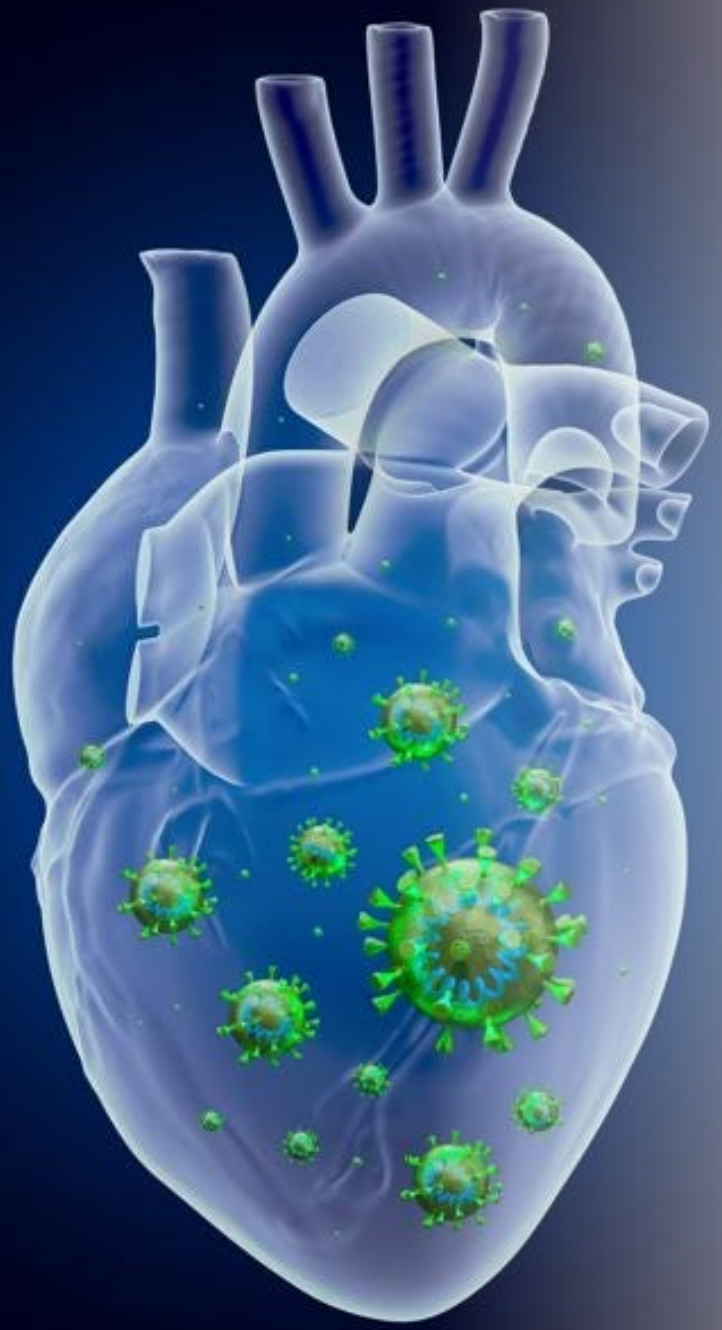
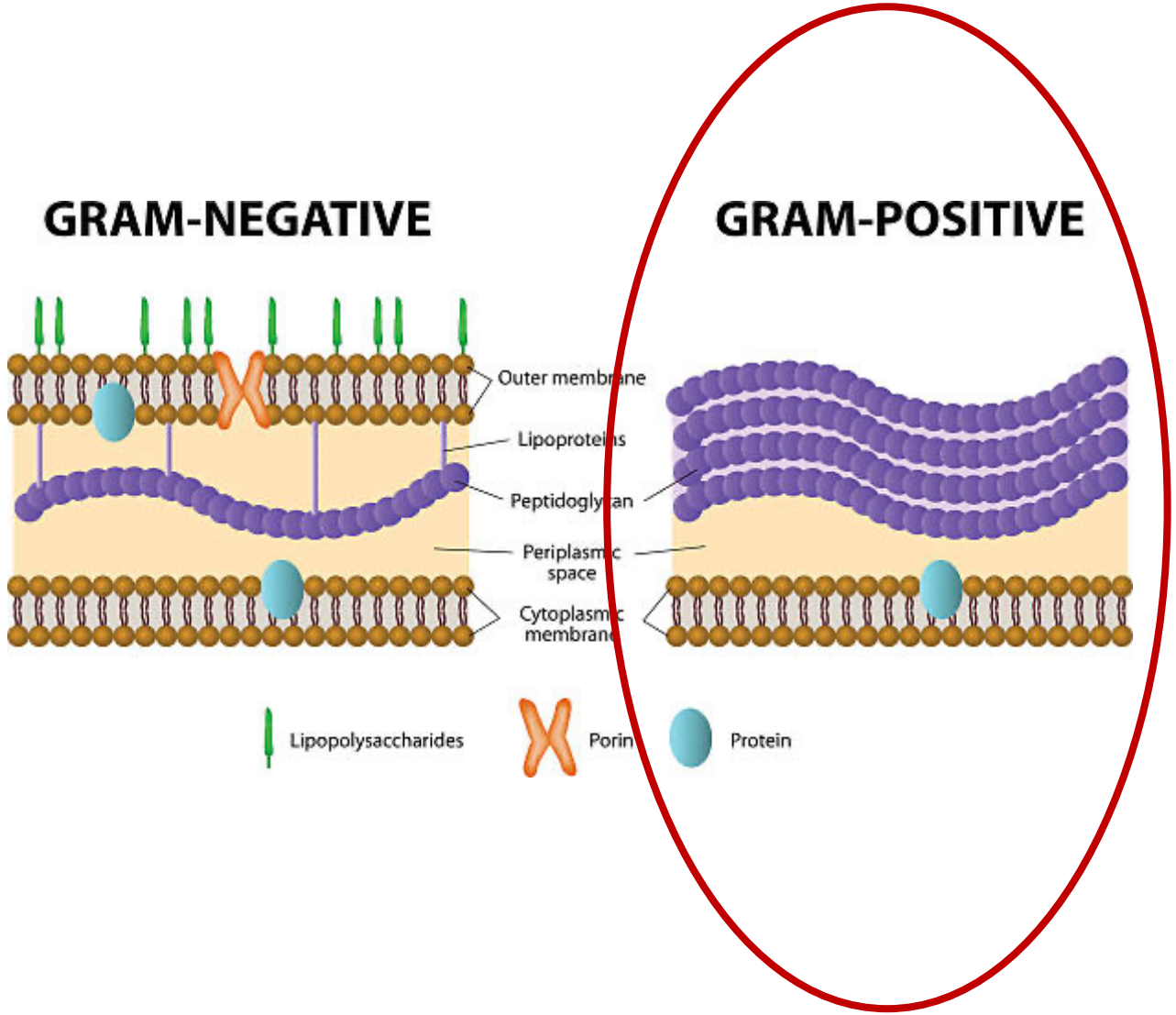


