Is Central venous catheter Tip Colonization (CTC) diagnosed at central venous catheter (CVC) removal an indication for antibiotic treatment ?

Is *isolated* Central venous catheter Tip Colonization (CTC) diagnosed at central venous catheter (CVC) removal *bloodstream* infection (BSI) an indication for antibiotic treatment ?

Is isolated Central venous catheter Tip Colonization (CTC) diagnosed at central venous catheter (CVC) removal associated with a high risk for subsequent bloodstream infection (sBSI) ?

Is isolated Central venous catheter Tip Colonization (CTC) diagnosed at central venous catheter (CVC) removal associated with a high risk for subsequent bloodstream infection (sBSI) / distal focus of infections attributed to the hematogenous spread ?

Background

- Definitions
- Main limits of studies

Literature review / impact of antibiotics administered at or after CVC removal

- Overall epidemiology of CTCs
- Epidemiology of CTCs due to
  Staphylococcus aureus
  Acinetobacter baumannii
  Pseudomonas aeruginosa
  Candid spp

Guidelines / Conclusion

Isolated central venous catheter tip colonized (CTC) and subsequent bloodstream infection (sBSI)

Central venous catheter tip colonized (CTC) = CVC removal

- Semiquantitative
  Maki roll Maki-roll catheter-tip culture
  ≥15 cfu/catheter-tip as a cutoff – exoluminal –
- Quantitative, vortex / sonification – exoluminal and endodoluminal -
  ≥1000 cfu/catheter tip as a cutoff - exoluminal and endoluminal -
  - Vortex, Brun Buisson, Arch Intern Med 1987 with 1000 cfu/catheter tip as a cutoff
  - Sonification, Sheretz, J Clin Microbiol 1990 (threshold 10^2 > 10^3 cfu/ml?)
  - Combined both sonification & vortex (threshold?)

Isolated CTC, without concomitant BSI (CRBSI)

Positive blood culture obtained from CVC - with concomitant negative peripheral blood cultures by venipuncture: blood culture contamination or CTC ?

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Isolated central venous catheter tip colonized (CTC) and subsequent bloodstream infection (sBSI)

Subsequent (secondary) bacteriemia (sBSI)

- BSI due to the microorganism of the positive catheter culture
  Phenotypical methods, same species
  Identical antimicrobial susceptibility profile
  Identical strain based on molecular methods
- Exclusion
  Patients with concurrent / concomitant bacteremia (CRBSI) (!)

Catheter Colonization and BSI

17% of patients with positive catheter cultures had CRBSI

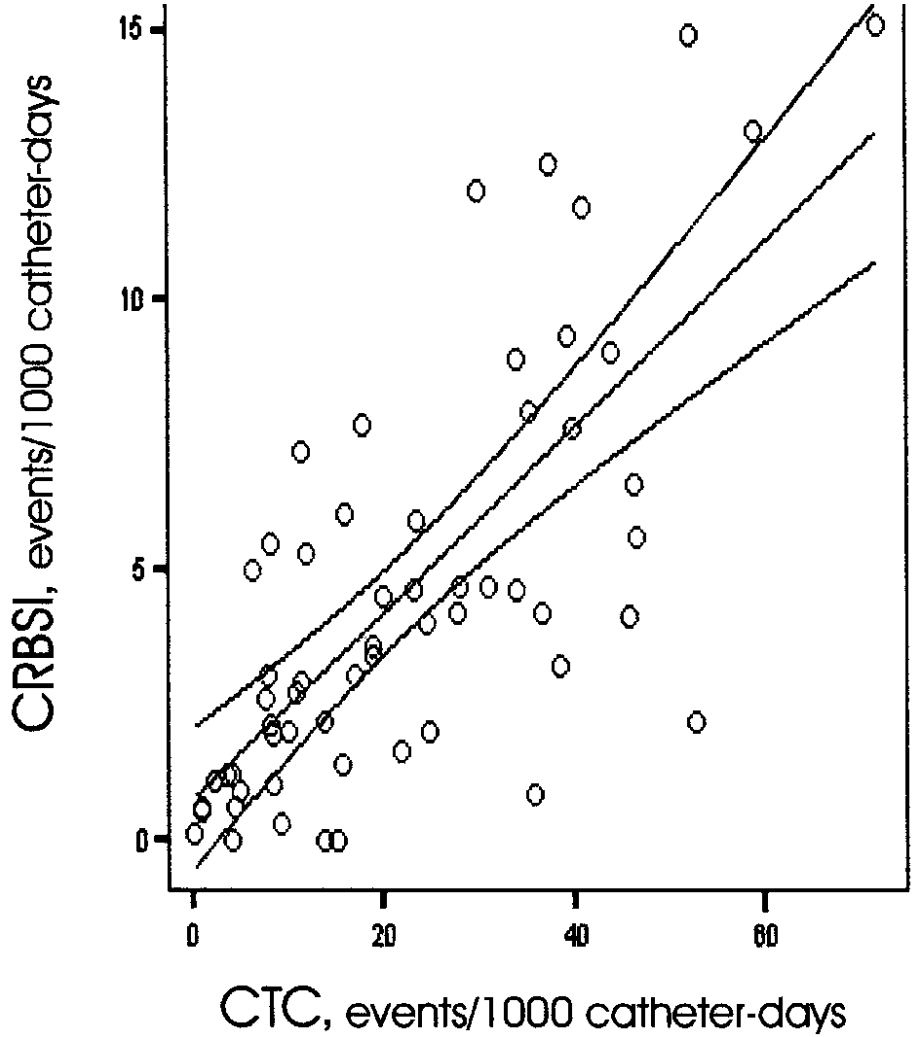


Figure 2. Linear regression of catheter tip colonization (CTC) and catheter-related bloodstream infection (CRBSI), with mean 95% prediction intervals. Incidence of BSI $= 0.73 + 0.17 \times$ incidence of CTC.

Rijnders BJA, Clin Infect Dis 2002

Isolated central venous catheter tip colonized (CTC) and subsequent bloodstream infection (sBSI)

Subsequent (secondary) bacteriemia (sBSI)

- BSI due to the microorganism of the positive catheter culture
- Exclusion

  Patients with concurrent / concomitant bacteremia (CRBSI) (!)

  sBSI diagnosed >24 h after CVC removal, distinction between CRBSI and sBSI (day-2)?

  cBSI diagnosed ≥24/48h BEFORE CVC removal

Other focus of infections attributed to the hematogenous spread of the strain isolated from CTC

Septic arthritis, osteomyelitis, soft tissue abscess, infective endocarditis, septic thrombophlebitis, septic pulmonary embolism, or septic endophthalmitis

UTI?

The precise risk of a subsequent BSI in cases of isolated CTC is uncertain

No RCT has identified ICU patients at increased risk of sBSI after a CTC

Single center observational retrospective studies, not specifically carried out in ICUs

Most studies focused on a single etiologic agent

Indications for CVC removal not systematically reported and differ between studies

- CVC tip cultures systematically performed or for suspected CVC infection
- Differences in definition of suspected CVC infection

Presence of SIRS criteria or local signs not predictive of subsequent infections in ICU cohorts

Other focus of infection, previous CVC infection

Systematic clinical surveillance / monitoring in patients after CVC removal

Follow-up systematic / duration

- The longer the follow–up, the lower the relationship between isolated CTC and subsequent infection?

How to cope with isolated CTC at the bedside

Clinical surveillance and follow-up

Watchful waiting

Work-up

- Blood cultures (BCs)
- PCT, BD glucan
- Venous ultrasound examination
- Echocardiography

Systematic antibiotics

Duration of antibiotics

Arterial catheter

Development of bacteraemia or fungaemia after removal of colonized central venous catheters in patients with negative concomitant blood cultures

Variable	Cases without subsequent BSI (*n* = 304)	Cases with subsequent BSI (*n* = 8)	p[a]
Duration of hospital stay after CVC removal, median days (IQR)	24 (11–48)	24 (15–78)	0.20
Duration of catheter use, median days (IQR)	10 (6–16)	11 (6–18)	0.82
Type of catheter (%)			
Non-tunnelled	279 (92)	8 (100)	1.00
Tunnelled	25 (8)	0 (0)	
Catheter insertion site (%)			
Internal jugular vein	200 (66)	5 (63)	0.07
Subclavian vein	88 (29)	1 (12)	
Femoral vein	16 (5)	2 (25)	
Haemodialysis catheter (%)	29 (10)	2 (25)	0.18
Exit-site or tunnel infection (%)	15 (5)	1 (13)	0.35
Body temperature >38°C (%)	211 (69)	5 (63)	0.71
Duration of fever before CVC removal, median days (IQR)[c]	1 (0–3)	4 (1–9)	0.34
Receipt of parenteral nutrition (%)	183 (60)	6 (75)	0.49
Immunosuppressive therapy (%)	46 (15)	0 (0)	0.61
Systemic corticosteroid use (%)	89 (29)	1 (13)	0.45
Antibiotic treatment (%)	148 (49)	1 (13)	0.07
28-day mortality rate (%)	60 (20)	2 (25)	0.67

sBSI positive BCs between 2 and 28 days after CVC removal

13 292 CVC tip cultures , 1961 CTCs, 312 included

sBSI, 8/312 (2.6%; 95% CI 1.2–5.1)

Park KH, Clin Microbiol Infect 2010; 16: 742–746

Organism	Underlying conditions	Onset of BSI after CVC removal, days	Appropriate antibiotics
Staphylococcus aureus	ICH	9	No
S. aureus	Pneumonia ARDS	3	Yes
Pseudomonas aeruginosa	CAD (3VD)	24	No
P. aeruginosa	ESLD	16	No
E. faecium	ALF	4	No
Candida albicans	Necrotizing pancreatitis	13	No
C. albicans	CAD (3VD)	9	No
Non-*albicans Candida*	Acute mesenteric ischaemia	11	No

sBSI

- *S. aureus* 2/58 (3.5%; 95% CI 0.3–12.4),
- Enterococcus 1/11 (9.1%; 95% CI 0–39.9)
- *P. aeruginosa* 2/17 (11.8%; 95% CI 2.0–35.6)
- Candidaemia 3/39 (7.7%; 95% CI 1.9–21.0)

