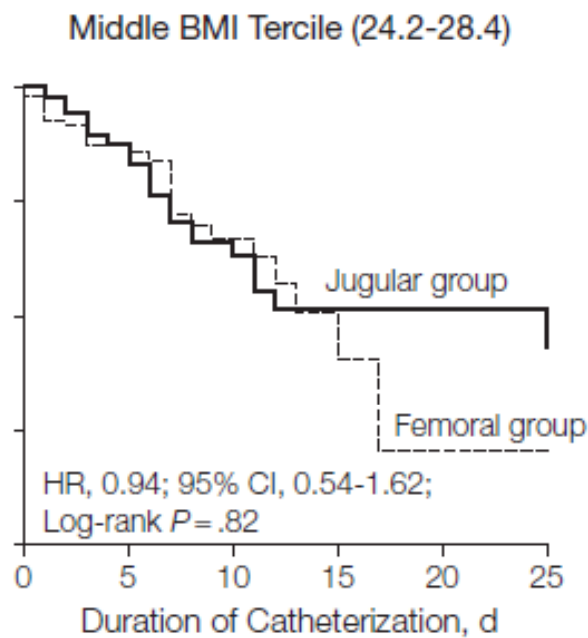
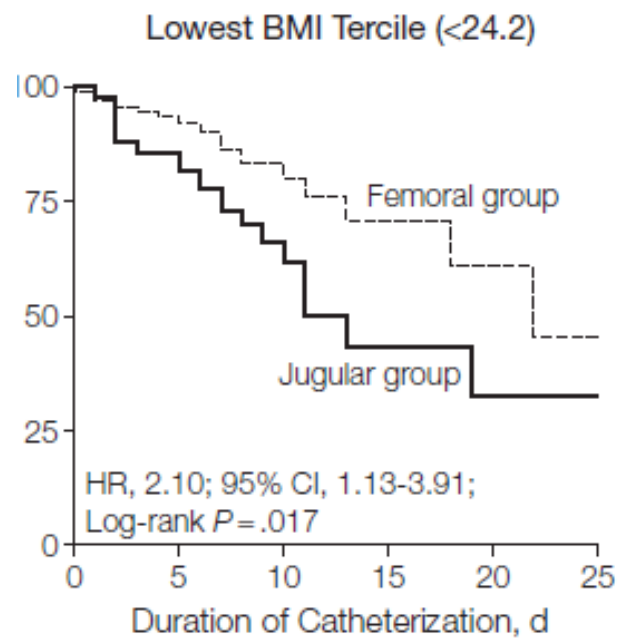
Proportion of CVCs and DCs free from positive quantitative cultures



CVC, No	150	125	95	67	51	24	12	07	06
DC, No	130	102	66	45	31	15	06	04	01

Table 2. Microorganisms Recovered From Colonized Catheters and Bloodstream Infections

	Femoral (n = 324)	Jugular (n = 313)	P Value ^a
No. of catheter colonizations	84	78	.79
No. of microorganisms			
Gram-positive	41	51	.04
<i>Staphylococcus epidermidis</i>	28	43	.007
<i>Staphylococcus aureus</i>	5	5	>.99
<i>Enterococcus species</i>	4	2	.69
Other	4	1	.37
Gram-negative	30	15	.03
<i>Escherichia coli</i>	10	1	.01
<i>Proteus species</i>	5	0	.06
<i>Pseudomonas aeruginosa</i>	7	6	>.99
<i>Enterobacter species</i>	5	3	.73
Other	3	5	.49
Fungi	11	5	.20
Polymicrobial	2	8	.06