The challenge of MDR and XDR infections 2023

Marta Hernández-Meneses
Infectious diseases Department
Hospital Clinic de Barcelona
Universidad de Barcelona

E-mail address: mhmeneses@clinic.cat

Clinical Case



Clinical Case

79 years-old male patient

- **Atrial fibrillation**: CHADS2-vasc 4. HAS BLED 4
- Received a **DDD PCM** implant in 2013 following a 3rd degree AV block. Generator change in Oct 2018
- **Diabetes mellitus 2**
- **Cirrhosis** and chronic liver disease child pugh B

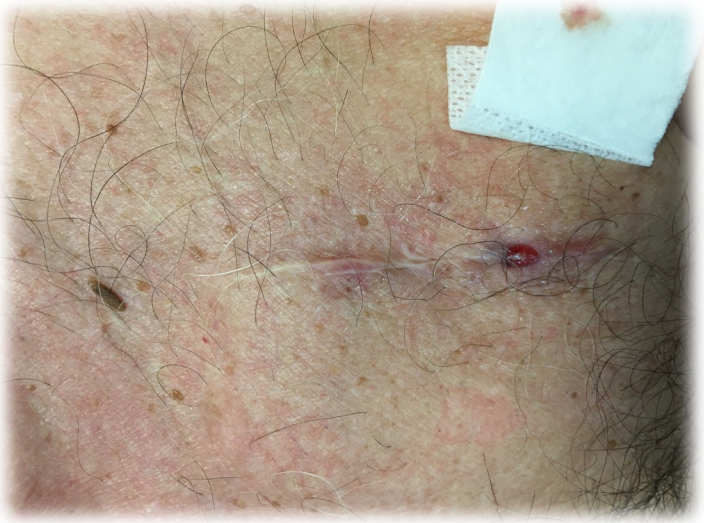
BI 100/100. Charlson comorbidities index (CCI): 4

Treatment: apixaban 2.5 mg/q2d, espironolactone 50 mg/24h, sitapliptin/metformin 1/q2d omeprazol 20 mg/24h

Clinical Case

December 2018 → **Exposed pacemaker generator** and signs of infection at the pocket site.

