Hammamet 22-24 Mai 2025

IAS à ABRI dans les services de Réanimation Tunisiens: état des lieux et perspectives

Sami Abdellatif
REA MED – CHU, La RABTA, Tunis

ABRI / CRAB

- **OMS : Pathogène d'urgence mondiale**

Tunis Med. 2008 Nov;86(11):992-5.

[Surveillance of multidrug resistant bacteria in a Tunisian hospital]

[Article in French]

Lamia Thabet [1], Amen allah Messadi, Mondher Mbarek, Amel Turki, Balkis Meddeb, Saida Ben Redjeb

(ESBL). The rate of MRSA was 70.4% among 371 strains of S. aureus. ESBL represented 23,6% among 1096 isolates. Concerning A. baumannii and P. aeruginosa, 51.7% and 20.5% were resistant to both imipenem and ceftazidime among 170 and 264 isolates. Antibiotic resistance evolution showed a

ELSEVIER MASSON

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Médecine et maladies infectieuses

Médecine et maladies infectieuses 40 (2010) 126–128

Profil de sensibilité aux antibiotiques des souches *d'Acinetobacter baumannii* isolées dans la région de Mahdia

Susceptibility patterns of Acinetobacter baumannii strains isolated in the Mahdia region

Tableau 1
Résistance aux antibiotiques des souches d'*A. baumannii* en fonction des services.
Resistance to antibiotics of A. baumannii strains according to units.

	Réanimation médicale ($n=261$) (%)	Chirurgie ($n=66$) (%)	Urologie ($n=19$) (%)	Pédiatrie ($n=11$) (%)	Gynécologie ($n=11$) (%)	Taux moyen (%)
Ticarcilline	68,5	64	48	41	37	51,7
Ticarcilline/Ac clavulanique	46	41	37	29	31	36,8
Pipéracilline	69	63	56	53	51	58,4
Pipéracilline-Tazobactam	55,5	48	42	35	39	32,2
Céftazidime	71	67	51	45	42	55,2
Céfépime	57	53	51	46	48	51
Imipénème	37	33	31	26	28	31
Amikacine	34,5	32,7	29,4	26	27	35,9
Tobramycine	72	68	66	60	58,5	64,9
Gentamycine	82	75	70	67	66	72
Ciprofloxacine	72	65	60,9	62	61,6	64,3
Lévofloxacine	82	81	75	77	76	78,2
Colistine	4,6	0	0	0	0	0,9

Tunisie Medicale
Volume 95, Issue 3, March 2017, Pages 179-184

ARTICLE ORIGINAL

Infections nosocomiales: état des lieux dans un service de réanimation

Nosocomial infections: current situation in a resuscitation-unit

Ahlem Trifi[1], Sami Abdellatif[1], Mouna Oueslati[1], Meriem Zribi[2], Foued Daly[1], Rochdi Nasri[1], Rahma Mannai[1], Chadlia Fandri [2], Salah Ben Lakhal[1]

1-Service de réanimation médicale CHU la Rabta, Tunis,Tunisie
2-Service de bactériologie CHU la Rabta, Tunis, Tunisie

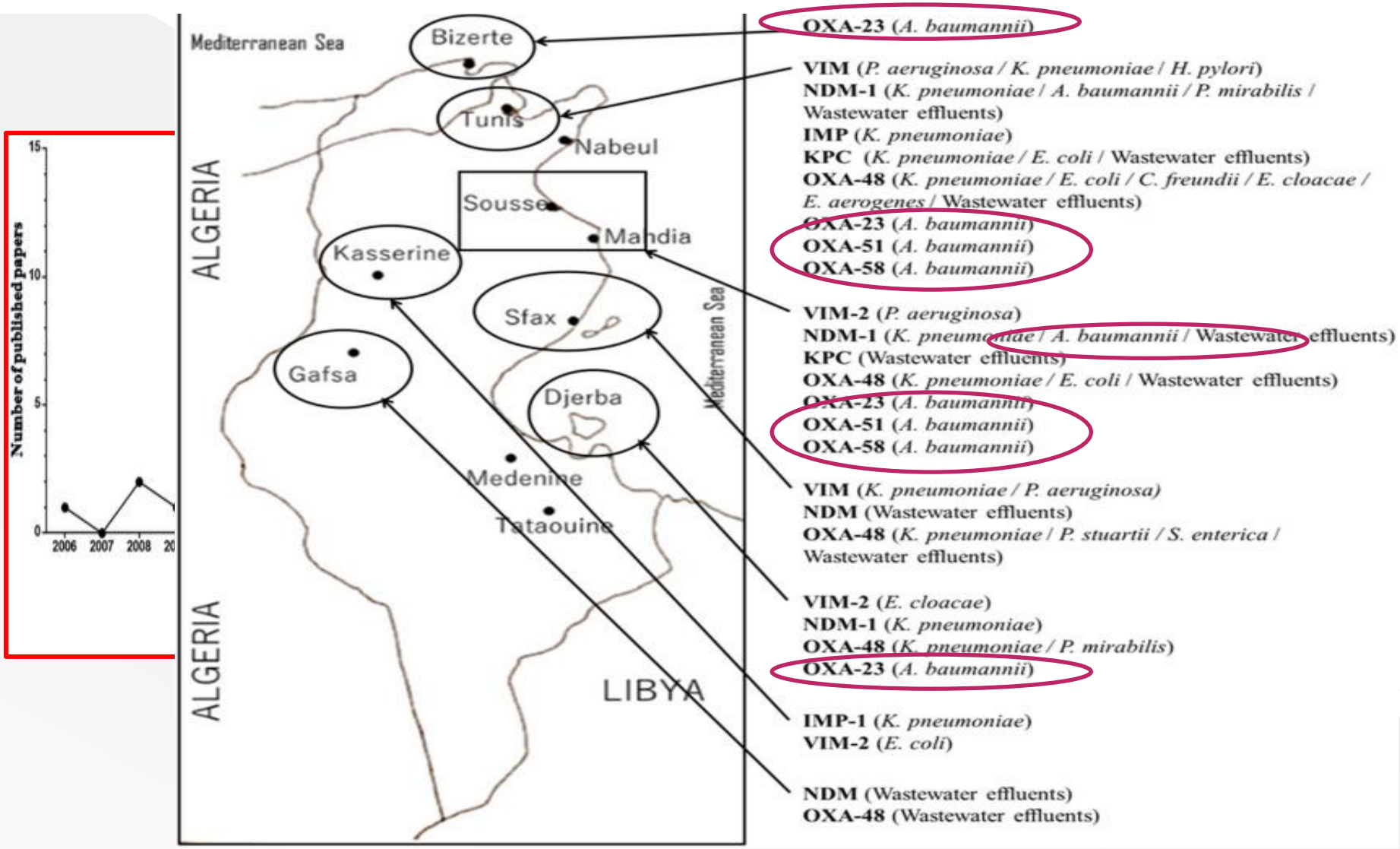
- **Profil de sensibilité:**

GERMES	PROFIL DE SENSIBILITE
•**Acineto B** •**Pseudomonas** •**Steno M** •**Enterobactéries** •**Staphylocoques** •**Enterocoques**	**IMP R: 91.6%** Colistine S: 87.5% Cefta R: 55% **IMP R: 33.6%** Quinolones S: 33% Tygécycline R: 20% C3G R: 42% (EBLSE) **P Carbapenemases: 12%** SARM: 41.7% St spp. metiR: 66% GP S: 100% Ampi R: 86% **Vanco R (EVR): 28.6% EGR: 14%**

Infect Drug Resist. 2020 Nov 23;13:4177–4191. doi: 10.2147/IDR.S259562

Carbapenemase Producing Gram-Negative Bacteria in Tunisia: History of Thirteen Years of Challenge

Olfa Dziri [1,2], Raoudha Dziri [1], Allaaeddin Ali El Salabi [3,4], Chedly Chouchani [1,2]



LA TUNISIE MEDICALE - 2018 ; Vol 96 (10/11)

ARTICLE ORIGINAL

The prevalence of healthcare-associated infection in medical intensive care units in Tunisia. Results of the multi-centre NOSOREA1 study.

Prévalence des infections associées aux soins en réanimation médicale en Tunisie. Résultats de l'étude multicentrique NOSOREA1

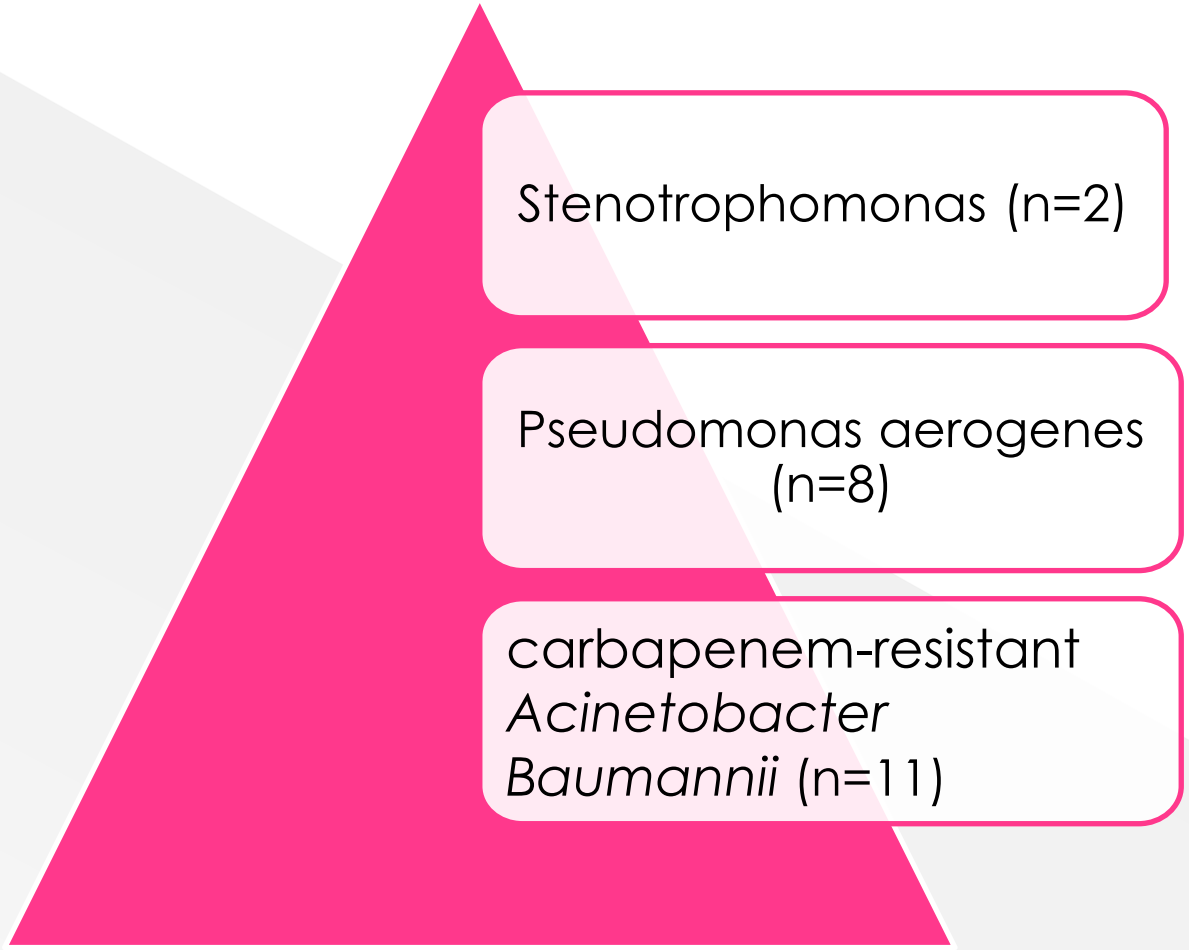
A. Jamoussi[1], S. Ayed[1], K. Ben Ismail[1], K. Chtara [2], M. Bouaziz[2], A. Mokline[3], A. Messaadi[3], T. Merhebene[1], N.Tilouche[4], S. El Atrous[4], M. Boussarsar[5], F. Daly[6], S. Benlakhel[6], I. Fathallal[7], N.Kouraichi[7], Y.Z. El Hechmi[8], Z. Jerbi[8], R. Attigue[9], H. Hamouda[9], H. Ghadhoun[10], H. El Ghord[10], K. Ben Romdhane[11], S. Khedher[12], R. Allala[13], H. Mateur[14], N. Brahmi[15], J. Ben Khelil[1] and M. Besbes[1]

Results: One hundred and three patients were collected from 15 Tunisian medical ICUs. HAI prevalence was 25.2% CI 95% [15-35].The most frequent HAIs were hospital acquired pneumonia in 19 cases (59%) and catheter related infection in 5 cases (15%). Independent factors associated with HAI occurrence were SAPSII score ≥ 33 with OR 1.047; CI 95% [1.015-1.077], p=0.003 and recent hospitalization with OR 4.14 CI 95% [1.235-13.889], p=0.021. Non-fermenting pathogens were the most frequent microorganisms reported in ICUs ecology, prior colonization and HAIs of the screened patients

- NOSOREA 2: Prevalence 41.6 % IC [33.6 – 49.6]

A Jamoussi et al Sep 2022

Non-fermenting pathogens (15/16)

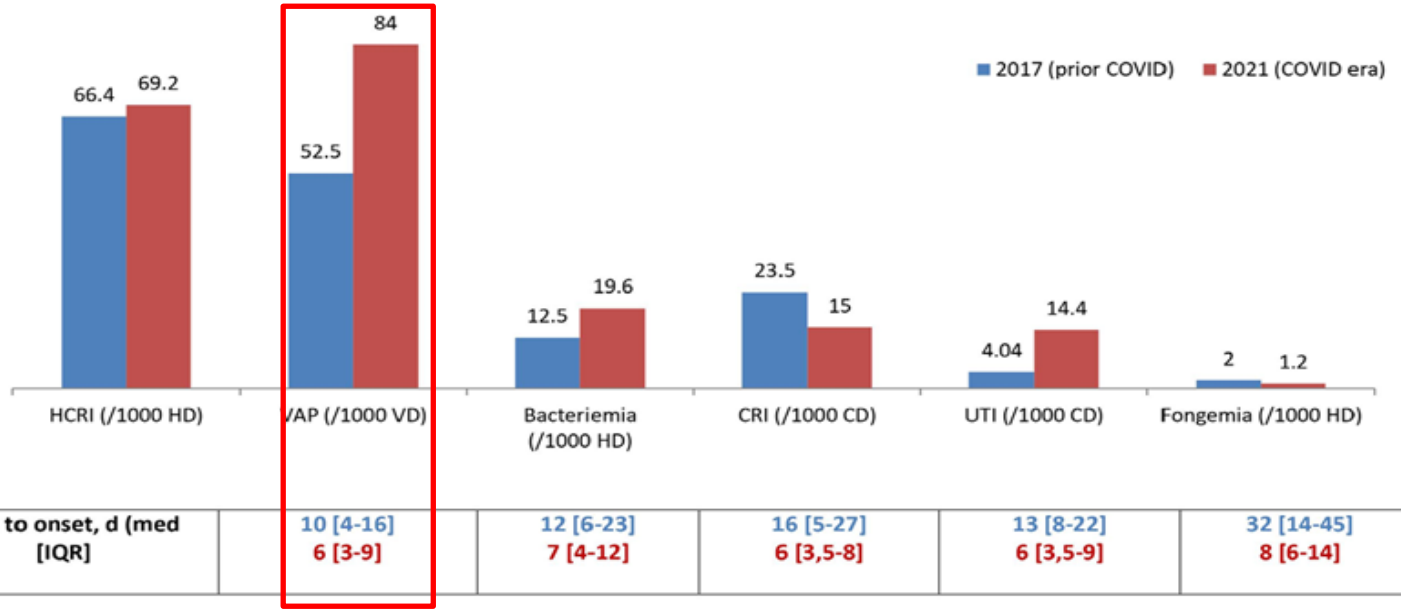


COVID?

