16e Journée des Référents en Antibiothérapie

lundi 30 août 2021
MONTPELLIER, Le Corum

Actualités dans la prise en charge des bactériémies à staphylocoques dorés

Vincent Le Moing, Montpellier

Bernard Castan, Perigueux

Déclaration de liens d'intérêt avec les industries de santé
en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant :CASTAN Bernard

Titre :Bactériémies à staphylocoques dorés

L'orateur ne souhaite pas répondre ☐

Consultant ou membre d'un conseil scientifique:	☐ OUI	☑ NON
Conférencier ou auteur/rédacteur rémunéré d'articles ou documents: BMS	☐ OUI	☑ NON
Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations: MSD-CORREVIO	☑ OUI	☐ NON
Investigateur principal d'une recherche ou d'une étude clinique:	☑ OUI	☐ NON

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Le Moing Vincent

Titre : Intitulé de l'intervention

Consultant ou membre d'un conseil scientifique	**OUI**
Conférencier ou auteur/rédacteur rémunéré d'articles ou documents	**OUI**
Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations	**OUI**
Investigateur principal d'une recherche ou d'une étude clinique	**NON**

Déclarations d’intérêts de 2015 à 2021 V LE MOING

- **Intérêts financiers : aucun**
- **Liens durables ou permanents : aucun**
- **Interventions ponctuelles : Gilead, Pfizer, Shionogi**
- **Intérêts indirects : aucun**

Epidémiologie

Infection sur cathéter

- Incidence entre 0.5 et 2/1000 jours de cathétérisation
- Importante morbidité et mortalité
  - mortalité attribuable = 3-25%
- Augmente les durées et coûts du séjour hospitalier (en réanimation)
- Augmente la durée d'hospitalisation
  - de 6 à 20 jours
  - surcoût de 16 000 à 28 000 dollars

Digiovine B. AJRCCM 1999

Incidence des bactériémies à *S. aureus* au Danemark

Registre en population 2008-2015: incidence+ 48 %
Explications ??

Mortalité J30 24% stable

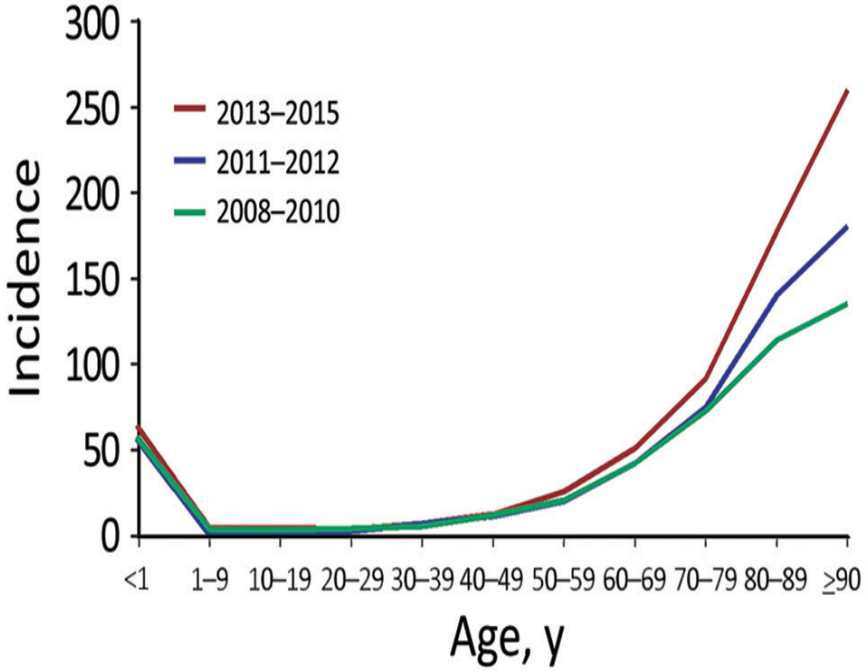
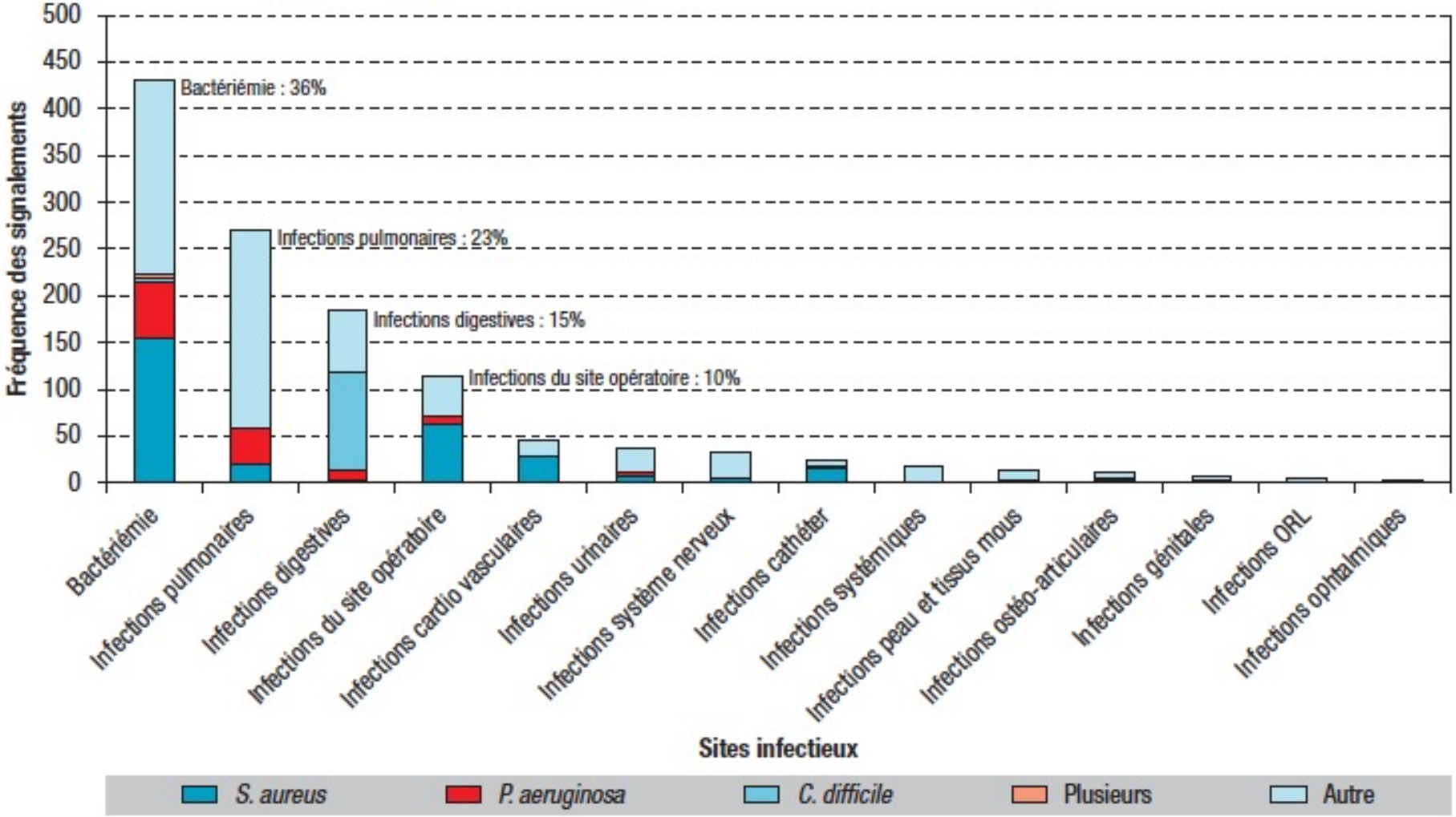


Figure 1. Temporal changes in *Staphylococcus aureus* bacteremia incidence (cases per 100,000 person-years), by age group and years, Denmark, 2008–2015.

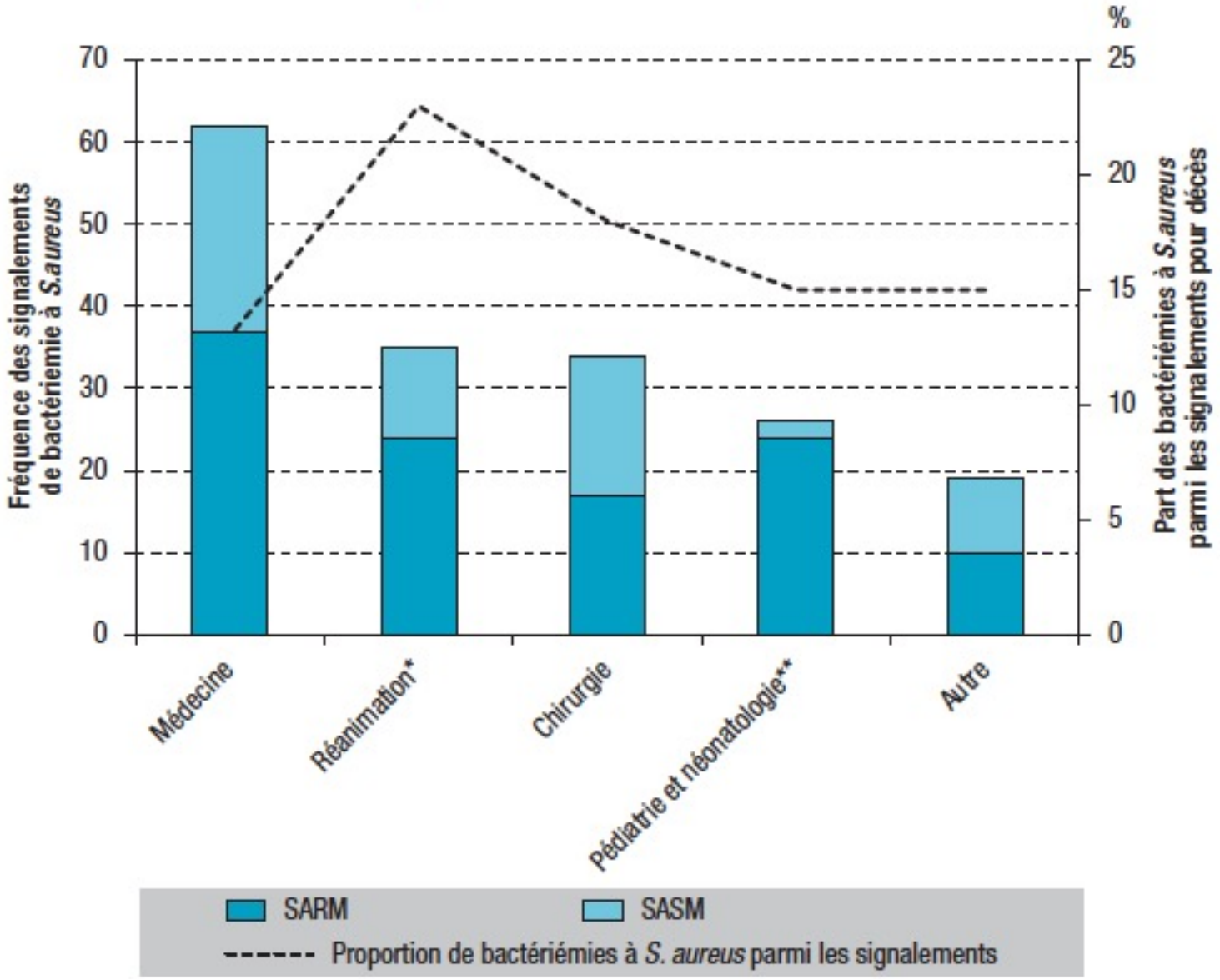
Thorlacius-Ussing L. et al, Emerg Infect Dis 2019

DÉCÈS LIÉS AUX INFECTIONS NOSOCOMIALES : BILAN 2008-2017 DES SIGNALEMENTS EXTERNES EN FRANCE – FOCUS SUR LES BACTÉRIÉMIES À *STAPHYLOCOCCUS AUREUS*

Répartition des sites et germes rapportés dans les signalements avec le critère « décès », France 2008-2017



Distribution annuelle par type de service des signalements de bactériémies à SASM et SARM et de la part de celles-ci dans les signalements avec le critère « décès », France 2008-2017



Hassoun et al. Critical Care (2017) 21:211
DOI 10.1186/s13054-017-1801-3

Critical Care

REVIEW Open Access

Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment

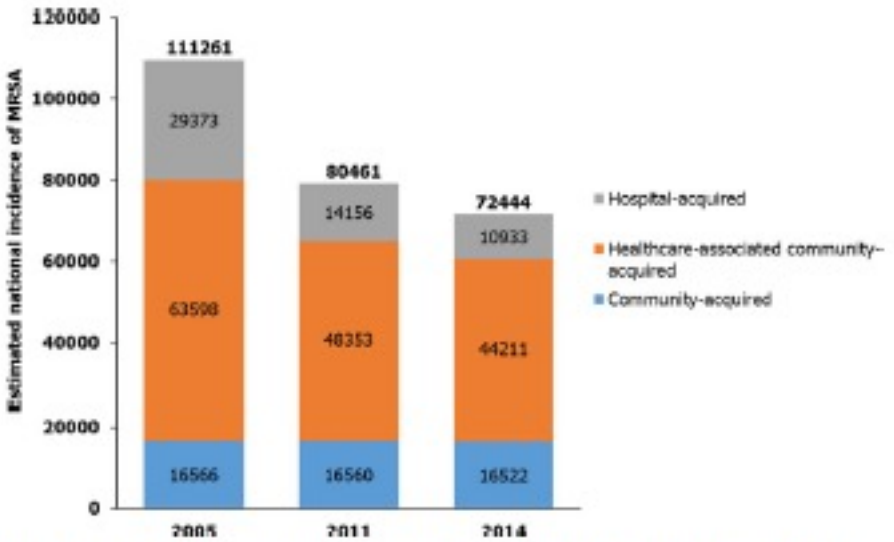
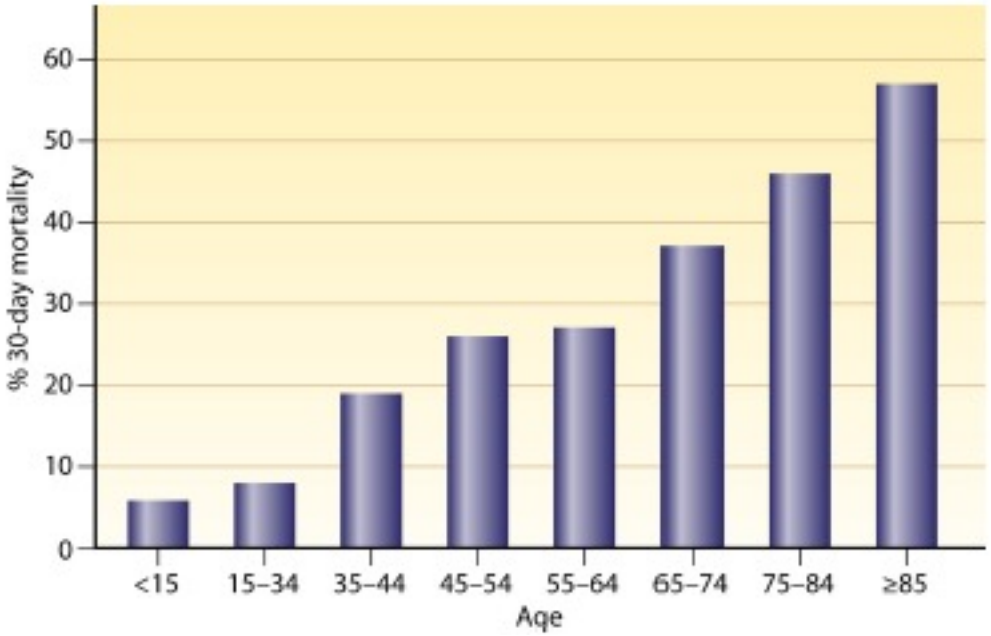


Fig. 1 The national estimated number of MRSA infections in the US, stratified by infection setting. Adapted from data reported by the Center for Disease Control and Prevention [27] and Dantes et al. [28]. *MRSA* methicillin-resistant *S. aureus*

CMR
Journals.ASM.org

Predictors of Mortality in *Staphylococcus aureus* Bacteremia

Sebastian J. van Hal,[a,b] Slade O. Jensen,[b,c] Vikram L. Vaska,[d] Björn A. Espedido,[b,c] David L. Paterson,[d] and Iain B. Gosbell[a,b,c]



Mortalité hospitalière et à J90:

Age
Bactériémie compliquée
Endocardite (cœur gauche)
SAMR < SAMS

Médecine et maladies infectieuses

Les infections à *Staphylococcus aureus* résistant à la méticilline (SARM) d'acquisition communautaire

Community-acquired methicillin-resistant Staphylococcus aureus (MRSA) infections

P. Tattevin [a,*,b,c]

OÙ EN SOMMES NOUS AUJOURD'HUI EN FRANCE AVEC LE CLONE ST80?

Dauwalder O, Lina G, Durand G, et al. Epidemiology of invasive MRSA clones in France, 2006–2007. J Clin Microbiol 2008;46(10):3454–8.

Robert J, Etienne J, Bertrand X. Methicillin-resistant *Staphylococcus aureus* producing Panton-Valentine leukocidin in a retrospective case series from 12 French hospital laboratories, 2000–2003. Clin Microbiol Infect 2005;11(7):585–7.