He denied history of recent fever, trauma, or infection



Emergency room → Physical examination results were normal despite signs of CIED local infection.

WBC and C reactive-protein were also normal.

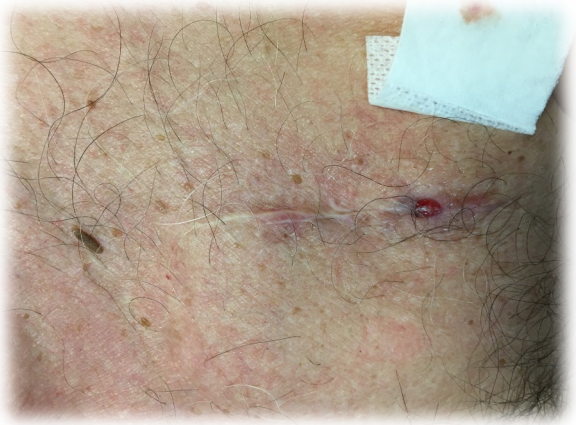
Clínic Barcelona

Local swabs were taken.

Augmentin 875/125 mg/8h was started.

Clinical Case

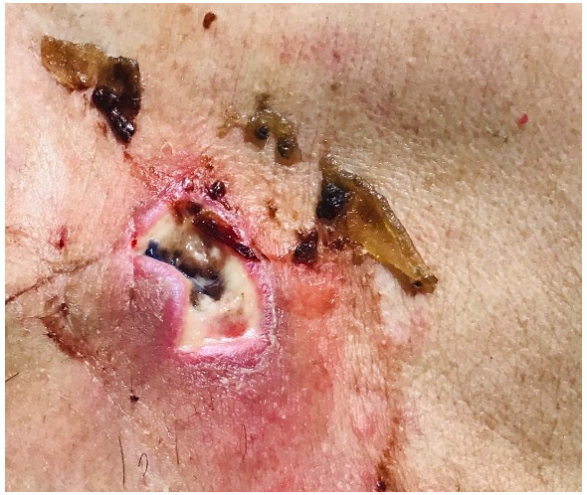
Despite antibiotics, signs of local purulence continued. After five days, he went to his GP at his **primary care center**, and antibiotics were switched **to clindamycin 600 mg/8 h.**



One week later

He developed deeper involvement of the wound with more purulence, erythema and there was a concern for fluid collection in the pacemaker.

NO FEVER. No systemic signs of infection



Question…

CIED pocket infection (at least) was suspected. Should we start empirical treatment? If yes, what regimen/s? What microorganisms should be targetted?

Both GPC and GNB → Ciprofloxacin (750 mg/bid) + Linezolid 600 mg/bid initiated empirically by the cardiology/ID Ward. The patient was admitted.

Both GPC and GNB → Meropenem (1g/8) + daptomycin (10 mg/kg/24h) initiated empirically by the cardiology/ID Ward. The patient was admitted.

We decided to delay the antibiotics, but the patient was admitted to complete diagnosis and management of local CIED infection.