Healthcare-related infections in critical patients with COVID-19: epidemiology, risk factors and outcomes

TRIFI Ahlem[1], MASSEOUD Lynda[1], MEFTEH Amal[1], SELLAOUTI Selim[1], ABDENNEBI Cyrine[1], ABDELLATIF Sami[1], BEN LAKHAL Salah[1]
[1]Medical ICU, la Rabta hospital, Faculty of Medicine of Tunis, Tunis, Tunisie
Correspondence: Ahlem TRIFI (trifiahlem2@gmail.com)
Annals of Intensive Care 2022, **12(1):**FC-135

Figure. Difference in incidence densities of HCRI before COVID versus COVID era



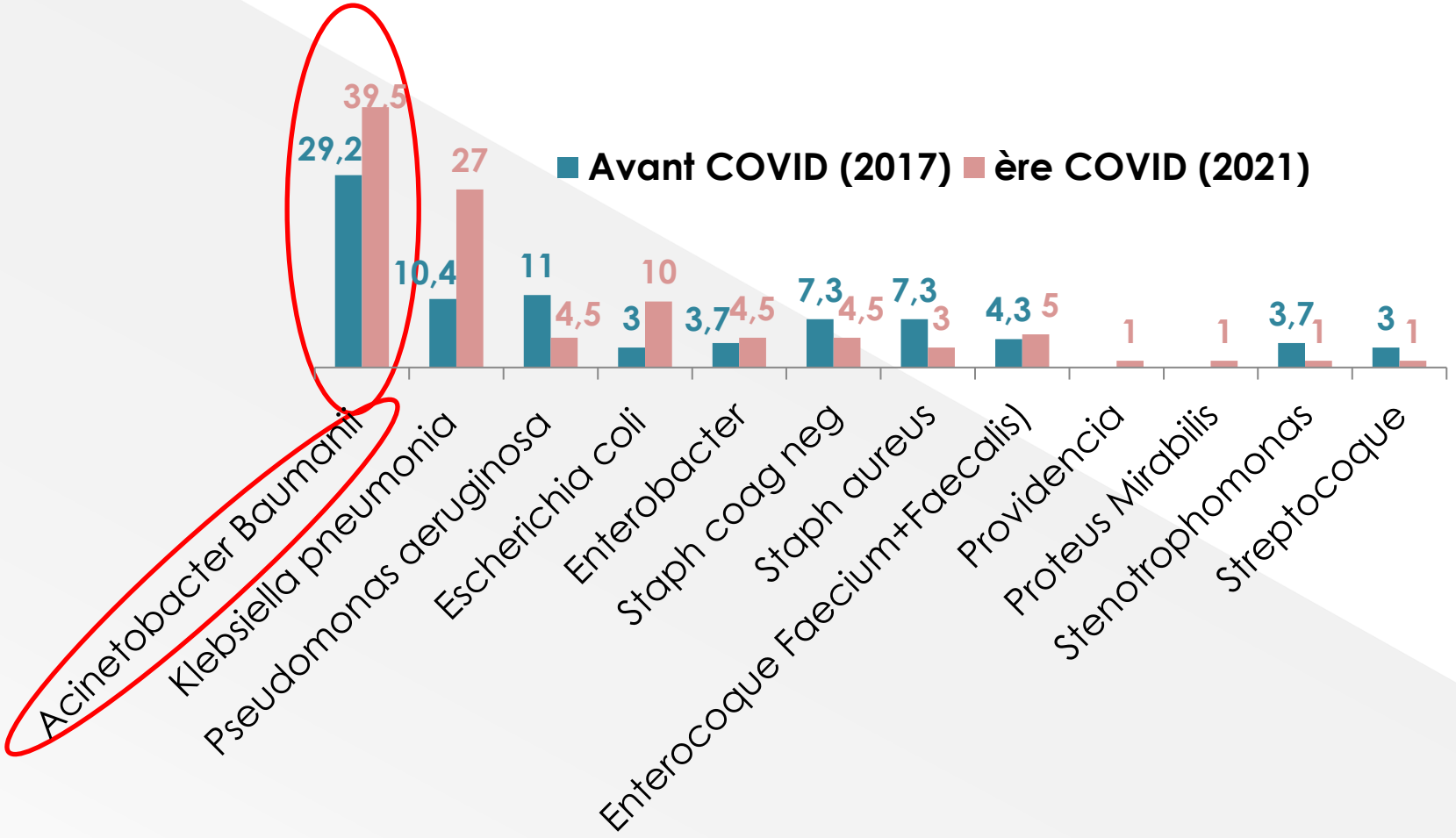
Time to onset, d (med [IQR]	10 [4-16] 6 [3-9]	12 [6-23] 7 [4-12]	16 [5-27] 6 [3,5-8]	13 [8-22] 6 [3,5-9]	32 [14-45] 8 [6-14]

HCRI: healthcare-related infection, VAP : ventilator acquired pneumonia, CRI : catheter related infection, UTI: urinary tract infection, HD : hospitalization days, VD : ventilation days, CD : catheterization days

Healthcare-related infections in critical patients with COVID-19: epidemiology, risk factors and outcomes

TRIFI Ahlem[1], MASSEOUD Lynda[1], MEFTEH Amal[1], SELLAOUTI Selim[1], ABDENNEBI Cyrine[1], ABDELLATIF Sami[1], BEN LAKHAL Salah[1]
[1]Medical ICU, la Rabta hospital, Faculty of Medicine of Tunis, Tunis, Tunisie
Correspondence: Ahlem TRIFI (trifiahlem2@gmail.com)

Annals of Intensive Care 2022, **12(1):**FC-135



Acute and Critical Care

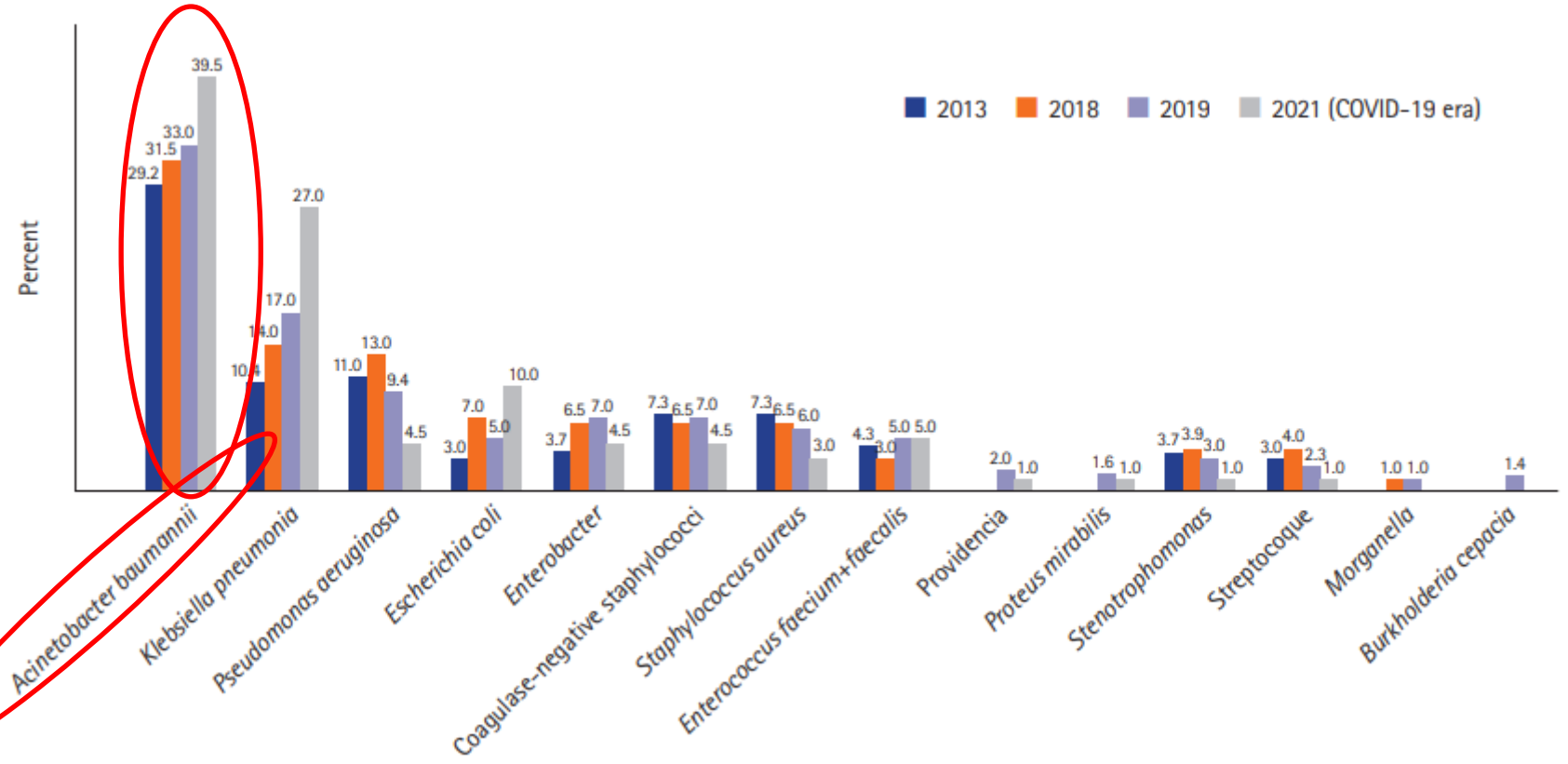
Acute and Critical Care 2023 November 38(4):425-434
https://doi.org/10.4266/acc.2023.00773

| pISSN 2586-6052 | eISSN 2586-6060

Healthcare-associated infections in critical COVID-19 patients in Tunis: epidemiology, risk factors, and outcomes

Ahlem Trifi, Selim Sellaouti, Asma Mehdi, Lynda Messaoud, Eya Seghir, Badis Tlili, Sami Abdellatif

Medical Intensive Care Unit, La Rabta Hospital, Tunis, Tunisia



RéaRIR. Données Pr Madani (SMAAR 2024)

- Étude d'incidence prospective sur 6 mois
- 41 centres
- 2841 patients
- 7 pays :
  - Algérie
  - Congo
  - Mali
  - Maroc
  - Niger
  - Tunisie
  - Sénégal

- IAS 21.7%
  - *Acineto baumannii* : 39%
    - ABRI 94,6%
    - AMK R : 86.6%
    - CST R : 7.1%
    - Mortalité : 65%
    - PAVM : 70%
    - Bactériémies : 16.7%
    - IUS : 9.7%

IAS Réa Tun T 1 2025

- 12 services participants
  - Capacité totale= 159 lits
  - Capacité moyenne = 13 lits (4 – 22 lits)
  - N admissions : 1507 patients
  - 129 épisodes IAS à ABRI chez 127 malades

- Incidence = **8,5 %** soit **85 cas par 1000 patients**

- Densité d'incidence = **4,06 cas par 1000 patient-jours**

C'est pratiquement le double des résultats de cette meta-analyse

Meta-Analysis > Emerg Microbes Infect. 2019;8(1):1747-1759.
doi: 10.1080/22221751.2019.1698273.

The incidence and prevalence of hospital–acquired (carbapenem–resistant) *Acinetobacter baumannii* in Europe, Eastern Mediterranean and Africa: a systematic review and meta–analysis

Olaniyi Ayobami [1], Niklas Willrich [1], Thomas Harder [1], Iruka N Okeke [2], Tim Eckmanns [1], Robby Markwart [1]