Park KH, Clin Microbiol Infect 2010; 16: 742–746

Single ICU, retrospective study, 109 patients with 138 CTCs, 149 microorganisms

Causative micro-organisms	149
Gram-positive cocci	81
Methicillin-sensitive *Staphylococcus aureus*	3
Methicillin-resistant *S. aureus*	3
Staphylococcus epidermidis	22
Staphylococcus warneri	5
Staphylococcus hominis	1
Staphylococcus capitis	1
Coagulase-negative *Staphylococcus spp.*	33
Enterococcus faecalis	13
Gram-negative bacilli	66
Pseudomonas aeruginosa	25
Proteus mirabilis	12
Enterobacter spp.	7
Morganella morganii	5
Klebsiella pneumoniae	5
Escherichia coli	5
Acinetobacter spp.	3
Providencia rettgeri	2
Serratia marcescens	2
Fungi	2
Candida albicans	2

	No.
Catheter types	
Central venous	61
Dialysis	39
Arterial	38
Emergency insertion	4
Guidewire exchange	8
Reasons for removal	
No longer needed	72
Suspicion of infection	54
Dysfunction	12
Duration of catheter placement, days[a]	9 ± 5

sBSI, identification of CTC causative organism in BCs taken between day 3 and day 30

87 microorganisms different from CNS;

- 66 GNB
- 13 enterococci, 6 *S aureus*
- 2 *Candida spp*

Mrozek N, CCM 2011

CTC is associated with a low risk of sBSI in ICU patients

	Patient 1	Patient 2
Type of catheter	Central venous	Central venous
Insertion site	Femoral	Internal jugular
Number of lumens	3	2
Cause of removal	No longer needed	Suspicion of infection
Results of positive catheter culture	*Escherichia coli* *Enterobacter aerogenes*	*Staphylococcus epidermidis*
Etiological organism[a]	*Escherichia coli* 1/5	*Staphylococcus epidermidis* 1/22
Antibiotics at catheter removal	No	Yes[b]
Timing of subsequent bacteremia[c]	5 days	4 days
Alive at hospital discharge	Yes	Yes

sBSI: 2/138; 87 microorganisms different from CNS, 1/87

In 8 patients, 2 sBSI and 6 nosocomial pneumonia;

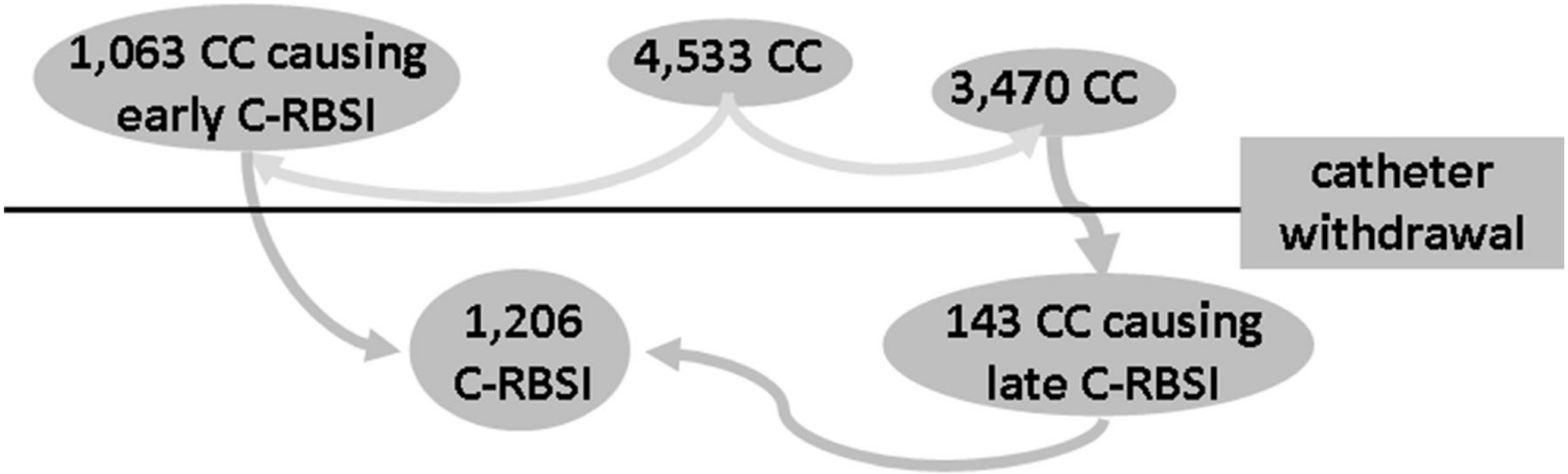
Subsequent nosocomial infection 0/23 with active antibiotics and in 8/121 without (P=0,36)

In 5 cases of CTC with CNS, AB susceptibility was not available.

Mrozek N, CCM 2011

CVC tips cultured: 17,981; CTC: 4,533 (25.2 %); Total C-RBSI: 1,206 (26.6 %)

- Late C-RBSI, 143/1206 (11.9 %)
- Late CRBSI, 4.1 % of CTCs without early C- RBSI episodes (3,470)



CTCs between 2003 and 2010 in patients without bacteremia
Early C-RBSI, positive blood cultures obtained ≤24 h after CVC withdrawal (concomitant BSI, CRBSI)
Late C-RBSI, positive blood cultures obtained **≥24 h after CVC withdrawal** (= sBSI)

Short term, long-term CVCs and, artery catheters
Follow-up, (10 days?)

Guembe M, Eur J Clin Microbiol Infect Dis (2014) 33:729–734

Table 1 Risk of late C-RBSI according to the etiology of the colonized catheters

Microorganism	CC without associated C-RBSI, *n* (%)	CC from late C-RBSI episodes, *n* (%)	Risk (%)
Gram-positive	4,112 (78.2)	87 (60.0)	2.1
Staphylococcus epidermidis	2,336 (44.4)	47 (32.4)	2.0
CoNS	684 (13.0)	0 (0.0)	0.0
MRSA	233 (4.4)	23 (15.9)	**9.9**
MSSA	88 (1.7)	11 (7.6)	**12.5**
Other Gram-positive	771 (14.7)	6 (4.1)	0.8
Gram-negative	679 (12.9)	29 (20.0)	4.3
Fungi	469 (12.9)	29 (20.0)	6.2
Total	5,260	145	

5260 microorganisms isolated from 3470 CTCs without concomitant BSI,

Guembe M, Eur J Clin Microbiol Infect Dis (2014) 33:729–734

Table 2 Characteristics of late and early C-RBSI episodes

Characteristics	Overall	Late C-RBSI	Early C-RBSI	*p*-Value
No. of patients	286	143	143	–
Age, years (median, IQR)	45.63 (0.07–69.00)	36.71 (0.06–68.79)	49.74 (0.13–69.00)	0.204
Male sex, no. (%)	188 (65.7)	96 (67.1)	92 (64.3)	0.884
No. (%) of deaths	70 (24.5)	43 (30.1)	27 (18.9)	**0.030**
Time to obtain BCs (mean, SD)	0.94 (4.944)	3.89 (5.39)	−1.94 (1.97)	<0.001
Overall time to obtain BCs, no. (%)				

Risk factors associated with late C-RBSI by comparing late episodes with a selected group of early C- RBSI episodes that had occurred close together in time.

No statistically significant differences in demographics between the groups.

Guembe M, Eur J Clin Microbiol Infect Dis (2014) 33:729–734

Eur J Clin Microbiol Infect Dis (2014) 33:729–734
DOI 10.1007/s10096-013-2004-8

ARTICLE

The risk of catheter-related bloodstream infection after withdrawal of colonized catheters is low