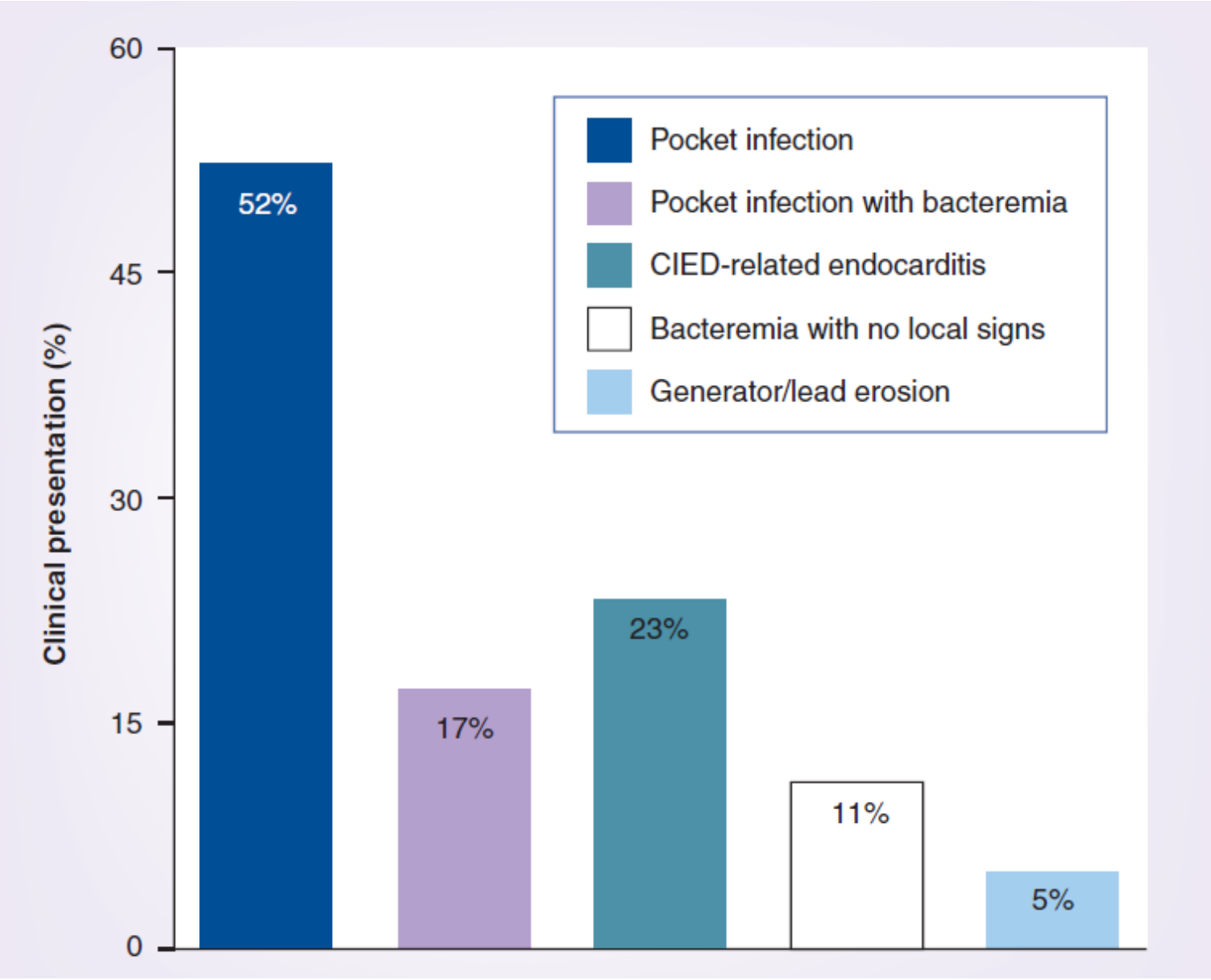
We decided to delay the antibiotics, and the patient was discharge to complete diagnosis and management in the outpatient clinic.

Question…

CIED pocket infection (at least pocket infection) it is suspected. Should we start empirical treatment? If yes, what regimen/s? What microorganisms should be targetted?

Both GPC and GNB → Meropenem (1g/8) + daptomycin (10 mg/kg/24h) initiated empirically by the cardiology/ID Ward. The patient was admitted.

Clinical presentation of CIED infections



Risk and prevalence of bacteremic infection?