Médecine et maladies infectieuses 41 (2011) 167–175

doi:10.1016/j.medmal.2010.11.017

Définitions

Uncomplicated bactériemia due to Staphylococcus aureus

- Definition selon Twaites
- Définition uncomplicated bacteriemia (V. fowler CID):

- **Absence de localisation secondaire**
- **ETT/ETO**
- **Bilan systématisé ?**

« Bactériémie non compliquée »

- Définition IDSA

  (i) EI exclue par échographie systématique

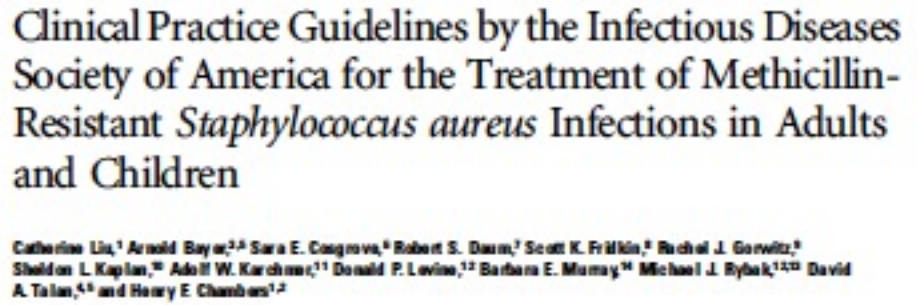
  (ii) Absence de matériel et/ou prothèse

  (iii) Hémoculture négative en 2-4j

  (iv) Apyrexie à **72H** de traitement efficace

  (v) Pas de localisation secondaire

- Si un seul de ces critères manquent : **Bactériémie compliquée**



Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[2,3] Sara E. Cosgrove,[4] Robert S. Daum,[5] Scott K. Fridkin,[6] Rachel J. Gorwitz,[7] Sheldon L. Kaplan,[8] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[15] and Henry F. Chambers[1,2]

Liu C, et al. Clin Infect Dis 2011

EI or not EI? That is the question

- Time to blood positivity
- PREDICT Early (J0) Late (72H)
- VIRSTA+++

Time to blood culture positivity in *Staphylococcus aureus* bacteraemia to determine risk of infective endocarditis*

- Retrospective population-based study: 10 Swiss hospitals
- **New POSITIVE score** was compared to PREDICT and VIRSTA scores

- **Results**:
  - 465 episodes → 38 (8.2%) IE
  - **Cutoff at 13 hours**: TTP had a sensitivity of 100% (95%CI 91-100) and specificity of 52% (95%CI 47-57)

POSITIVE score

Variable	Score
TTP <9 hours	5
TTP >9 but <11 hours[a]	3
TTP >11 but <13 hours[a]	2
IV drug use[a]	3
Vascular phenomena	6
Predisposing heart disease	5

Characteristic	Complete cases			
	n	Sens	Spec	AUC
Predict day 1	531	0.15 (0.04–0.34)	0.95 (0.93–0.97)	0.68 (0.59–0.78)
Predict day 5	284	0.95 (0.74–1.00)	0.46 (0.40–0.52)	0.77 (0.68–0.85)
VIRSTA	284	1.00 (0.82–1.00)	0.44 (0.38–0.50)	0.89 (0.83–0.96)
TTP	531	1.00 (0.87–1.00)	0.44 (0.40–0.49)	0.84 (0.79–0.89)
POSITIVE	531	0.93 (0.76–0.99)	0.70 (0.66–0.74)	0.92 (0.86–0.97)

Kahn F, et al. Clin Microbiol Infect. 2020:S1198-743X(20)30700-X.

Source control & BSI duration

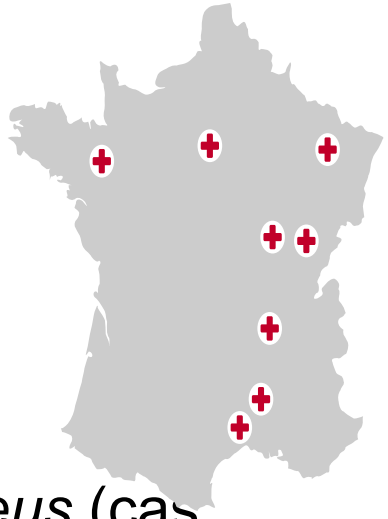
- Multicenter, prospective, observational study 884 hospitalized patients
- Patients were grouped by bacteremia duration (BD):
  - Short (1-2d): 63%
  - Intermediate (3-6d): 28%
  - Prolonged (≥7d): 9%

- **Results**:
  - **Time to source control ↔ BD:** 3.5d vs 3d vs 1d, p<0.0001
  - **Metastatic complications and 30-day mortality** were progressively worse as BD increased (p<0.0001).
  - Every continued day of bacteremia ↔ RR of death of 1.16 (95% CI 1.10-1.22, p<0.0001), with **significant increase in risk starting at 3 days as determined by ROC analysis**.

Minejima E, et al. *Clin Infect Dis* 2020;70(4):566-573.

Etude VIRSTA

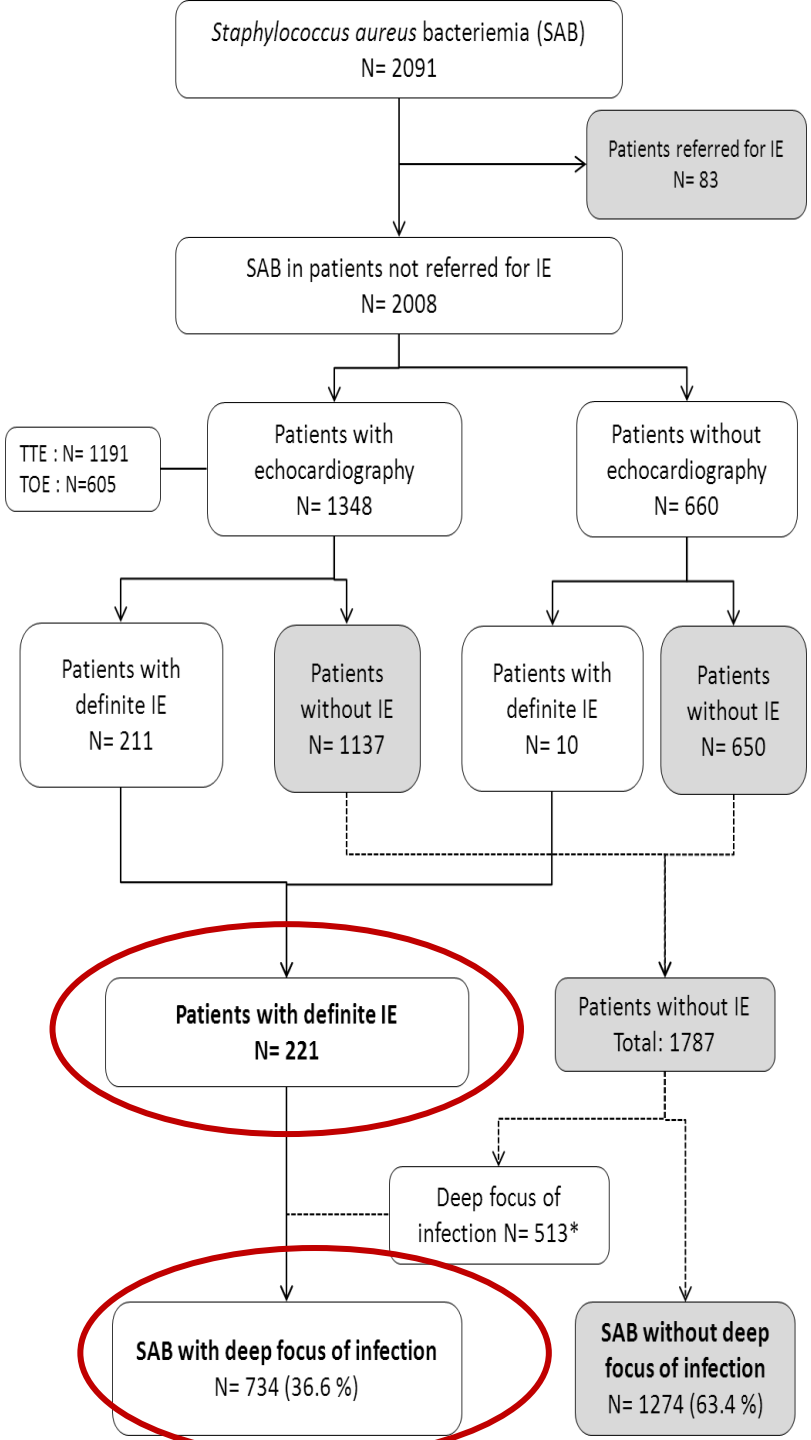
- Cohorte observationnelle prospective
- 8 CHU français
- Avril 2009 – octobre 2011
- 2091 patients consécutifs
  dont 2008 non admis pour EI



- Inclusion: 1ère hémoculture positive à *S. aureus* (cas incidents)
- ETO encouragée mais pas obligatoire

- Exclusion: colonisation de cathéter sans bactériémie

mineurs, adultes protégés, femmes enceintes



Etude VIRSTA
2009-2011
8 CHU français

VIRSTA –
% d'EI en fonction du contexte

Setting of acquisition	Predisposing heart disease			Total
	Yes, prosthetic	Yes, native	No	
Community associated – IVDU	2/2 (100%)	1/3 (33.3%)	18/38 (47.4%)	21/43 (48.8%)
Community associated – non IVDU	20/30 (66.7%)	31/80 (38.8%)	35/369 (9.5%)	86/479 (18.0%)
Non-nosocomial healthcare associated	6/13 (46.2%)	15/66 (22.7%)	21/274 (7.7%)	42/353 (11.9%)
Nosocomial	18/94 (19.1%)	20/191 (10.5%)	31/790 (3.9%)	69/1075 (6.4%)

21%

The VIRSTA score, to estimate the risk of IE in patients with SAB

	.632 Bootstrap procedure	
	β′	Weight
Cerebral or peripheral emboli	2.37	***5***
Meningitis	2.31	***5***
Permanent intracardiac device or previous IE	2.02	***4***
Pre-existing native valve disease	1.29	***3***
Intravenous drug use	1.77	***4***
Persistent bacteremia	1.40	***3***
Vertebral osteomyelitis	1.15	**2**
Community or non nosocomial health care associated acquisition	0.96	**2**
Severe sepsis or shock	0.72	**1**
C-reactive protein >190 mg/L	0.65	**1**

Tubiana S, J Infection 2014

Performances du score VIRSTA pour prédire l'existence d'une EI

Score	Sensitivity	Specificity	PPV	NPV	Patients with IE with the corresponding value	Total Nb of patients with the corresponding value
0	**99.29** (99.23 ;99.34)	**18.4**8 (17.29 ;19.60)	**13.14** (12.15 ; 14.20)	**99.52** (99.49 ; 99.55)	**1**	331
1	**97.16** (96.06 ;98.65)	**32.20** (30.80. 33.51)	**15.09** (13.93 ; 16.24)	**98.92** (98.42 ; 99.47)	**5**	250
2	**95.83** (94.31 ; 97.79)	**44.18** (42.60 ;45.59)	**17.55** (16.22 ;18.86)	**98.83** (98.41 ; 99.40)	**3**	217
3						341
4						239
5						174
6						169
7						99
8						55
9	**26.70** (23.18 ; 30.24)	**98.71** (98.39 ; 99.04)	**71.95** (65.42 ; 78.43)	**91.59** (90.77 ; 92.38)	26	51
≥ 10	**20.36** (17.02 ; 23.81)	**99.44** (99.21 ; 99.65)	**81.82** (75.00 ; 88.24)	**90.99** (90.12 ; 91.79)	59	82

Score VIRSTA < 3

- **VPN: 98,8%**
- **LR - = 0.2**
- **40% de la population**
- **Probabilité d'EI : 1.1%**

Tubiana S., J. Infect 2016

Performances du score VIRSTA pour prédire l'existence d'une EI

Score VIRSTA > 5

- **VPP: 44,6%**
- **LR+ = 6**
- **19% de la population**
- **Probabilité d'EI de 32%**

Score	Sensitivity	Specificity	PPV	NPV	Patients with IE with the corresponding value	Total Nb of patients with the corresponding value
				49 ;	**1**	331
				42 ;	**5**	250
				41 ;	**3**	217
				54 ;	23	341
				38 ;	16	239
				09 ;	18	174
				90 ;	27	169
	62.06)	92.02)	48.37)	95.26)		
7	**45.70** (41.51 ; 49.65)	**95.13** (94.47 ; 95.84)	**53.72** (49.14 ; 58.57)	**93.41** (92.67 ; 94.10)	27	99
8	**38.46** (34.55 ; 42.35)	**97.31** (96.83 ; 97.80)	**63.91** (58.38 ; 69.14)	**92.75** (91.97 ; 93.45)	16	55
9	**26.70** (23.18 ; 30.24)	**98.71** (98.39 ; 99.04)	**71.95** (65.42 ; 78.43)	**91.59** (90.77 ; 92.38)	26	51
≥ 10	**20.36** (17.02 ; 23.81)	**99.44** (99.21 ; 99.65)	**81.82** (75.00 ; 88.24)	**90.99** (90.12 ; 91.79)	59	82

Stratification du risque d'EI pour guider la réalisation de l'échographie ???

Trois groupes de patients atteints de bactériémie à *S. aureus* pourraient être distingués:

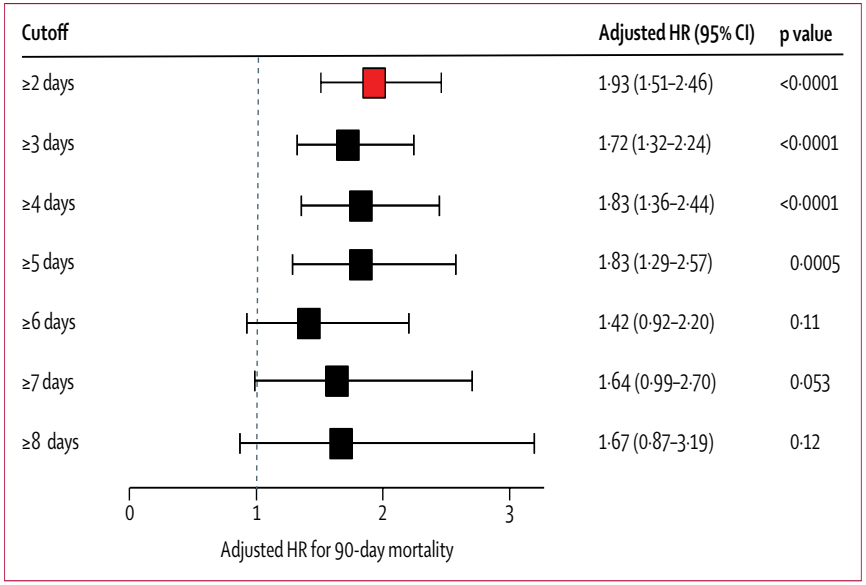
- **faible risque d'EI = ETT dispensable**
- **risque intermédiaire d'EI = ETT et ETO si anormale**
- **risque élevé d'EI = ETO systématique**

En fonction du score VIRSTA:

- **faible risque d'EI =**
  Score VIRSTA < 3
- **risque élevé d'EI =**
  Score VIRSTA > 5

Bactériémie persistante, c'est bien 48 heures

Cohorte ISAC-10
987 patients
17 centres
Durée de bactériémie **sous AB efficace**



	1 day (n=672)	2–4 days (n=218)	5–7 days (n=69)	>7 days (n=28)	Total (n=987)	p value
Outcome						
30-day mortality	84 (13%)	60 (28%)	21 (30%)	9 (32%)	174 (18%)	<0·0001
90-day mortality	148 (22%)	85 (39%)	30 (43%)	10 (36%)	273 (28%)	<0·0001
In-hospital mortality	101 (15%)	72 (33%)	26 (38%)	9 (32%)	208 (21%)	<0·0001
Any new metastatic focus*	39 (6%)	22 (10%)	15 (22%)	3 (11%)	79 (8%)	<0·0001
New metastatic focus >7 days†	22 (3%)	8 (4%)	6 (9%)	3 (11%)	39 (4%)	0·040

Kuehl et al., Lancet Infect Dis 2020

Etude TEPSTAR: recherche d'un consensus sur la recherche des autres foyers profonds

- Objectif: harmonisation des pratiques
- Méthode Delphi

- Accord fort (2ème tour):
  - IRM crâne si EI ou manifestations neurologiques
  - IRM rachidienne orientée par symptômes (après J7)
  - TDM thorax et/ou abdomen si symptômes

- Consensus mou (4ème tour)
  - Pas d'imagerie urinaire si ECBU positif à S. aureus

- **Pas de consensus:**
  - **TDM TAP systématique**
  - **Diagnostic des thrombophlébites septiques**

Dufour S, JNI 2018

Pour les experts, une bactériémie à *S. aureus* correspond à une forte suspicion d'EI

- Recommandations ESC 2015 de prise en charge de l'EI:

  « *In patients with* S. aureus *bacteraemia, echocardiography is justified in view of the frequency of IE in this setting, the virulence of this organism and its devastating effects once intracardiac infection is established.* »

- IE AHA guidelines 2015:

  « *TEE should be the first examination in adults with suspected IE, particularly in the setting of staphylococcal bacteremia. Further work is needed to better define the subgroup of patients who need only TTE* [in this setting] »

- Catheter-related infections guidelines IDSA 2009:

  « *Patients with* S. aureus *CRBSI should receive 4–6 weeks of antimicrobial therapy, unless they have exceptions*

  Patients who are being considered for a shorter duration of therapy should have a transesophageal echocardiograph (TEE) obtained. »

La réalisation de l'écho cœur n'est pas universelle en cas de bactériémie à *S. aureus*

Données issues des études observationnelles récentes

1er auteur	Localisation	Période	N patients	ETT	ETO
Khatib	USA	2002-2009	960	37%	20%
Showler	Toronto	2007-2010	833	65%	14%
Kaasch	Europe-USA	2006-2011	3395	57%	
Joseph	Oxford	2006-2011	668	45%	7%
Le Moing	France	2009-2011	2008	67%	30%
Heriot	Australia	2009-2015	1167	74%	35%

Khatib, Medicine 2013; Joseph, JAC 2013; Kaasch, J Infect 2013; Showler, JACC Imaging 2015; Le Moing Plos One 2015; Heriot EJCMID 2018