Affiliations + expand

PMID: 31805829 PMCID: PMC6913636 DOI: 10.1080/22221751.2019.1698273

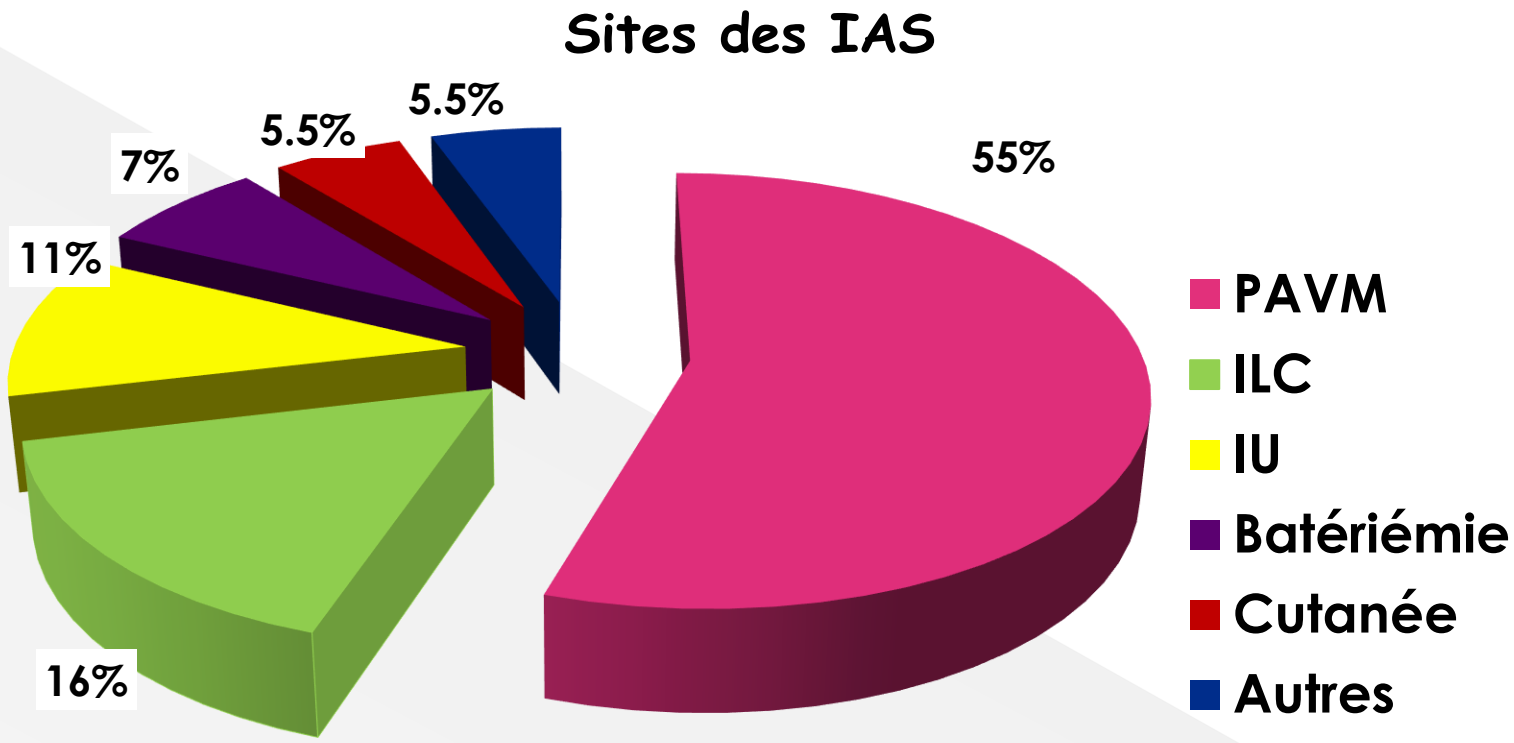
Abstract

Due to therapeutic challenges, hospital-acquired infections (HAIs) caused by *Acinetobacter baumannii* (HA-AB), particularly carbapenem-resistant strains (HA-CRAB) pose a serious health threat to patients worldwide. This systematic review sought to summarize recent data on the incidence and prevalence of HA-AB and HA-CRAB infections in the WHO-defined regions of Europe (EUR), Eastern Mediterranean (EMR) and Africa (AFR). A comprehensive literature search was performed using MEDLINE, EMBASE and GMI databases (01/2014-02/2019). Random-effects meta-analyses were performed to determine the pooled incidence of HA-AB and HA-CRAB infections as well as the proportions of *A. baumannii* among all HAIs. 24 studies from 3,340 records were included in this review (EUR: 16, EMR: 6, AFR: 2). The pooled estimates of incidence and incidence density of HA-AB infection in intensive care units (ICUs) were 56.5 (95% CI 33.9-92.8) cases per 1,000 patients and 4.4 (95% CI 2.9-6.6) cases per 1,000 patient days, respectively. Five studies conducted at a hospital-wide level or in specialized clinical departments/wards (ICU + non-ICU patients) showed HA-AB incidences between 0.85 and 5.6 cases per 1,000 patients. For carbapenem-resistant *A. baumannii* infections in ICUs, the pooled incidence and incidence density were 41.7 (95% CI 21.6-78.7) cases per 1,000 patients and 2.1 (95% CI 1.2-3.7) cases per 1,000 patient days, respectively. In ICUs, *A. baumannii* and carbapenem-resistant *A. baumannii* strains accounted for 20.9% (95% CI 16.5-26.2%) and 13.6% (95% CI 9.7-18.7%) of all HAIs, respectively. Our study highlights the persistent clinical significance of hospital-acquired *A. baumannii* infections in the studied WHO regions, particularly in ICUs.

Caractéristiques cliniques des patients

	Population étudiée (n=127)
Age, ans (med [IQR])	56 [30-67]
Sex-ratio (M/F)	93/34 (2,73)
Scores de gravité : • IGS II, (med [IQR]) • APACHE II, (med [IQR])	 41 [29-54] 17 [14-24]
Motif d'admission: n (%) • Respi • Neuro • ESG • HD hors ESG • Metab • Autres	 52 (41%) 43 (34%) 16 11 (dont choc hypoV / brulures) 3 2

Sites


Sites des IAS
55%
16%
11%
7%
5.5%
5.5%
PAVM
ILC
IU
Batériémie
Cutanée
Autres

Délais de survenue

	Délai de survenue, j (med [IQR])
PAVM	9 [5-12,2]
ILC	6 [5-19]
IU	12 [5,5-20,5]
Bactériémie	4,5 [3-6]

Antibiothérapie instaurée

- **Probabiliste « Empirique »:** n=83 (64,4%)
  - ✓ **Molécule la plus utilisée :** colistine : n=47 dont association avec :
    - ✓IMP dans 35 fois
    - ✓Tygé dans 12 fois
    - ✓Aminosides 8 fois
- **Adaptée :** n=46 (35,6%)
  - ✓ **Molécules utilisées en adaptée :** Colistine a été administrée dans tous les cas (n=46) avec :
    - ✓En monothérapie : 12 cas
    - ✓En association avec :
      - ✓IMP dans 15 fois
      - ✓IMP+aminosides : 8 cas
      - ✓Autres B Lact : 5 cas
      - ✓Tygé, quinolones, rifa : 6 fois
      - ✓Coli en AS : 6 cas

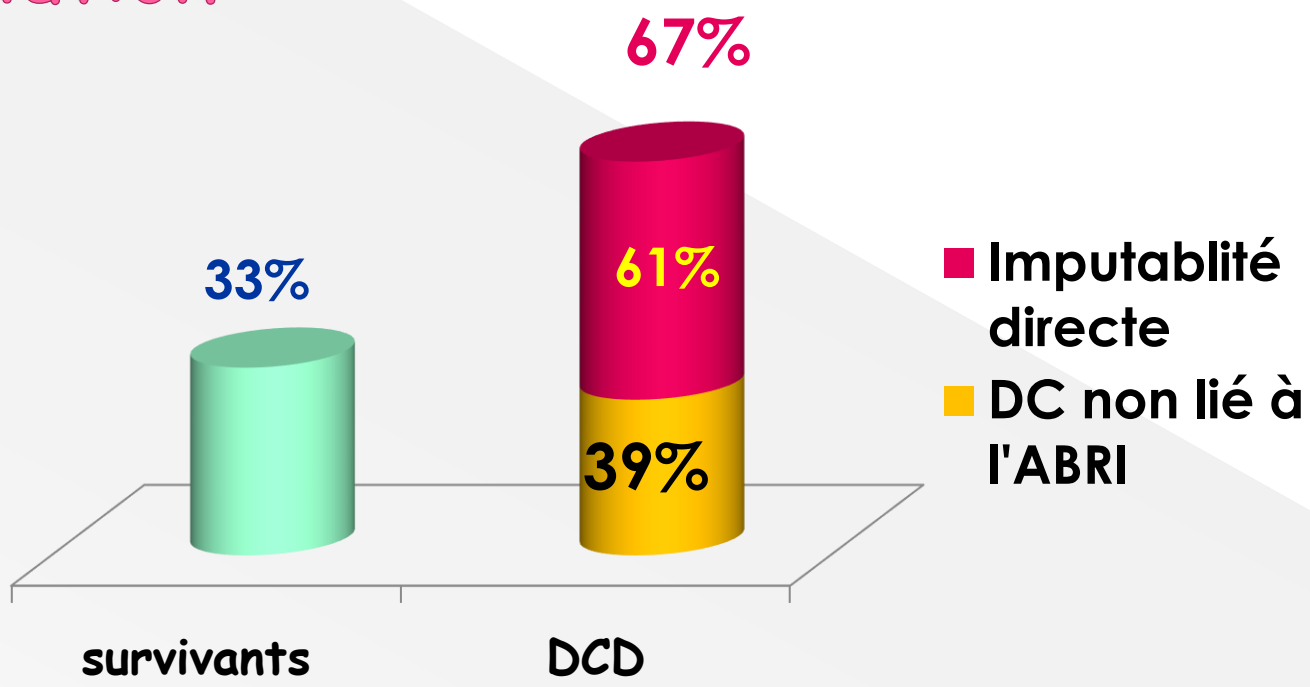
Durée ATB

- Durée médiane= 7 j [2-10]
- Min-max= 2-14 j
- Dans 24,5% des cas, durée > 10 j

Durée Séjour

- med [IQR]=19 J [8,5-28,5]
- min-max= 1-106 J

Evolution



frontiers in Medicine

REVIEW
published: 24 March 2022
doi: 10.3389/fmed.2022.793615

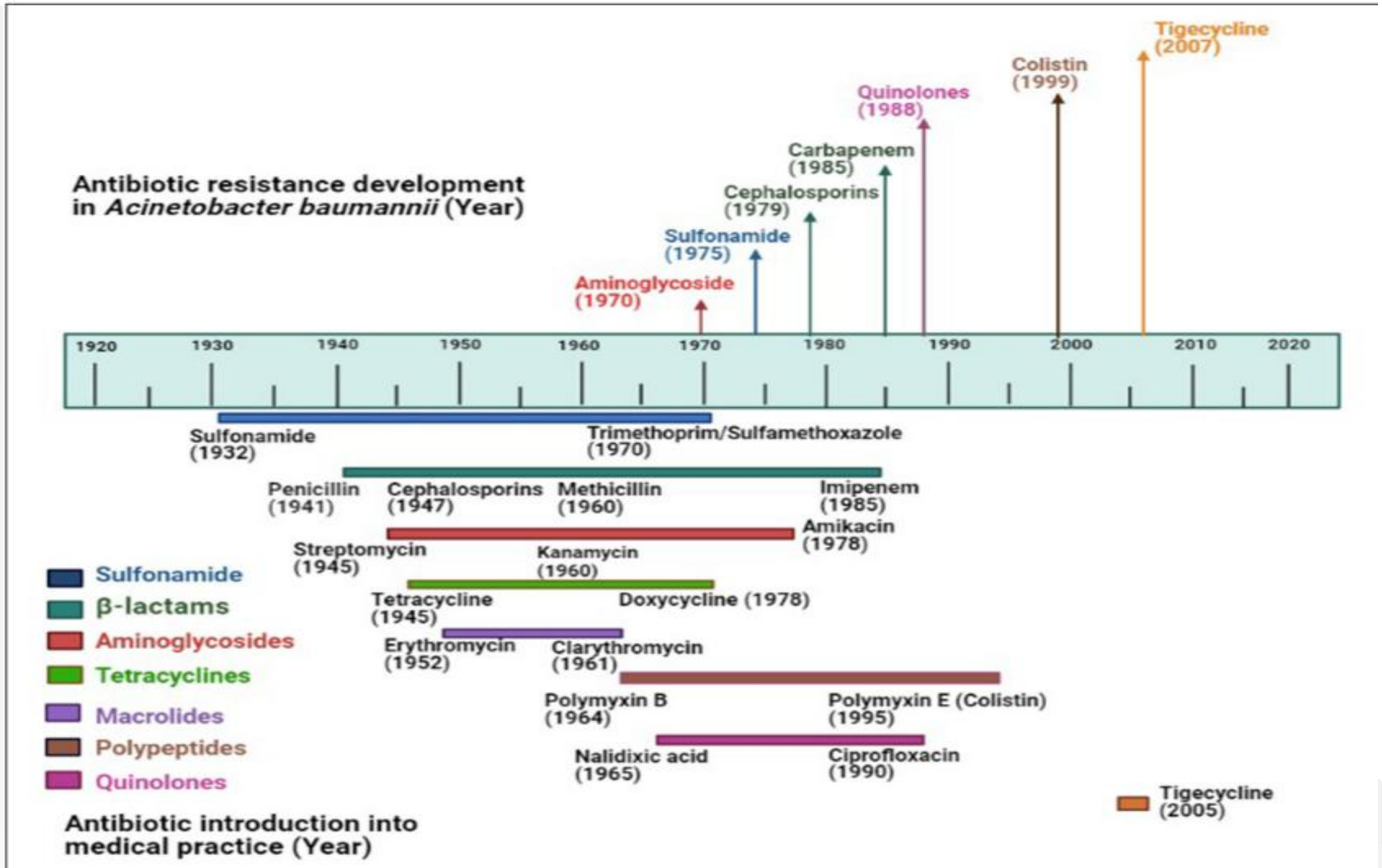
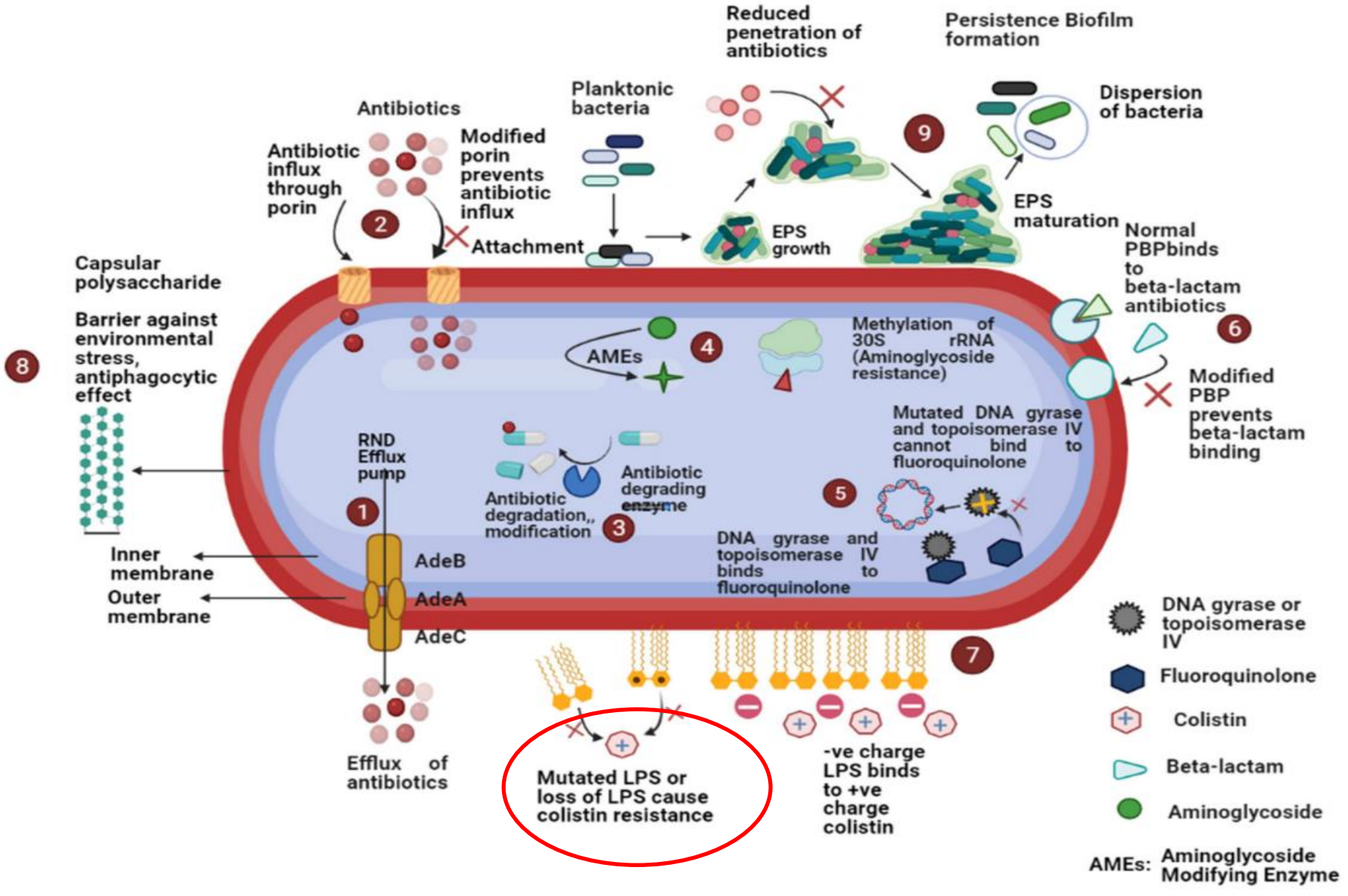


FIGURE 1 | Evolution of antimicrobial resistance among *Acinetobacter baumannii*: Top portion of the diagram shows the year of the first report of antimicrobial resistance in *A. baumannii*; the lower portion shows the year of introduction of antimicrobials (approximate year) in the market where colored lines indicate different antimicrobial groups.