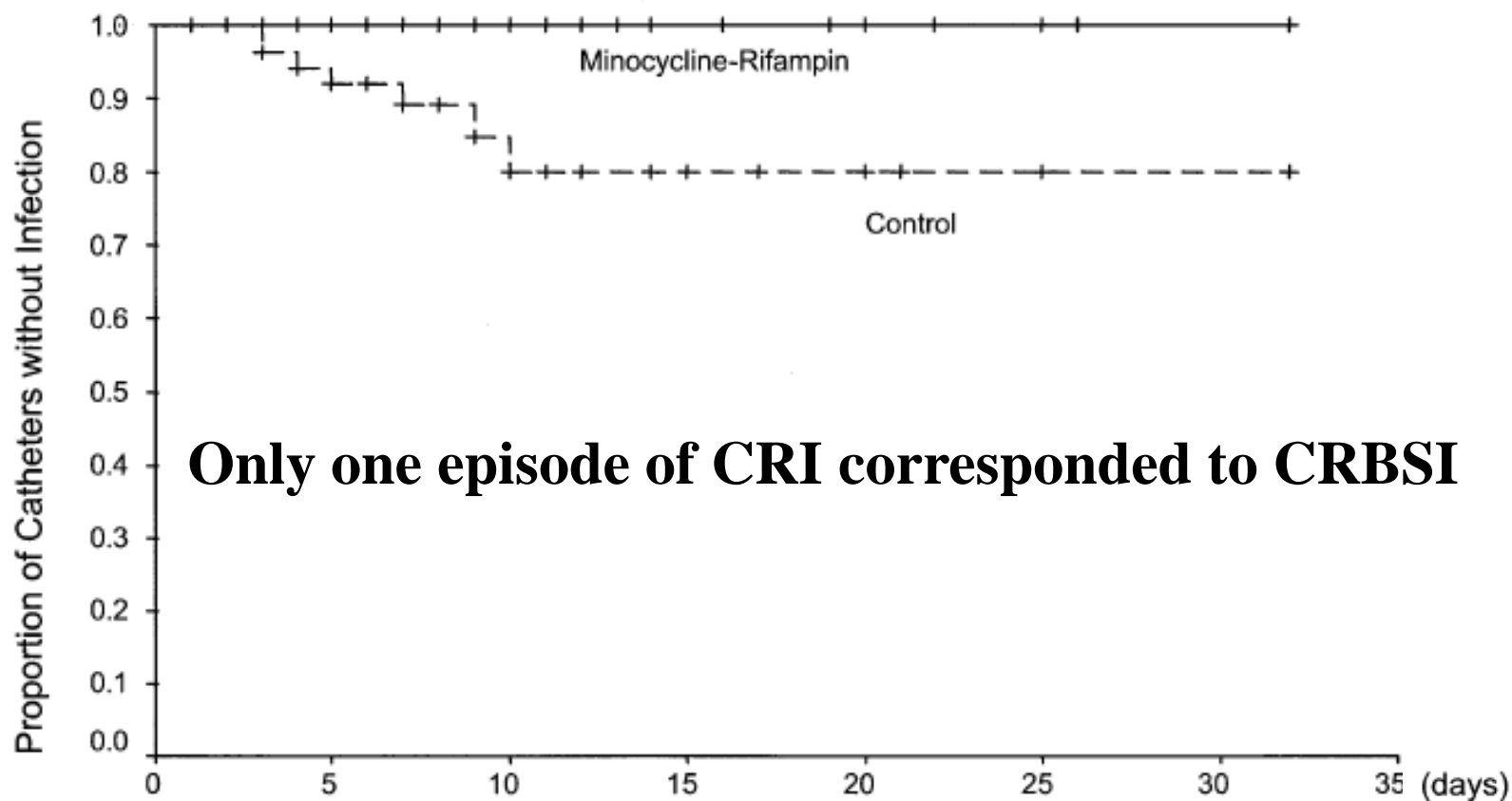


p 101 50 14 5 3
n 94 62 25 9 5

101 48 20 5 1
101 57 23 9 8

102 61 24 7 4
100 66 36 18 9

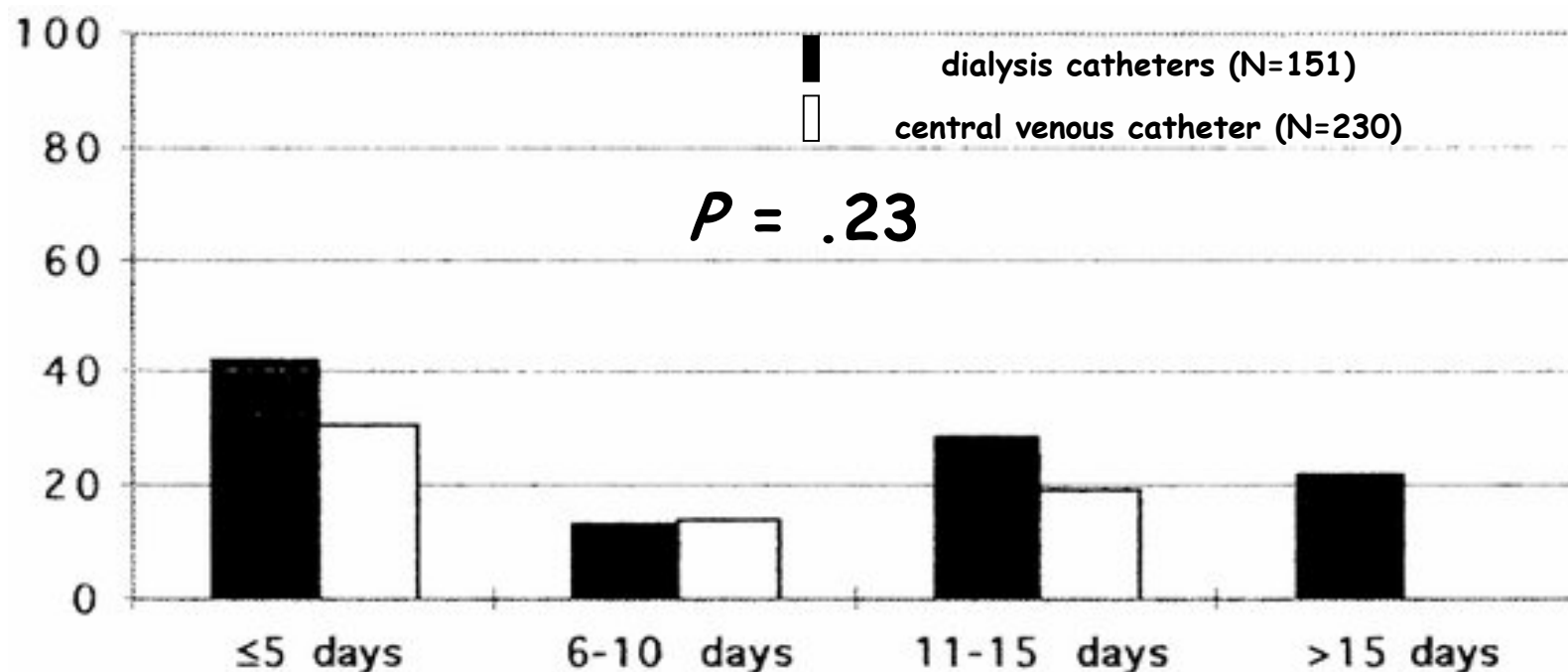
Characteristic	Minocycline- Rifampin-Coated (n = 66)	Uncoated (n = 64)	P Value
Catheter colonization	13 (20)	16 (25)	0.6
Catheter-related infections	0	7 (11)	0.006