Sohail MR, JACC 2007;49:1851

ETIOLOGY

Medicine
OBSERVATIONAL STUDY

Current Epidemiology and Outcome of Infective Endocarditis

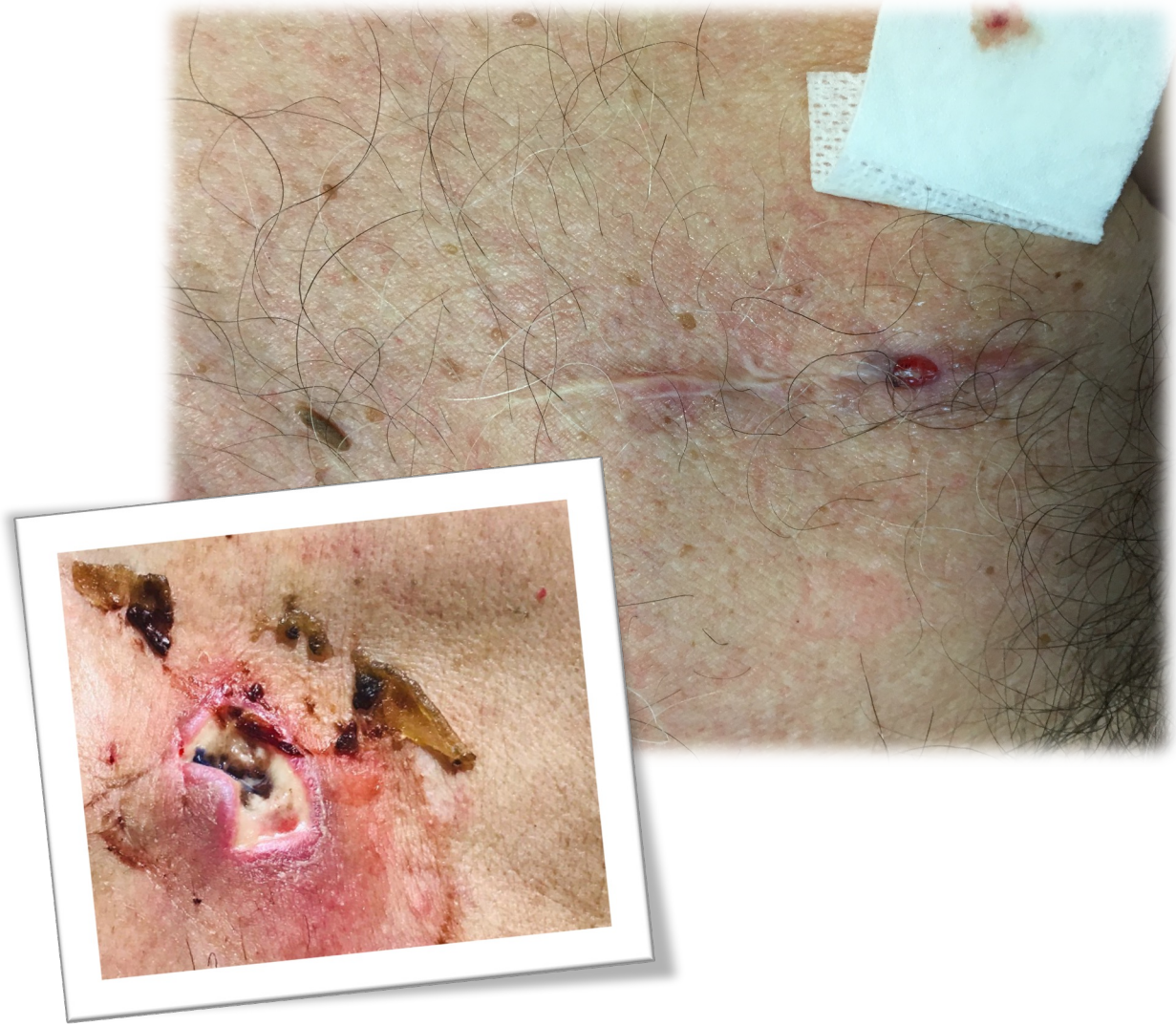
A Multicenter, Prospective, Cohort Study

TABLE 2. Etiology, Diagnosis, and Outcome of 1804 Episodes of Infective Endocarditis Prospectively Collected in Spain