M. Guembe · M. Rodríguez-Créixems · P. Martín-Rabadán · L. Alcalá · P. Muñoz · E. Bouza

Clinical Microbiology and Infection 24 (2018) 548.e1–548.e3

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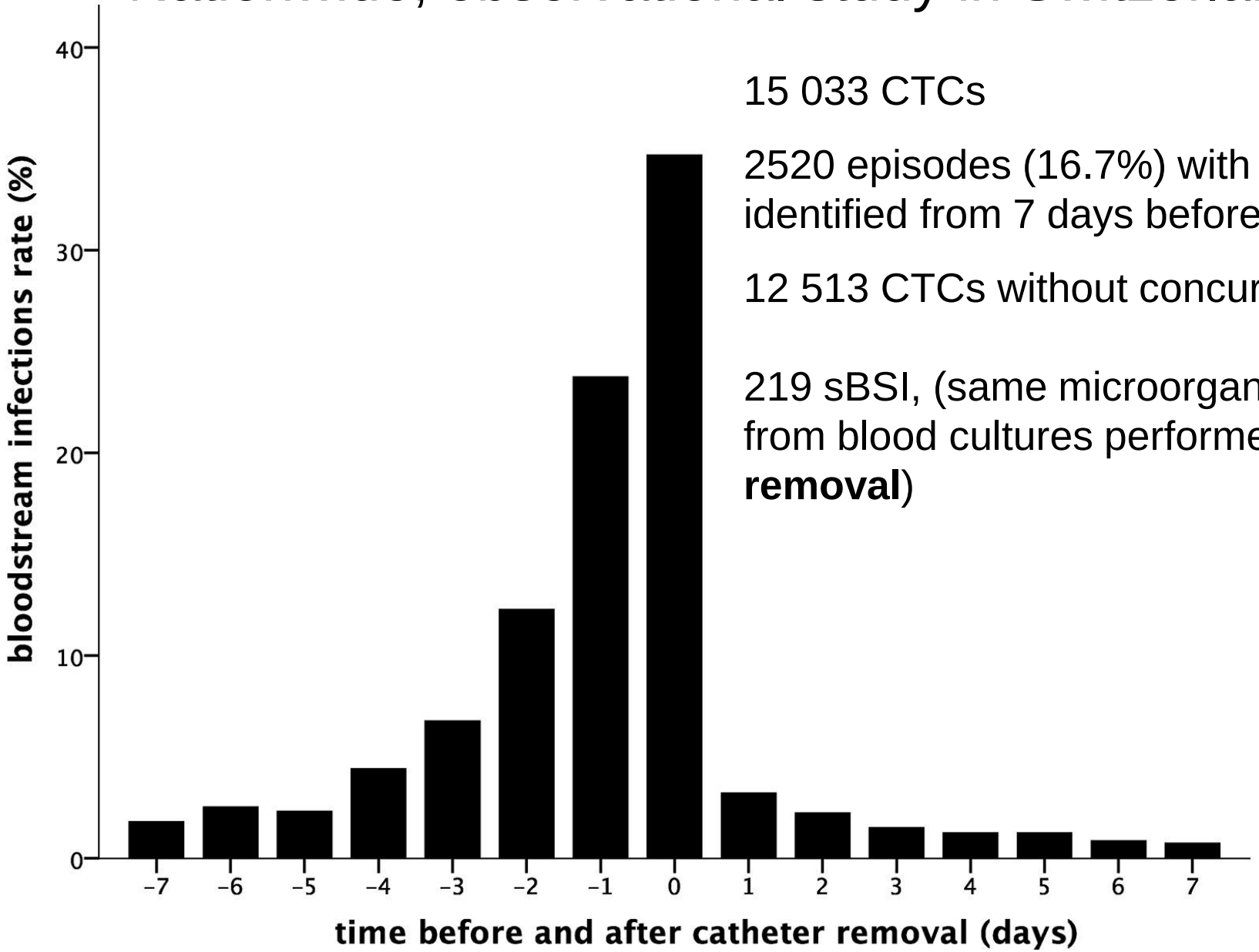
Research note

Low incidence of subsequent bacteraemia or fungaemia after removal of a colonized intravascular catheter tip

N. Buetti [1, *], E. Lo Priore [1], A. Atkinson [1], A. Kronenberg [2], J. Marschall [1] on behalf of the Swiss Centre for Antibiotic Resistance (ANRESIS)

[1)] *Department of Infectious Diseases, University Hospital Bern, Bern, Switzerland*
[2)] *Institute for Infectious Diseases, University of Bern, Bern, Switzerland*

Nationwide, observational study in Switzerland from 2008 to 2015



15 033 CTCs

2520 episodes (16.7%) with concurrent BSI (same microorganism identified from 7 days before to 2 days after CVC removal)

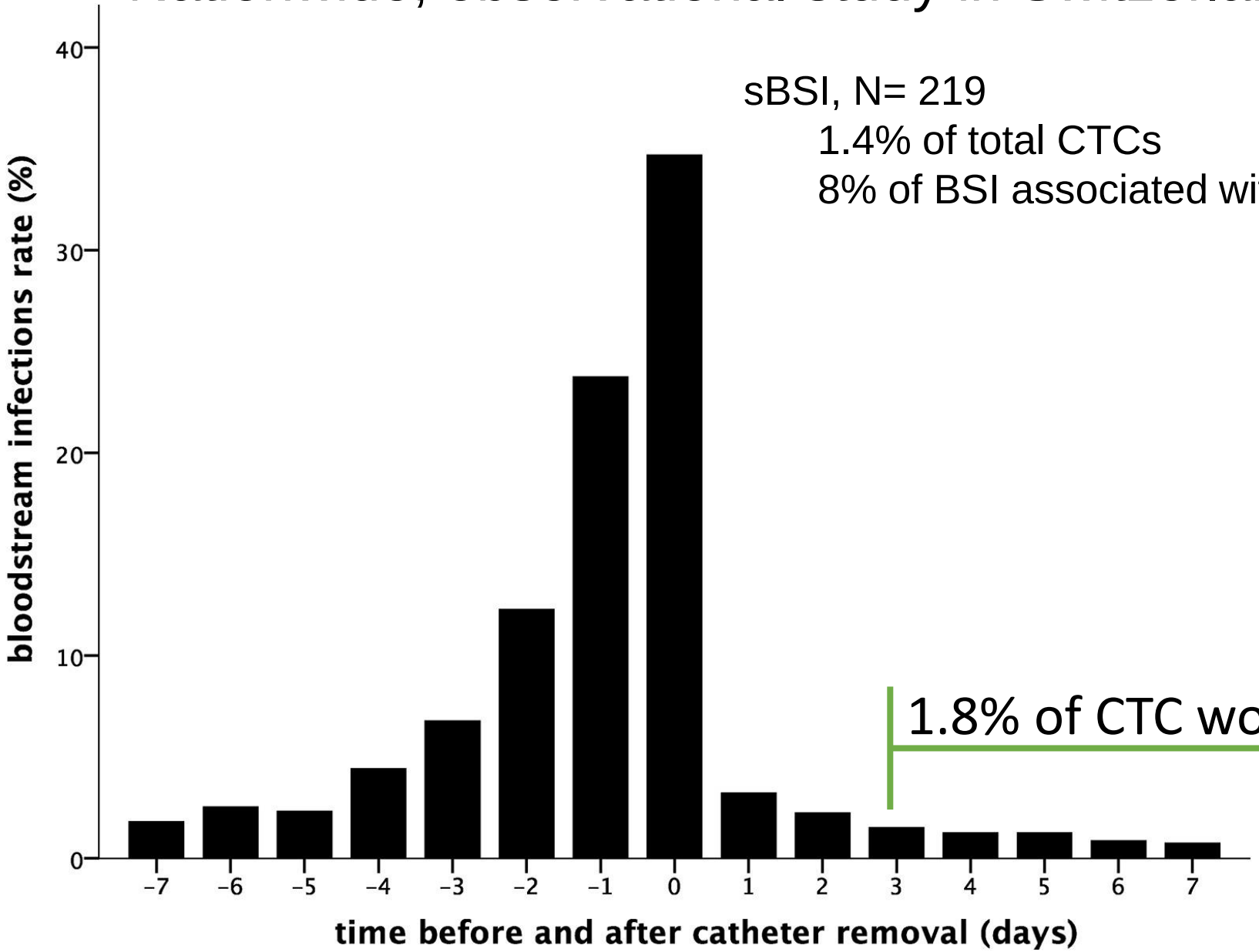
12 513 CTCs without concurrent BSI

219 sBSI, (same microorganism recovered from the CVC tip and from blood cultures performed **> 2 days up to 7 days after CVC removal**)

sBSI, Same microorganism recovered from the CVC tip and from blood cultures performed > 2 days up to 7 days after CVC removal,

Buetti N, Clin Microbiol Infect. 2018;24:548

Nationwide, observational study in Switzerland from 2008 to 2015



sBSI, N= 219

1.4% of total CTCs

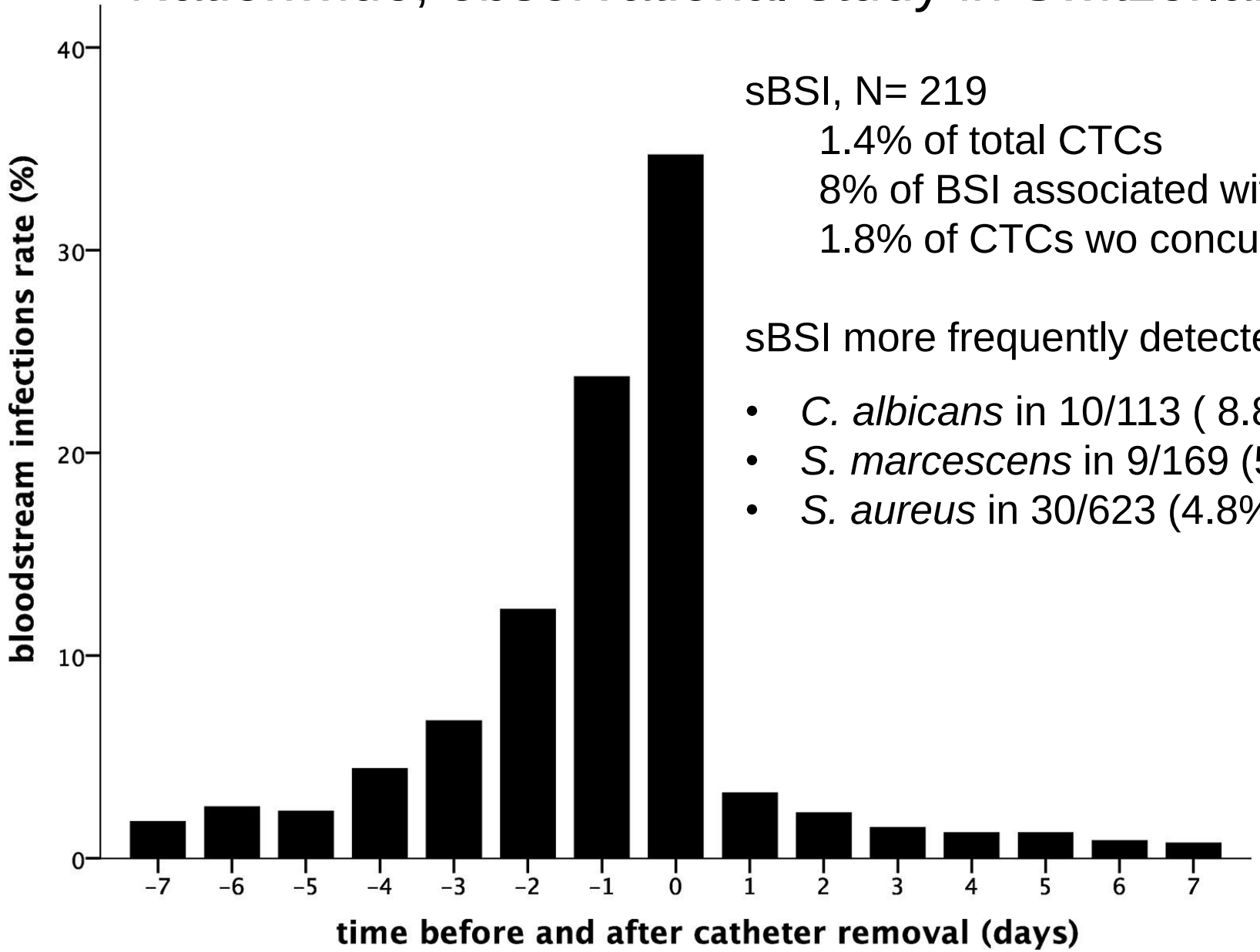
8% of BSI associated with CVCs (concurrent + subsequent)