Only one episode of CRI corresponded to CRBSI

The stable low risk for DC-associated infections over time do not support the rationale for scheduled replacement

DC and CVC durations were both associated with catheter infection: $p < 0.001$ and $p = .04$



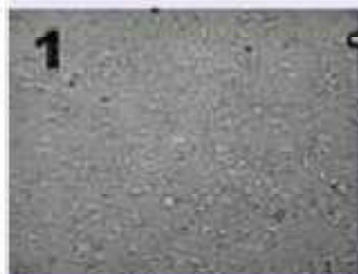
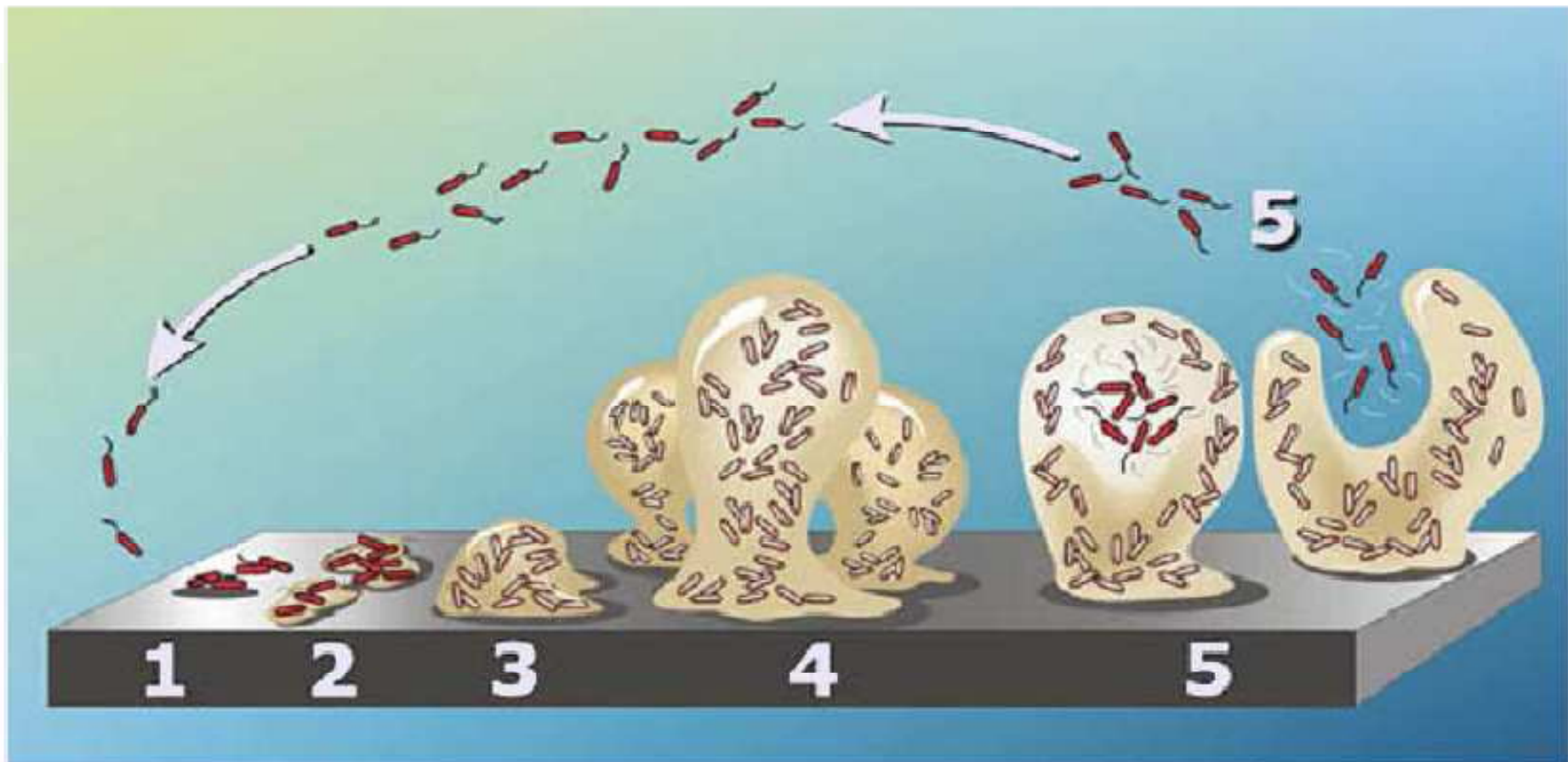
Incidence rates per 1000 days of catheter use for dialysis and central venous catheter infections examined over 5-day intervals

Take-home message number 1

Hygiene procedures for insertion and maintenance of catheters must not differ between CVCs and DCs

DCs must be removed of as soon as they are no longer necessary +++

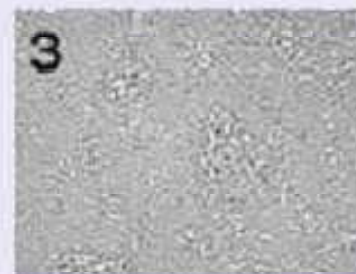
Use internal jugular site for DC insertion if BMI > 28 and femoral if BMI < 24.