	Total N = 1804	Native Non-IVDU N = 1079	Native IVDU N = 52	Prosthetic N = 504	Device N = 169	*P*
Definite IE	1498 (83.0)	919 (85.6)	48 (92.3)	409 (81.3)	122 (72.2)	<0.01
Possible IE	300 (16.6)	155 (14.4)	4 (7.7)	94 (18.7)	47 (27.8)	<0.01
Etiology						
Staphylococcus spp.	728 (40.3)	382 (35.3)	30 (55.8)	218 (43.2)	98 (58.0)	<0.01
S. aureus	426 (23.6)	278 (25.8)	26 (50.0)	77 (15.3)	45 (26.6)	<0.01
MSSA	360 (84.5)	235 (84.5)	24 (92.3)	64 (83.2)	37 (82.3)	0.46
MRSA	66 (15.5)	43 (15.5)	2 (7.7)	13 (16.8)	8 (17.7)	
CoNS	302 (16.7)	104 (9.7)	4 (7.7)	141 (28.0)	53 (31.5)	<0.01
Streptococcus spp.	440 (24.4)	329 (30.5)	8 (15.4)	86 (17.1)	17 (10.1)	<0.01
S. bovis	117 (6.4)	80 (7.4)	0	32 (6.5)	5 (3.0)	0.036
S. viridans group	223 (12.3)	171 (16.0)	7 (13.5)	38 (7.5)	7 (4.1)	<0.01
Others	100 (5.5)	79 (7.3)	1 (1.9)	15 (3.0)	5 (5.3)	0.001
Enterococcus spp.	230 (12.7)	142 (13.2)	5 (9.6)	77 (15.3)	6 (3.6)	0.001
Other Gram-positives*	26 (1.4)	14 (1.3)	2 (3.8)	8 (1.5)	2 (1.1)	0.48
Gram-negatives**	93 (5.2)	53 (4.9)	–	25 (5.0)	15 (8.9)	0.05
Fungi***	44 (2.4)	21 (1.9)	2 (3.8)	15 (3.0)	6 (3.6)	0.38
Negative BC	264 (14.7)	152 (14.0)	5 (9.6)	75 (14.8)	32 (18.9)	0.67
Echocardiogram						

Muñoz P. et al. Medicine Volume 94, Number 43, October 2015

Clinical Case



Clinical Case

Staphylococcus aureus

Estudi de bacteris i fongs - Local swab -

Cultiu

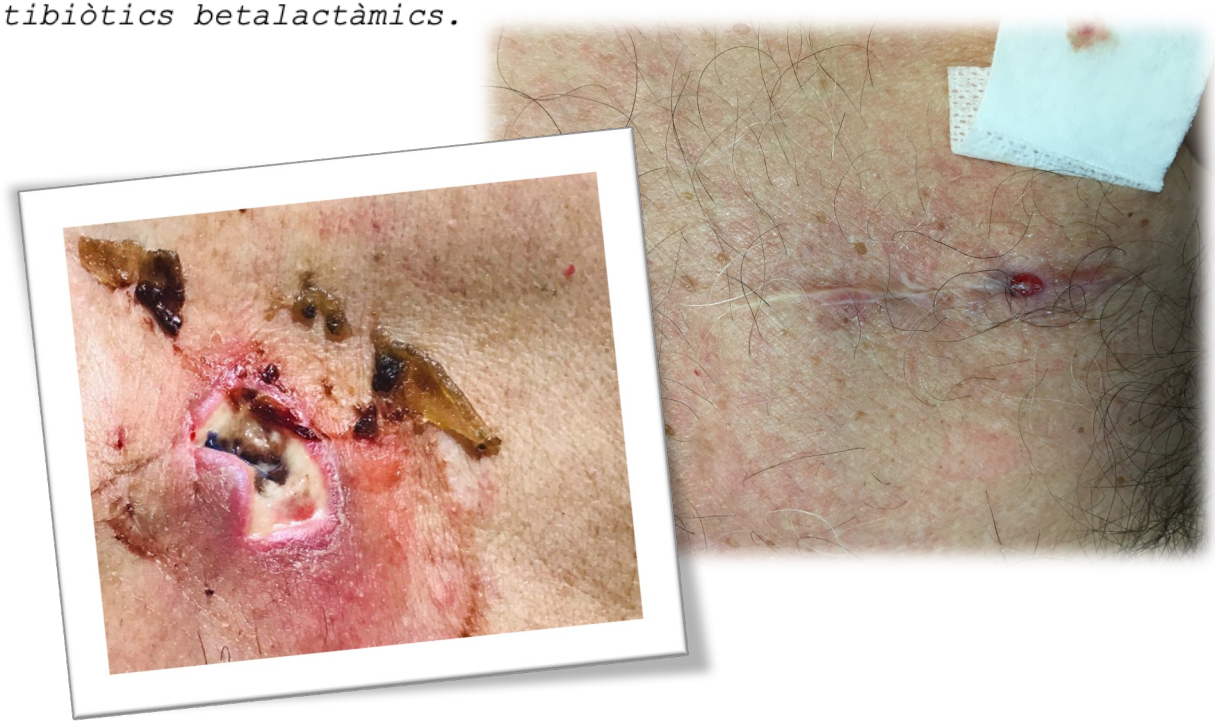
1 S'aïllen escasses colònies de: Staphylococcus aureus

Soca resistent a l'oxacil.lina i a tots els antibiòtics betalactàmics.