Mécanismes Res

frontiers in Medicine

REVIEW
published: 24 March 2022
doi: 10.3389/fmed.2022.793615



frontiers in Medicine

Convergence of Biofilm Formation and Antibiotic Resistance in *Acinetobacter baumannii* Infection

REVIEW
published: 24 March 2022
doi: 10.3389/fmed.2022.793615

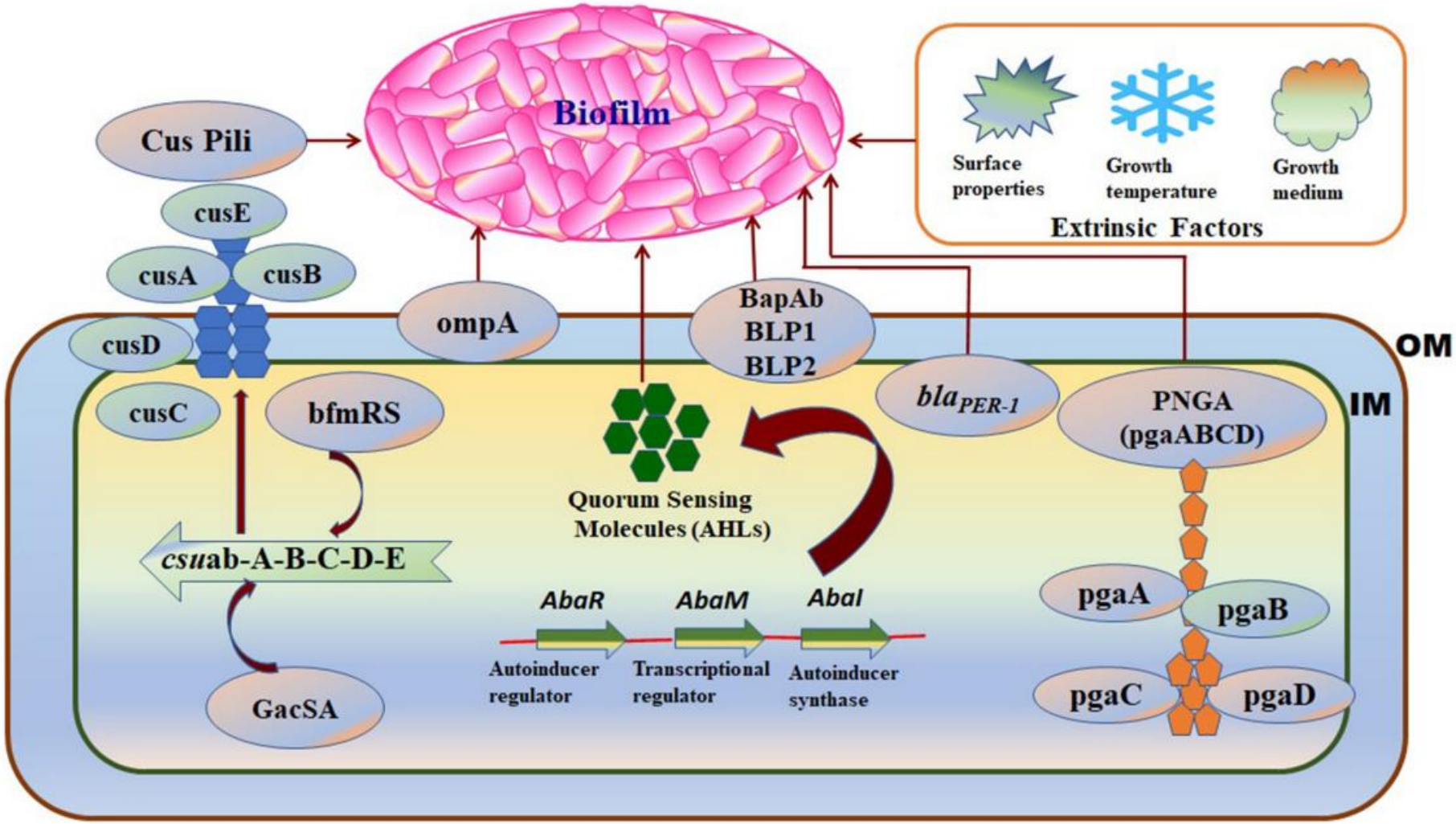


FIGURE 3 | A schematic diagram representing the intrinsic factors (genes) and the extrinsic factors that regulate biofilm formation in *A. baumannii:* OM, Outer membrane; IM, Inner membrane. **Intrinsic factors:** PNAG, Poly-(1–6)-N-acetylglucosamine; Csu, Chaperon/usher pilus system; OmpA, Outer membrane protein A; bla_{PER-1}, Beta-lactamase PER-1; bap-Ab, *A. baumannii* biofilm-associated protein; AHLs, N-acyl homoserine lactones; **Extrinsic factors:** surface properties, growth temperature, and growth medium.

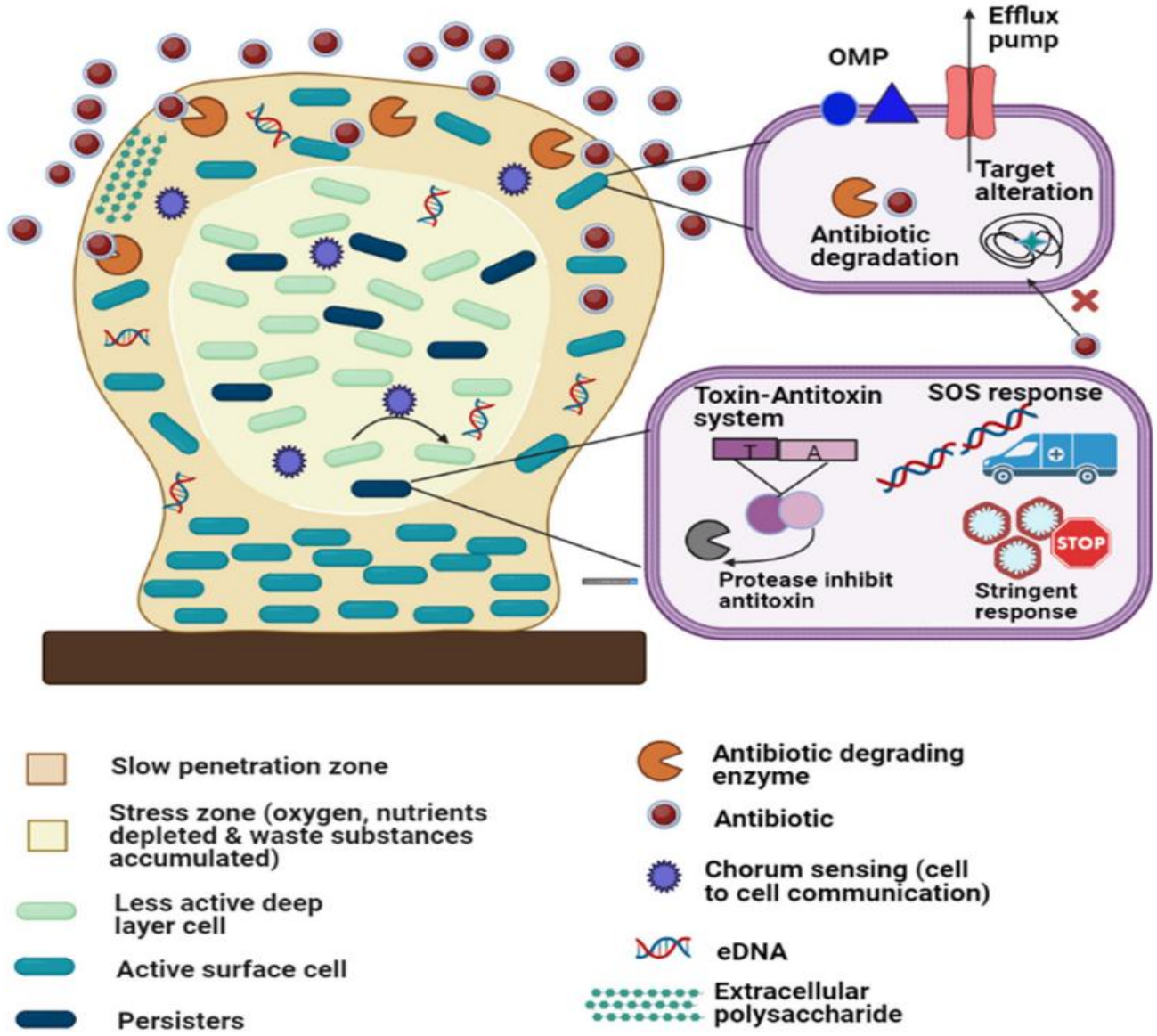


FIGURE 4 | Diagrammatic representation of the antibiotic resistance mechanisms of biofilm-embedded bacterial cells: The biofilm is attached to a biotic or abiotic surface (brown rectangle). Development of persister cells (dark green) and less active deep layer cells (light green) in the stress zone (the core of the biofilm, light cream color) where fewer nutrients are available. The various resistant mechanisms depicted in the figure are as follows: (1) matrix exopolysaccharides cause slow penetration of antibiotics; (2) extracellular DNA (eDNA); (3) multidrug efflux pumps; (4) outer membrane protein; (5) antibiotic degrading enzymes and target modifications (6) quorum sensing; (7) stress responses (oxidative stress response, stringent response, etc.); (8) toxin-antitoxin system and (9) SOS responses.

STRATEGIES OF PREVENTING A. baumannii BIOFILMS: FIGHTING BACK

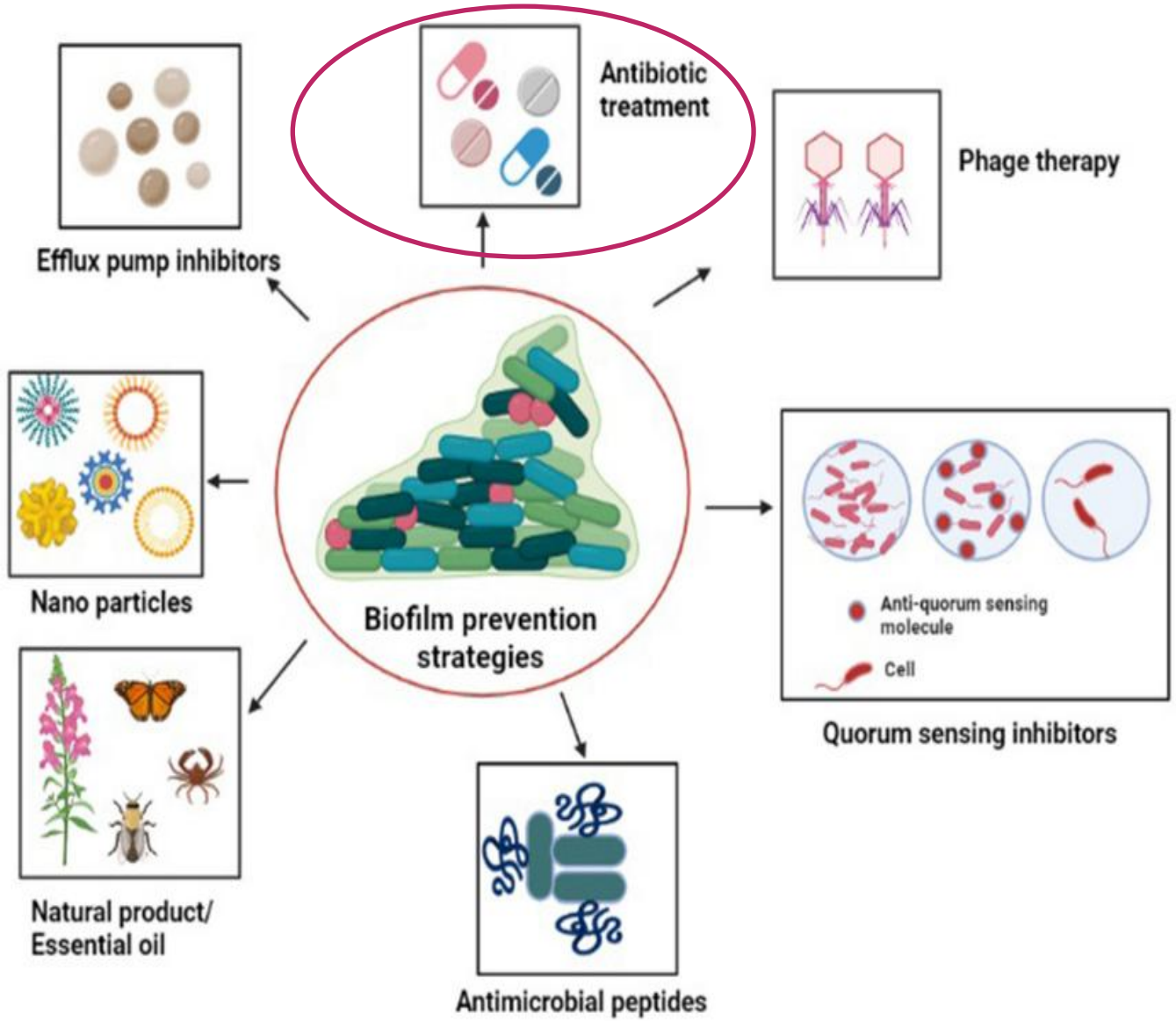
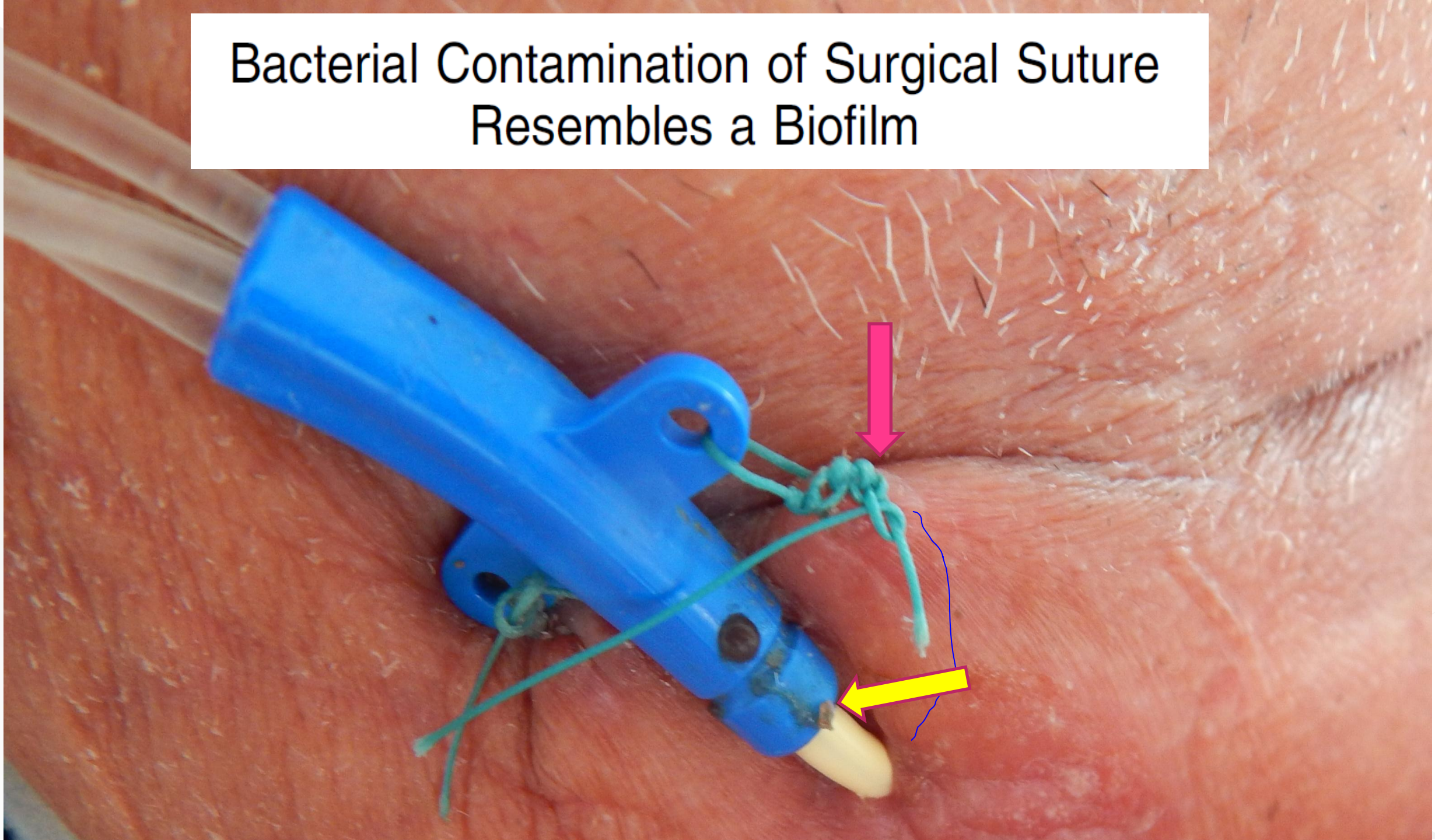