1.8% of CTC wo concurrent BSI (219 / 12513)

sBSI, Same microorganism recovered from the CVC tip and from blood cultures performed > 2 days up to 7 days after CVC removal,

Buetti N, Clin Microbiol Infect. 2018;24:548

Nationwide, observational study in Switzerland from 2008 to 2015



sBSI, N= 219

- 1.4% of total CTCs
- 8% of BSI associated with CVCs (concurent + subsequent)
- 1.8% of CTCs wo concurrent BSI

sBSI more frequently detected after identification on CTC of

- *C. albicans* in 10/113 (8.8%)
- *S. marcescens* in 9/169 (5.3%)
- *S. aureus* in 30/623 (4.8%)

sBSI, Same microorganism recovered from the CVC tip and from blood cultures performed > 2 days up to 7 days after CVC removal,

Buetti N, Clin Microbiol Infect. 2018;24:548

Microorganism distribution of positive catheter tip culture and subsequent bloodstream infection (sBSI)

	Total[a] *N* (%)	sBSI *N* (%)	sBSI/pathogen
Enterobacteriaceae	1552 (12.4)	40 (18.3)	2.6% (1.8–3.4)
S. marcescens	169 (1.4)	9 (4.1)	5.3% (1.9–8.7)
Gram-negative non-fermenters	431 (3.4)	8 (3.7)	1.9% (0.6–3.1)
P. aeruginosa	297 (2.4)	7 (3.2)	2.4% (0.7–4.1)
S. aureus	623 (5.0)	30 (13.7)	4.8% (3.1–6.5)
CoNS	8518 (68.1)	116 (53.0)	1.4% (1.1–1.6)
Streptococcus spp	51 (0.4)	0 (0)	0%
Enterococcus spp	733 (5.9)	12 (5.5)	1.6% (0.7–2.5)
Anaerobes	12 (0.1)	0 (0)	0%
Fungi	172 (1.4)	12 (5.5)	7.0% (3.2–10.8)
Candida albicans	113 (0.9)	10 (4.6)	8.8% (3.5–14.0)
Other	421 (3.4)	1 (0.5)	0.2% (-0.2–0.6)
Total	12513 (100.0)	219 (100.0)	1.8% (1.6–2.0)

CoNS, coagulase-negative staphylococci spp species; sBSI, subsequent bacteraemia or fungaemia; CI, confidence interval.

[a] Without episodes of bacteraemia 7 days before and 2 days after catheter removal.

sBSI more frequently detected after identification on CTC of

- *C. albicans* in 10/113 (8.8%)
- *S. marcescens* in 9/169 (5.3%)
- *S. aureus* in 30/623 (4.8%)

Buetti N, Clin Microbiol Infect. 2018;24:548

Isolated CTC and sBSI in ICUs

	sBSI N (%)	without sBSI N (%)	p-value	Total*
Department[1]				
ICU	92 (42.4)	2849 (23.9)	**<0.001**	2941
Non-ICU	125 (57.6)	9055 (76.1)		9180

Among episodes of catheter colonization with sBSI, 42.4% of cases were from ICU (vs. 23.9% in those without sBSI, p < 0.001

sBSI, isolating the same microorganism as the one recovered from the CVC tip from blood cultures performed > 2 days up to 7 days after CVC removal

Buetti et al. Critical Care (2018) 22:259

Isolated CTC and sBSI in ICUs

	Total*	sBSI	sBSI/pathogen isolated from catheter tip (95% CI)
***Enterococcus* spp**	252	4	1.6% (0.5-4.2)
Enterobacteriaceae	412	19	4.6% (3.3-7.2)
S. marcescens	40	4	10.0% (3.3-24)
Fungi	29	8	27.6% (11.3-43.9)
C. albicans	22	8	36.4% (18-59.2)
Gram-negative non-fermenters	133	4	3.0% (1-8)
P. aeruginosa	81	4	4.9% (1.6-12.8)
S. aureus	88	7	8.0% (3.5-16.2)
CoNS[1]	1925	49	2.5% (1.9-3.3)
Anaerobes	1	0	0%
Other	101	1	1% (0-6.2)
Total	2941	92	3.1% (2.5-3.8)

Buetti et al. Critical Care (2018) 22:259

Isolated CTC with *Staphylococcus aureus* and sBSI

Preventing *Staphylococcus aureus* Bacteremia and Sepsis in Patients With *Staphylococcus aureus* Colonization of Intravascular Catheters

A Retrospective Multicenter Study and Meta-Analysis

450 patients with an IV catheter colonized with *S. aureus* during the 6-year study period.

Follow-up = 6 months.

256 (57%) excluded because of *S. aureus* BSI between 7 days prior **until 24 h after CVC** removal

-> 192 patients included

Median duration of catheter insertion = 7 days.

74 antibiotics active against the cultured *S. aureus* within 24 hours

-> 18/192 (9%) sBSI at 10.7 days (range, 2-65 d) after CVC removal

Abs 3/74 (4%) vs no Abs 15/118 (13%), OR = 4.2; 95% CI, (1.1-15.6)

Hetem DJ, Medicine 2011

Isolated CTC with *Staphylococcus aureus* and sBSI (>48 hrs after CVC rem=oval)
- cohorts reported by Ekkelenkamp and Hetem combined -

TABLE 3. Risk Factors for Subsequent *S. aureus* Bacteremia in Patients With *S. aureus* Colonization of IV Catheters, Combined Analysis*

	Patients Without Subsequent SAB	Patients With Subsequent SAB After 48 h	Univariate Analysis		Multivariate Analysis	
Variable	**No. (%) (n = 259)**	**No. (%) (n = 32)**	**P**	**OR (95% CI)**	**P**	**OR (95% CI)**
No antibiotic therapy within 24 h	140 (54)	27 (84)	0.001	4.59 (1.71–12.35)	0.001	5.4 (2.0–15.1)
Documented exit-site infection	85 (33)	17 (53)	0.023	2.32 (1.11–4.87)	0.003	3.31 (1.5–7.4)
Corticosteroid therapy	46 (18)	12 (37)	0.007	2.87 (1.30–6.32)	0.013	2.9 (1.3–6.6)
Immunosuppressive therapy (all)	63 (24)	15 (47)	0.007	2.74 (1.30–5.81)	0.61	1.4 (0.3–5.6)

*Combining results from present report and results of the study by Ekkelenkamp et al.[1]

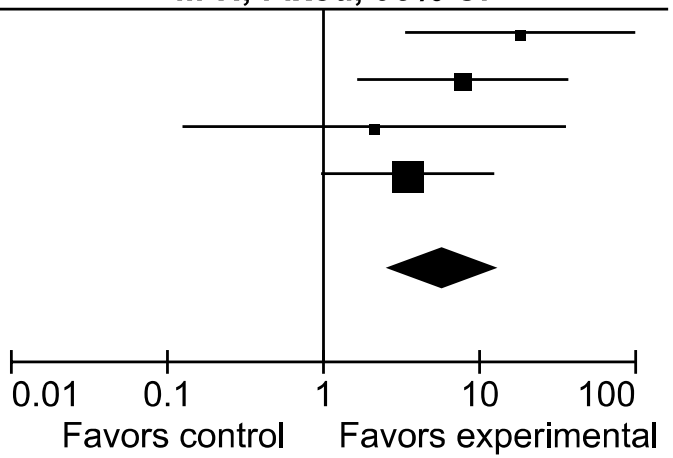
Hetem DJ, Medicine 2011

Protective effect of prophylactic antibiotic therapy for CTC with *S. aureus* to prevent subsequent *S. aureus bacteremia*, (> 24 h after CVC removal)

Study First Author, Ref., Year	Antibiotic Therapy Events	Antibiotic Therapy Total	No Antibiotic Therapy Events	No Antibiotic Therapy Total	Weight	Odds Ratio (Non-event) M-H, Fixed, 95% CI
Ruhe[7] 2006	2	59	7	18	9.7%	18.14 [3.32, 99.16]
Ekkelenkamp[1] 2008	2	50	12	49	25.3%	7.78 [1.64, 36.94]
Park[6] 2010	1	39	1	19	10.5%	2.11 [0.12, 35.70]
Hetem (PR) 2011	3	74	15	118	54.5%	3.45 [0.96, 12.35]
Total (95% CI)		**222**		**204**	**100.0%**	**5.83 [2.57, 13.19]**
Total events	8		35			

Heterogeneity: Chi² = 2.99, df = 3 (P = 0.39); I² = 0%

Test for overall effect: Z = 4.22 (P < 0.0001)



In the studies by Ruhe and Park, Abs were initiated within 48 hours

In the studies by Ekkelenkamp and Hetem, Abs were initiated within 24 hours.