Recomanem aplicar mesures d'aïllament.

Antibiograma

	1(CMI:µg/ml)
Clindamicina	R (>1)
Cotrimoxazol	S (<=0,5/9,)
Eritromicina	R (>4)
Gentamicina	S (<=1)
Levofloxacina	R (>4)
Linezolid	S (2)
Oxacil.lina	R (>2)
Penicilina	R (>0,25)
Rifampicina	S
Vancomicina	S (1)



CIED infection due to MRSA, initially without systemic signs of infection

What should we do to complete the diagnosis?

Wait for the blood culture results, if positive, TEE or TTE suspecting CIED infective endocarditis.

TEE

TEE and 18 FDP PET/CT regardless blood culture positivity

Device removal without TEE or 18 FDP PET/CT

CIED infection due to MRSA, initially without systemic signs of infections

What should we do to complete diagnosis?

TEE and 18 FDP PET/CT regardless blood culture positivity

Consensus statement	Statement class	Scientific evidence coding	Reference
'Definite' CIED clinical pocket/generator infection = generator pocket shows swelling, erythema, warmth, pain, and purulent discharge/sinus formation OR deformation of pocket, adherence, and threatened erosion OR exposed generator or proximal leads.			
'Definite' CIED/IE = presence of either two major criteria or one major + three minor criteria			
'Possible' CIED/IE = presence of either one major + one minor criteria or three minor criteria			
'Rejected' CIED/IE diagnosis = patients who did not meet the aforementioned criteria for IE			
Major criteria		E	59
Microbiology	A. Blood cultures positive for typical microorganisms found in CIED infection and/or IE (Coagulase-negative Staphylococci, *Staphylococcus aureus*)		
	B. Microorganisms consistent with IE from two separate blood cultures:		
	a. Viridans streptococci, *Streptococcus gallolyticus* (*Streptococcus bovis*), HACEK group, *S. aureus* or		
	b. Community-acquired enterococci, in the absence of a primary focus.		
	C. Microorganisms consistent with IE from persistently positive blood cultures:		
	a. ≥2 positive blood cultures of blood samples drawn >12 h apart; or		
	b. All of three or a majority of ≥4 separate cultures of blood (first and last samples drawn ≥1 h apart); or		
	c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre >1:800		
Imaging positive for CIED infections and/or IE	D. Echocardiogram (*including ICE*) positive for:		
	a. CIED infection:		
	i. Clinical pocket/generator infection		
	ii. Lead vegetation		
	b. Valve IE		
	i. Vegetations		
	ii. Abscess, pseudoaneurysm, intracardiac fistula;		
	iii. Valvular perforation or aneurysm;		
	iv. New partial dehiscence of prosthetic valve		
	E. [^{18}F]FDG PET/CT (caution should be taken in case of recent implants) or radiolabelled WBC SPECT/CT detection of abnormal activity at pocket/generator site, along leads or at valve site		
	F. Definite paravalvular leakage by cardiac CT		
Minor criteria		E	59
a. Predisposition such as predisposing heart condition (e.g. new onset tricuspid valve regurgitation) or injection drug use			
b. Fever (temperature >38°C)			
c. Vascular phenomena (including those detected only by imaging): major arterial emboli, septic pulmonary embolisms, infectious (mycotic) aneurysm,			