FIGURE 5 | Diagrammatic representation of the strategies to tackle antibiotic-resistant biofilm communities: antibiotic treatment, quorum sensing inhibitors, natural products/essential oils, antimicrobials peptides, efflux pump inhibitors, nanoparticles, and phage therapy.

Bacterial Contamination of Surgical Suture Resembles a Biofilm



Contamination / Colonisation / Infection

Contamination : mise en é… de microbes non présents dan… prélevé

Colonisation : pré… de microbes sans i… associée

Infection… …iques associés à la présence de mi… connus pour être à l'origine des symptômes observés

Infection ou Colonisation: une source importante du mésusage ATB

Infection / Colonisation (PAVM)

Techniques invasives

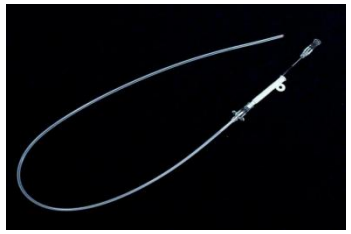
• bronchoscopie à fibres optiques ou lavage mini-broncho-alvéolaire

• personnel qualifié! Cout!

Techniques non invasives

obtenir des échantillons de sécrétions respiratoires pour une analyse quantitative ou qualitative

➢**Cathéter distal protégé (Combicath®)**
(seuil 10^3 UFC/ml)



➢**Aspirations trachéales quantitatives (seuil 10^6 UFC/ml):**
à l'aveugle, Risque de contaminations oro-pharyngées

Analyses quantitatives++
compte de croissance bactério pour aider à différencier infection vs colonisation

Analyses qualitatives
présence ou l'absence de pathogènes
simples et non invasives
moins spécifiques+

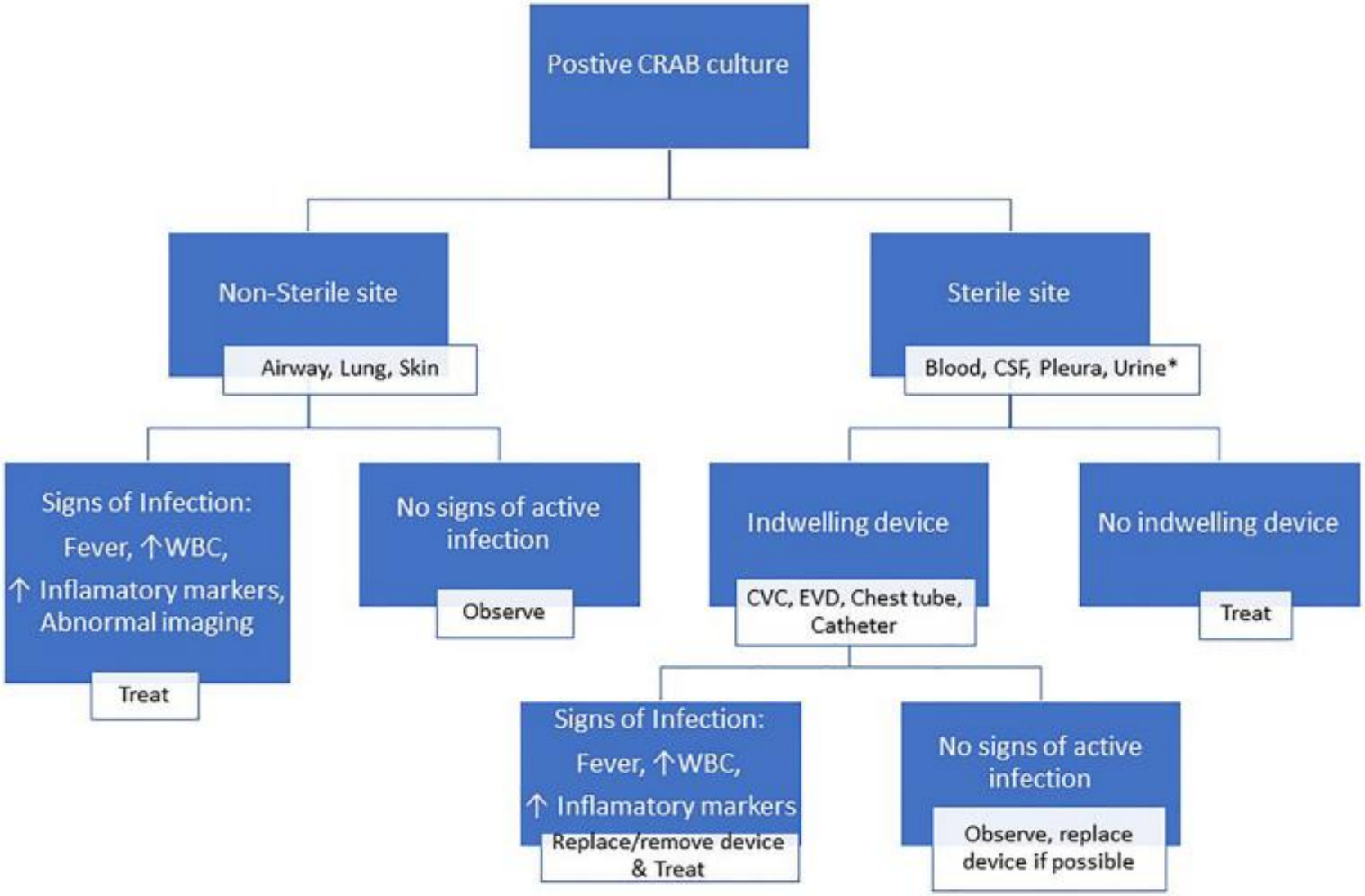
Infection / Colonisation (ILC)

- **Contamination:**
  - Présence "accidentelle" de germes sur le cathéter
  - En culture quantitative: taux non significatif (< 10^3ufc/ml).
- **Colonisation:**
  - Présence de germes en quantité significative (≥ 10^3ufc/ml)
  - en l'absence de signe infectieux (lié au cathéter)
- **Infection:**
  - Présence de germes en quantité significative (≥ 10^3ufc/ml)
  - en présence de signes infectieux cliniques (locaux ou systémiques) ou microbiologiques (bactériémie)

Infection / Colonisation

Infect Dis Ther (2022) 11:683–694
https://doi.org/10.1007/s40121-022-00597-w

REVIEW



Patient specific risk stratification for antimicrobial resistance and possible treatment strategies in gram-negative bacterial infections

Matteo Bassetti, Alessia Carnelutti & Maddalena Peghin

November 2016,

Multidrug resistant gram negative infection suspected

ESBL	CRE-KPC	MDR *A.baumanii*	MDR *P.aeruginosa*
- piperacillin-tazobactam +/- aminoglycoside - meropenem/imipenem - ceftolozane/tazobactam - ceftazidime/avibactam	- cabapenem + - tigecycline + -colistin or - gentamicin or - fosfomycin - ceftazidime/avibactam	- meropenem + colistin - colistin+ rifampicin - tigecycline+ rifampicin - colistin+ tigecycline	- ceftolozane/tazobactam - pipercillin/tazobactam or carbapenam or -ceftazidime or cefepime + aminoglycoside or colistin or fofomycin

Empirical treatment for suspected MDRGN infections.

Antibiotic Treatment: Active Combinations

- Monotherapy is generally inappropriate because of the high antibiotic tolerance of biofilm-embedded cells

- Combination therapies such as :
  - Imipenem-rifampicin,
  - colistin-rifampicin,
  - Imipenem-colistin-rifampicin,
  - Meropenem-sulbactam,
  - Tigecycline-sulbactam have shown significant inhibition of A. baumannii biofilms

World J Microbiol Biotechnol. (2014) 30:3015–25.
Antimicrob Agents Chemother. (2016) 60:4670–6
Frontiers. (2022)

Infect Dis Ther (2022) 11:683–694
https://doi.org/10.1007/s40121-022-00597-w

REVIEW

Carbapenem-resistant *Acinetobacter baumannii*: Colonization, Infection and Current Treatment Options

Carmi Bartal · Kenneth V. I. Rolston · Lior Nesher

Table 1 Antibiotics used for the treatment of CRAB infections

Agent	Adult dosage (assuming normal renal and liver function)	Remarks	Major toxicities to consider
[a]Ampicillin-sulbactam	3 g every 4 h if intolerance or toxicities preclude the use of higher dosages or for mild infections		Hepatotoxicity (1%)
[a]Ampicillin-Sulbactam	9 g every 8 h, each dose given over 4 h 27-g continuous infusion over 24 h	High dose, suitable for ampicillin-sulbactam-resistant CRAB	
Cefiderocol	2 g every 8 h infused over 3 h		Elevated liver tests (2–16%) Hypokalemia (11%)
Colistin	As per international consensus guidelines[b]		Nephrotoxicity (1–18%) Neurotoxicity (1–7%)
Eravacycline	1 mg/kg/dose every 12 h		GI (2–7%)
[c]Imipenem-cilastatin	500 mg every 6 h infused over 3 h		Seizures (1%)
[c]Meropenem	2 g every 8 h infused over 3 h		Seizures (< 1%)
Minocycline	200 mg every 12 h		CNS (1–3%)
Tigecycline	200 mg once, then 100 mg every 12 h	High dose	Hepatotoxicity (2–5%) Pancreatitis (< 1%),

Polymyxine E = Coli

- Activité sur les ABRI en diminution
  - Favorisé par la préexposition a la Coli ++
- In vitro : synergie avec d'autres antibiotiques même pour les souches ColiR

Pandrug-resistant Gram-negative bacteria: a systematic review of current epidemiology, prognosis and treatment options

Stamatis Karakonstantis [1], Evangelos I Kritsotakis [2 3], Achilleas Gikas [4]

J Antimicrob Chemother. 2020 Feb 1;75(2):271-282.

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Delivery of antibiotics

Recommendation
25. For adults with sepsis or septic shock, we **suggest** using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion *Weak recommendation, moderate quality of evidence*

Pharmacokinetics and pharmacodynamics

Recommendation
26. For adults with sepsis or septic shock, we **recommend** optimising dosing strategies of antimicrobials based on accepted pharmacokinetic/pharmacodynamic (PK/PD) principles and specific drug properties *Best Practice Statement*

Antimicrobial Section / Original Paper

Chemotherapy

Chemotherapy 2015–16;61:190–196
DOI: 10.1159/000442786

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Accepted: November 24, 2015
Published online: February 11, 2016

Efficacy and Toxicity of High-Dose Colistin in Multidrug-Resistant Gram-Negative Bacilli Infections: A Comparative Study of a Matched Series

Ahlem Trifi Sami Abdellatif Foued Daly Khaoula Mahjoub Rochdi Nasri
Mouna Oueslati Rahma Mannai Montassar Bouzidi Salah Ben Lakhal

Medical Intensive Care Unit, University Hospital Center of La Rabta, Tunis, Tunisia

- The study was conducted at the Medical Resuscitation Unit, Tunisian University Hospital Center of La Rabta,
  - over a period of 17 months (April 2013 to August 2014)
- In the high-dose colistin group,
  - CMS was administered at a loading dose of 9 MIU followed by a maintenance dose of 4.5 MIU/12 h.
- In the second group, retrospectively analyzed, colistin was administered at 6 MIU/day.