Hetem DJ, Medicine 2011

Significance of the isolation of *Staphylococcus aureus* from a central venous catheter tip in the absence of concomitant bacteremia: a clinical approach

Group 1, 67 patients with *S aureus* CTC with CRBSI (positive BCs drawn ≤ 48 h since the catheter removal yielding *S. aureus* with identical antimicrobial susceptibility profile)

Group 2, 46 patients with *S aureus* CTC without CRBSI (negative BCs drawn ≤ 48 h since the catheter removal)

Subsequent infection: 17/113 (15%) **(> 48** h after CVC removal due to *S. aureus* of CTC with identical antimicrobial susceptibility profile)

14/113 (12.4%) sBSI > 48 h after CVC removal
Hematogenous dissemination in 6 /113 patients

- 4 septic arthritis
- 2 septic pulmonary
- 1 infective endocarditis
- 1 cerebral abscess
- 1 splenic abscess
- 1 septic endophthalmitis

López-Medrano E, Eur J Clin Microbiol Infect Dis (2016) 35:1865–1869

Table 1 Patients with a CVC tip culture positive for *Staphylococcus aureus*

	All patients ($n = 113$)	Group 1 (BC[g] positive for *S. aureus*) ($n = 67$)	Group 2 (BC[g] negative for *S. aureus*) ($n = 46$)	p-Value[a] G1 vs G2
Temperature ≥38.0 °C (n [%])	100 (88.5)	60 (89.6)	40 (86.9)	0.671
Local signs of thrombophlebitis (n [%])	39 (34.5)	29 (43.3)	10 (21.7)	**0.018**
Treatment and endpoint				
Appropriate antibiotic therapy (n [%])	84 (74.3)	57 (85.1)[f]	31 (67.4)	**0.026**
Delayed *S. aureus* bacteremia and/or hematogenous dissemination (n [%])	17 (15.0)	17 (25.4)	0 (0.0)	**<0.001**
Delayed *S. aureus* bacteremia (n [%])	14 (12.5)	14 (20.9)	0 (0.0)	**0.001**
Delayed hematogenous dissemination (n [%])[e]	6 (5.3)	6 (9.0)	0 (0.0)	0.080
Death by any cause 6 months after removal of the catheter	21 (18.6)	14 (20.9)	7 (15.2)	0.446

López-Medrano E, Eur J Clin Microbiol Infect Dis (2016) 35:1865–1869

	All patients ($n = 113$)	Group 1 (BC[g] positive for *S. aureus*) ($n = 67$)	Patients in Group 2 that received antibiotic therapy[b] ($n = 31$)	Patients in Group 2 that did not receive antibiotic therapy[b] ($n = 15$)	p-Value[c] G1 vs G2 wo ABs
Temperature ≥38.0 °C (n [%])	100 (88.5)	60 (89.6)	29 (93.5)	11 (73.3)	0.110
Local signs of thrombophlebitis (n [%])	39 (34.5)	29 (43.3)	8 (26.7%	1 (6.7)	**0.008**
Treatment and endpoint					
Appropriate antibiotic therapy (n [%])	84 (74.3)	57 (85.1)[f]	31 (100)	0 (0.0)	–
Delayed *S. aureus* bacteremia and/or hematogenous dissemination (n [%])	17 (15.0)	17 (25.4)	0 (0.0)	0 (0.0)	**0.033**
Delayed *S. aureus* bacteremia (n [%])	14 (12.5)	14 (20.9)	0 (0.0)	0 (0.0)	0.062
Delayed hematogenous dissemination (n [%])[e]	6 (5.3)	6 (9.0)	0 (0.0)	0 (0.0)	0.334
Death by any cause 6 months after removal of the catheter	21 (18.6)	14 (20.9)	6 (19.4)	1 (6.7)	0.283

López-Medrano E, Eur J Clin Microbiol Infect Dis (2016) 35:1865–1869

	All patients ($n = 113$)	Group 1 (BC[g] positive for *S. aureus*) ($n = 67$)	Patients in Group 2 that received antibiotic ther…	P… antibiotic therapy[b] ($n = 15$)	p-Value[c] G1 vs G2 wo ABs
Temperature ≥38.0 °C (n [%])	100 (88.5)	60 (89.6)		11 (73.3)	0.110
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Treatment and endpoint					
Appropriate antibiotic therapy (n [%])	84 (74.3)		31 (100)	0 (0.0)	–
Delayed *S. aureus* bacteremia and/or hematogenous dissemi… (n [%])		(25.4)	0 (0.0)	0 (0.0)	**0.033**
Delayed *S. aur*… (n [%])	14 (12.5)	14 (20.9)	0 (0.0)	0 (0.0)	0.062
D… [%])[e]	6 (5.3)	6 (9.0)	0 (0.0)	0 (0.0)	0.334
…y cause 6 months after …oval of the catheter	21 (18.6)	14 (20.9)	6 (19.4)	1 (6.7)	0.283

CTC à S aureus isolé et hémocultures prélevées et négatives pendant les 48 h suivant le retrait même en cas de suspicion d'infection -> AB ?

López-Medrano E, Eur J Clin Microbiol Infect Dis (2016) 35:1865–1869

R3.12—The duration of the antibiotic therapy for documented catheter colonization without bacteremia depends on the species identified and the clinical setting in which the catheter was removed.

No treatment is required in the absence of signs of infection
The clinical surveillance, with blood cultures even in the absence of fever, is required in the case of colonization by *Staphylococcus aureus*

Table 3 Unexplained fever, catheter removed and positive microbiology (EXPERT OPINION)

Catheter removed in a context of fever and positive microbiology	Antibiotics and duration
Staphylococcus aureus,	
Negative blood culture	3–5 days
Positive blood culture with no remote complications	14 days
Positive blood culture with remote complications	4 to 6 weeks

-> Venous US, echocardiography

Isolated CTC with Gram negative bacteria and sBSI

Eur J Clin Microbiol Infect Dis (2012) 31:1027–1033
DOI 10.1007/s10096-011-1401-0

ARTICLE

Bacteremic complications of intravascular catheter tip colonization with Gram-negative micro-organisms in patients without preceding bacteremia

A. van Eck van der Sluijs · J. J. Oosterheert · M. B. Ekkelenkamp · I. M. Hoepelman · Edgar J. G. Peters

Bacteremic complications of intravascular catheter tip colonization with Gram-negative micro-organisms in patients without preceding bacteremia

BSI, positive BC **from 48 hrs before** to 90 days after catheter removal

BSI isolate identical (same species and same antibiotic resistance pattern) to that of the CVC tip.

BC(s) positive later than the catheter tip culture

Median time from CVC removal to sBSI = 4 days (IQR: 3–9 days).

213 CTCs in 181 patients, sBSI with GNB in 40 (19%) cases (CRBSI & sBSI)

No positive blood cultures with the same micro-organism after 10 days following catheter removal.

van Eck van der Sluijs A, Eur J Clin Microbiol Infect Dis (2012) 31:1027–1033

Isolated CTC with Gram negative bacteria and sBSI

	No subsequent GNB (n=173)	Subsequent GNB (n=40)	p-value	OR of difference (95% CI), univariate analysis
Immunosuppressive medication	129 (75)	33 (83)	0.05	0.38 (0.14–1.04)
Jugular vein*	51 (30)	5 (13)	0.05	0.38 (0.14–1.04)
Artery*	8 (5)	7 (18)	0.006	5.02 (1.68–14.99)
PICC	4 (2)	5 (13)	0.04	6.04 (1.54–23.62)
Tunneled	8 (5)	3 (8)	0.46	1.67 (0.42–6.61)
Catheter exit site infection[a]	34 (20)	3 (8)	0.12	0.38 (0.11–1.35)
SIRS	67 (39)	14 (35)	0.40	0.73 (0.36–1.51)
Antibiotic treatment[b]	147 (85)	37 (93)	0.085	5.54 (0.72–42.42)
Appropriate antibiotic treatment 24 h before to 48 h after catheter tip culture	58 (34)	16 (40)	0.44	1.32 (0.65–2.68)
No antibiotic treatment 24 h before to 48 h after catheter tip culture	26 (15)	3 (8)	0.21	0.45 (0.13–1.60)
SDD*	33 (19)	15 (38)	0.012	2.55 (1.21–5.36)

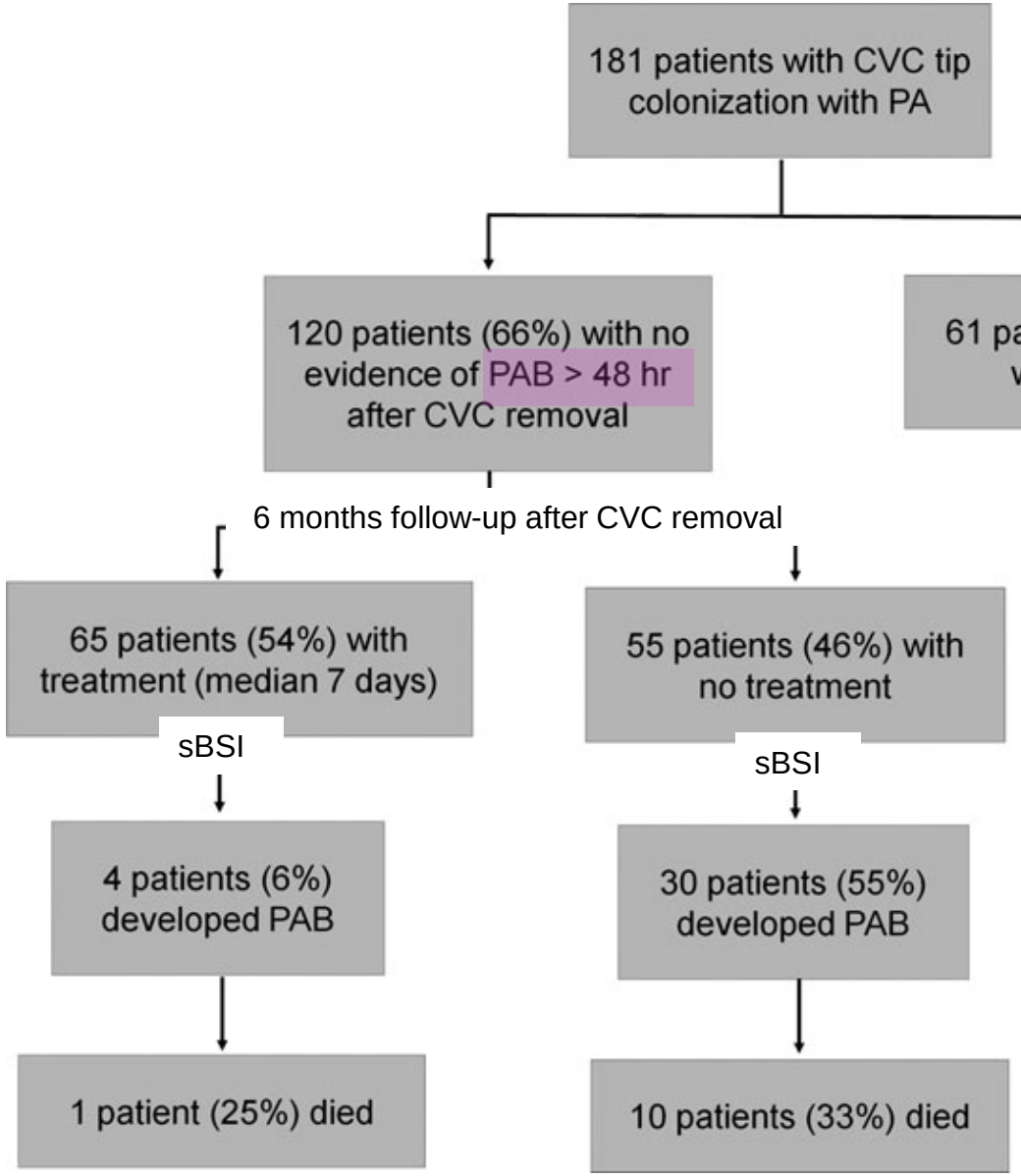
In the multivariate logistic regression analysis,