1
Adhésion réversible



2
Adhésion irréversible



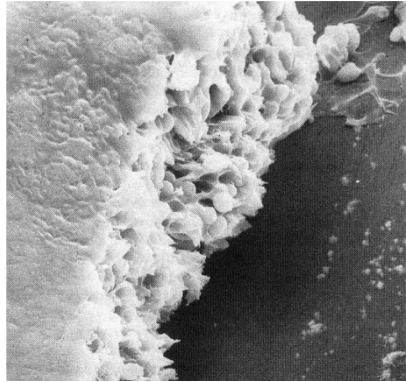
3
Multiplication et division = formation de micro-colonies



4
Production d'exopolymère et formation du biofilm



5
Libération de microorganismes



Susceptibility of biofilm organisms

Organism	Antibiotic	MIC or MBC (mcg/mL)	Effective [] vs. biofilm (mcg/mL)
<i>S. aureus</i> (NCTC 8325-4)	Vancomycin	2 (MBC)	20
<i>P. aeruginosa</i> (ATCC 27853)	Imipenem	1 (MIC)	>1,024 ^a
<i>E. coli</i> (ATCC 25922)	Ampicillin	2 (MIC)	512 ^a
<i>P. pseudomallei</i>	Ceftazidime	8 (MBC)	800
<i>S. sanguis</i>	Doxycycline	0.063 (MIC)	3.15

^a Minimal biofilm eradication

Adapted from Donlan RM, et al. *Clin Microbiol Rev.* 2002;15:167-93.

Verrou anti-infectieux

Principe

Concentration élevée anti-infectieux au contact du biofilm

Temps de contact

Verrou aspiré ou instillé en fin de procédure

Solution verrou: antimicrobiens

AB

Antiseptiques

Indications

Traitement préventif

Traitement curatif en association à AB systémique

Verrou anti-infectieux

Limites

Microorganisme

biofilm endoluminal

émergence de résistance

Solution verrou

stabilité chimique

efficacité anti-biofilm

Cathéter de dialyse

dégradation

thrombose

Patient

Échec +++

toxicité

A Meta-analysis of Hemodialysis Catheter Locking Solutions in the Prevention of Catheter-Related Infection

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Richard J. Fluck, MBBS,¹ and Christopher W. McIntyre, MD^{1,2}

American Journal of Kidney Diseases, Vol 51, No 2 (February), 2008: pp 233-241

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Antimicrobial Lock Solutions for the Prevention of Infections Associated with Intravascular Catheters in Patients Undergoing Hemodialysis: Systematic Review and Meta-analysis of Randomized, Controlled Trials

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Nephrol Dial Transplant (2008) 23: 1666–1672

doi: 10.1093/ndt/gfm847

Advanced Access publication 8 December 2007

Original Article

Preventing haemodialysis catheter-related bacteraemia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials

Laura Labriola¹, Ralph Crott² and Michel Jadoul¹

Journal of Hospital Infection 75 (2010) 1–11



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journal homepage: www.elsevierhealth.com/journals/jhin



Review

Antibiotic-based catheter lock solutions for prevention of catheter-related bloodstream infection: a systematic review of randomised controlled trials