Les infectiologues ne recommandent pas systématiquement l'écho cœur

Plusieurs études ont suggéré une efficacité spectaculaire et durable de l'intervention d'un infectiologue dans la prise en charge des patients atteints de bactériémie à *S. aureus*

Au sein du protocole proposé par les infectiologues espagnols: l'écho cœur est recommandée uniquement en cas de bactériémie compliquée définie par

- Bactériémie persistant > 3 jours
- Présence de foyers métastatiques
- Lésions cutanées ou muqueuses évocatrices d'infection systémique aiguë (érythème de Janeway, purpura, taches de Roth, hémorragie conjonctivale…)
- Prothèse permanente quelle qu'elle soit
- Hémodialyse

- **Echo réalisée chez seulement 33 % de 221 cas, en accord avec les recommandations chez 73%**

Lopez-Cortes CID 2013

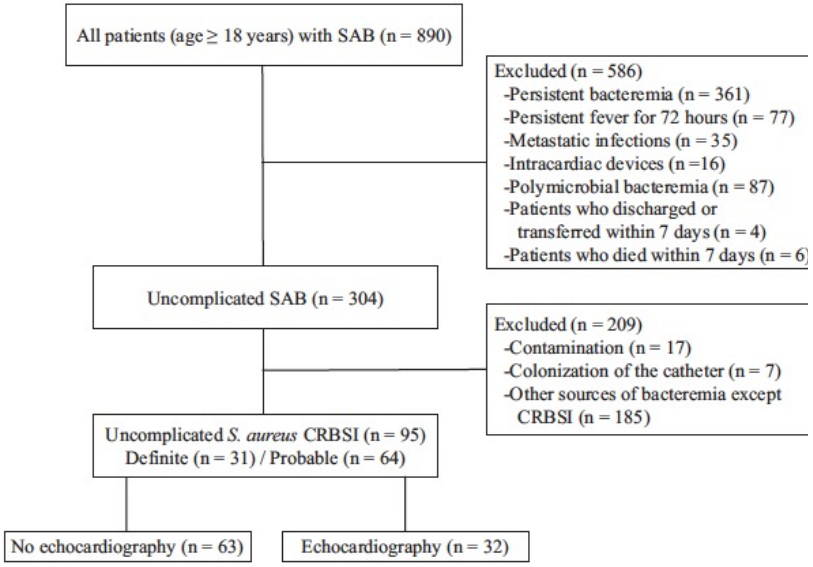
Observational Study

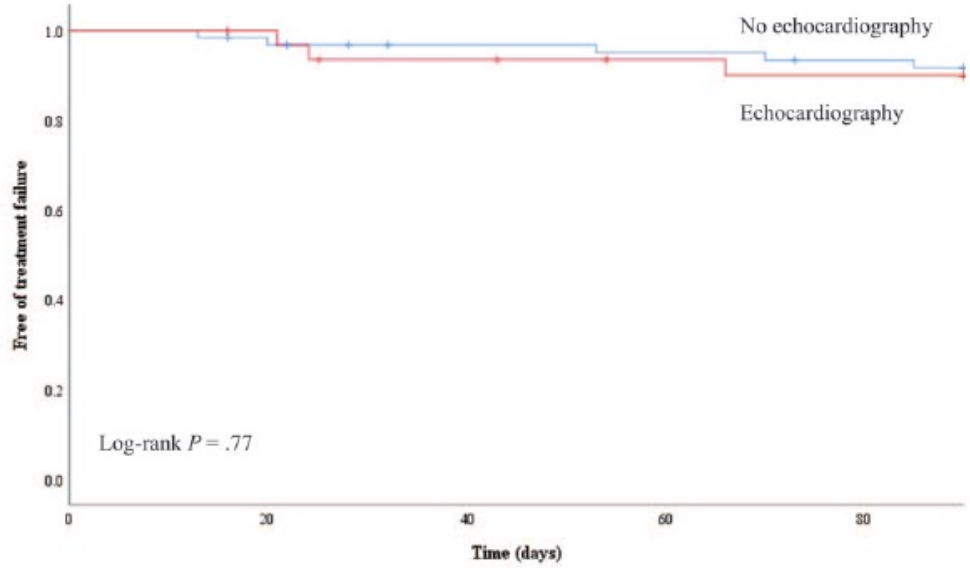
Medicine®

OPEN

Role of echocardiography in uncomplicated *Staphylococcus aureus* catheter-related bloodstream infections

Seok Jun Mun, MD[a], Si-Ho Kim, MD[b], Kyungmin Huh, MD[c], Sun Young Cho, MD[c], Cheol-In Kang, MD[c], Doo Ryeon Chung, MD[c], Kyong Ran Peck, MD[c,*]





Diagnostic microbiologique

Accélération du rendu des résultats des hémocultures

A-Méthode conventionnelle : à JO (jour où l'hémoculture se positive), il est possible de faire :

1- **L'Identification à partir du bouillon d'hémoc de tous types de germes par Spectro de masse (MaldiTof)** : résultat dans la journée

Avantage : orientation rapide pour le clinicien

Inconvénient : aspect technique pour la labo : manipulation plus longue et plus consommatrice de temps technicien (difficile à mettre en oeuvre sur toutes les hémoc+)

2**- L' Antibiogramme à partir du bouillon d'hémoculture**

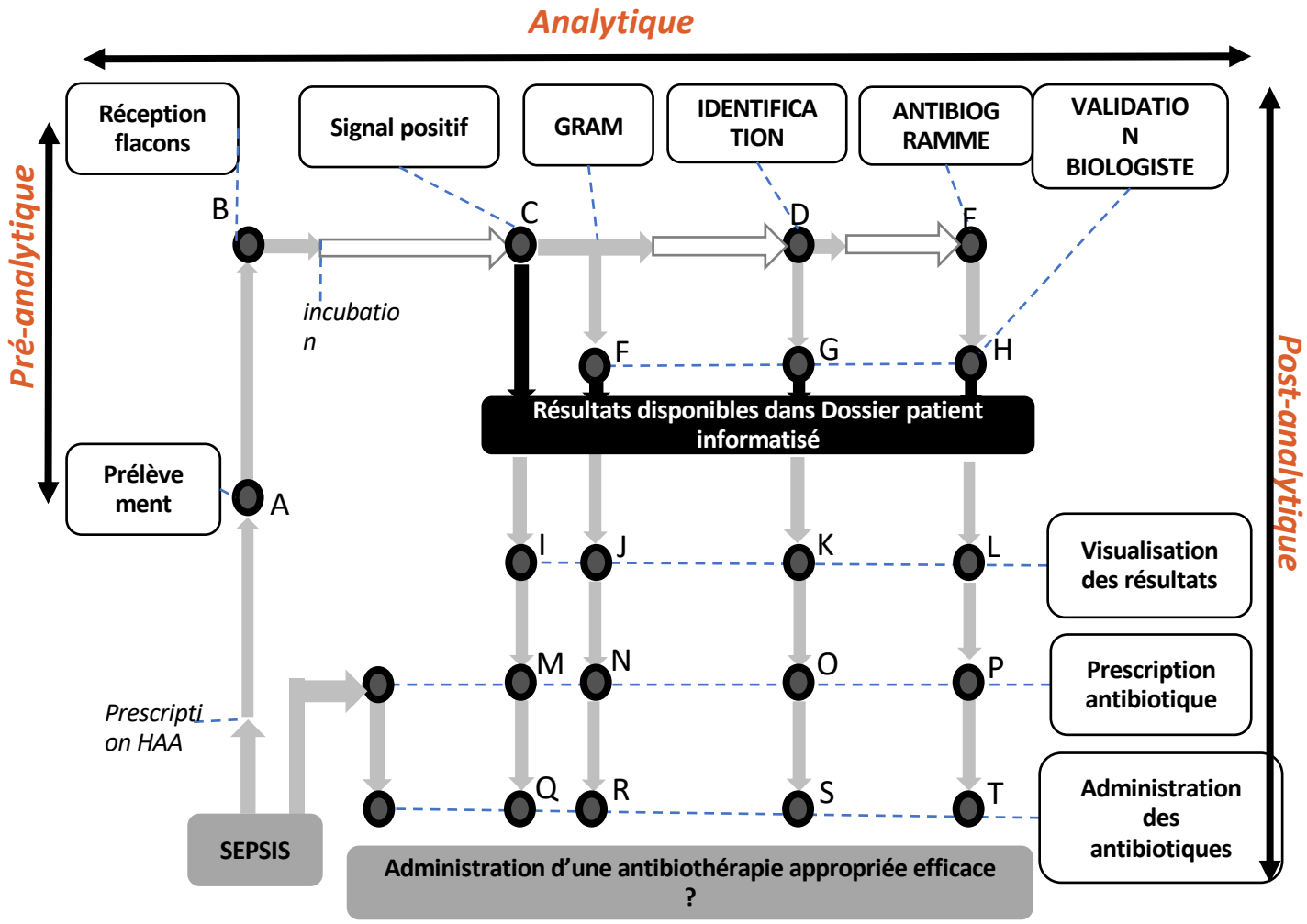
2-1 Antibiogramme en milieu gélosé (diffusion sur boite) : validé par le CA-SFM pour Staph-Strepto-BGN (entérobactéries et bacilles non fermentants)

2-2 Si Antibiogramme en milieu liquide (type VITEK) : non validé encore à ce jour mais des études solides montrent une excellente concordance pour les entérobactéries et les staphylocoques

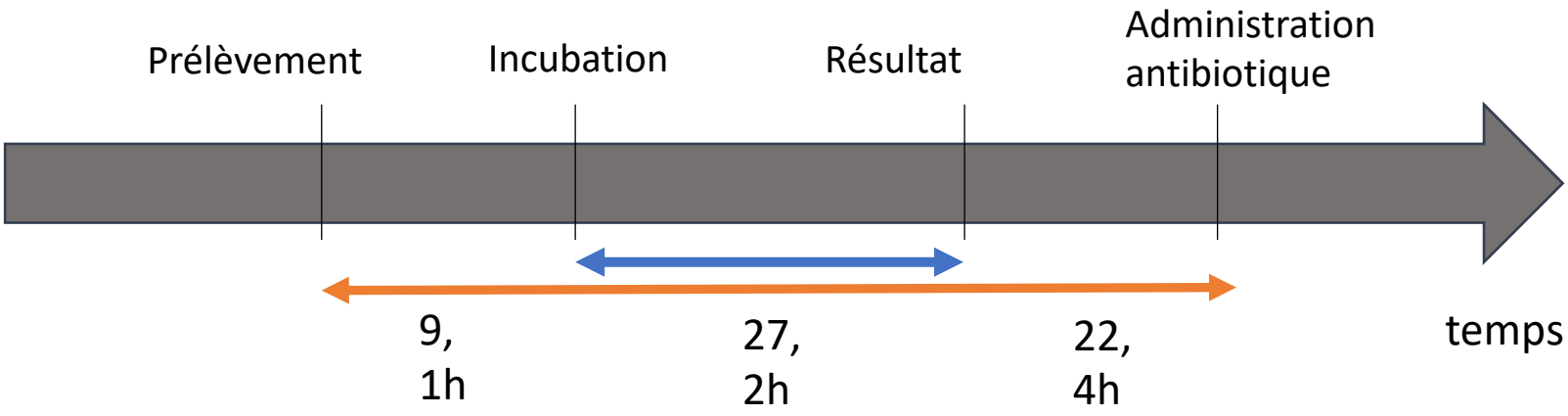
B-Biologie Moléculaire : **à JO sur le bouillon il est possible de faire en 1 H avec 2 mn de temps technique:**

- l'identification de 24 pathogènes parmi les plus fréquents (Gram+ , Gram- , Levures)
- de détecter 3 gènes de résistances (Mec A, VanA/B , KPC).

Inconvénient : coût



Thèse Jordan Lejeune Faculté Montpellier-Nîmes



- Temps microbiologique ⇔ 46% du circuit complet
- Temps de prise en compte des résultats > 1/3 du processus

- **Pré-analytique** organisé mais très dépendant des effectifs et donc des horaires des techniciens du laboratoire qui enregistrent les flacons.

- **Analytique** dépend du temps de la bactérie et de la technique : recommandations de bonnes pratiques de laboratoire, optimisation du circuit du flacon au laboratoire, démarches qualité, nombreux protocoles de recherche déjà faits ou à venir.

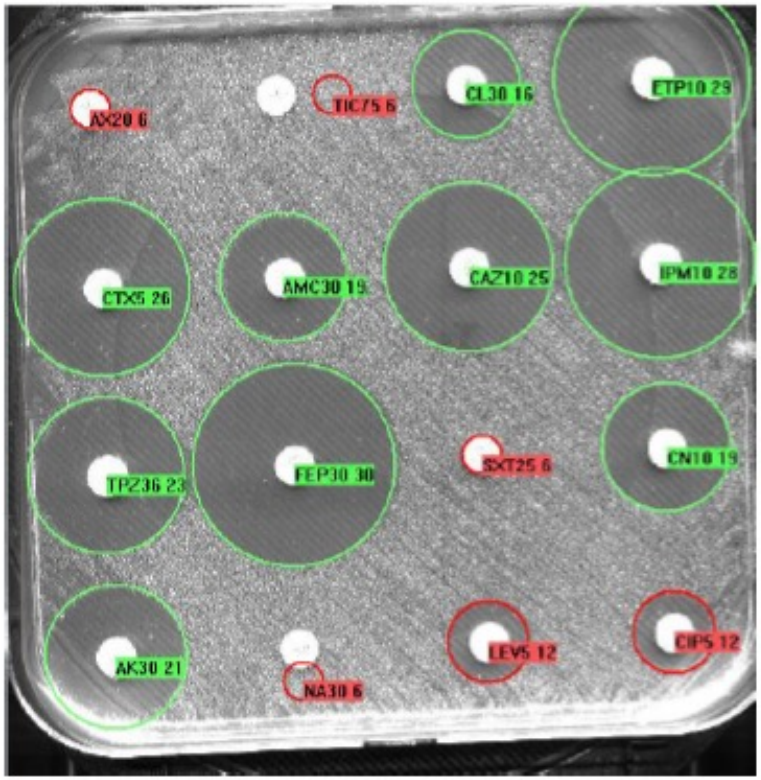
- **Post-analytique** : grande hétérogénéité, temps perdu identifié, perspectives d'amélioration

Diagn Microbiol Infect Dis. 2019 Jan;93(1):14-21. doi: 10.1016/j.diagmicrobio.2018.07.016. Epub 2018 Jul 31.

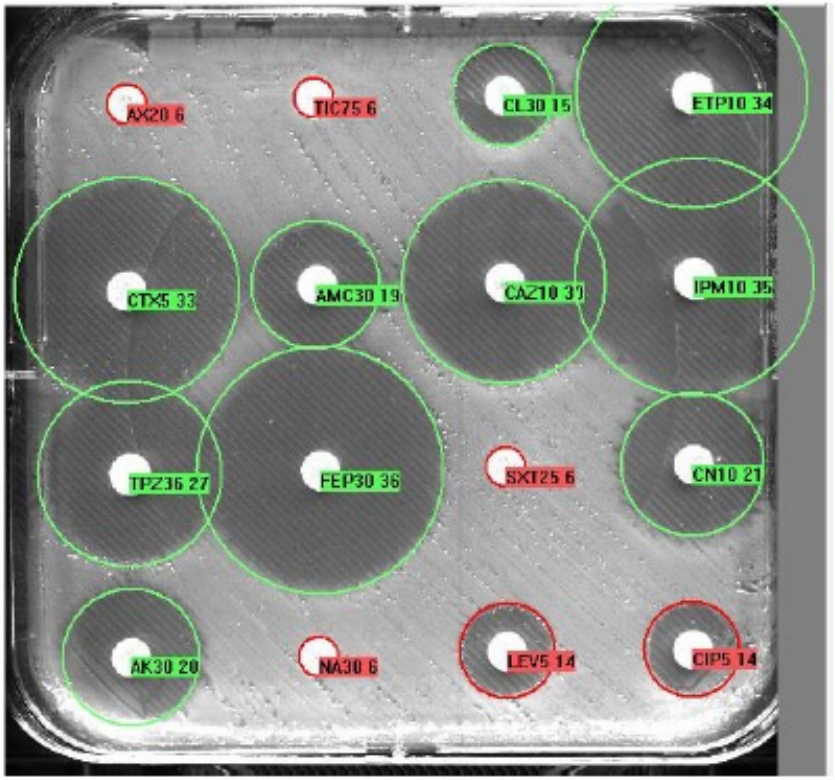
Prospective evaluation of rapid antimicrobial susceptibility testing by disk diffusion on Mueller-Hinton rapid-SIR directly on blood cultures.

Périllaud C[1], Pilmis B[2], Diep J[2], Péan de Ponfilly G[1], Vidal B[2], Couzigou C[2], Mizrahi A[1], Lourtet-Hascoët J[1], Le Monnier A[1], Nguyen Van JC[3].