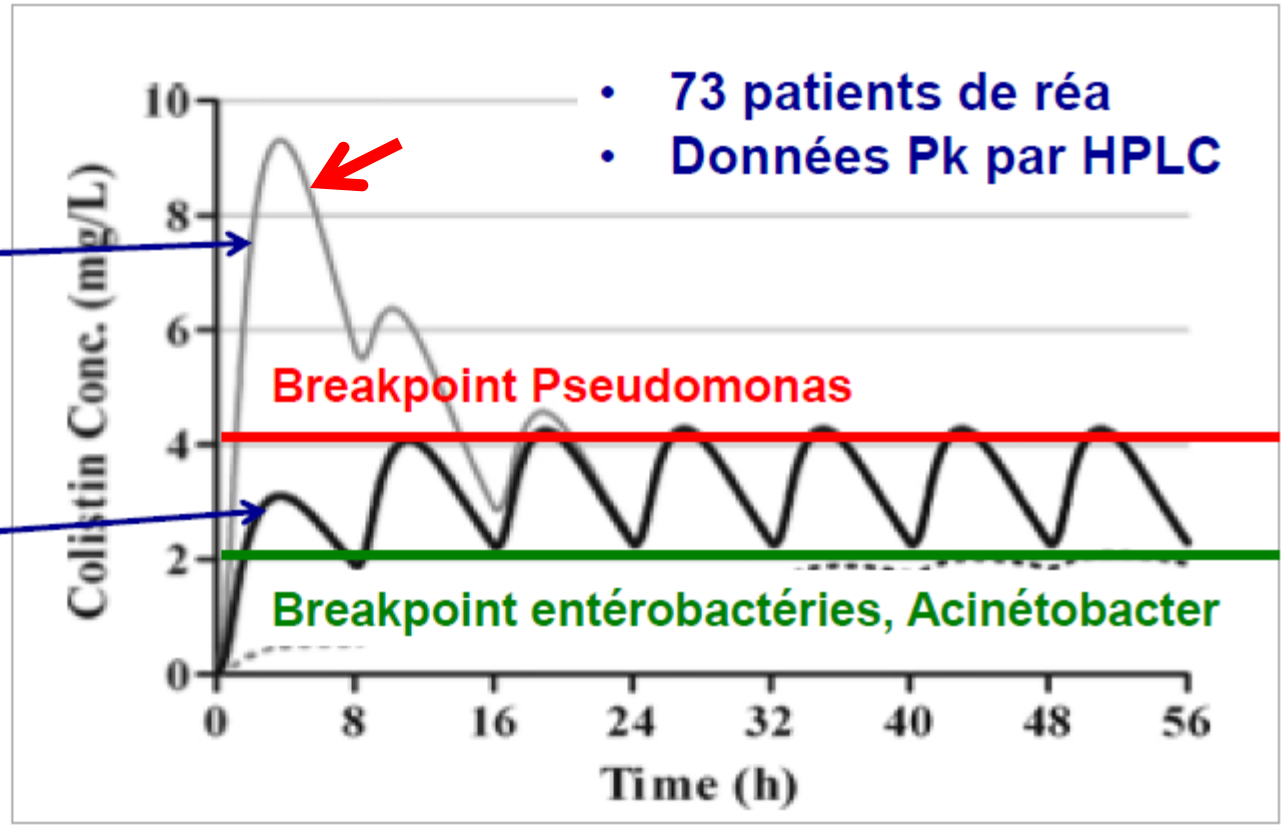
New Colistin Population Pharmacokinetic Data in Critically Ill Patients Suggesting an Alternative Loading Dose Rationale

AAC Antimicrobial Agents and Chemotherapy
Dec 2014

N. Grégoire,[a,b] O. Mimoz,[a,b,c] B. Mégarbane,[d] E. Comets,[e,f,g] D. Chatelier,[e] S. Lasocki,[h] R. Gauzit,[i] D. Balayn,[e] P. Gobin,[a,c] S. Marchand,[a,b,c] W. Couet[a,b,c]

Dose de charge
9 MUI

Pas de dose
de charge



Confirmation du modèle de Plachouras

Dose de charge 9 M UI , puis 4,5 M UI/12 h

Table 1. Clinical characteristics of patients

	High-dose colistin group (n = 46)	Standard-dose colistin (n = 46)	p value

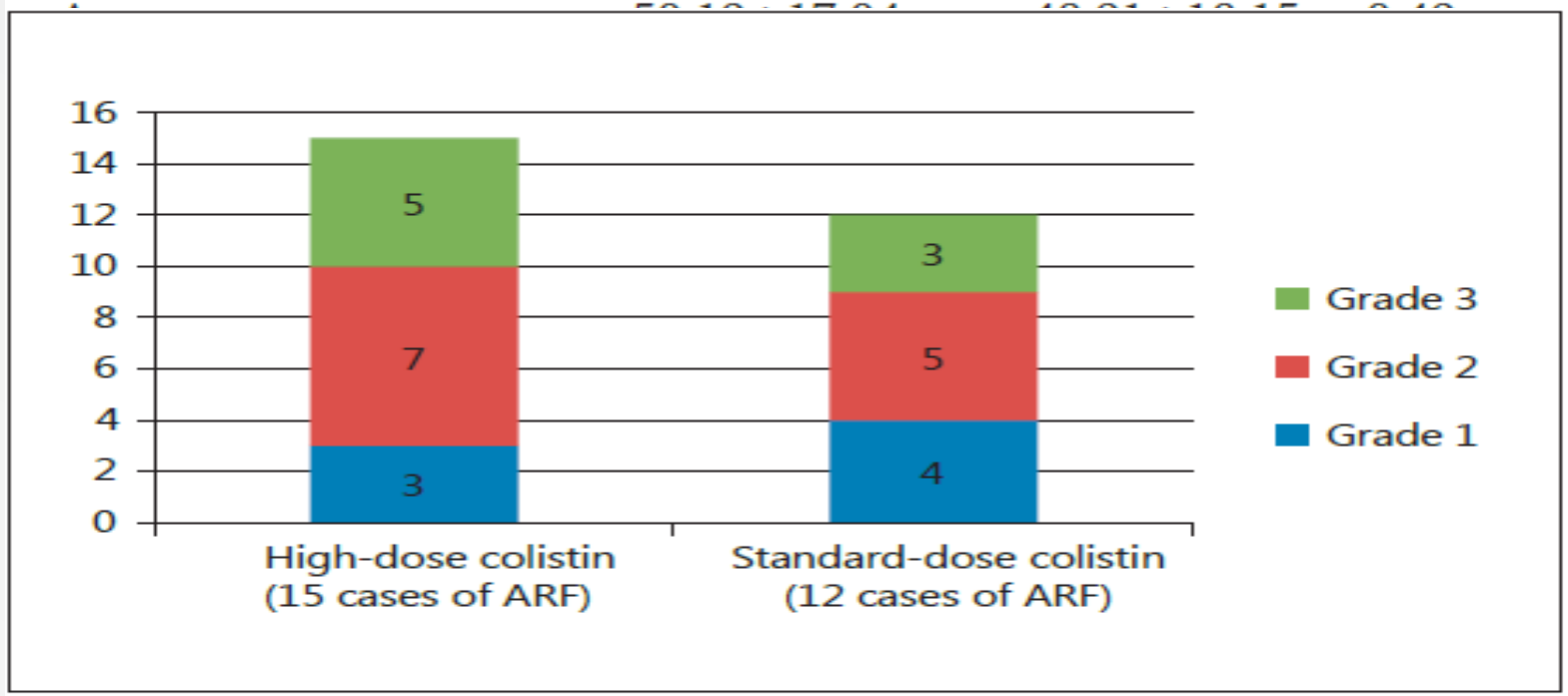


Fig. 2. Distribution of patients in the 2 groups according to the AKIN classification. ARF = Acute renal failure.

Table 2. Outcome parameters of the 2 groups

Studied variables	High-dose colistin group (n = 46)	Standard-dose colistin group (n = 46)	p value
Cure rate	63	41.3	0.04
Duration of treatment, days	13.63±8.1 (12)	15.63±6.3 (15)	0.25
Recurrent infection	4.3	13	0.21
AKI	32.2	26	0.64
Time to AKI onset, days	8.32±4.3 (7)	11±6.4 (9.5)	1
Renal replacement therapy	26.6	41	1
Neurotoxicity	6.5	2.1	0.25
Mortality	23	27.5	0.6

Values are expressed as percentages or mean ± standard deviation (median).

Abdellatif *et al. Ann. Intensive Care* (2016) 6:26
DOI 10.1186/s13613-016-0127-7

Annals of Intensive Care

RESEARCH Open Access

Efficacy and toxicity of aerosolised colistin in ventilator-associated pneumonia: a prospective, randomised trial

Sami Abdellatif, Ahlem Trifi*, Foued Daly, Khaoula Mahjoub, Rochdi Nasri and Salah Ben Lakhal

ClinicalTrials.gov PRS
Protocol Registration and Results System

ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 02/05/2016

ClinicalTrials.gov ID: [Not yet assigned]

Study Identification

Unique Protocol ID:	Tunis university
Brief Title:	Effect of Aerosolised Colistin in Ventilator Associated Pneumonia
Official Title:	Efficacy and Toxicity of Aerosolised Colistin in Ventilator Associated Pneumonia: a Prospective, Randomized Trial.
Secondary IDs:	

Trial registration ClinicalTrials.gov Identifier: NCT02683603

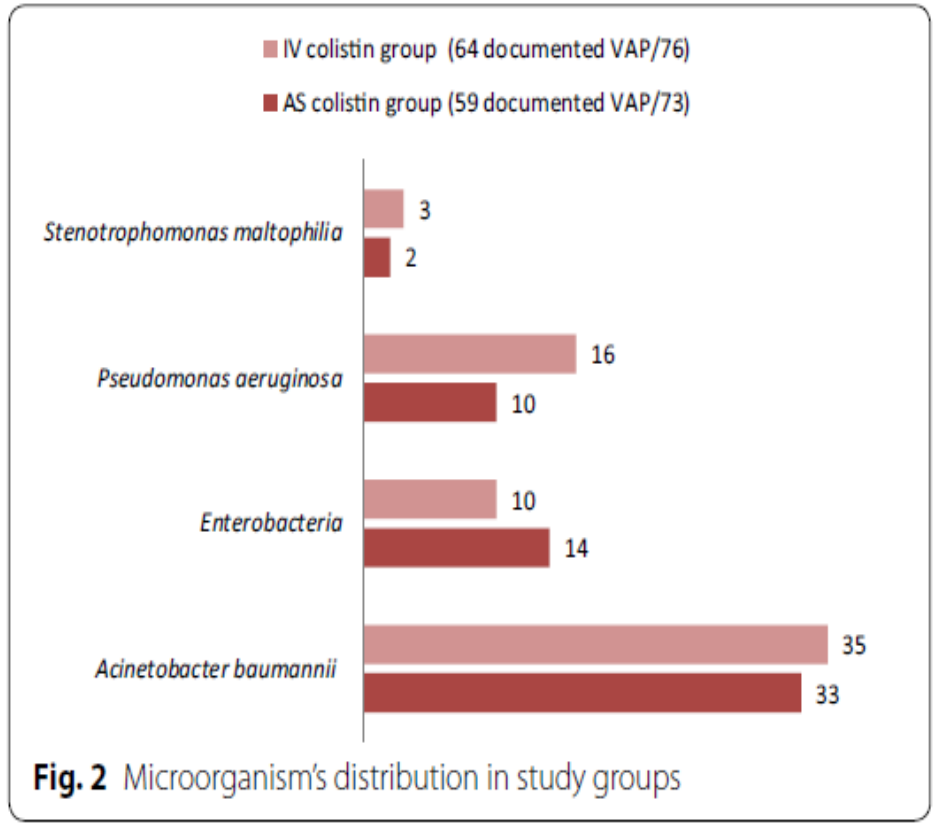


Fig. 2 Microorganism's distribution in study groups

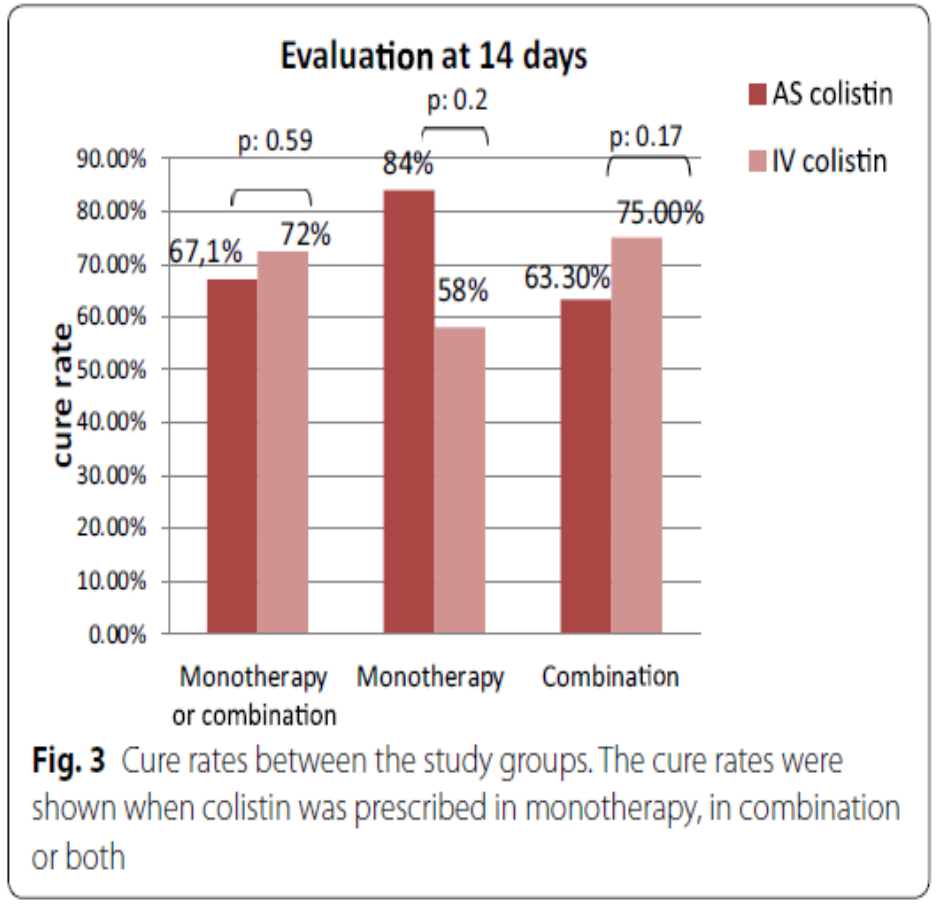


Fig. 3 Cure rates between the study groups. The cure rates were shown when colistin was prescribed in monotherapy, in combination or both