M. Snaterse^{a,*}, W. Rüger^b, W.J.M. Scholte op Reimer^c, C. Lucas^d

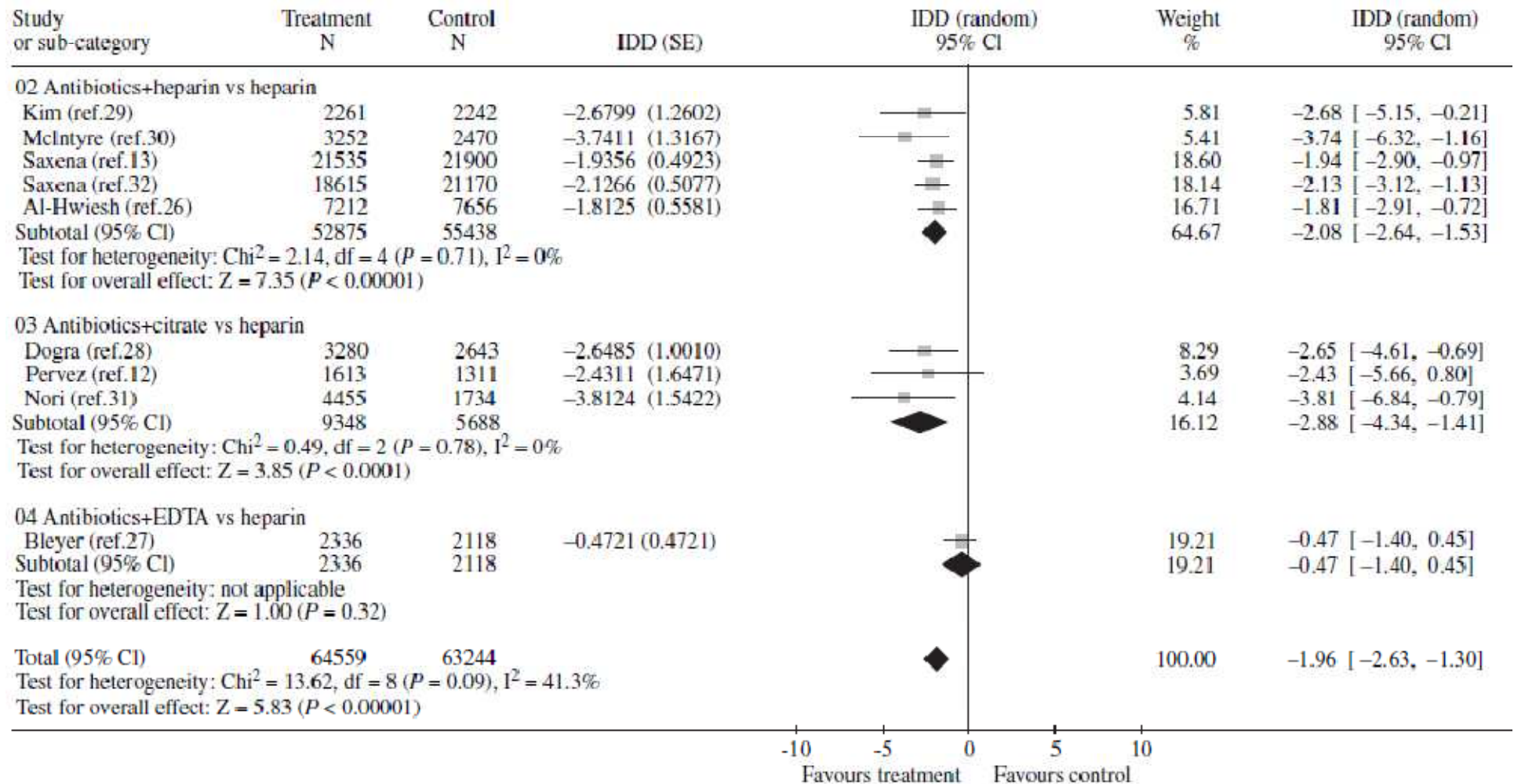
AB locking as prophylaxis

Study populations, interventions and definition of catheter-related bloodstream infection

Study	Setting	Type of CVC	Interventions (total no. of study catheters)	Duration of CVC catheterisation, mean or median days (total catheter-days)	No. of episodes	Baseline incidence density per 1000 catheter-days in C	Definition of outcome
Al-Hwiesh and Abdul-Rahman ²⁶	Haemodialysis	Tunnelled Cuffed	T (37): VA (25 mg/mL), GE (40 mg/mL), H (5000 U/mL) ^a	T: (7212) C: (7656)	CRBSI T: 2 C: 26	2.1	CRBSI: Isolation of the same MO from the CVC blood and peripheral blood.
Bleyer <i>et al.</i> ²⁷	Haemodialysis	Tunnelled Non-tunnelled	T (30): MI (3 mg/mL), EDTA (30 mg/mL) ^d C (27): H ^d	T: 77.9 (2336) C: 78.4 (2118)	CRBSI T: 0 C: 1	0.5	CRBSI: Febrile episode + CVC colonised with the same MO as isolated from peripheral blood.
Dogra <i>et al.</i> ²⁸	Haemodialysis	Tunnelled Cuffed	T (53): GE 40 mg/mL (2 mL) and 3.13% trisodium citrate (1 mL) ^b C (55): H (5000 U/mL) ^b	T: (3280) C: (2643)	CRBSI T: 0 C: 7	2.6	CRBSI: Febrile episode with no other apparent source of infection + (a) isolation of the same MO from catheter and catheter blood and peripheral blood;
Kim <i>et al.</i> ²⁹	Haemodialysis	Non-tunnelled	T (60): CEF (10 mg/mL), GE (5 mg/mL), H (1000 U/mL) ^a C (60): H (1000 U/mL) ^a	T: 37.68 (2261) C: 37.37 (2242)	CRBSI T: 1 C: 7	3.1	CRBSI: Isolation of the same MO from catheter and catheter blood and peripheral blood.
McIntyre <i>et al.</i> ³⁰	Haemodialysis	Tunnelled Cuffed	T (25): GE (5 mg/mL), H (5000 U/mL) ^d C (25): H (5000 U/mL) ^d	T: 130.1 (3252) C: 103 (2470)	CRBSI T: 1 C: 10	4.0	CRBSI: Febrile episode with no other apparent source of infection + isolation of the same MO from catheter and catheter blood and peripheral blood.
Nori <i>et al.</i> ³¹	Haemodialysis	Tunnelled Cuffed	T1 (20): GE (4 mg/mL), 3.13% trisodium citrate ^a T2 (21): MI (3 mg/mL), EDTA (30 mg/mL) ^a C (20): H (5000 U/mL) ^a	T1: (2002) T2: (2453) C: (1734)	CRBSI T1: 0 T2: 1	4.0	CRBSI: Febrile episode with no other apparent source of infection + (a) catheter colonisation + positive catheter blood or peripheral blood; (b) defervescence of symptoms after antibiotic therapy + positive catheter blood or positive peripheral blood; (c) defervescence of symptoms after antibiotic therapy and catheter removal + catheter colonisation.
Pervez <i>et al.</i> ¹²	Haemodialysis	Tunnelled Cuffed	T (14): Tricetasol (46.7%), GE (40 mg/mL) ^g C (22): H (1000 U/mL) ^g	T: (1613) C: (1311)	CRBSI T: 1 C: 4	3.0	CRBSI: Febrile episode with no other apparent source of infection + positive blood culture (not specified whether peripheral and/or catheter blood).
Saxena <i>et al.</i> ¹³	Haemodialysis (patients > 65 years)	Tunnelled Cuffed	T (59): CEFT (10 mg/mL), H (5000 U/mL) ^a C (60): H (5000 U/mL) ^a	T: (21 535) C: (21 900)	CRBSI T: 36 C: 79	3	CRBSI: Febrile episode with no other apparent source of infection + positive blood culture (not specified whether peripheral and/or catheter blood).
Saxena <i>et al.</i> ³²	Haemodialysis	Tunnelled Cuffed	T (51): CEFT (10 mg/mL), H (5000 U/mL) ^a C (58): H (5000 U/mL) ^a	T: (18 615) C: (21 170)	CRBSI T: 29 C: 78	3.7	CRBSI: Febrile episode with no other apparent source of infection + positive blood culture (not specified whether peripheral and/or catheter blood).