Lecture de l'antibiogramme < 8h et après 18 heures d'incubation
Concordance : 97,4 % pour les BGN / > 98% pour les Staphylocoques



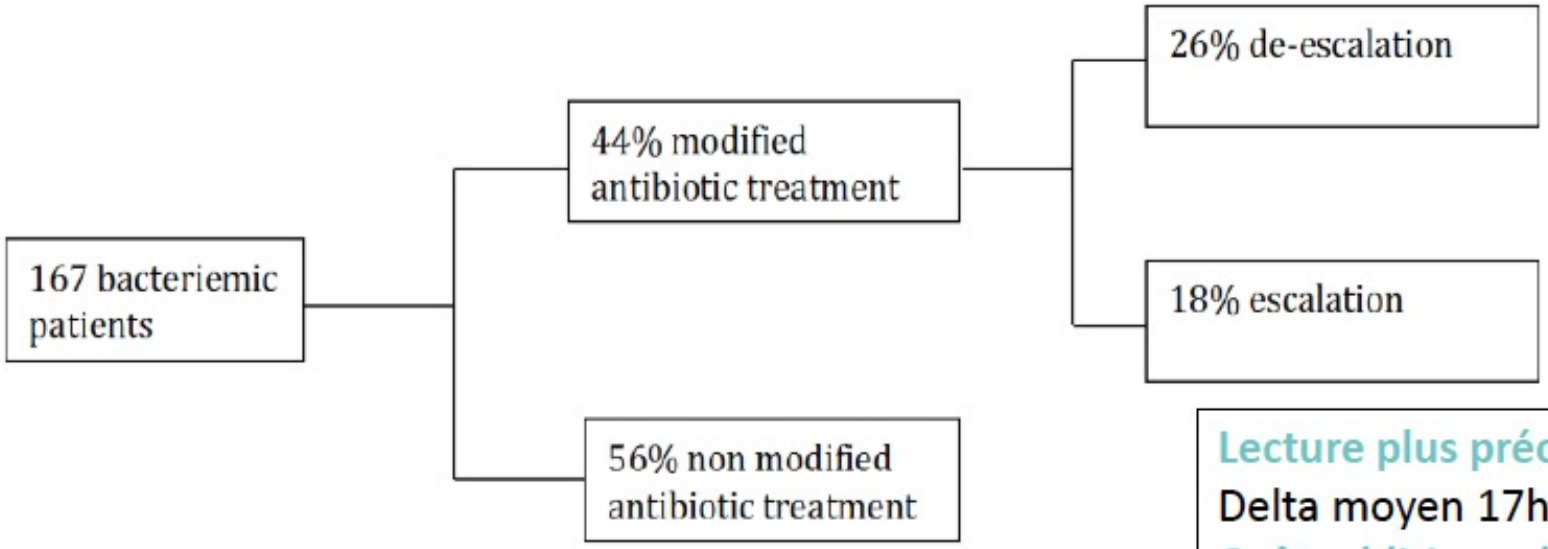
< 8 heures sur gélose MHR



18 heures sur MH à partir de la culture

Evaluation de l'impact clinique d'une lecture précoce < 8H

Etude prospective (janvier à août 2018)
167 épisodes de bactériémies consécutives
79% à Entérobactéries dont 12 BLSE et 21% à *Staphylococcus aureus*



Lecture plus précoce :
Delta moyen 17h
Coût additionnel :
+ 0,5 € pour la gélose MHR

Impact significatif sur adaptation précoce des antibiothérapies et mise en isolement mais importance de l'intervention de l'antimicrobial stewardship

B Pilmis et al - Clinical Impact of Rapid Susceptibility Testing on MHR-SIR, Directly from Blood Cultures. Journal antimicrobial chemotherapy (*sous presse*)

Approche par biologie moléculaire ciblée
Exemple de la PCR SARM

Principe

- Détection gène *mecA* et casette *SSCmec* (support génétique de la résistance)
- TAT très courts
- Délai pour les résultats 1h

Applications

- A partir de prélèvements (orthopédie septique, ponction articulaire préopératoire, dépistage portage nasal pré-opératoire, …)
- Sur flacon hémoculture positive (SA/SARM BC) :

- Simple, rapide et sensible
- Baisse des coûts
- Diminution délai mise en route traitement anti staphylocoque adapté
- Diminution des durées d'hospitalisation
- Diminution de la prescription d'ATB en cas de SCoN

- Coût des tests
- Pas de de différence si pas de référent ATB associé à la prise de décision
- Pas de différence si pas de rendu en temps réel
- Peu de réactivité sur l'émergence de variants (ex *mecC*)
- Pas d'impact sur la mortalité

Bauer et al CID 2014

RAPID DIAGNOSTICS WITH RAPID ACTION PLAN: HOLY GRAIL

What are the benefits of a combination of rapid diagnostic tests and an active re-evaluation of antibiotic therapy 72 h after the onset of bloodstream infection (BSI)?

- ✓ More de-escalation, discontinuation and appropriate escalation
- ✓ Decreased DOT
- ✓ Shorter LOS
- ✓ Mortality similar

Laboratory Survey Across Europe: 209 laboratories in 25 European countries.

- 33% use the classical processing of positive blood cultures (BC), two-thirds applied rapid technologies
- 42% were able to start incubating BC in automated BC incubators around-the-clock
- But, only 13% had established a 24-h service to start immediate processing of positive BC
- ONLY 5% of laboratories validated, transmitted the results to clinicians 24 h/day

Laboratories have started to implement novel technologies for rapid identification and susceptibility testing for positive BC. However, progress is severely compromised by limited operating hours

Murri R et al; Eur J Clin Microbiol Infect Dis 2018; 37
Idelevich EA et al; Clin Microbiol Infect 2019; 25

Evaluating the Impact of the Accelerate PhenoTest® BC Kit (AXDX) on Patients with Bloodstream Infections Receiving Ineffective Empirical Antibiotic Treatment: IOAS Study Experience of 4 Hospitals

Contact: Shawn MacVane
smacvane@axdx.com
Abstract number: 664

S. H. MacVane[1], A. A. Bhalodi[1], R. M. Humphries[2], M. A. Ben-Aderet[3], J. Kolev[3], M. Madhusudhan[3], M. A. Morgan[3], R. K. Dare[4], E. R. Rosenbaum[4], K Wolfe[4], D. N. Bremmer[5], D. R. Carr[5], T. L. Walsh[5], P. M. Kinn[6], K. M. Percival[6], D. Ince[6], B. Ford[6]

[1]Accelerate Diagnostics, Inc., [2]Vanderbilt University Medical Center, [3]Cedars-Sinai Med. Ctr., [4]Univ. of Arkansas for Med. Sci., [5]Allegheny Health Network, Pittsburgh, PA, [6]Univ. Of Iowa., Iowa City, IA

RESULTS

Fig 1. Kaplan-Meier analysis of time to effective therapy

Median time (hours) to effective therapy: SOC: 12.6 (2.7-37.1) vs AXDX: 5.9 (2.9-13.6)

***P*=0.027**

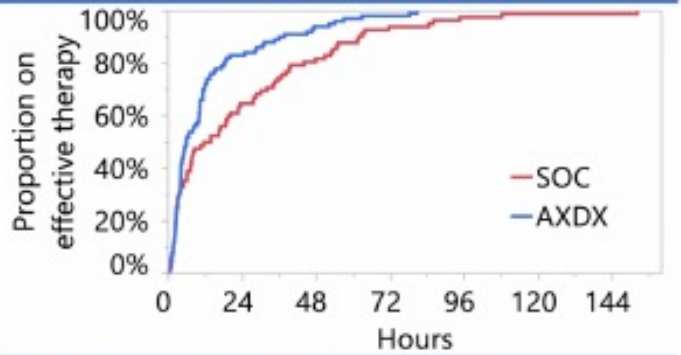


Table 2. Antimicrobial modifications

Parameter*	SOC (n=82)	AXDX (n=100)	Difference	*P*
Achievement of effective therapy within 24h, n (%)	53 (64.6)	83 (83.0)	18.4%	**0.005**
Time to first gram-positive antimicrobial modification	18.2 (7.6-44.7)	9.9 (4.0-28.4)	8.3 h	0.10
Time to first gram-negative antimicrobial modification	25.4 (6.3-53.2)	10.2 (4.0-20.4)	15.2 h	**0.004**
Time to first de-escalation	44.4 (25.5-59.1)	31.1 (17.3-49.2)	13.3 h	**0.05**
Time to optimal therapy	40.5 (17.1-62.9)	12.4 (5.3-12.4)	28.1 h	**<0.0001**

*Evaluated at 96h after blood culture positivity and reported as median (IQR), unless otherwise noted

Table 3. Risk factors for 30-day mortality in patients who received IET*

Factor	Adjusted Odds Ratio (95% Conf. Int.)	*P*
SOC group	4.29 (1.36-13.46)	0.013
Pitt Bacteremia Score ≥ 4	14.33 (4.67-44.03)	<0.0001

*As determined by multivariable logistic regression

CONCLUSION

In this interim analysis of patients who received IET for BSI, use of AXDX was associated with decreased time to effective therapy and 30-day mortality. Additional patient enrollment is ongoing.

31st ECCMID Online 9 – 12 July 2021
ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

The Potential impact on clinical decision making times of direct identification of bacteria in positive blood cultures using a FilmArray panel compared to conventional automated identification and antimicrobial susceptibility testing: A pilot study

B. RATHISH [1], A. WILSON[1], A. WARRIER[1], S. PRAKASH[1], R. BABU[1], S. JOY[1]
[1]Aster Medcity, Kochi, India

INTRODUCTION

Rapid administration of antibiotic therapy is indicated in sepsis, and the time taken for prescription of appropriate antibiotics is critical in the outcome of sepsis [1]. Conventional phenotypic techniques generally have a slow turn around time (TAT) which can have implications on clinical decision making times.

In a medical emergency such as sepsis, the use of newer techniques including genotypic multiplex PCR arrays may have a role by significantly reducing the TAT associated with test results and subsequently leading to faster clinical decisions. We evaluated the role of such a modality in a cohort of patients with culture positive sepsis.

AIM

We conducted a pilot study with an aim to evaluate the role of a FilmArray direct identification of bacteria in positive blood cultures compared to the conventional automated system.

METHODS

Design and setting:

This was a pilot study conducted prospectively over 6 months in a tertiary care centre in South India. In a group of patients with a positive blood culture, we compared the accuracy and TAT of the FilmArray Direct from Positive Blood Culture system (BCID) (BioFire Diagnostics, Salt Lake City, UT, USA) versus the VITEK®2 Automated ID/AST (bioMerieux, Durham, NC, USA) in patients having a positive blood culture. The time from blood collection to ID/AST by VITEK®2 and time to report by FilmArray were analysed.

Tools:

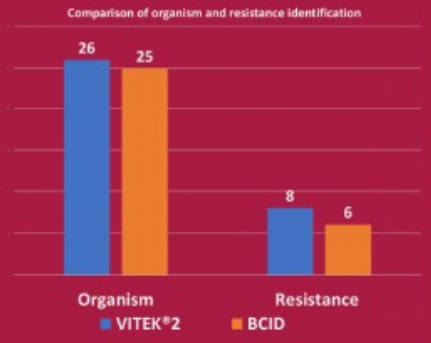
Blood cultures were performed in patients with suspected sepsis with a high SOFA score, using BD BACTEC Plus™ aerobic and anaerobic media [2]. BIOFIRE® FILMARRAY® performs the extraction, amplification and detection in a closed system with a TAT of about an hour [3]. VITEK®2 is an automated system that uses conventional phenotypic methods of organism identification and AST estimation[4].

Statistical methods:

Patient characteristics were described using descriptive statistics. The sensitivity, specificity, Positive predictive value (PPV), negative predicitive value (NPV), and accuracy of filmarray was calculated. Group comparisons were made using paired t-tests. A p-value of <0.05 was considered significant.

RESULTS

26 patients with a positive blood culture were studied. VITEK2 identified organisms in all 26 (100%) patients while BCID identified the organism in 25 (96.2%) patients with a sensitivity of 96.2% and Positive predictive value (PPV) of 100%. VITEK®2 identified multi-drug resistant (MDR) organisms in 8 (30.8%) samples while BCID identified genes suggestive of resistance in 6 (23.1%) patients with sensitivity of 75%, specificity of 100%, PPV of 100%, negative predictive value of 90%, and accuracy of 92.3%. VITEK®2 ID/AST was obtained in a mean (M) ± standard deviation (SD) of 50.22 ± 19.29 hours. BCID was obtained in a mean (M) ± standard deviation (SD) of 19.43 ± 11.62 hours. There was a statistically significant difference in time taken (t=6.835, p<0.001).



OBJECTIVES

Our primary objective for this study was taken as TAT of both the tests. The secondary objectives were to assess accuracy of filmarray in identifying the organism and potential resitance causing genes to predict resistance patterns as compared to VITEK®2 results.

CONFLICTS OF INTEREST

None of the authors have any affiliation to Biofire and have no COI to declare.

CONTACT INFORMATION

Balram Rathish: balramrnair@gmail.com
Arun Wilson: drarun.wilson@asterhospital.com

CONCLUSIONS

BCID was comparable to conventional VITEK®2 in the identification of organisms from positive blood cultures and detecting presence of MDR status of the organisms. However BCID had significantly lower TAT with less than half that of VITEK®2. BCID may be useful in faster decision making in patients with bacteremia, and thereby improve clinical outcomes.

REFERENCES

1. Kumar A. Optimizing antimicrobial therapy in sepsis and septic shock. Crit Care Clin 2009;25(4):733–51.
2. https://www.bd.com/en-us/offerings/capabilities/microbiology-solutions/blood-culture/blood-culture-media. Accessed 27 May 2021.
3. https://www.biomerieux-diagnostics.com/filmarray. Accessed 27 May 2021.
4. https://www.biomerieux-usa.com/vitek-2. Accessed 27 May 2021.

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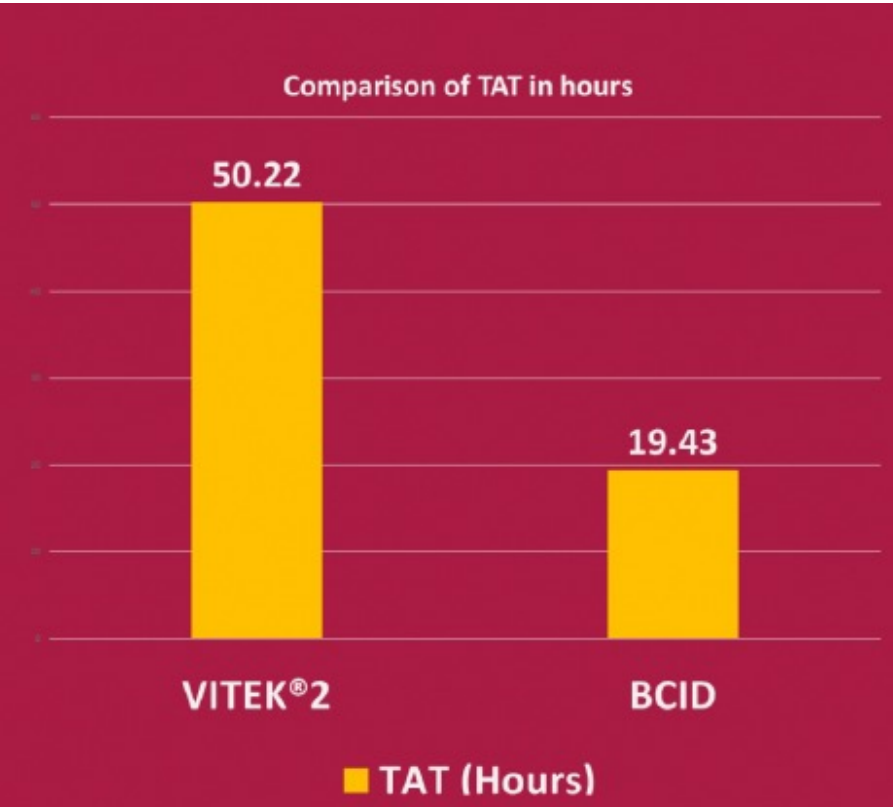
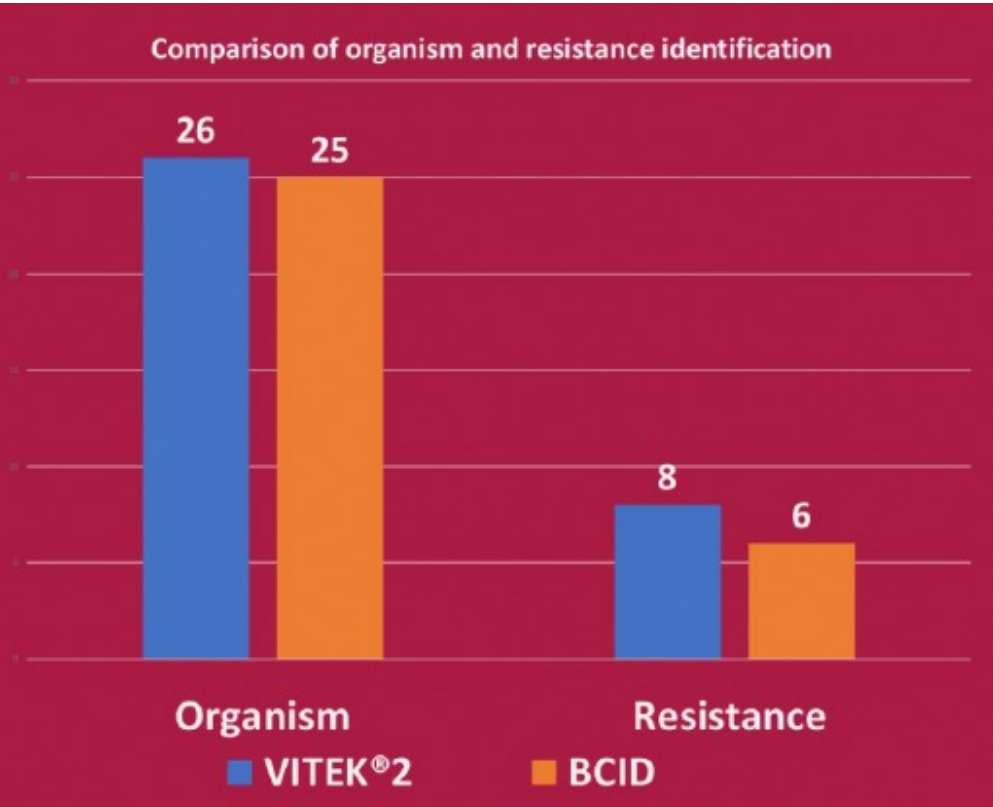
The Potential impact on clinical decision making times of direct identification of bacteria in positive blood cultures using a FilmArray panel compared to conventional automated identification and antimicrobial susceptibility testing: A pilot study

B. RATHISH [1], A. WILSON[1], A. WARRIER[1], S. PRAKASH[1], R. BABU[1], S. JOY[1]
[1]Aster Medcity, Kochi, India

AsterMedcity
We'll Treat You Well





Clinical Infectious Diseases

MAJOR ARTICLE

Defining the Breakpoint Duration of *Staphylococcus aureus* Bacteremia Predictive of Poor Outcomes

Emi Minejima,[1,2] Nikki Mai,[1] Nancy Bui,[1] Melissa Mert,[3] Wendy J. Mack,[4] Rosemary C. She,[5] Paul Nieberg,[6] Brad Spellberg,[2,7] and Annie Wong-Beringer[1,8]

No. of Days of Bacteremia	Total N	Mortality, %	Relative Risk (95% CI)	*P* Value
1	446	4.5	Reference	Reference
2	108	8.3	1.86 (0.87–3.97)	.11
3	98	9.2	2.05 (0.96–4.36)	.06
4	74	12.2	2.71 (1.28–5.73)	.01
5	46	8.7	1.94 (0.69–5.43)	.21
6	33	18.2	4.05 (1.75–9.40)	.001
7	28	21.4	4.78 (2.09–10.94)	<.001
8–10	30	20.0	4.46 (1.94–10.27)	<.001
11+	21	23.8	5.31 (2.21–12.76)	<.001
Per day	…	…	1.16 (1.10–1.22)	<.001

N = 884. The numbers of days of infection at 8–10 and 11+ were collapsed to account for the observed sample sizes.