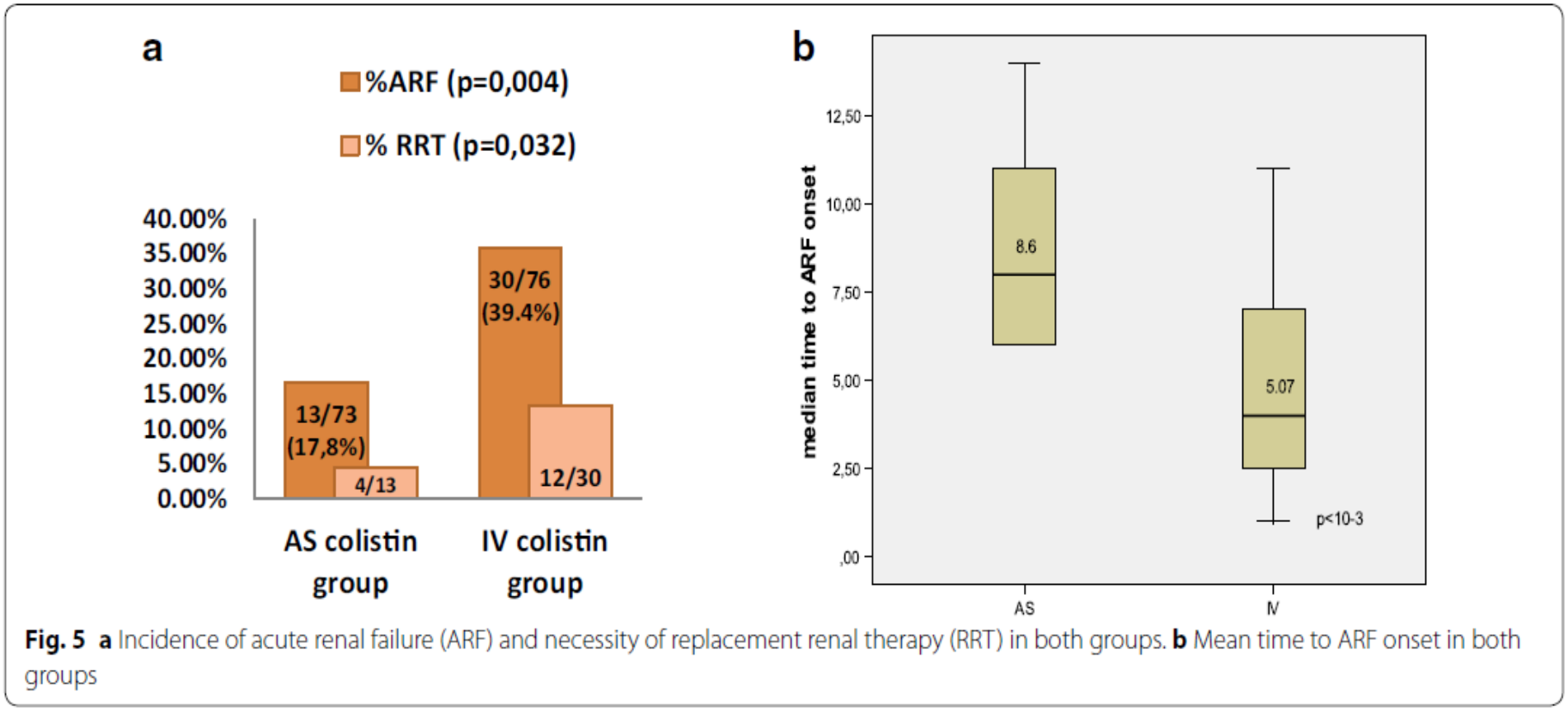


Fig. 5 **a** Incidence of acute renal failure (ARF) and necessity of replacement renal therapy (RRT) in both groups. **b** Mean time to ARF onset in both groups

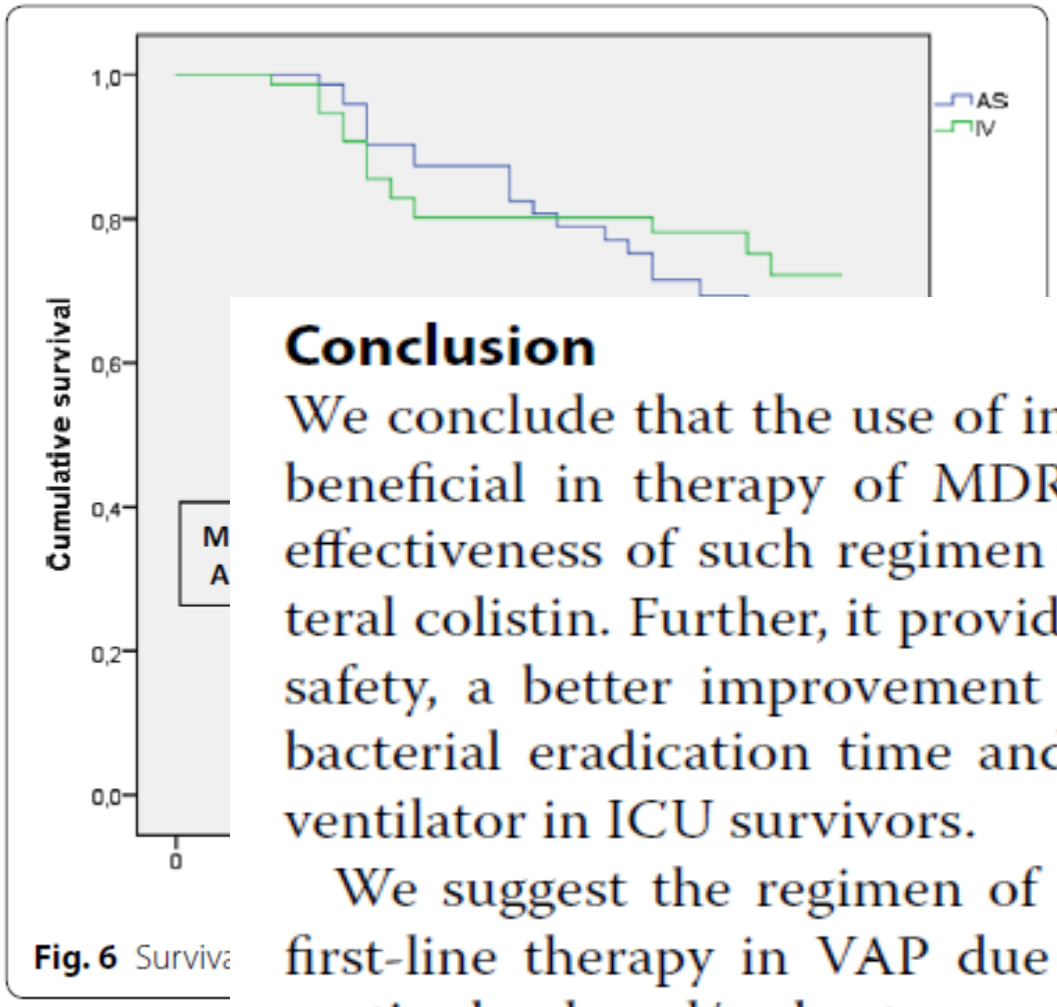


Fig. 6 Surviva

Conclusion

We conclude that the use of inhaled colistin seems to be beneficial in therapy of MDR bacilli VAP. Therapeutic effectiveness of such regimen was as effective as parenteral colistin. Further, it provided several benefits: a renal safety, a better improvement of *P*/*F* ratio, a shortened bacterial eradication time and an earlier weaning from ventilator in ICU survivors.

We suggest the regimen of aerosolised colistin as the first-line therapy in VAP due to MDR bacilli outside a septic shock and/or bacteraemia.

Les nébulisations d'ATB

- AMK
- Fosfo
- Coli
- Règles de Nébulisation :
  - Molécule
  - Nébuliseur à plaques
  - VMC et réglage spécifique
  - Toxicité ?

En cas de pneumonie à BGN (GNB), les aminosides et la colistine sont souvent les seuls antibiotiques conservant (au moins *in vitro*) *une activité contre ces souches*

Trifi *et al. Ann Clin Microbiol Antimicrob* (2018) 17:39
https://doi.org/10.1186/s12941-018-0292-7

Annals of Clinical Microbiology and Antimicrobials

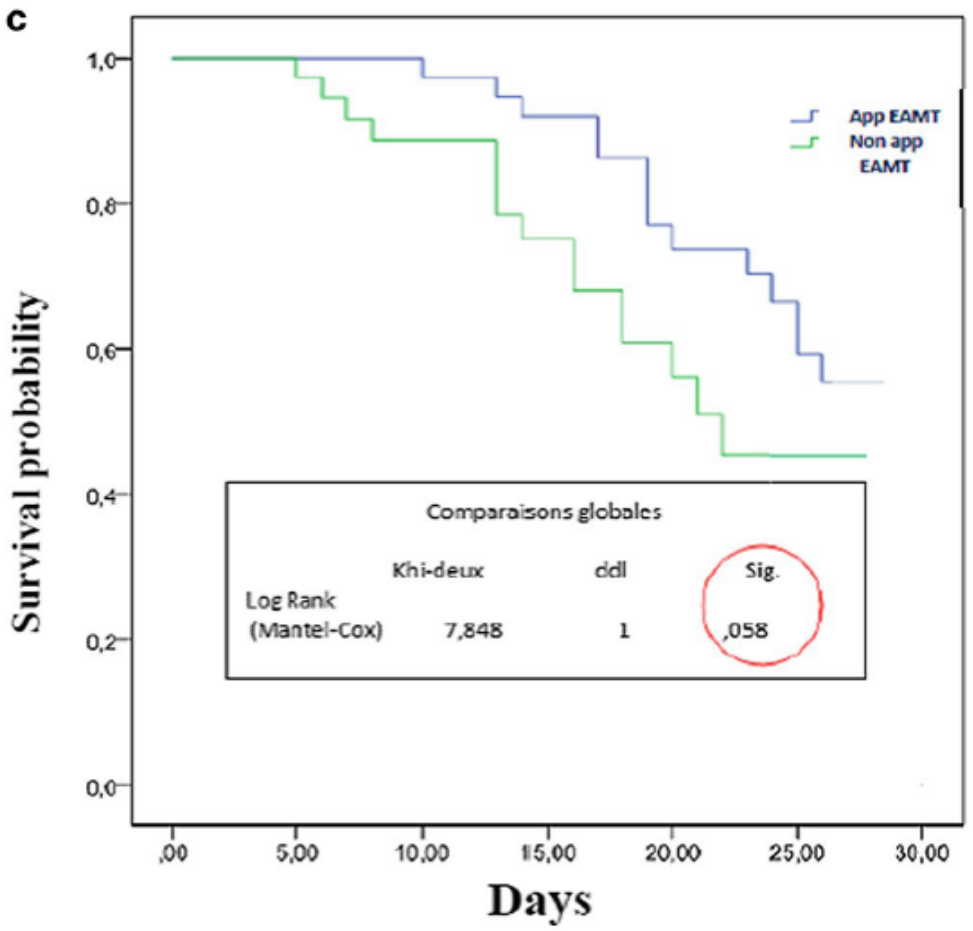
RESEARCH Open Access

Appropriateness of empiric antimicrobial therapy with imipenem/colistin in severe septic patients: observational cohort study

Ahlem Trifi[1,2*], Sami Abdellatif[1,2], Cyrine Abdennebi[1,2], Foued Daly[1,2], Rochdi Nasri[1,2], Yosr Touil[1,2] and Salah Ben Lakhal[1,2]

Appropriate EAMT group (n = 41)	Inappropriate EAMT group (n = 38)		
	Enlargement (n = 22)	Change (n = 9)	De-escalation (n = 7)
Imipenem/colistin	Imipenem/colistin/Glycopeptid (n = 8)	Other betalactam (for resistance to impenem) + tygecycline, amino-glycoside or quinolone (n = 6)	Piperacilline (n = 2)
	Imipenem/colistin/antifungal (n = 7)	Glycopeptide ± aminoside (n = 2)	Ceftazidime (n = 3)
	Imipenem/colistin/Tygecycline/ aminglyosides (n = 3)	Antifungal (n = 1)	Cefotaxime (n = 2)

c



Conclusions

Despite the high proportion of MDR-GNB in the cause of nosocomial sepsis, empiric antimicrobial therapy using imipenem-colistin was only appropriate in half of cases and increased mortality. It would therefore be judicious to revise this empiric therapy with the elaboration

Table 2 Microbiological data in study groups

Subgroups	Appropriate EAMT group (n = 41)	Inappropriate EAMT group (n = 38)		
		Enlargement (n = 22)	Change (n = 9)	De-escalation (n = 7)
Bacteriologic documentation, n	28/41	18/22	9/9	7/7
NI location				
VAP	22	11	2	4
Bacteraemia	3	7	3	2
CRI	2	5	3	0
CRB	1	1	0	1
UI	0	1	1	0
Isolates (n)				
Acinetobacter B	14	6	0	0
Klebsiella pneumonia	6	4	0	0
Pseudomonas spp.	5	5	3	5
Enterobacter	2	4	1	0
E. coli	0	1	0	0
Staphylococcus	0	4	1	0
Enterococcus	0	3	1	0
Stenotrophomonas M	0	3	2	0
Burkholderiacepacia	1	0	0	0
Streptocoque spp.	0	0	0	2
Candida species	0	7	1	0

70%

De Pascale *et al. Critical Care* 2014, **18**:R90
http://ccforum.com/content/18/3/R90

CRITICAL CARE

RESEARCH Open Access

High dose tigecycline in critically ill patients with severe infections due to multidrug-resistant bacteria

Gennaro De Pascale[1*], Luca Montini[1], Mariano Alberto Pennisi[1], Valentina Bernini[1], Riccardo Maviglia[1], Giuseppe Bello[1], Teresa Spanu[3], Mario Tumbarello[2] and Massimo Antonelli[1]

- All patients consecutively admitted to our ICU
- between 1 June 2009 through 31 May 2012 who received TGC for a microbiologically documented infection were evaluated.

Drugs. 2025 January ; 85(1): 21–40.

Treatment approaches for carbapenem-resistant *Acinetobacter baumannii* infections

Alina Iovleva[1], Vance G. Fowler Jr.[2,3], Yohei Doi[1,4]

- Tigecycline is still frequently used as part of combination therapy,
- but the benefit of this practice has not been definitively demonstrated.
- High-dose tigecycline improves probability of attaining pharmacodynamic targets for pneumonia and appears to be tolerated in most patients,
- but controlled studies that demonstrate clinical benefits are needed before its use can be broadly recommended.