Arterial catheter (p = 0.048, OR = 3.67, 95% CI: 1.01–13.26)

SDD (p = 0.033, OR = 2.47, 95% CI: 1.07–5.69)

van Eck van der Sluijs A, Eur J Clin Microbiol Infect Dis (2012) 31:1027–1033

CTC with *P.aeruginosa* is associated with a 28% incidence of sBSI



IV antibiotics ≥3 days for which the isolated strain was susceptible (timing?)

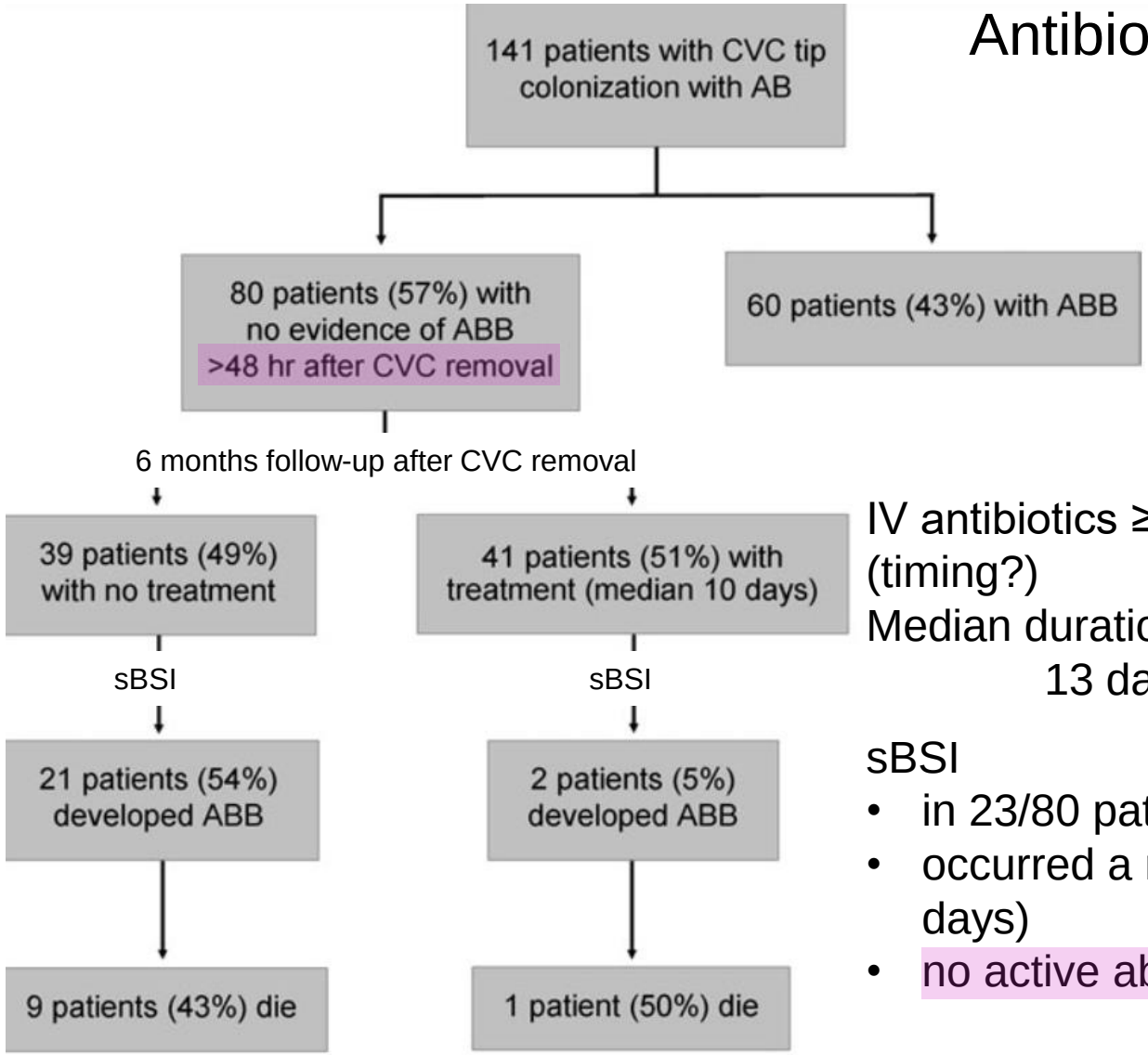
Median duration of catheterization, 16 days with antibiotics vs 15 without (P =0.79)

sBSI

- in 34/120 patients (28%),
- occurred a median of 8 days after CVC removal (range, 3–24 days)
- no active Abs, RR = 8.86; 95% CI, 3.3–23.6 (P=0.001)

Apisarnthanarak A, CID 2012:54

CTC with MDR *A. baumannii* was associated with a 28.8% incidence of sBSI



Antibiotics associated with 91% lower risk of sBSI

IV antibiotics ≥3 days for which the isolated strain was susceptible (timing?)

Median duration of catheterization:

13 days with AB vs 12 without (P =0.79)

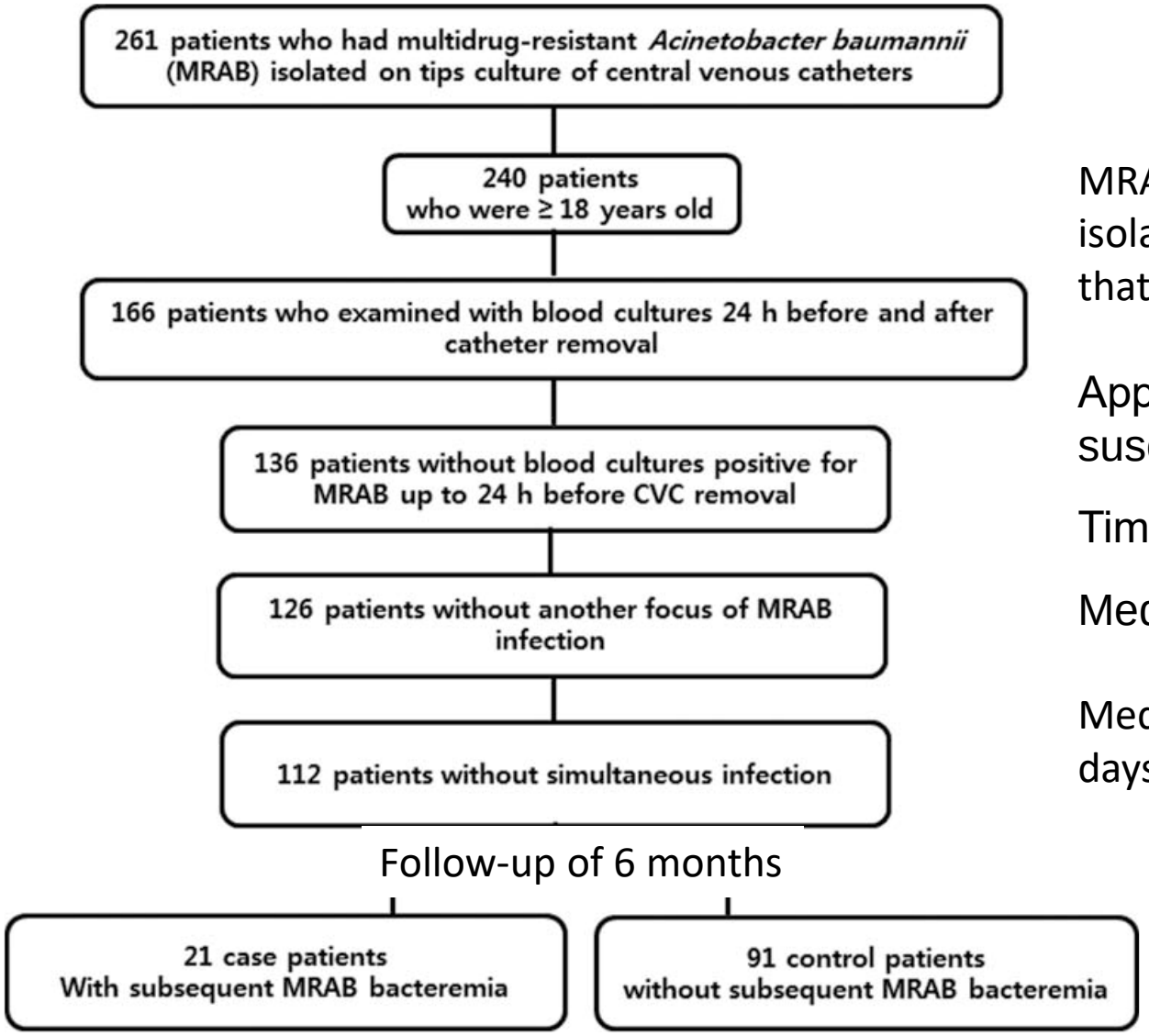
sBSI

- in 23/80 patients (28%),
- occurred a median of 10 days after CVC removal (range, 3–30 days)
- no active abtibiotics RR = 22.54; 95% CI, 2.7–42.8 (P <0.001)