Abbreviation: CI, confidence interval.

Clinical Infectious Diseases

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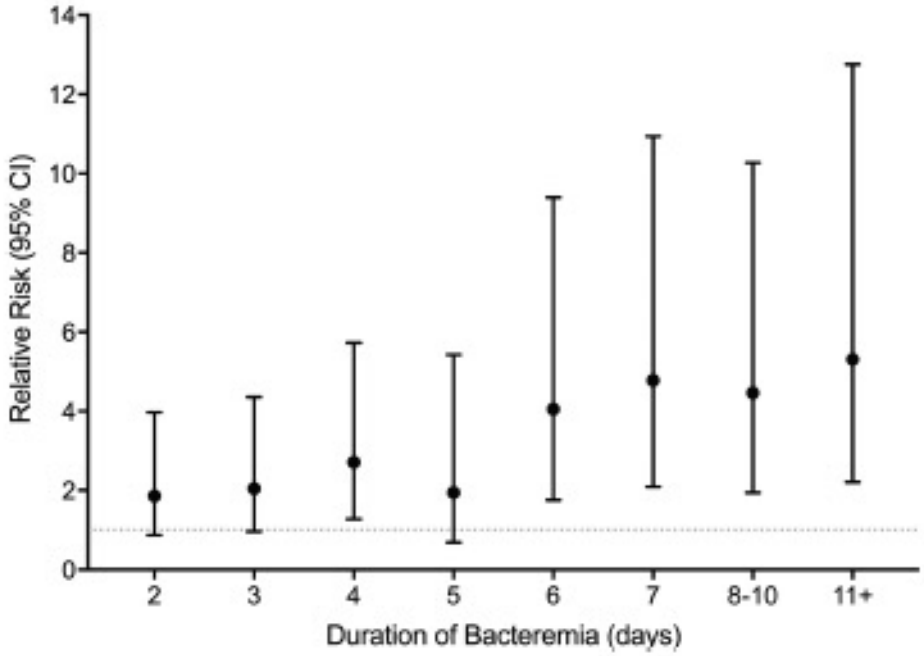


Figure 1. Relative risk (95% confidence interval) of mortality by duration of bacteremia (N = 884). The numbers of days of infection at 8–10 and 11+ were collapsed to account for the observed sample sizes.

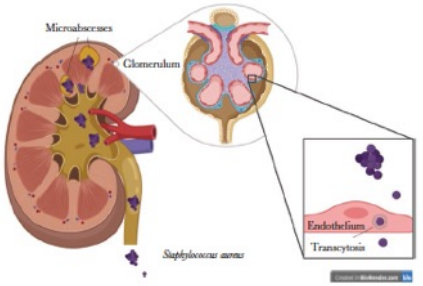
Open Forum Infectious Diseases

REVIEW ARTICLE

A Narrative Review on the Role of *Staphylococcus aureus* Bacteriuria in *S. aureus* Bacteremia

Franziska Schuler,[1] Peter J. Barth,[2] Silke Niemann,[1] and Frieder Schaumburg[1]

[1]Institute of Medical Microbiology, University Hospital Münster, Münster, Germany, and [2]Gerhard Domagk Institute of Pathology, University Hospital Münster, Münster, Germany



Effector	Function	Design	Reference
Sortase A and sortase A anchored surface proteins	Formation of abscess lesions and persistence of bacteria in host tissues	Murine infection model	[44]
Coagulase	Proposed cessation of the capillary flow followed by bacterial growth in the capillaries; coagulative necrosis of the tubules	In vivo animal studies (rabbit model)	[45]
		In vivo animal studies (guinea pigs, mice)	[46]
Staphylokinase	Activation of plasminogen (antivirulence properties)	Murine infection model	[47]
Urease	Promoting bacterial fitness in the low-pH, urea-rich kidney	Murine infection model	[48]
Superantigens	Increased virulence (lethal sepsis, infective endocarditis, kidney infections) in MRSA strain MW2 (especially staphylococcal enterotoxin C)	In vivo animal studies (rabbit model)	[49]
Staphylococcal enterotoxin B	Proposed induction of renal proximal tubule epithelial cells leading to dysregulation of the vascular tone	Cell cultures	[50]
Adhesion factors, ie, FnBPs, Eap, clumping factor A and B, or protein A	Binding to extracellular matrix proteins (eg, fibronectin, fibrinogen/fibrin, von Willebrand factor), this attachment might also be the first step in the uptake from the blood into the tissue via a transcellular or paracellular route (see Knowledge Gaps)	Animal infection models, cell cultures	[36, 51, 52]
α-hemolysin	Dispensable for renal abscess lesions	Murine infection model	[53]
Siderophore production	Renal abscess formation	Murine infection model	[54]
Surface polysaccharide (poly-*N*-acetylglucosamine)	Renal abscess formation	Murine infection model	[55]
Extracellular complement-binding protein and extracellular fibrinogen-binding protein	Impairment of complement activation followed by a decrease in renal abscess formation	Murine infection model	[56]
Eukaryotic-like serine/threonine-kinase	Renal abscess formation	Murine infection model	[57]

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

Management

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

III. What is the management of MRSA bacteremia and infective endocarditis?

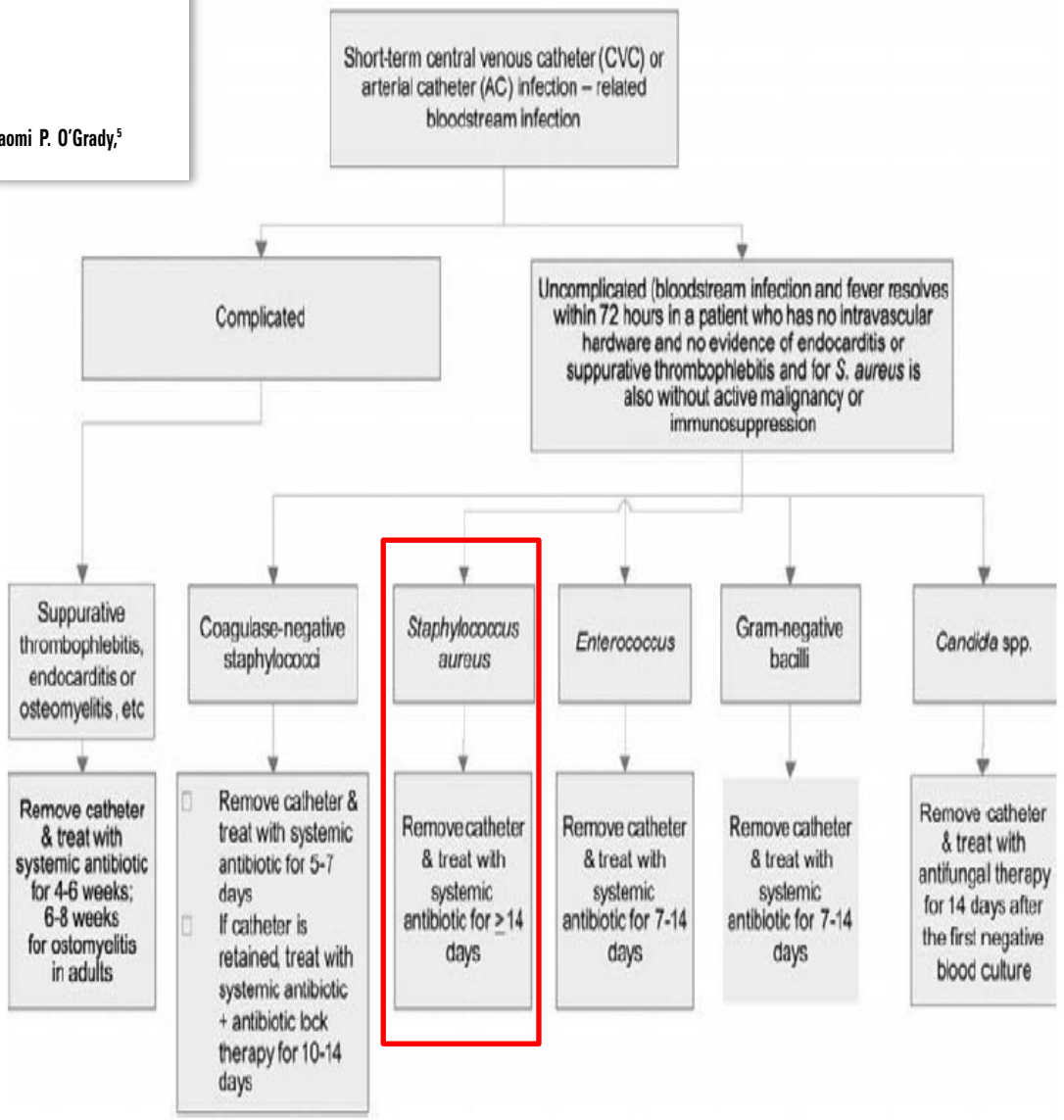
Bacteremia and Infective Endocarditis, Native Valve

19. For adults with uncomplicated bacteremia (defined as patients with positive blood culture results and the following: exclusion of endocarditis; no implanted prostheses; follow-up blood cultures performed on specimens obtained 2–4 days after the initial set that do not grow MRSA; defervescence within 72 h of initiating effective therapy; and no evidence of metastatic sites of infection), vancomycin (**A-II**) or daptomycin 6 mg/kg/dose IV once daily (**AI**) for at least 2 weeks. For

CID 2011

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,[1] Michael Allon,[2] Emilio Bouza,[9] Donald E. Craven,[3] Patricia Flynn,[4] Naomi P. O'Grady,[5] Issam I. Raad,[6] Bart J. A. Rijnders,[10] Robert J. Sherertz,[7] and David K. Warren[8]



Mermel *et al.* IDSA guidelines. CID 2009

Infection Prevention in Practice 2 (2020) 100037

Available online at www.sciencedirect.com

Infection Prevention in Practice

journal homepage: www.elsevier.com/locate/ipip

Management of *Staphylococcus aureus* bacteraemia (SAB) in the oncology patient: Further evidence supports prompt removal of central venous catheters and shorter duration of intravenous antimicrobial therapy

Colum P. Dunne [a,*], Phelim Ryan [a], Roisin Connolly [b], Suzanne S. Dunne [a], Mohammed A. Kaballo [b], James Powell [b], Bernie Woulfe [c], Nuala H. O'Connell [a,b], Rajnish K. Gupta [c]

Background: *Staphylococcus aureus* bacteraemia (SAB) is associated with relatively high risk of complications and high levels of mortality. Internationally, SAB management guidelines lack consensus and especially so regarding oncology patients. This is likely a reflection of insufficient randomised control trials (RCT) and the diversity of SAB patient populations. However, there are 2011 guidelines recommending a minimum of 14 days of appropriate IV antibiotic therapy for SAB.

Objective: We wished to determine whether our practice of shortened duration of intravenous antimicrobial therapy in favour of oral administration proved as effective as recommended guidelines in a mixed oncology patient cohort.

Methods: Retrospective review of patient records that included any SAB episode among oncology patients from January 2002 to December 2015. Medical chart reviews were undertaken to determine patient demographics, clinical management & antimicrobial therapy, duration of stay, presence of a central venous catheter (CVC) and outcome.

Results: Our CVC removal rate was just 73% in SAB where CVC was the identified source of infection, with an attributable mortality rate (<4%) far lower than would be expected. Antimicrobial therapy durations were considerably lower (10 days) than current recommendations of 14 days IV therapy. The recurrence rate of 15% was also significantly lower than has been reported previously.

Conclusions: Our observations contribute new insights concerning the management of SAB in oncology patients. Our findings suggest that therapeutic approaches should perhaps

Bactériémie sur cathéter !!

Logistic regression model analysing the risk factors for cumulative 30-day mortality in patients treated for infective endocarditis

Covariate	Odds ratio	95% confidence interval	*P*-value
Age/year	1.028	0.991–1.070	0.156
Male	3.19	0.86–14.70	0.104
Non-native valve	1.20	0.99–12.41	0.060
Catheter-related bloodstream infection	5.51	1.09–27.67	0.034
Staphylococcus aureus	15.96	4.25–75.82	<0.001

Ahmed *et al* . JHI 2012

Optimal Duration of Therapy for Catheter-Related *Staphylococcus aureus* Bacteremia: A Study of 55 Cases and Review

Issam I. Raad and Mouin F. Sabbagh

From the Division of Infectious Diseases, Department of Medicine, University of Florida School of Medicine, Gainesville, Florida

Variable	Treatment groups according to duration of iv antibiotics			
		≥10 days		
	<10 (n = 18)	10–14 days (n = 18)	>14 days (n = 10)	P*
No. of patients developing late complications	3	0	0	.05
Age, mean, years†	39.5	35.7	40.8	NS
No. of ICU patients	3	3	3	NS
No. of immunocompromised patients	2	7	4	.04
No. of patients with CVC	13	14	10	NS
No. of patients treated with				
Vancomycin	6	8	3	NS
β-lactam‡	8	7	4	NS
β-lactam + aminoglycoside	4	3	3	NS

Table 3. Cases of vascular catheter-related *Staphylococcus aureus* bacteremia (CRSB).

Reference	Follow-up	No. of patients with catheter-related bacteremia	Mean duration of iv therapy, d	No. of cases of endocarditis (%)	No. of related deaths (%)	No. of cases with other complications (%)
[19]	R	22	10.6	0	0	0
[14]	R	21	28	8 (39)	3 (14)	0
[18]	R	20	18.5	0	1 (5)	4 (20)
[13]	R/P*	28	15.2	0	6 (21)	0
[12]	P	13	9.1	1 (8)	0	0
[22]†	R	27	17.1	1 (4)	3 (11)	5 (19)

CID 1992

Short-Course Therapy of Catheter-related *Staphylococcus aureus* Bacteremia: A Meta-analysis

John A. Jernigan, MD; and Barry M. Farr, MD, MSc

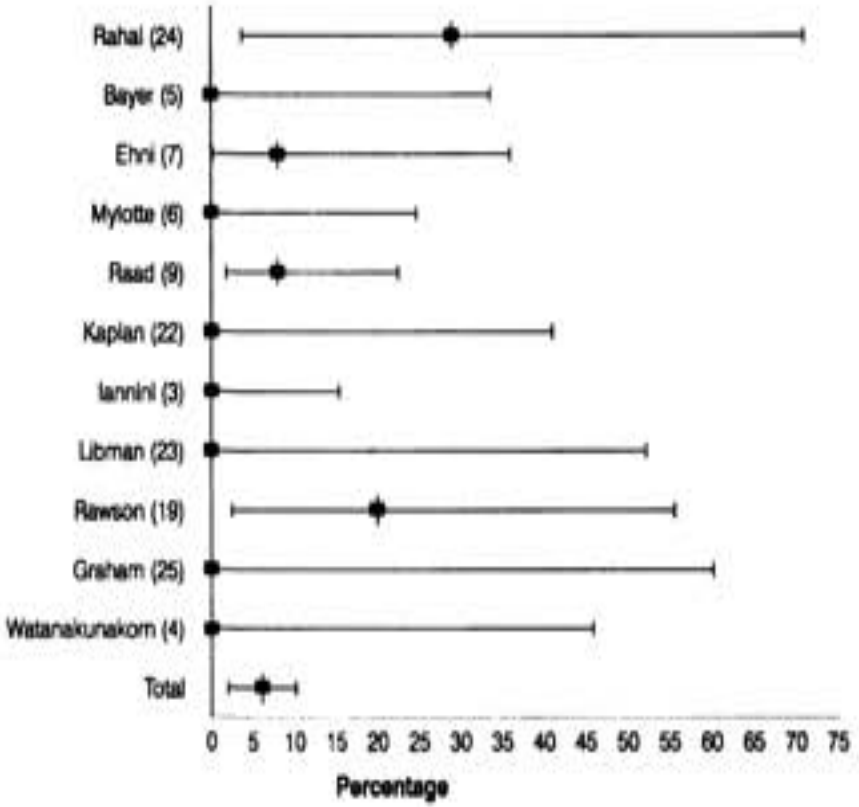


Figure 1. Statistical precision of reported relapse rates for short-course therapy (≤2 weeks) of catheter-related *Staphylococcus aureus* bacteremia. Boxes mark the estimated relapse rate reported in corresponding study. Surrounding interval indicates the 95% confidence interval.