Table 3 Logistic regression analysis of factors associated with clinical cure in 63 patients with ventilator-associated pneumonia

Variable	Multivariate analysis		
	Odds ratio	95% CI	*P*-value
SOFA score at infection occurrence	0.66	0.51, 0.87	0.003
Initial inadequate treatment	0.18	0.05, 0.68	0.01
High-dose tigecycline group	6.25	1.59, 24.57	0.009

Conclusions

These data suggest that TGC, used at doses higher than standard treatment, can be administered without relevant toxicity for the treatment of serious infections in critically ill sedated patients. The regimen with higher TGC doses (that is, 100 mg every 12 hours after a 200 mg loading dose) may be useful to improve the clinical outcome of patients with MDR Gram-negative VAP. Pharmacokinetic investigations and multicenter, prospective clinical trials are needed to confirm these preliminary results and investigate the efficacy of HD TGC in severe infections.

Garnacho-Montero *et al. BMC Infectious Diseases* 2014, **14**:135
http://www.biomedcentral.com/1471-2334/14/135

BMC Infectious Diseases

REVIEW Open Access

How to treat VAP due to MDR pathogens in ICU patients

José Garnacho-Montero[1,2,3*], Yael Corcia-Palomo[1], Rosario Amaya-Villar[1,3] and Luis Martin-Villen[1]

Table 2 Recommended doses of antimicrobials use in VAP caused by MDR pathogens in patients with normal renal function

Antibiotic	Loading dose	Daily dose	Observations
Imipenem*	Not required	1 g/6-8 h	Extended or prolonged infusion is not possible due to drug instability
Meropenem*	Not required	1-2 g/8 h	Extended infusion (3-4 hours) is recommended.
Doripenem*	Not required	500 mg-1 g/8 h	Extended infusion (3-4 hours) is recommended.
Colistin*	4.5-9 UI	9 UI/day in 2 or 3 dose	Loading dose is necessary.
Tigecycline	200 mg	100 mg/ 12 h	Without approval by regulatory agencies.
Fosfomycin*	Not required	24 g/day (in four doses)	Always in combination therapy.
Vancomycin*	25-30 mg/kg (based on ABW)	15-20 mg/kg (based on ABW) every 8-12 hours	Monitor trough concentrations after the forth dose; serum trough levels of 15-20 mg/L for MRSA VAP.
Linezolid	Not required	600 mg/ 12 h	It should be changed to vancomycin in the directed therapy of patients with good clinical evolution and *S aureus* with vancomycin MIC ≤ 1 mg/L

*Dose adjustment is necessary in case of renal dysfunction.

Conclusions: Empirical treatment of VAP due to MDR pathogens should be based on knowledge of local ecology. A strategy combining early high doses of effective agents with subsequent simplification in the light of microbiologic information is recommended.

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Réanimation 15 (2006) 168–175
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Mise au point

Durée de l'antibiothérapie des infections sévères en réanimation

Duration of antimicrobial therapy for severe infections in critically-ill patients

M. Wolff [a,*], J. Chastre [b]

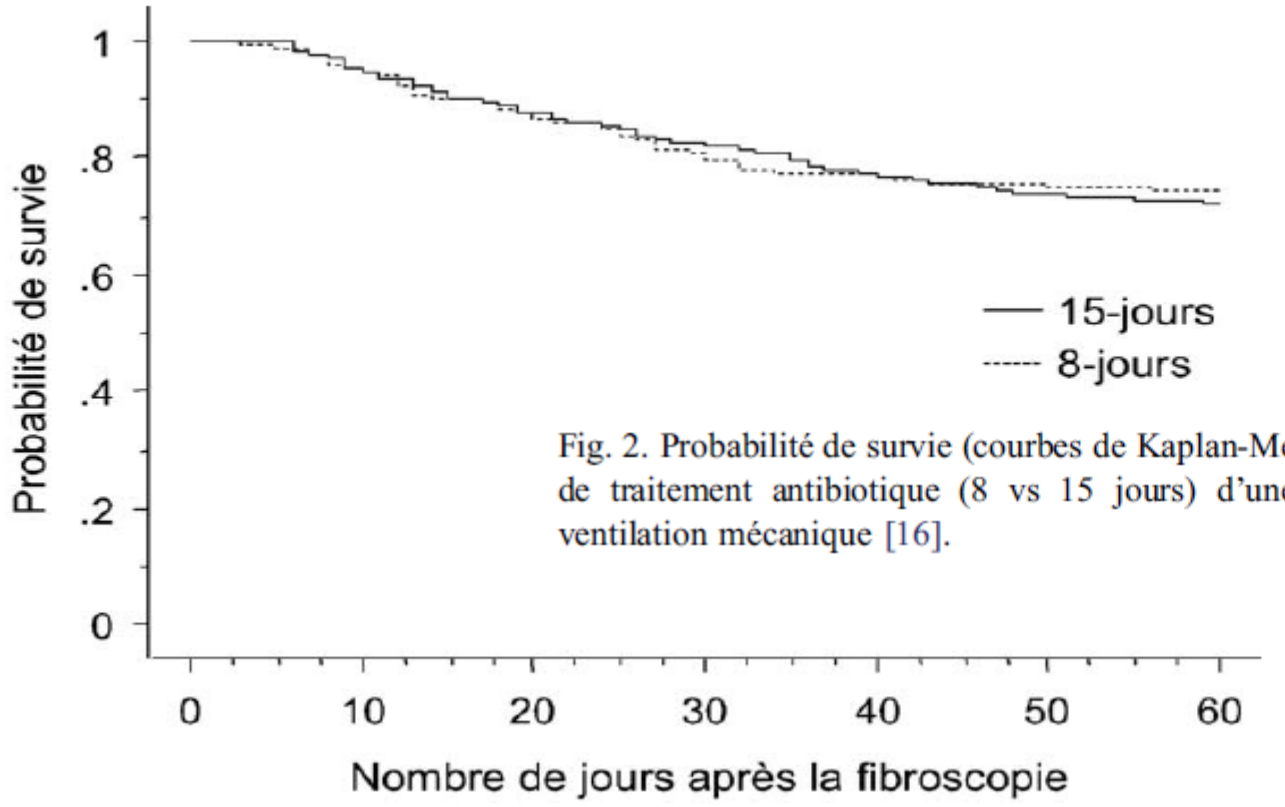
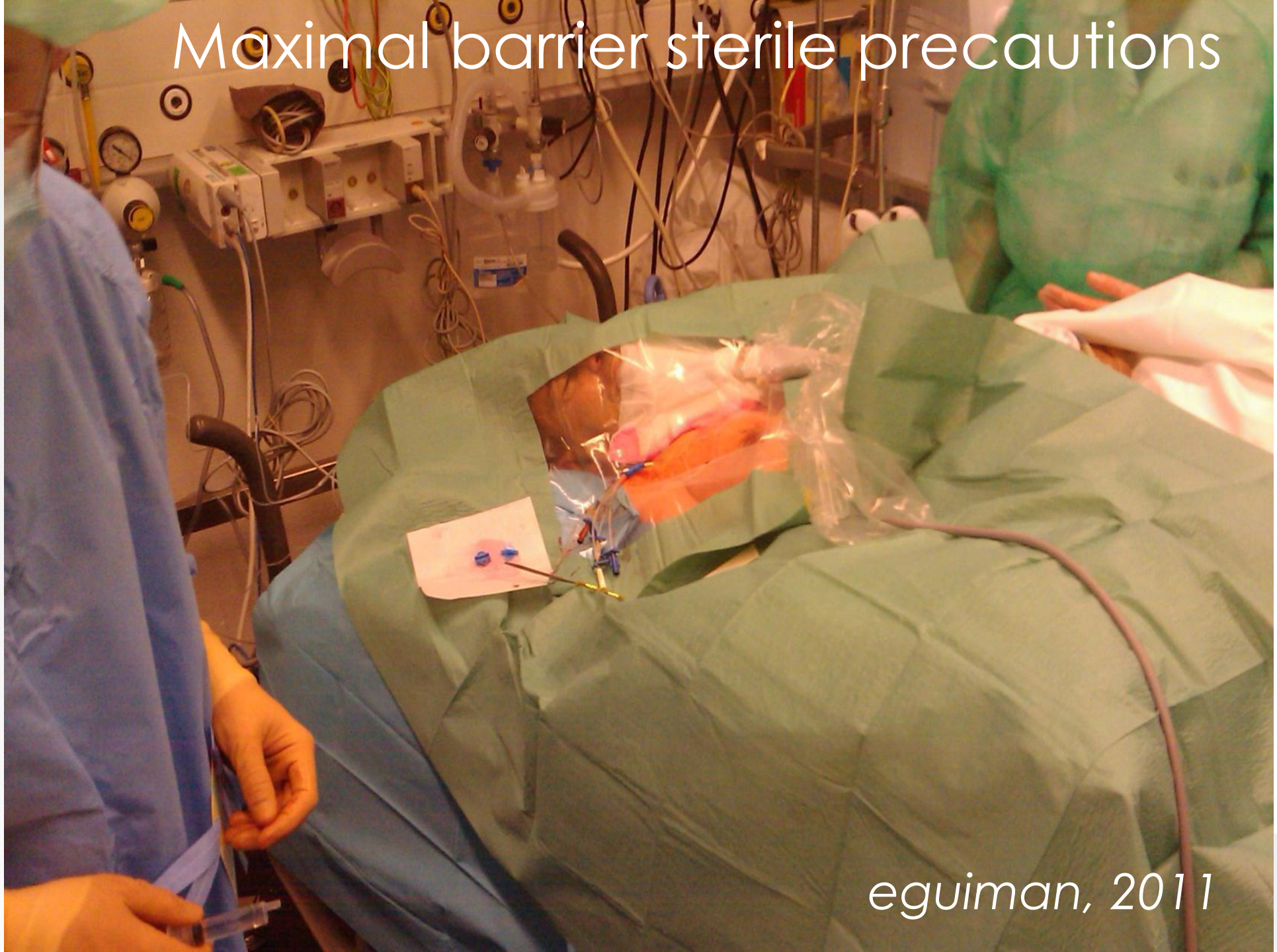
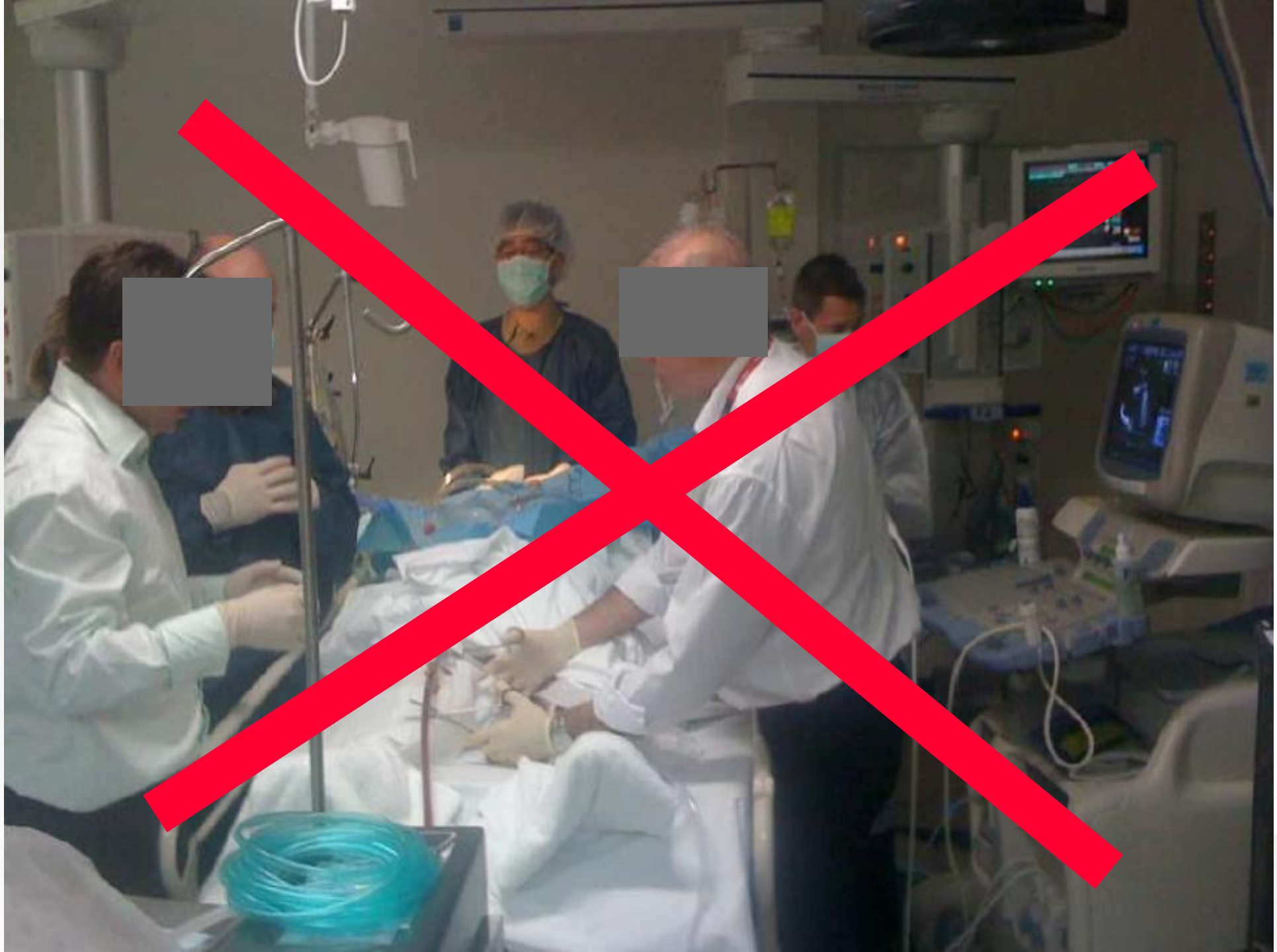


Fig. 2. Probabilité de survie (courbes de Kaplan-Meier) en fonction de la durée de traitement antibiotique (8 vs 15 jours) d'une pneumonie acquise sous ventilation mécanique [16].

Maximal barrier sterile precautions



eguiman, 2011



Conclusion

- Bactérie usuellement nosocomiale
- Incidence croissante
- La résistance à la coli en augmentation
- Pas de panique / cohabitation / stewardship
- Eviter le sur traitement
- Optimisation pk/pd : dose de charge, vd élevé, poso H24 indépendante de la clairance
- Association plus utile qu'ailleurs
  - Coli fortes doses / Aérosol
  - IMP
  - TIG oui (pneumonies) Mais…
  - Ampi/sulbactam fortes doses (9g/3g x 3)
  - Cefiderocol ?
- Durée : 10 j si succès clinique (PCT)

Merci pour votre attention