MDR *Acinetobacter baumannii*, isolate resistant to >3 classes of the following Abs: cephalosporins, β-lactam/β-lactamases inhibitors, aminoglycosides, fluoroquinolones, and carbapenems

Apisarnthanarak A, CID 2011:52

CTC with MDR *A. baumannii* was associated with a 18.8% incidence of sBSI



ICU setting

MRAB sBSI ≥1 positive BC **within 6 months of CVC removal** with an isolate that demonstrated an antibiotic resistance pattern identical to that of the CTC

Appropriate Abs, IV ABs ≥3 days to which the MRAB strain was susceptible

Timing ≤3 d of removal in 8/112 with ABs

Median duration of catheterization (9 sBSI vs 11 days no-sBSI)

Median time from CVC removal until sBSI = 7.0 days (IQR, 4.0–12.0 days)

MRAB, MDR *Acinetobacter baumannii*, isolate resistant to >3 classes of the following Abs: cephalosporins, β-lactam/β-lactamases inhibitors, aminoglycosides, fluoroquinolones, and carbapenems

Yoon YK, Scand J Infect Dis 2013 Dec;45(12):900-6

CTC with MDR *A. baumannii* was associated with a 18.8% incidence of sBSI

Table I. Clinical and demographic characteristics of 112 patients with a positive central venous catheter tip culture caused by multidrug-resistant Acinetobacter baumannii, without concurrent bacteremia.

Variables[a]	All ($N = 112$)	No subsequent bacteremia ($n = 91$, 81.2%)	Subsequent bacteremia ($n = 21$, 18.8%)	p-Value[b]
Duration of intravascular catheter in situ, days, median	11 (7.0–17.0)	11 (8.0–18.0)	9.0 (7.0–15.0)	0.455
Prior antibiotic use, *n* (%)	120 (91.1)	81 (89.0)	21 (100)	0.204
Clinical severity at the time of catheter removal				
Catheter exit site infection [6], *n* (%)	5 (4.5)	4 (4.4)	1 (4.8)	1.000
Systemic inflammatory response syndrome, *n* (%)	89 (79.5)	68 (74.7)	21 (100)	0.006
APACHE II score,[f] mean (SD)	15.3 (6.6)	15.1 (6.7)	15.9 (6.1)	0.647
Laboratory results at the time of catheter removal				
C-reactive protein, mg/l, median (IQR)	15.7 (6.7–51.3)	14.5 (6.5–42.7)	91.7 (51.4–254.3)	0.010
WBC > 12,000/μl, *n* (%)	39 (34.8)	30 (33.0)	9 (42.9)	0.391
Albumin < 3.0 mg/dl, *n* (%)	71 (63.4)	59 (64.8)	12 (57.1)	0.510
Antibiotic treatment for CVC tip colonization caused by MRAB, *n* (%)				
Antibiotic treatment	8 (7.1)	6 (6.6)	2 (9.5)	0.643

Yoon YK, Scand J Infect Dis 2013 Dec;45(12):900-6

CTC with MDR *A. baumannii* was associated with a 18.8% incidence of sBSI

Table II. Multivariable Firth logistic regression analysis of predictive factors associated with subsequent bacteremia due to multidrug-resistant Acinetobacter baumannii.[a]

Variables	OR	95% CI	*p*-Value
Gender, male sex	3.16	0.95–10.49	0.061
C-reactive protein ≥40 mg/l	18.11	2.22–148.07	0.007
Prior receipt of carbapenems	7.04	1.43–34.77	0.017
Prior receipt of corticosteroids	6.67	1.19–37.44	0.031
Prior MRAB colonization at a site other than the catheter	0.10	0.03–0.39	0.001

Yoon YK, Scand J Infect Dis 2013 Dec;45(12):900-6

R3.12—The duration of the antibiotic therapy for documented catheter colonization without bacteremia depends on the species identified and the clinical setting in which the catheter was removed.

No treatment is required in the absence of signs of infection
The clinical surveillance, with blood cultures even in the absence of fever, is required in the case of colonization by *Pseudomonas aeruginosa* and other non-fermenting Gram-negative bacilli

Catheter removed in a context of fever and positive microbiology	**Antibiotics and duration**
Enterobacteriaceae, enterococci, coagulase-negative *Staphylococcus*	
Negative blood culture	No antibiotics[a]
Positive blood culture with no distant complications	7 days
Positive blood culture with remote complications	4 to 6 weeks
Pseudomonas aeruginosa, *Acinetobacter baumannii*	
Negative blood culture	3–5 days[a]
Positive blood culture with no distant complications	7 days
Positive blood culture with distant complications	4 to 6 weeks

Isolated CTC with *Candida spp* and sBSI

Candidemic complications in patients with intravascular catheters colonized with Candida species: an indication for preemptive antifungal therapy?

	Definite candidemia ($n=3$) n (%) or median (range)	No definite candidemia ($n=65$) n (%) or median (range)
Unit at time of catheter removal		
ICU	2 (67)	43 (66)
Systemic antifungal therapy	3 (100)	24 (37)
Total duration, days[a]	19 (14–44)	13 (2–41)
Start, days after catheter removal[a]	4 (3–6)	2 (0–9)
Stop, days after catheter removal[a]	25 (17–48)	15 (1–43)
Adequate therapy[a]	3 (100)	24 (100)
Adequate dose[a]	2 (67)	22 (92)
Catheter time in situ, days[b]	17 (8–665)	8 (1–23)
Time in situ >8 days	2 (67)	21 (38)
Time in situ >10 days	2 (67)	15 (27)

Definite, N=3 (4%)

Concomitant candidemia (N=2); Day +1

Subsequent candidemia, N= 1 (Day 5)

5 cases of possible IC

CTC with *Candida spp* and without preceding candidemia associated with 4% of subsequent definite candidemia and with up to 12% of combined definite and possible candidemia, invasive candidiasis without positive BC (EORTC)

Leenders NHJ, Int Soc Infect Dis. 2011;15:e453-458.

Is Candida colonization of central vascular catheters in non-candidemic, non-neutropenic patients an indication for antifungals?

215 patients with CTC with Candida species

- **Study population, N=58**; CTC with *Candida spp* and no concomitant candidemia, 7 days before or after CVC withdrawal
- Exclusion, N = 157, including 64 concomitant BSI and 14 with antifungal therapy initiated before CVC withdrawal

Follow-up period, 2.3 (0.5–6.6) months;
Poor outcome, sBSI or mortality

- Mortality, 25/58 (43.1%); in-hospital mortality, 18/58, (31.0%).
- Candidemia, N=1 (1.7%)

Independent predictors for poor outcome (multivariate analysis)

- Ultimately fatal underlying disease: OR 11.98; 95% CI, 1.37–104.97; (P = 0.025)
- Maximum severity reached before CVC removal (severe sepsis, septic shock, MOF: OR 6.16; 95% CI, 1.00–37.93; (P=0.05)

Perez-Parra A, Intensive Care Med (2009) 35:707–712

Clinical significance of Candida colonization of intravascular catheters in the absence of documented candidemia

CVC tip culture yielding ≥15 cfu/ml of *Candida spp*. AND

No concomitant blood culture (48 h before to 48 h after CVC removal) either taken or negative for *Candida spp*.

Subsequent candidemia defined as ≥1 blood culture obtained **48 h after CVC removal**

122 patients with CVC tip culture positive for *Candida spp*

Exclusion :

- 66 (54.1%) concomitant candidemia
- 16 (13.1%) insufficient clinical data

The final cohort therefore consisted of 40 patients, concomitant blood cultures in 27

Follow-up ?

López-Medrano F, Diagn Microbiol Infect Dis. 2012

Clinical significance of Candida colonization of intravascular catheters in the absence of documented candidemia (sBSI > 48 hrs after CVC removal)

Variable	Overall ($N = 40$)	Good outcome ($n = 21$)	Poor outcome ($n = 19$)	P value[a]
Species distribution				NS
C. albicans	29 (72.5%)	16 (76.2%)	13 (68.4%)	
C. parapsilosis	7 (17.5%)	4 (19.1%)	3 (15.8%)	
C. glabrata	3 (7.5%)	1 (4.8%)	2 (10.5%)	
C. guilliermondii	1 (2.5%)	0 (0.0%)	1 (5.3%)	
Clinical signs at the time of IVC removal				
Temperature >38 °C	25 (62.5%)	12 (57.1%)	13 (68.4%)	NS
IVC exit site infection	5 (12.5%)	4 (19.1%)	1 (5.3%)	0.20
Severity reached at the time of IVC removal				
Sepsis	9 (22.5%)	3 (14.3%)	6 (31.6%)	0.26
Septic shock	8 (20.0%)	3 (14.3%)	5 (26.3%)	NS
Multiple organ dysfunction syndrome	4 (10.0%)	1 (4.8%)	3 (15.8%)	NS
ICU admission	24	12 (57.1%)	12 (63.1%)	NS
Antifungal therapy	22 (55.0%)	10 (47.6%)	12 (63.1%)	NS
Days of treatment, mean ± SD	14.0 ± 4.4	13.2 ± 4.1	14.7 ± 4.7	NS
Type of antifungal				NS
Fluconazole	19 (47.5%)	10 (47.6%)	9 (47.4%)	
Voriconazole	1 (2.5%)	0 (0.0%)	1 (5.3%)	
Echinocandin	2 (5.0%)	0 (0.0%)	2 (10.5%)	

Poor outcome

Overall mortality, 16/40 (40%)

No death attributed to Candida spp. infection.