AM, amikacin; C, control; CEF, cefazolin; CEFT, cefotaxime; cfu, colony-forming units; CI, ciprofloxacin; CoNS, coagulase-negative staphylococci; (CR)BSI, (catheter-related) bloodstream infection; CVC, central venous catheter; EDTA, ethylenediamine tetra-acetic acid; GE, gentamicin sulphate; H, heparin; ICVC, indwelling central venous catheter; MI, minocycline; MO, micro-organism; PICC, peripherally inserted central catheter; T, treatment; VA, vancomycin hydrochloride

Three haemodialysis patients needed to be treated with antibiotics to prevent one CRBSI, given a mean insertion time of 146 days (range: 37-365) and an average baseline risk of 3.0 events per 1000 catheter-days.



Inadvertent postdialysis anticoagulation due to heparin line locks

Hemodialysis International 2007; 11:430–434

Loss of Catheter Lock Fluid Is Caused by Hydraulic Effects and Not by Diffusion

Blood Purif 2009;28:226

Measuring of the heparin leakage into the circulation from central venous catheters—an *in vivo* study

Nephrol Dial Transplant (2009) 24: 1550–1553

AML with gentamicin at high concentrations (40 mg/mL) resulted in significant systemic exposure, with median predialysis serum gentamicin levels of 2.8 mg/L (range, 0.6 to 3.5 mg/L),¹

whereas lower concentrations of gentamicin (5 mg/mL) did not produce serum levels greater than 0.2 mg/L.²

Gentamicin (1mg/mL), serum level below the limit of detection (<0.3 mg/L)³

1, Dogra GK, *J Am Soc Nephrol* 2002;13:2133-9

2, McIntyre CW, *Kidney Int* 2004;66:801-5

3, Abbas SA, *Am J Kidney Dis* 2009

Toxicity can arise from systemic aminoglycoside exposure with AMLs containing these antibiotics

Saxena et al¹ reported severe ototoxicity with a serum amikacin level of 24.6 g/L by using 25 mg of amikacin to lock a patient's tunneled catheter.

Dogra et al² also reported symptoms of ototoxicity in patients with mean serum gentamicin levels of 2.8 mg/L by using 80 mg of gentamicin to lock their tunneled catheters.

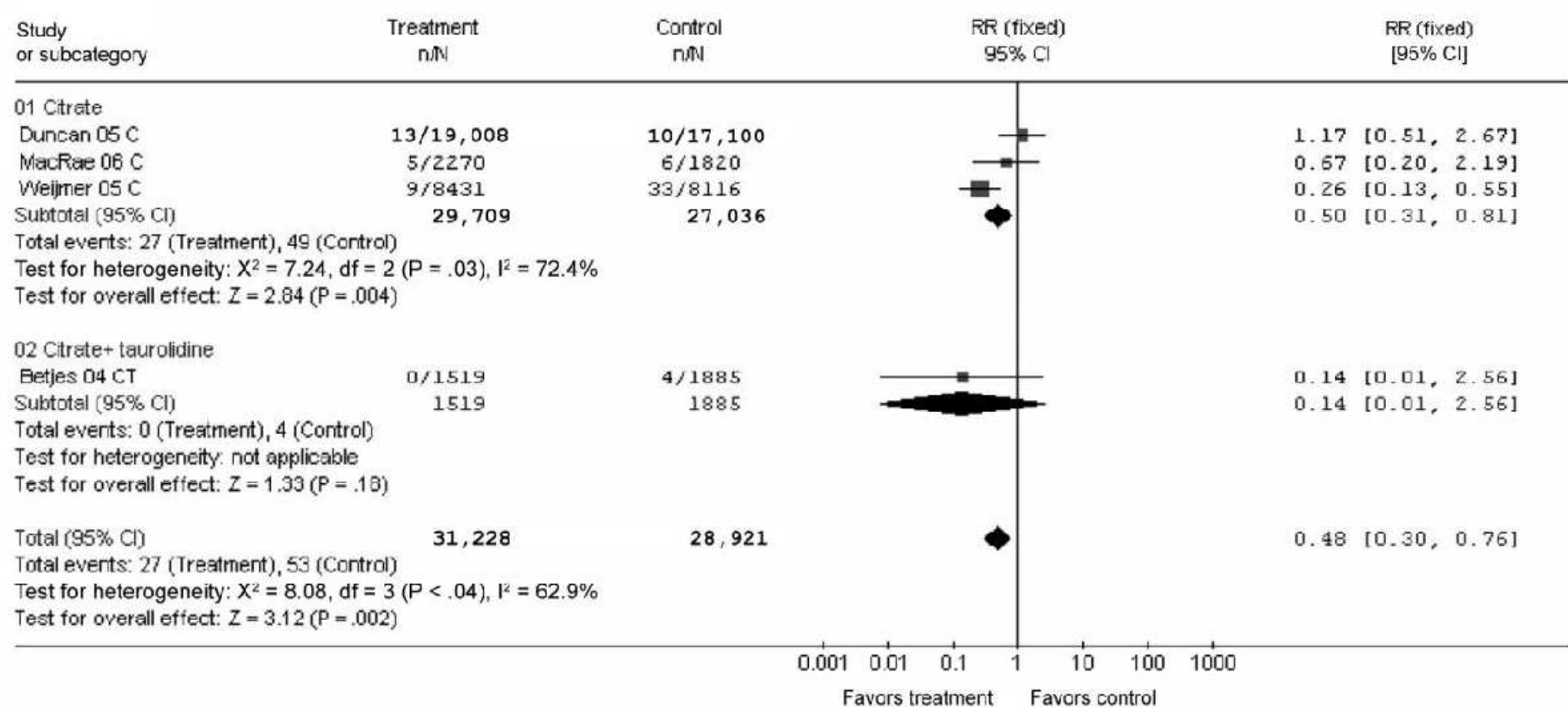
Table 5. Bacterial Resistance Profiles of Isolates From CA-BSIs Tabulated by AML Exposure