« Investigators suggest the data are flawed by bias and statistical imprecision and optimum duration of therapy remains **unknown** They suggest a **controlled trial is required** »

11 études

Ann intern med 1993

Eur J Clin Microbiol Infect Dis (2001) 20:380–384

Article

Long-Term Infectious Complications and Their Relation to Treatment Duration in Catheter-Related *Staphylococcus aureus* Bacteremia

M.M.P. Zeylemaker, C.A.J.J. Jaspers, M.G.J. van Kraaij, M.R. Visser, I.M. Hoepelman

Table 4 Denominator data. For comparison between groups, chi-square = 0.36; *P* value = 0.546328; and odds ratio (95% CI) = 1.50 (0.40–5.62)

Duration of antibiotic therapy	No. with complications	No. without complications	Total patients[a]
>14 days	8	5	13
≤14 days	16	15	31
Total patients	24	20	44

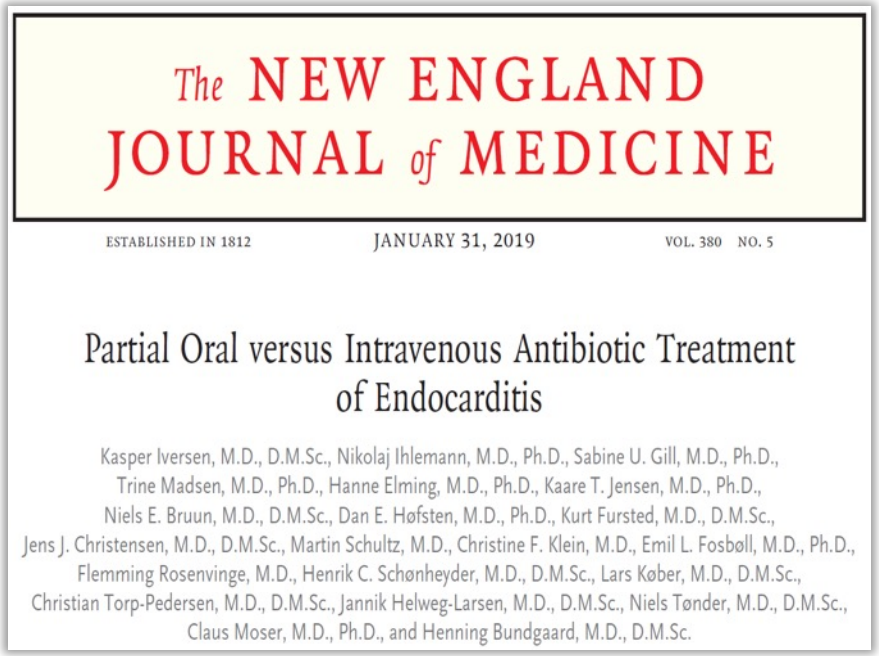
RELAIS PER OS

STUDY PROTOCOL Open Access

Efficacy of seven and fourteen days of antibiotic treatment in uncomplicated *Staphylococcus aureus* bacteremia (SAB7): study protocol for a randomized controlled trial

Louise Thorlacius-Ussing[1*], Christian Østergaard Andersen[2], Niels Frimodt-Møller[3], Inge Jenny Dahl Knudsen[2], Jens Lundgren[4] and Thomas Lars Benfield[1]

Thorlacius-Ussing *et al. Trials* (2019) 20:250
https://doi.org/10.1186/s13063-019-3357-9



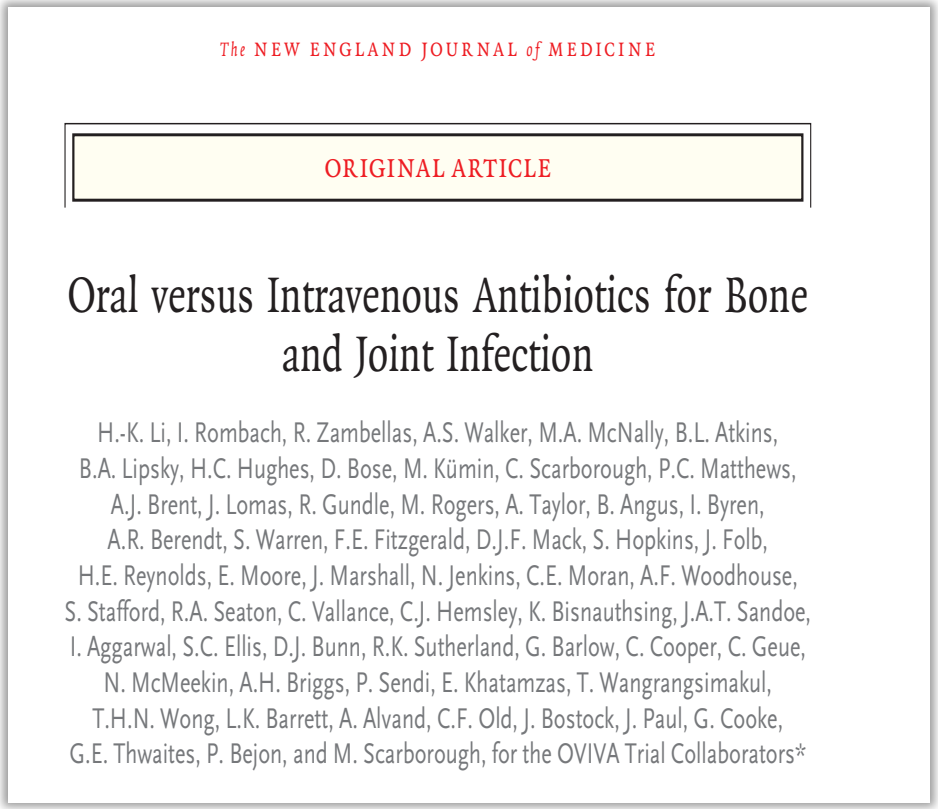
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

Iversen et al NEJM 2019



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

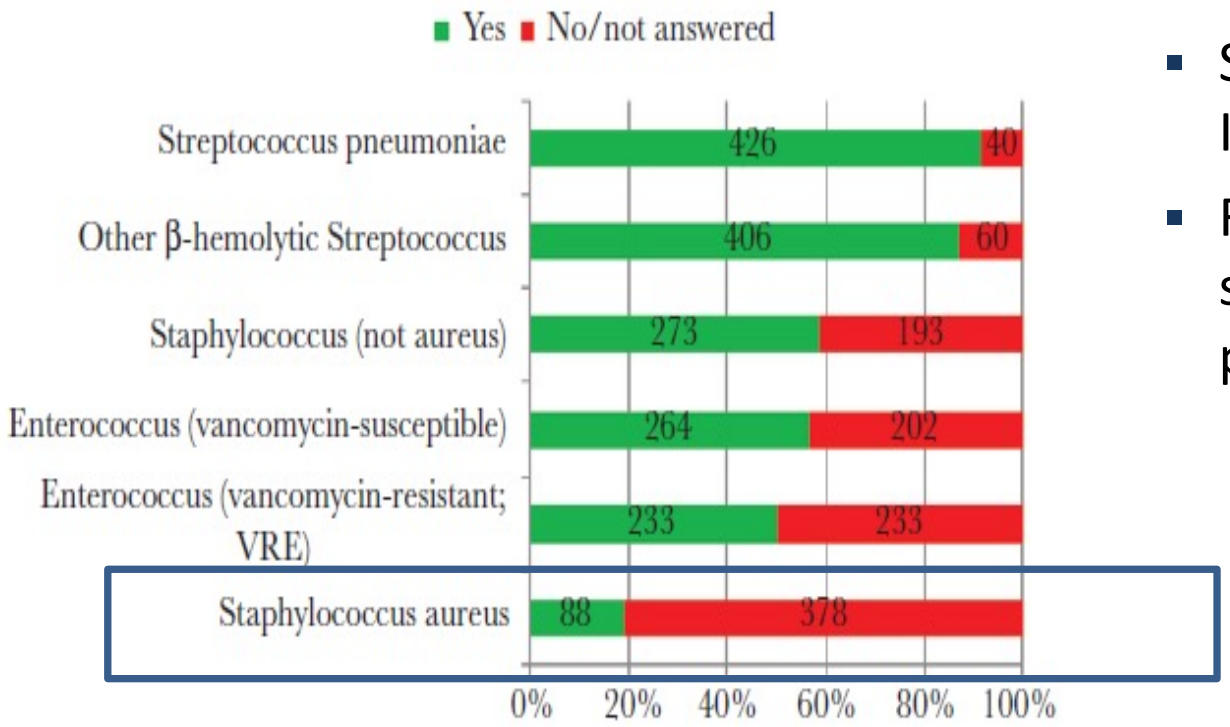
Rombach et al NEJM 2019

Open Forum Infectious Diseases

MAJOR ARTICLE

Practice Patterns of Infectious Diseases Physicians in Transitioning From Intravenous to Oral Therapy in Patients With Bacteremia

Duane R. Hospenthal,[1,2] C. Dustin Waters,[3] Susan E. Beekmann,[4] and Philip M. Polgreen[4]



- Survey : 655 Infectiologues (IDSA)
- Relais per os en cas de septicémie chez patient « stable »

Oral Antibiotic Treatment of Right-sided Staphylococcal Endocarditis in Injection Drug Users: Prospective Randomized Comparison with Parenteral Therapy

Alan W. Heldman, MD, Tina V. Hartert, MD, Stuart C. Ray, MD, Emile G. Daoud, MD, Thomas E. Kowalski, MD, Vincent J. Pompili, MD, Stephen D. Sisson, MD, William C. Tidmore, MD, Keith A. vom Eigen, MD, Steven N. Goodman, MD, PhD, Paul S. Lietman, MD, PhD, Brent G. Petty, MD, Charles Flexner, MD, *Baltimore, Maryland*

- In a prospective, randomized, non-blinded trial, febrile injection drug users were assigned to begin oral or intravenous (IV) treatment
- Oral therapy consisted of ciprofloxacin and rifampin.
- Parenteral therapy was oxacillin or vancomycin, plus gentamicin for the first 5 days

TABLE II

Reasons for Attrition of Subjects with Sustained Staphylococcal Bacteremia

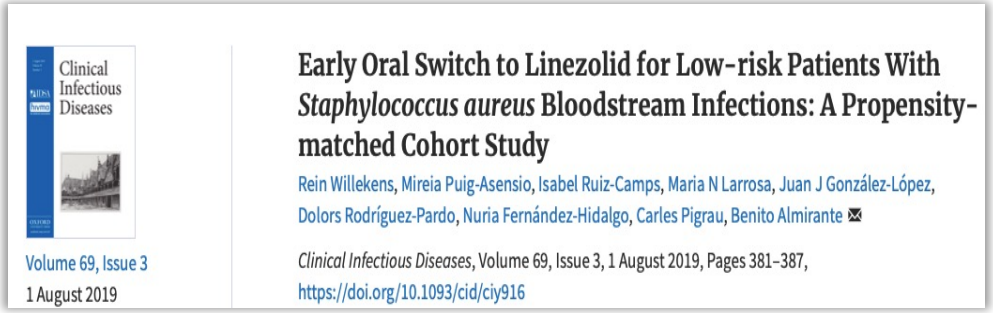
	Oral Therapy	Intravenous Therapy
Did not satisfy criteria for endocarditis upon entry	5	3
Exclusion criteria after entry	6	6
Antibiotic violation	4	7
Organism not sensitive to assigned antibiotic	1	0
Withdrawn by physician	3	0
Withdrawal by patient	1	2
Elopement or discharge against medical advice	6	5
Total	26	23
Total for subjects with right-sided staphylococcal endocarditis	21	20

TABLE III

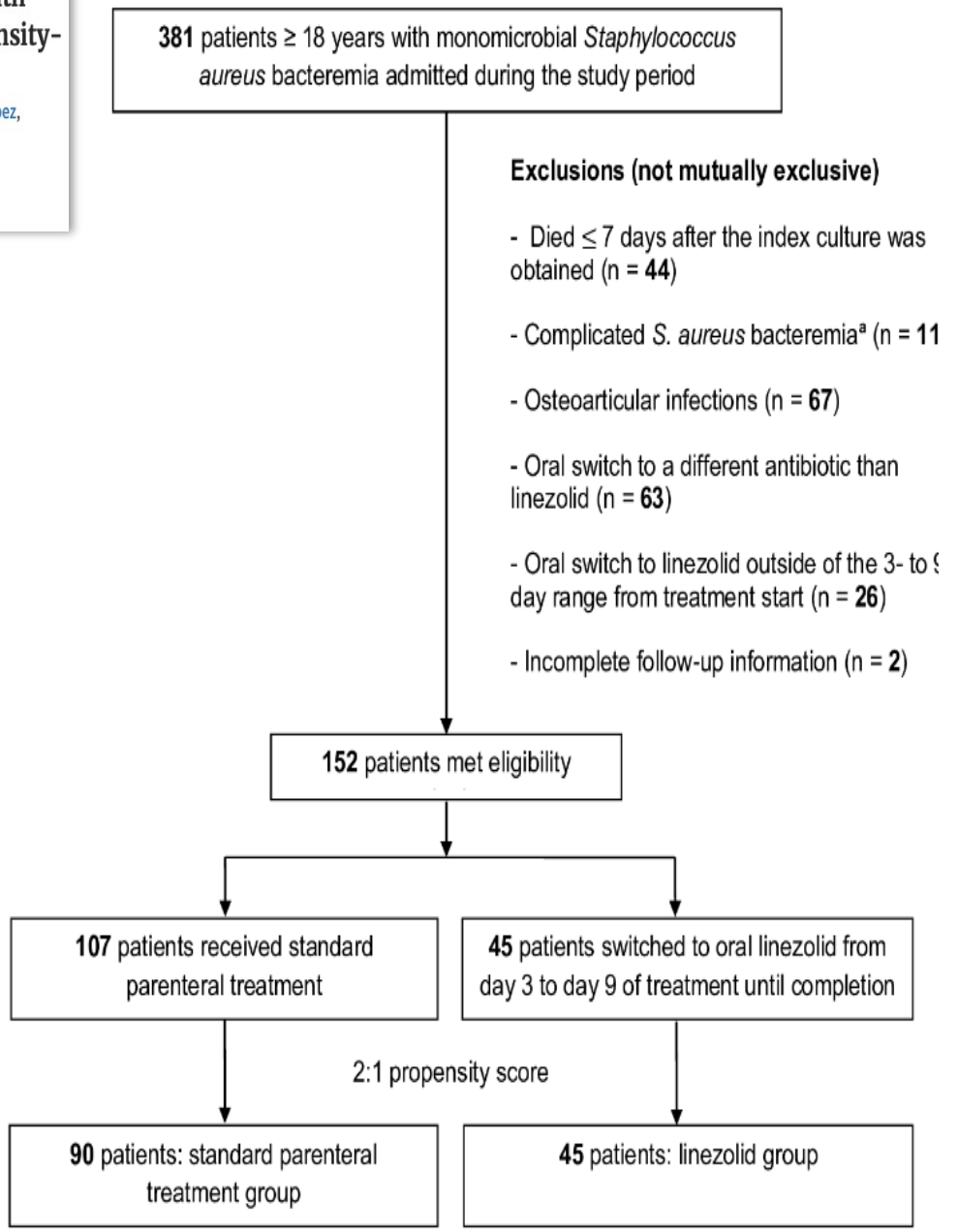
Efficacy of Oral Versus Parenteral Antibiotics

	Oral	Intravenous
a. Bacteriologic evaluation of outcome		
Cured	18	22
Failed	1	3($P = 0.6$)
b. Combined bacteriologic and projected clinical evaluations of outcome		
Cured	26	30
Failed	3	3($P = 0.9$)

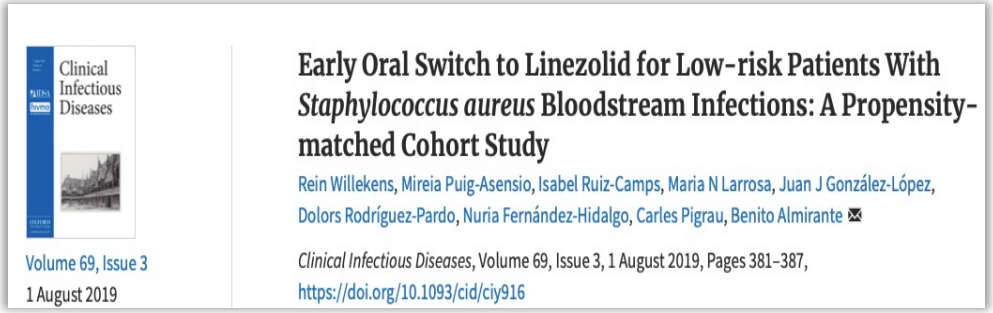
The American Journal of Medicine 1996



- Cohorte prospective 2013-2017
- Monocentrique
- BSIs non compliquée
- Relais per os entre J3 et J9
- Score de propension 2:1



CID 2018



Outcome	Whole cohort			Propensity score-matched cohort		
	Oral linezolid (n=45)	Standard treatment (n=107)	*P* value	Oral linezolid (n=45)	Standard treatment (n=90)	*P* value
90-day relapse in survivors	1 (2.2)	4 (3.7)	1.00	1 (2.2)	4 (4.4)	0.87
14-day mortality	0 (0.0)	10 (9.3)	0.08	0 (0.0)	6 (6.7)	0.18
30-day mortality	1 (2.2)	17 (15.9)	0.04	1 (2.2)	12 (13.3)	0.08
Length of hospital stay after index culture, days, median (IQR) [a]	8 (7-10)	19 (15-32)	<0.01	8 (7-10)	19 (15-30)	<0.01

CID 2018

HEINRICH HEINE
UNIVERSITÄT DÜSSELDORF

TRIAL PROTOCOL

EARLY ORAL SWITCH THERAPY IN LOW-RISK STAPHYLOCOCCUS AUREUS BLOODSTREAM INFECTION

ACRONYM: SABATO (Staphylococcus aureus Bacteremia Antibiotic Treatment Options)

Sponsor:

Heinrich-Heine-Universität Düsseldorf

Universitätsstr.1

40225 Düsseldorf

Germany

Principal Coordinating Investigator:

Prof. Dr. med. Achim Kaasch

Institute of Medical Microbiology and Hospital Hygiene

Düsseldorf University Hospital

Universitätsstr.1

When are Oral Antibiotics a Safe and Effective Choice for Bacterial Bloodstream Infections? An Evidence-Based Narrative Review

Andrew J. Hale, MD[1,2*], Graham M. Snyder, MD, SM[3,4], John W. Ahern, PharmD[5,6], George Eliopoulos, MD[3,4], Daniel N. Ricotta, MD[4,7], W. Kemper Alston, MD, MPH[1,2]

[1]Department of Infectious Diseases, University of Vermont Medical Center, Burlington, Vermont; [2]Department of Medicine, Larner College of Medicine at the University of Vermont, Burlington, Vermont; [3]Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts; [4]Department of Medicine, Harvard Medical School, Boston, Massachusetts; [5]Department of Pharmacy, University of Vermont Medical Center, Burlington, Vermont; [6]Larner College of Medicine at the University of Vermont, Burlington, Vermont; [7]Hospitalist, Beth Israel Medical Center, Boston, Massachusetts

Gram-Positive Cocci, *Staphylococcus* Species

Staphylococcus species include *S. aureus* (including methicillin susceptible and resistant strains: MSSA and MRSA, respectively) and coagulase-negative species, which include organisms such as *S. epidermidis*. *S. aureus* is the most common cause of BSI mortality in the United States,[1] with mortality rates estimated at 20%–40% per episode.[46] Infectious disease consultation has been associated with decreased mortality and is recommended.[47] The guidelines of the Infectious Diseases Society of America for the treatment of MRSA recommend the use of parenteral agents for BSI.[48] It is important to consider if a patient with *S. aureus* BSI has infective endocarditis.