2 patients with abdominal abscess due to C. albicans.

1 (2.5%) - /27 with concomitant blood cultures obtained - developed a metastatic complication attributable to a transient, occult episode of candidemia (chorioretinitis) = possible candidemia

No (definite) subsequent candidemia!

López-Medrano F, Diagn Microbiol Infect Dis. 2012

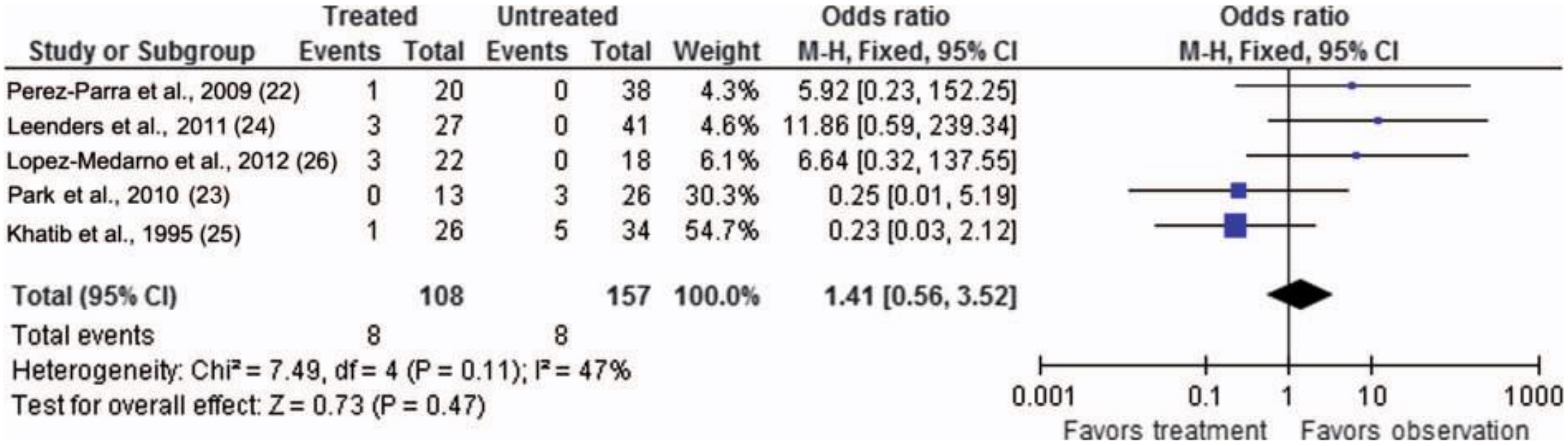


Figure 2. Forest plot of antifungal therapy or catheter colonization and outcome (invasive candidiasis). 'Events' includes patients with invasive candidiasis and 'Total' includes the patients with candidiasis plus those without candidiasis.

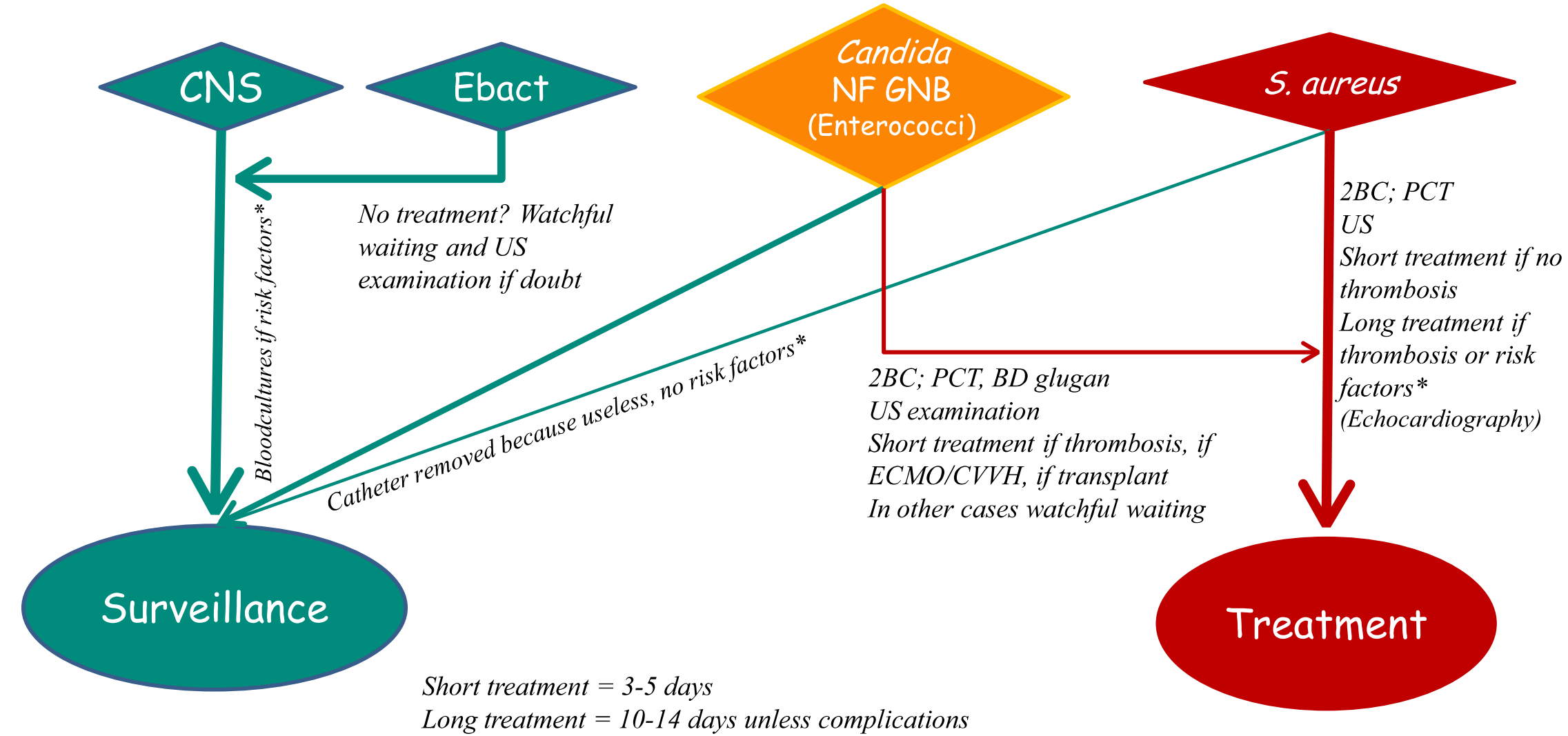
De Almeida BM, Scand J Infect Dis. 2014;46:854–61.

R3.12—The duration of the antibiotic therapy for documented catheter colonization without bacteremia depends on the species identified and the clinical setting in which the catheter was removed.

No treatment is required in the absence of signs of infection.
The clinical surveillance, with blood cultures even in the absence of fever, is required in the case of colonization by *Candida spp*

Table 3 Unexplained fever, catheter removed and positive microbiology (EXPERT OPINION)

Catheter removed in a context of fever and positive microbiology	Antibiotics and duration
Staphylococcus aureus, *Candida* spp.	
Negative blood culture	3–5 days
Positive blood culture with no remote complications	14 days
Positive blood culture with remote complications	4 to 6 weeks



*Risk factors: implantable devices or immunosuppression

Timsit *et al. Intensive Care 2018*

Conclusion

The rate of sBSI in patients with CTC is very low

The risk of subsequent bacteremia in patients in whom a colonized CVC was removed depends on several factors, including

- Immunocompromized status
- Thrombosis of the catheterized vein
- Microbial species
- Probably the magnitude of the inoculum

Complementary studies are required to establish an adequate policy in these patients

Antibiotics for documented catheter colonization without bacteraemia depends on the species identified and the clinical setting in which the catheter was removed.

The experts suggest the following:

a. no treatment is required in the absence of signs of infection
However, the clinical surveillance, with blood cultures even in the absence of fever, is required in the case of colonisation by *Staphylococcus aureus*, *Candida spp*., and *Pseudomonas aeruginosa* and other non-fermenting Gram-negative bacilli.

b. When the catheter was removed in a context of unexplained sepsis:

- b-1 In the case of colonisation by *S. aureus*, *Candida spp*. or non-fermenting Gram-negative bacilli, the total duration of treatment should be 3 to 5 days, in the absence of bacteraemia or complications.
- b-2 In the case of colonisation by coagulase-negative *Staphyloccoci* or enterobacteria: no antibiotic therapy is required.

Timsit JF, Ann. Intensive Care (2020) 10:118

Table 3 Unexplained fever, catheter removed and positive microbiology (EXPERT OPINION)

Catheter removed in a context of fever and positive microbiology	Antibiotics and duration
Staphylococcus aureus, *Candida* spp.	
Negative blood culture	3–5 days
Positive blood culture with no remote complications	14 days
Positive blood culture with remote complications	4 to 6 weeks
Enterobacteriaceae, enterococci, coagulase-negative *Staphylococcus*	
Negative blood culture	No antibiotics[a]
Positive blood culture with no distant complications	7 days
Positive blood culture with remote complications	4 to 6 weeks
Pseudomonas aeruginosa, *Acinetobacter baumannii*	
Negative blood culture	3–5 days[a]
Positive blood culture with no distant complications	7 days
Positive blood culture with distant complications	4 to 6 weeks

[a] These proposals are based on poor-quality epidemiological data and are only presented as a guide. They must be modulated according to the presence of signs of clinical sepsis, intravascular devices, and underlying immunosuppression