CA-BSI Bacterial Isolates	No AML	Transitional	AML	P
Enterobacteriaceae and nonfermenting Gram-negative bacilli				
Gentamicin sensitive	18	6	4	0.4
Gentamicin resistant	1	0	1	
<i>Staphylococcus aureus</i>				
Methicillin sensitive	9	3	10	0.6
Methicillin resistant	2	0	1	
Coagulase-negative staphylococci*				
Gentamicin sensitive	5	3	3	0.1
Gentamicin resistant	4	2	12	
Methicillin sensitive	2	1	2	0.8
Methicillin resistant	7	4	13	
Quinolone sensitive	6	5	10	0.3
Quinolone resistant	3	0	5	

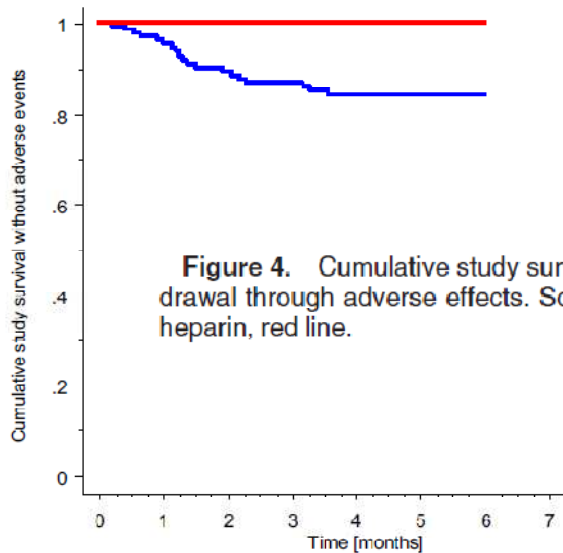
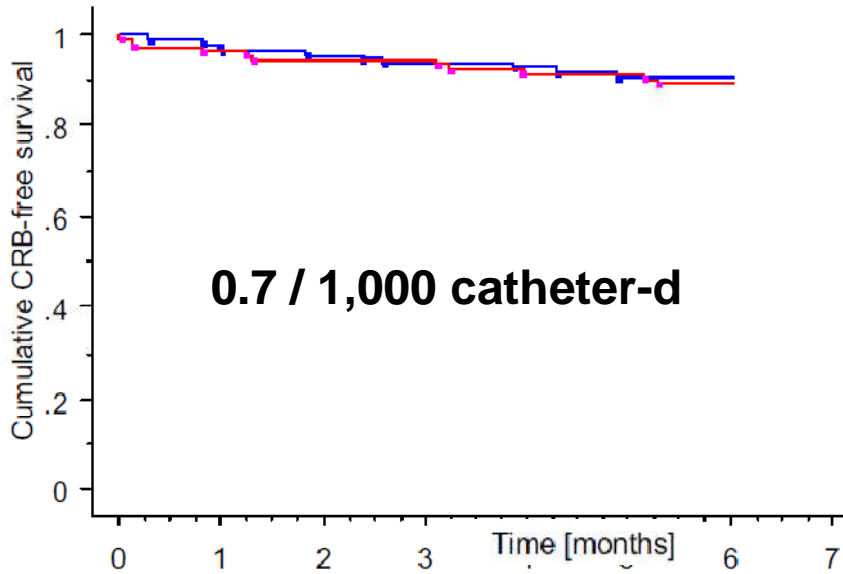
Abbreviations: AML, antimicrobial lock; CA-BSI, catheter-associated bloodstream infection.

*Data missing for 3 coagulase-negative staphylococci isolates from April 5, 2003; July 24, 2003; and August 12, 2003.

Non-antibiotics antimicrobial locks?