Oral antibiotic therapy for *S. aureus* BSI is not currently standard practice. Although trimethoprim-sulfamethoxazole (TMP-SMX) has favorable pharmacokinetics and case series of using it successfully for BSI exist,[49] TMP-SMX showed inferior outcomes in a randomized trial comparing oral TMP-SMX with intravenous vancomycin in a series of 101 *S. aureus* infections.[50] This observation has been replicated.[51] Data on doxycycline or clindamycin for *S. aureus* BSI are limited, and IDSA guidelines advise against their use in this setting because they are predominantly bacteriostatic.[48] Linezolid has favorable pharmacokinetics, with approximately 100% bioavailability, and *S. aureus* resistance to linezolid is rare.[52] Several randomized trials have compared oral linezolid with intravenous vancomycin for *S. aureus* BSI; for instance, Stevens et al. randomized 460 patients with *S. aureus* infection (of whom 18% had BSI) to linezolid versus vancomycin and observed similar clinical cure rates.[53] A pooled analysis showed oral linezolid was noninferior to vancomycin specifically for *S. aureus* BSI.[54] However, long-term use is often limited by hematologic toxicity, peripheral or optic neuropathy (which can be permanent), and induced serotonin syndrome. Additionally, linezolid is bacteriostatic, not bactericidal against *S. aureus*. Using oral linezolid as a first-line option for *S. aureus* BSI would not be recommended; however, it may be used as a second-line treatment option in selected cases. Tedizolid has similar pharmacokinetics and spectrum of activity with fewer side effects; however, clinical data on its use for *S. aureus* BSI are lacking.[55] Fluoroquinolones such as levofloxacin and the newer agent delafloxacin have activity against *S. aureus*, including MRSA, but on-treatment emergence of fluoroquinolone resistance is a concern, and data on delafloxacin for BSI are lacking.[56,57] Older literature suggested the combination of ciprofloxacin and rifampin was effective against right-sided *S. aureus* endocarditis,[58] and other oral fluoroquinolone-rifamycin combinations have also been found to be effective[59] However, this approach is currently not a standard therapy, nor is it widely used. Decisions on the duration of therapy for *S. aureus* BSI should be made in conjunction with an infectious diseases specialist; 14 days is currently regarded as a minimum.[47,48]

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ESCMID EUROPEAN SOCIETY OF MICROBIOLOGY AND IN

bacteraemia: partial oral
eral treatment

	IV (n=65)	IV to oral (n=38)	P value
Death during admission	25 (38%)	7 (18%)	0.034
30-day mortality	24 (37%)	6 (16%)	0.023
90-day relapse	1 (2%)	1 (3%)	0.698
Length of stay - median, days	22	14	0.0521

Table 2: Outcome data for 103 patients with uncomplicated SAB who received antibiotics

RESULTS

237 episodes of SAB were included between November 2018 and February 2020. Of these, 104 (44%) were uncomplicated. Descriptive data is shown in Table 1.

Of 103 patients with uncomplicated SAB who received antibiotics, 38 (37%) had an IV-PO switch within 14 days. The PO antibiotic of choice was flucloxacillin in 84% of cases (Figure 1).

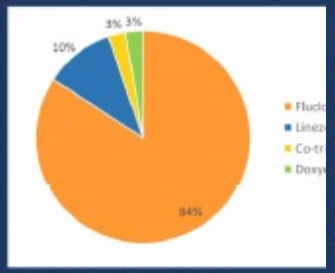

Figure 1: Oral antibiotic of choice

The median duration of antibiotics for both groups was 15 days. For the IV-PO switch group, the median IV duration was 8 and the medial PO duration was 7 days.

There is clinical equipoise in whether patients in our centre receive a parenteral to oral switch for uncomplicated *S. aureus* bacteraemia. Treatment of uncomplicated *S. aureus* bacteraemia with a parenteral to oral switch within 14 days, with total antibiotic duration of 7 days or more, demonstrated similar clinical outcomes to standard parenteral therapy with reduced length of stay. Further work should be done in a larger, prospective randomised study to evaluate this including economic analysis.

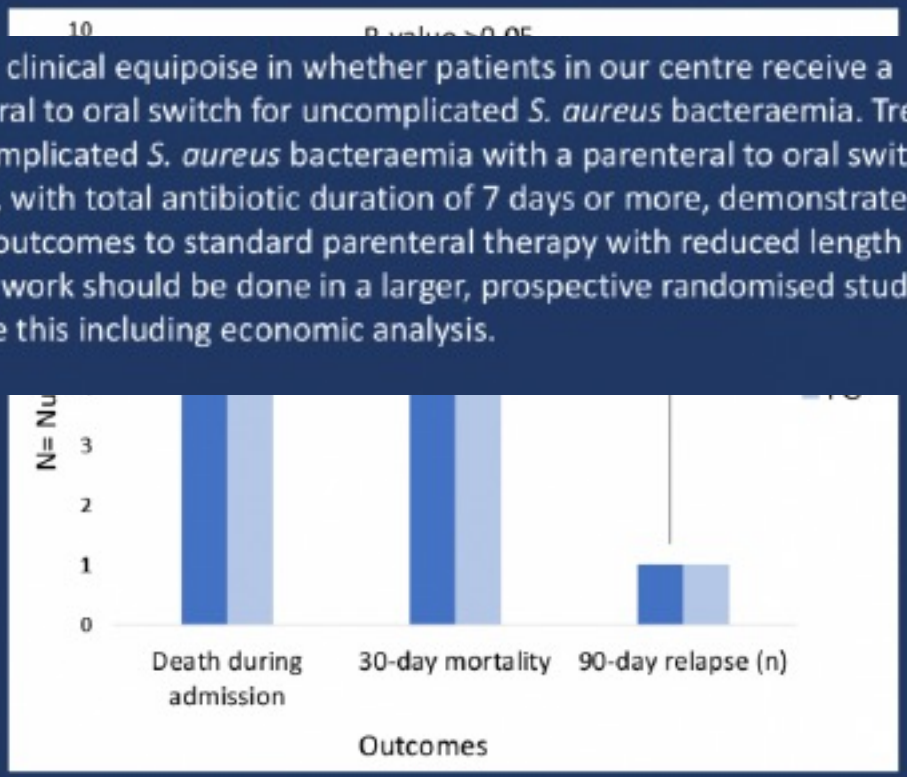

Figure 2: Outcome data for 85 patients with uncomplicated SAB who received ≥7 days antibiotics

	IV (n=65)	IV to oral (n=38)	P value
Death during admission	25 (38%)	7 (18%)	0.034
30-day mortality	24 (37%)	6 (16%)	0.023
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Table 2: Outcome data for 103 patients with uncomplicated

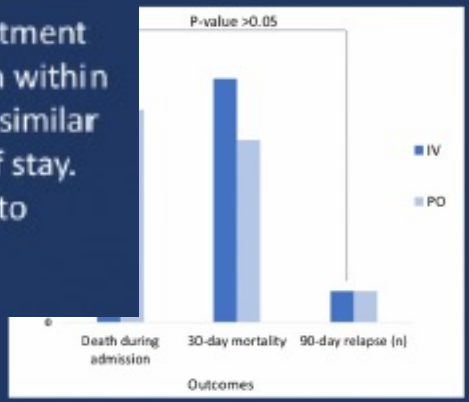

Figure 2: Outcome data for 85 patients with uncomplicated SAB who received ≥7 days antibiotics

Consultation infectiologue

- Meilleure prise en charge
- Au cours des bactériémie à Staphylocoque
- Quel que soit le critère
  - Obtention d'hémoculture de contrôle systématiques >> clairance
  - Réalisation d'une échographie cardiaque
  - Recherche de foyers infectieux à distance
  - Ablation du matériel infecté
  - Durée de traitement adapté en cas de localiisation secondaire
  - Prescription de béta lactamine en cas d'infection à MSSA
- > 11 études concluent à réduction de la mortalité

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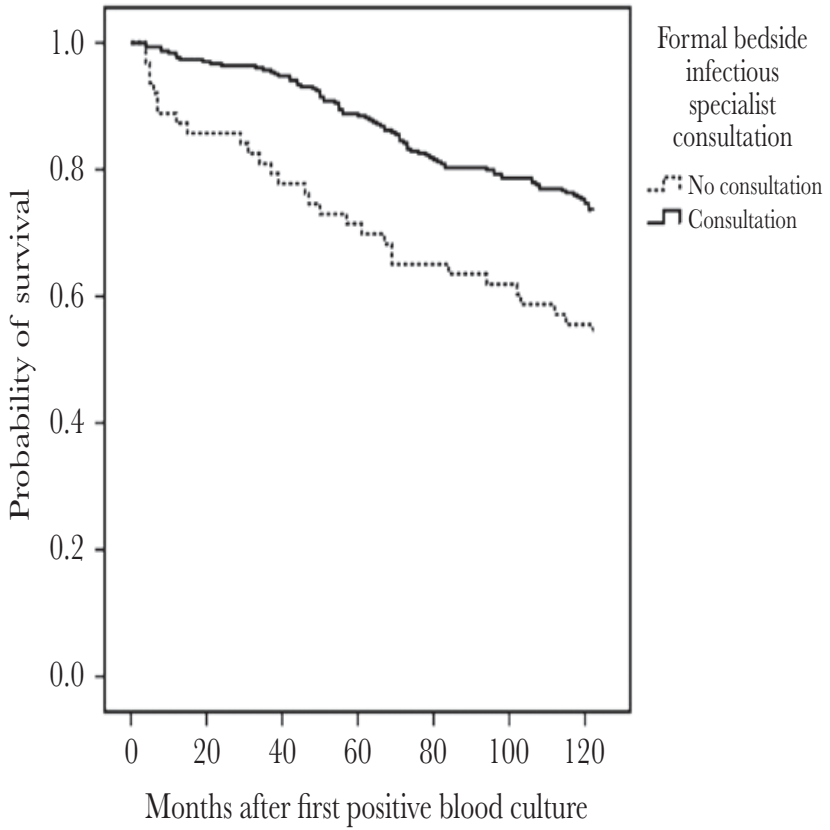
Open Forum Infectious Diseases

MAJOR ARTICLE

Formal Infectious Diseases Specialist Consultation Improves Long-term Outcome of Methicillin-Sensitive *Staphylococcus aureus* Bacteremia

Erik Forsblom,* Hanna Frilander,* Eeva Ruotsalainen, and Asko Järvinen



Impact of an Evidence-Based Bundle Intervention in the Quality-of-Care Management and Outcome of *Staphylococcus aureus* Bacteremia

Systematic review

1. Follow-up blood cultures
2. Early source control
3. Echocardiography in patients with clinical indications
4. Early use of intravenous cloxacillin for MSSA as definitive therapy
5. Adjustment of vancomycin dose according to trough levels
6. Treatment duration according to the complexity of infecti

Table 7. Multivariate Analyses of Variables Associated With 14- and 30-Day Mortality Among Patients With *Staphylococcus aureus* Bacteremia

Variables	OR (95% CI)	*P* Value
14-day mortality		
Age >60 y	2.97 (1.51–5.87)	.002
Pitt score >2	3.04 (1.74–5.33)	<.001
High-risk source[a]	2.80 (1.32–5.92)	.007
Intervention	0.49 (.28–.87)	.016
30-day mortality		
Age >60 y	3.48 (1.89–6.41)	<.001
Pitt score >2	2.34 (1.40–3.92)	.001
High-risk source[a]	3.11 (1.54–6.26)	.001
Intervention	0.59 (.36–.97)	.04

López-Cortés LE, et al. *Clin Infect Dis* 2013;579:1225-33.

Infectious Diseases Consultation Is Associated With Decreased Mortality in Enterococcal Bloodstream Infections

- Retrospective cohort single-center study (January 2015 to June 2016)
- 205 patients → 64% received IDC
- IDC was associated with higher rates of:
  - Follow-up BC (**99%** vs 74%; P < .001)
  - Echocardiography (**79%** vs 45%; P < .001)
  - Surgical intervention (**20%** vs 7%; P = 0.01)
  - Appropriate antibiotic duration (**90%** vs 46%; P < .001)

Multivariable logistic regression model of variables associated with **30-day mortality**

Variable	Crude Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)	*P* Value
Infectious diseases consultation	0.38 (0.181–0.782)	0.35 (0.16–0.76)	.007
Hypotension	2.20 (1.06–4.55)	1.85 (0.83–4.12)	.13
Ventilation at time of bacteremia	2.95 (1.36–6.42)	2.20 (0.93–5.23)	.07
Enterococcus species			
Enterococcus faecium	2.38 (1.14–4.95)	2.39 (1.09–5.23)	.03
Other *Enterococcus* species	1.58 (0.16–15.65)	2.18 (0.18–26.04)	.55
Enterococcus faecalis	Referent	Referent	

Lee RA, et al. Open Forum Infect Dis. 2020;7(3):ofaa064.

ESCMID QCI compliance

Management of bloodstream infections by infection specialists: an international ESCMID cross-sectional survey

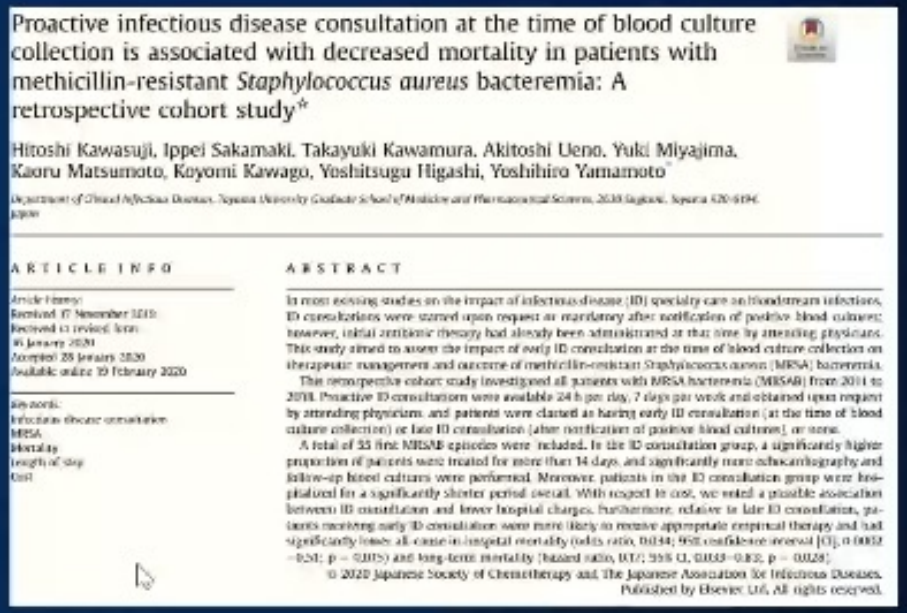
- International ESCMID cross-sectional survey (Dec 2016 to Feb 2017) exploring the management of BSIs by infection specialists.
- 616 professionals from 56 countries participated → 54% ID specialists.

	MSSA	MRSA	*Enterococcus faecalis*
Investigations [% (n/N)]			
Echocardiography	78 (400/510)	81 (373/459)	60 (262/438)
CT scan	11 (57/510)	13 (59/459)	14 (63/438)
Chest radiography	7 (38/510)	7 (33/459)	2 (7/438)
Abdominal ultrasound	5 (27/510)	6 (28/459)	13 (58/438)
Urine culture	2 (11/510)	2 (11/459)	14 (62/438)
Colonoscopy	0 (0/510)	0 (0/459)	10 (42/438)
Fundus examination	3 (14/510)	3 (13/459)	0.5 (2/438)
Other	6 (33/310)	6 (29/459)	1 (5/438)
Targeted antimicrobial therapy			
Combination therapy [% (n/N)]	20 (87/440)	27 (114/420)	39 (155/393)
Most frequently prescribed antimicrobial	Antistaphylococcal penicillins	Vancomycin	Amoxicillin/ampicillin
Most frequent daily dose (g)	12	2	12
Follow-up blood cultures [% (n/N)]	83 (365/440)	86 (357/417)	64 (249/391)
Intravenous-to-oral switch [% (n/N)]			
Yes, after 48–72 h of therapy	17 (73/438)	9 (38/418)	27 (105/388)
Yes, after 10 days	26 (116/438)	25 (105/418)	23 (90/388)
Yes, in specific situations	33 (146/438)	34 (142/418)	29 (111/388)
Never	23 (99/438)	32 (132/418)	21 (80/388)
Not applicable (already started an oral treatment)	1 (4/438)	0.2 (1/418)	1 (2/388)

Diallo K, et al. Int J Antimicrob Agents. 2018 ;51(5):794-798.

ROLE OF INFECTIOUS DISEASES CONSULTANTS

- Proactive ID consultations for MRSA bacteremia upon request by attending physicians
- ***In the ID consultation group***
  - ✓ ***Shorter hospitalization***
  - ✓ ***lower hospital charges, appropriate empiric therapy***
  - ✓ ***lower all-cause in-hospital and long-term mortality***
- Limitations: retrospective in nature, small sample size



Proactive infectious disease consultation at the time of blood culture collection is associated with decreased mortality in patients with methicillin-resistant *Staphylococcus aureus* bacteremia: A retrospective cohort study*

Hitoshi Kawasuji, Ippei Sakamaki, Takayuki Kawamura, Akitoshi Ueno, Yuki Miyajima, Kaoru Matsumoto, Koyomi Kawago, Yoshitsugu Higashi, Yoshihiro Yamamoto*

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ARTICLE INFO

Article History:
Received 17 November 2019
Received in revised form
16 January 2020
Accepted 28 January 2020
Available online 19 February 2020

Keywords:
Infectious disease consultation
MRSA
Mortality
Length of stay
Cost

ABSTRACT

In most existing studies on the impact of infectious disease (ID) specialty care on bloodstream infections, ID consultations were started upon request or mandatory after notification of positive blood cultures; however, initial antibiotic therapy had already been administrated at that time by attending physicians. This study aimed to assess the impact of early ID consultation at the time of blood culture collection on therapeutic management and outcome of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia.

This retrospective cohort study investigated all patients with MRSA bacteremia (MRSAB) from 2014 to 2018. Proactive ID consultations were available 24 h per day, 7 days per week and obtained upon request by attending physicians, and patients were classified as having early ID consultation (at the time of blood culture collection) or late ID consultation (after notification of positive blood cultures), or none.

A total of 55 first MRSAB episodes were included. In the ID consultation group, a significantly higher proportion of patients were treated for more than 14 days, and significantly more echocardiography and follow-up blood cultures were performed. Moreover, patients in the ID consultation group were hospitalized for a significantly shorter period overall. With respect to cost, we noted a possible association between ID consultation and lower hospital charges. Furthermore, relative to late ID consultation, patients receiving early ID consultation were more likely to receive appropriate empirical therapy and had significantly lower all-cause in-hospital mortality (odds ratio, 0.134; 95% confidence interval [CI], 0.033–0.531; p = 0.015) and long-term mortality (hazard ratio, 0.17; 95% CI, 0.033–0.83; p = 0.028).

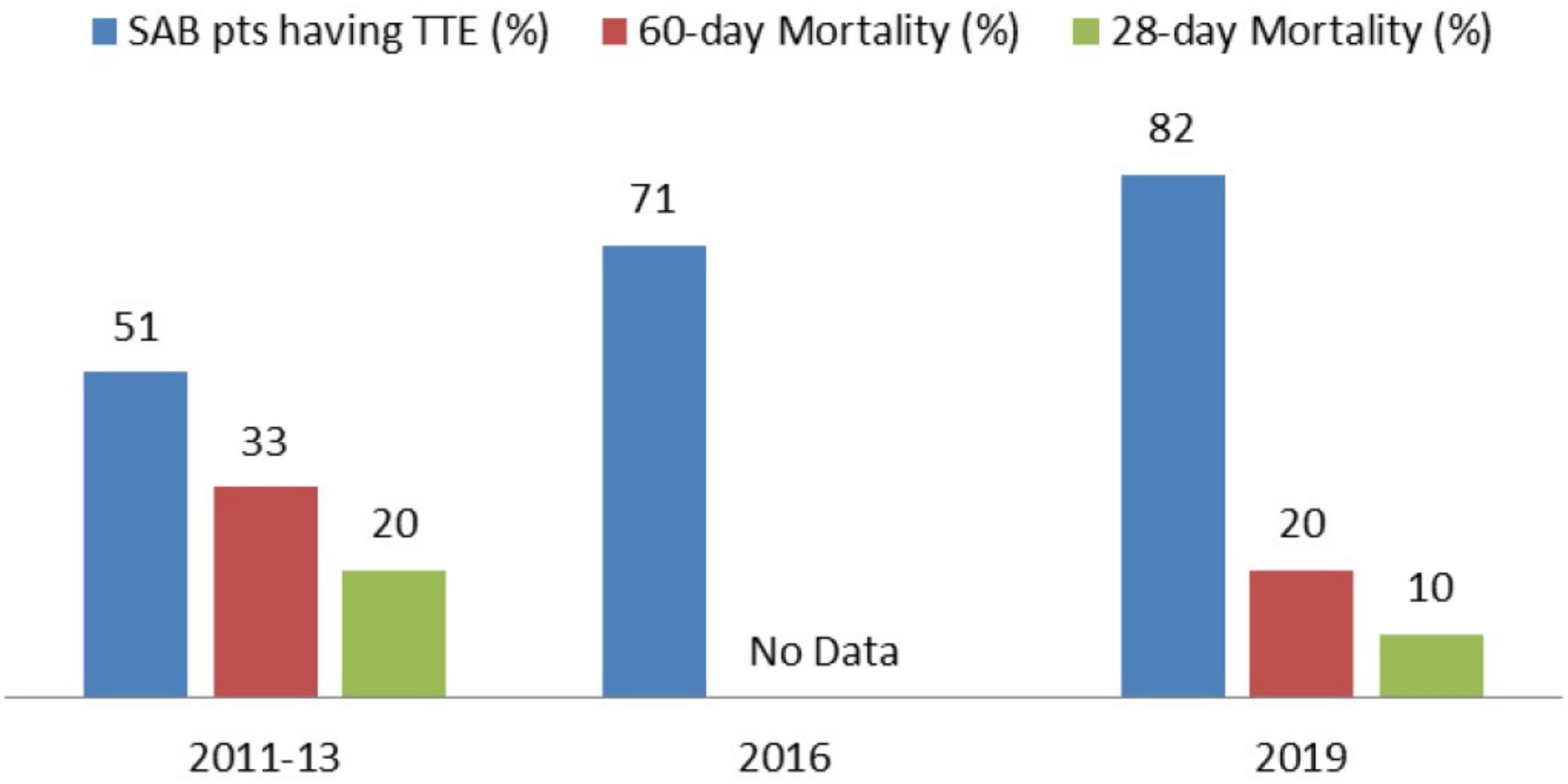
Kawasuji H et al; J Infect Chemother 2020; 26

Gunning. Poster 00684 ECCMID 2021

Timeline of Quality Improvement Interventions

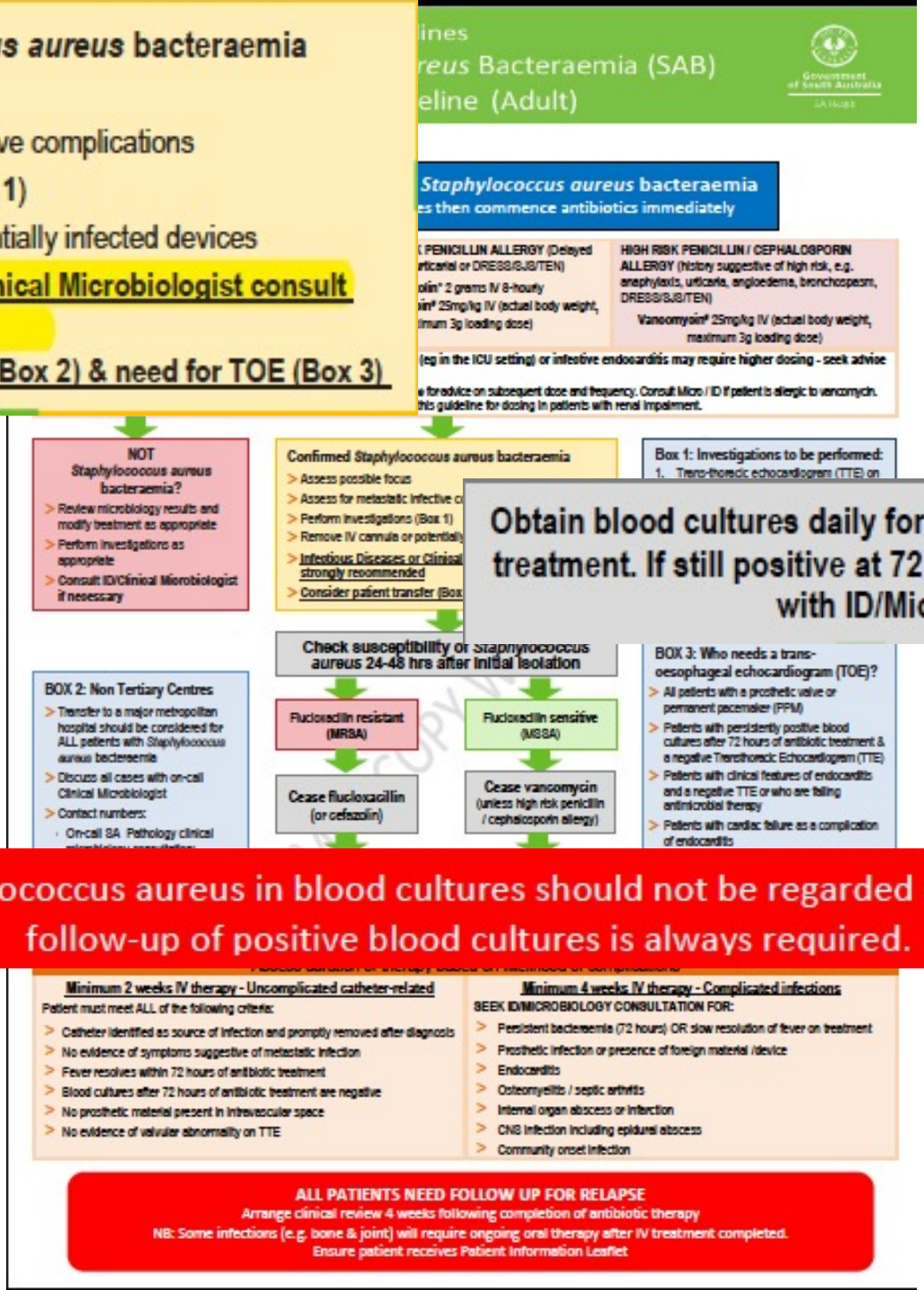
2013- 2016	Nov 2016 – Jan 2017	Apr 2017 – May 2017	June 2017	November 2017-January 2018		
Uploading flowchart for the investigation of IE onto the intranet	Reviewing the impact of previous recommendations	Educational tutorials for junior doctors and consultants	Uploading guidelines onto Hospital digital platform	Enable Infection specialists to request echocardiograms	Improve digital requesting for echo and blood cultures	Improve communication between MDT members

SAB-clinical outcomes



Confirmed *Staphylococcus aureus* bacteraemia

- Assess possible focus
- Assess for metastatic infective complications
- Perform investigations (**Box 1**)
- Remove IV cannula or potentially infected devices
- **Infectious Diseases or Clinical Microbiologist consult strongly recommended**
- **Consider patient transfer (Box 2) & need for TOE (Box 3)**



Obtain blood cultures daily for 72 hours after starting treatment. If still positive at 72 hours, discuss further with ID/Micro

Isolation of Staphylococcus aureus in blood cultures should not be regarded as a 'contaminant' – follow-up of positive blood cultures is always required.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Staphylococcus aureus Bacteremia
This new guideline is currently in development.
Projected publication: Fall 2020

Conclusion

- 14j IV probablement excessif si bactériémie non compliquée
- RCT à faire (SAMS)
- Etude sur relais per os >> SABATO
- Etude sur simplification administration IV >> Dalicath
- Nécessité de standardiser les bilans ETT/Eto/Pet TDM en fonction de la population cible : +âgé + de matériel ou en fonction des populations

Rien à voir

Mais intéressant pour la desescalde thérapeutique

ECCMID 2021

Article

Definitive Cefazolin Treatment for Community-Onset Enterobacteriaceae Bacteremia Based on the Contemporary CLSI Breakpoint: Clinical Experience of a Medical Center in Southern Taiwan

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Antibiotics **2019**, *8*, 216; doi:10.3390/antibiotics8040216

Abstract: Cefazolin is traditionally active against Escherichia coli, Klebsiella species, and Proteus mirabilis (EKP) isolates. The Clinical and Laboratory Standards Institute (CLSI) has twice updated cefazolin susceptibility breakpoints for EKP since 2010, but its role in the definitive treatment of cefazolin-susceptible EKP bacteremia remains debated. To assess its efficacy as a definitive agent, the 8-year cohort study consisted of 941 adults with monomicrobial cefazolin-susceptible EKP bacteremia, based on the CLSI criteria issued in 2019, was retrospectively established in a medical center. Based on the definitive antimicrobial prescription, eligible patients were categorized into the cefazolin (399 patients, 42.4%) and broader-spectrum antibiotic (BSA) (542, 57.6%) groups. Initially, fewer proportions of patients with fatal comorbidities (the McCabe classification) and the critical illness (a Pitt bacteremia score ≥4) at the onset and day 3 of the bacteremia episode were found in the cefazolin group, compared to the BSA group. After propensity-score matching, no significant difference of patient proportions between the cefazolin (345 patients) and BSA (345) groups was observed, in terms of the elderly, types and severity of comorbidities, bacteremia severity at the onset and day 3, major bacteremia sources, and the 15-day and 30-day crude mortality. In early outcomes, lengths of time to defervescence, intravenous (IV) antimicrobial administration, and hospitalization were similar in the two matched groups; lower costs of IV antimicrobial administration were observed in the cefazolin group. Notably, for late outcomes, lower proportions of post-treatment infections caused by antimicrobial-resistant pathogens (ARPs) and post-treatment mortality rates were evidenced in the cefazolin group. Conclusively, cefazolin is definitively efficacious and cost-effective for adults with community-onset cefazolin-susceptible EKP bacteremia in this one-center study, compared to BSAs. However, a prospective multicenter study should be conducted for external validation with other communities.

Antibiotics **2019**, *8*, 216; doi:10.3390/antibiotics8040216

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Extra slides:

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Laupland KB et al; Int J Infect Dis 2021; 104

CAS CLINIQUE

- M. A., 45 ans, 126 kg, IMC 42, diabétique insuliné, dépendant aux opiacés, substitué par Subutex®
- Cirrhose compensée (VHC guéri, OH, NASH…)
- EI à *Enterococcus faecalis* en 2016 => bioprothèse

- 23/05/21: confusion fébrile:
  - Choc septique
  - EP bilatérale
  - Bactériémie à SAMS
  - ETT normale, ETO épaississement d'un feuillet de la prothèse sans dysfonctionnement: « traiter comme une EI »
  - Cloxacilline IV 12 g/24h
  - Héparine

- 28/05: sortie de réanimation
  - ETO végétation 5 mm
  - TDM TAP pas d'autre embole
  - Diminution DFG à 50: relai céfazoline malgré l'absence de cristallurie
  - Coumadine

- 15/06: DFG: 42; demandeur de sortie, Piccline bouché (mésusage ??)

????

- Relais oral le 15/6: clindamycine 600 mg x 3/j + cotrimoxazole (800/160) 2 cps x 3/j
- Sortie le 21/6 (DFG 39)
- Rapidement: asthénie, vomissements
- Le 30/6: DFG 15, K 7,6, PNN 1200/mm3

- Evolution rapidement favorable à l'arrêt du cotrimoxazole
- Reprise Céfazoline poursuivie jusqu'au 9/07: 6 semaines
- ETO stable

Relais oral: quelques précautions

- Les recommandations (anciennes) des sociétés savantes ne le proposent pas

- Le patient doit être stabilisé et les hémocultures stériles
- Le ou les antibiotiques choisis doivent diffuser aux foyers profonds

- Pas de monothérapie pour fluoroquinolones, rifampicine, acide fusidique

- La rifampicine est pourvoyeuse d'interactions: anticoagulants, **opiacés**, …

Relais oral: peu de données

- Dans l'EI:
  - Quelques études anciennes montrent une bonne efficacité de fluoroquinolone-rifampicine dans l'EI droite
  - Les données de l'IHU Méditerranée Infection suggèrent une efficacité de clindamycine-cotrimoxazole fortes doses après J7
  - Les données de l'essai POET suggèrent la possibilité d'un relai à partir de J10
  - Etude RODEO en cours

- Dans les autres BSA:
  - Pas de données; étude SABATO en attente
  - Qui peut le plus peut le moins
  - Durée de traitement = celle des foyers profonds

Heldman, Am J Med 1996, Tissot-Dupont IJAA 2019, Iversen NEJM 2019, Lemaignen BMJ Open 2020

Etude POET: antibiothérapie orale utilisée

Antibiotic regimens in the POET trial.

	Oral regimens	Frequency n (%)
Staphylococcus aureus	Dicloxacillin and rifampicin	15 (33)
	Amoxicillin and rifampicin	13 (29)
	Moxifloxacin and rifampicin	3 (7)
	Amoxicillin and fusidic acid	2 (4)
	Dicloxacillin and fusidic acid	2 (4)
	Fusidic acid and linezolid	2 (4)
	Rifampicin and linezolid	2 (4)
	Penicillin and rifampicin	1 (2)
	Amoxicillin and clindamycin	1 (2)
	Ampicillin and rifampicin	1 (2)
	Moxifloxacin and fusidic acid	1 (2)
	Moxifloxacin and linezolid	1 (2)
	Linezolid and clindamycin	1 (2)

Iversen NEJM 2019