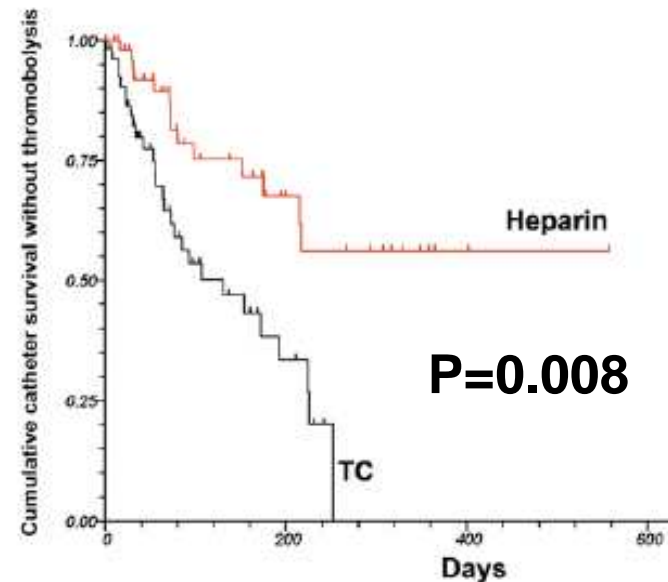
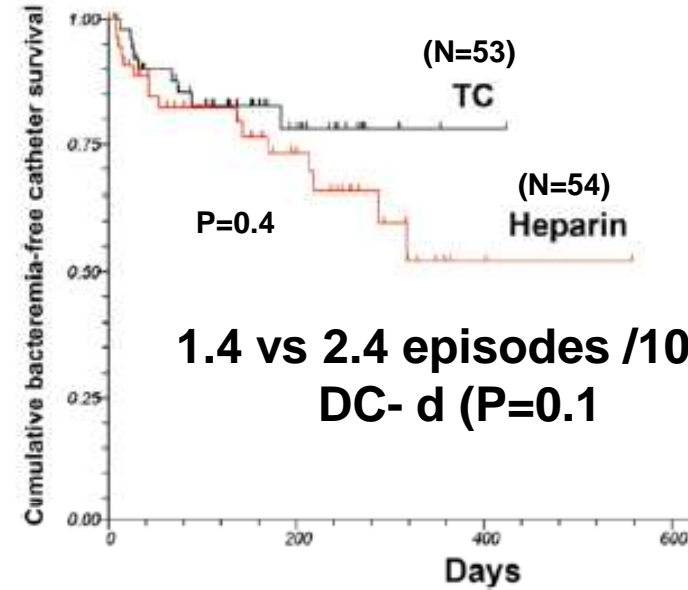


**Open RCT, 232 twin- DC
46.7% sodium citrate
vs 5% heparin locks**



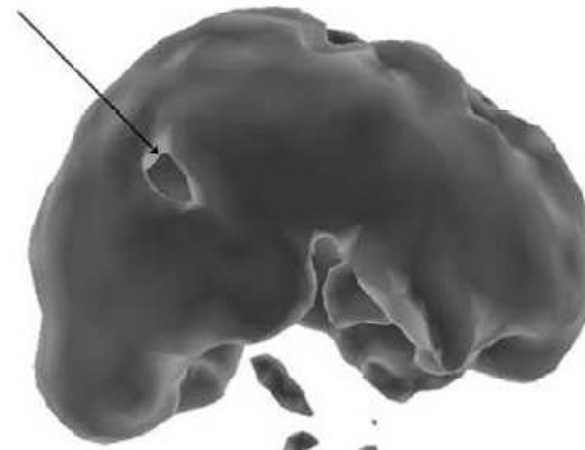
Power A, *Am J Kidney Dis* 2009

**DB RCT, 110 t DC
1.35% taurolidine and 4% citrate
vs 5% heparin locks**



Embotic Complications From Central Venous Hemodialysis Catheters Used With Hypertonic Citrate Locking Solution

Patient No.	Age (y)	Sex	Catheter Position	Duration (mo)	Anticoagulant	Hypotension	Embolus
1	32	F	Right subclavian catheter	24	Tinzaparin 1,500 IU	No	Cerebrovascular accident
2	79	M	Left internal jugular central venous catheter	4	Daily tinzaparin	Yes	Pulmonary embolus
3	64	F	Right internal jugular central venous catheter	3	Tinzaparin 3,500 IU	Yes	Pulmonary embolus
4	86	M	Left internal jugular central venous catheter	6	Tinzaparin 2,500 IU	Yes	Pulmonary embolus
5	68	F	Right internal jugular central venous catheter	5	Tinzaparin 2,500 IU	Yes	Pulmonary embolus
6	30	M	Right internal jugular central venous catheter	3	Warfarin	Yes	Pulmonary embolus
7	23	F	Right internal jugular central venous catheter	1	Tinzaparin 1,500 IU	Yes	Pulmonary embolus
8	56	M	Right internal jugular central venous catheter	3	Tinzaparin 4,500 IU	No	Pulmonary embolus



Dialysis catheter salvage by combining systemic ABs in conjunction with antibiotic locks.

Advantages

Preservation of HD access
Uninterrupted HD schedule
Low immediate costs
Convenience

Dialysis catheter salvage by combining systemic ABs in conjunction with antibiotic locks.

Indications (?)^a

- Hemodynamically stable patient**
- No sign of tunnel infection**
- No sign of metastatic infection**
- Microorganisms medically treatable**
- Blood culture sterile in 48-72 hrs**
- No persistent fever**
- Difficult to replace catheters**

Dialysis catheter salvage by combining systemic ABs in conjunction with antibiotic locks.

Potential drawbacks

**Osteomyelitis
Septic arthritis
Epidural abscess
Endocarditis...**

**Septic shock
Death**

Catheter salvage is always risky in patients with CRB

Verrous AB comme traitement des bactériémies liées aux cathéters de dialyse.

40 - 70% de succès

Pas de différence par rapport aux stratégies classiques (retrait + AB) mais contrôles historiques

Résultats décevants en cas d'infection à *S aureus*

Table 4. Outcome of catheter-related bacteraemia treated with the antibiotic lock protocol, sorted by type of organism

Type of organism	Infections (<i>n</i>)	Success (<i>n</i>) (%)	Failures (<i>n</i>)	
			Persistent fever	Positive survival cultures
Gram negative	15	13 (87%)	1	1
<i>S.epidermidis</i>	16	12 (75%)	1	3
<i>S.aureus</i>	10	4 (40%)	5	1

Conclusion

Appliquer au CD toutes les mesures de prévention élémentaires proposées pour prévenir les infections de CVC (hygiène, formation, surveillance, restitution, check list)

Voie jugulaire si BMI > 28 et fémorale si BMI <24

Retrait du CD dès qu'il n'est plus nécessaire

Place des « accessoires » : domaine de recherche clinique