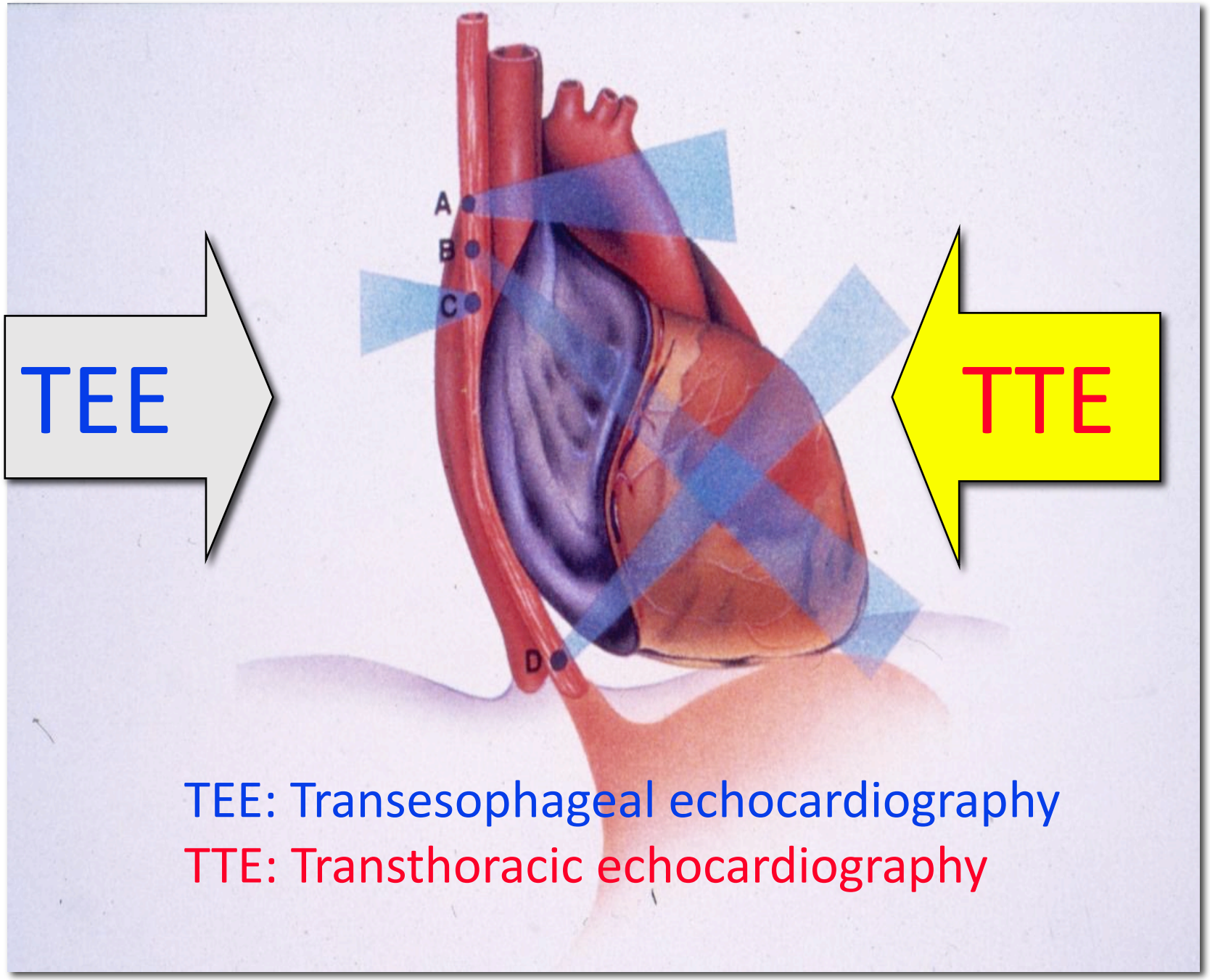
European Heart Journal (2020) 41, 2012–2032

Diagnosis - Summary of recommendations

COR	LOE	Recommendations
IIa	B-NR	TEE can be useful for patients with CIED pocket infection with and without positive blood cultures to evaluate the absence or size, character, and potential embolic risk of identified vegetations.
IIa	C-EO	Evaluation by physicians with specific expertise in CIED infection and lead extraction can be useful for patients with suspected CIED infection.
IIb	C-LD	Additional imaging may be considered to facilitate the diagnosis of CIED pocket or lead infection when it cannot be confirmed by other methods.

- The failure → **mass adherent to a lead** with TEE does not exclude lead infection
- TEE may be useful in CIED-related IE→ TTE poor sensitivity.
- Prognostic features better in TTE → pericardial effusion, ventricular dysfunction and dyssynchrony, and pulmonary vascular pressure estimations.

Habib G. Eur Heart J. 2015 Nov 21;36(44):3075-3128.



TEE is the gold standard for the detection of lead vegetations!

PET's usefulness is not well characterized

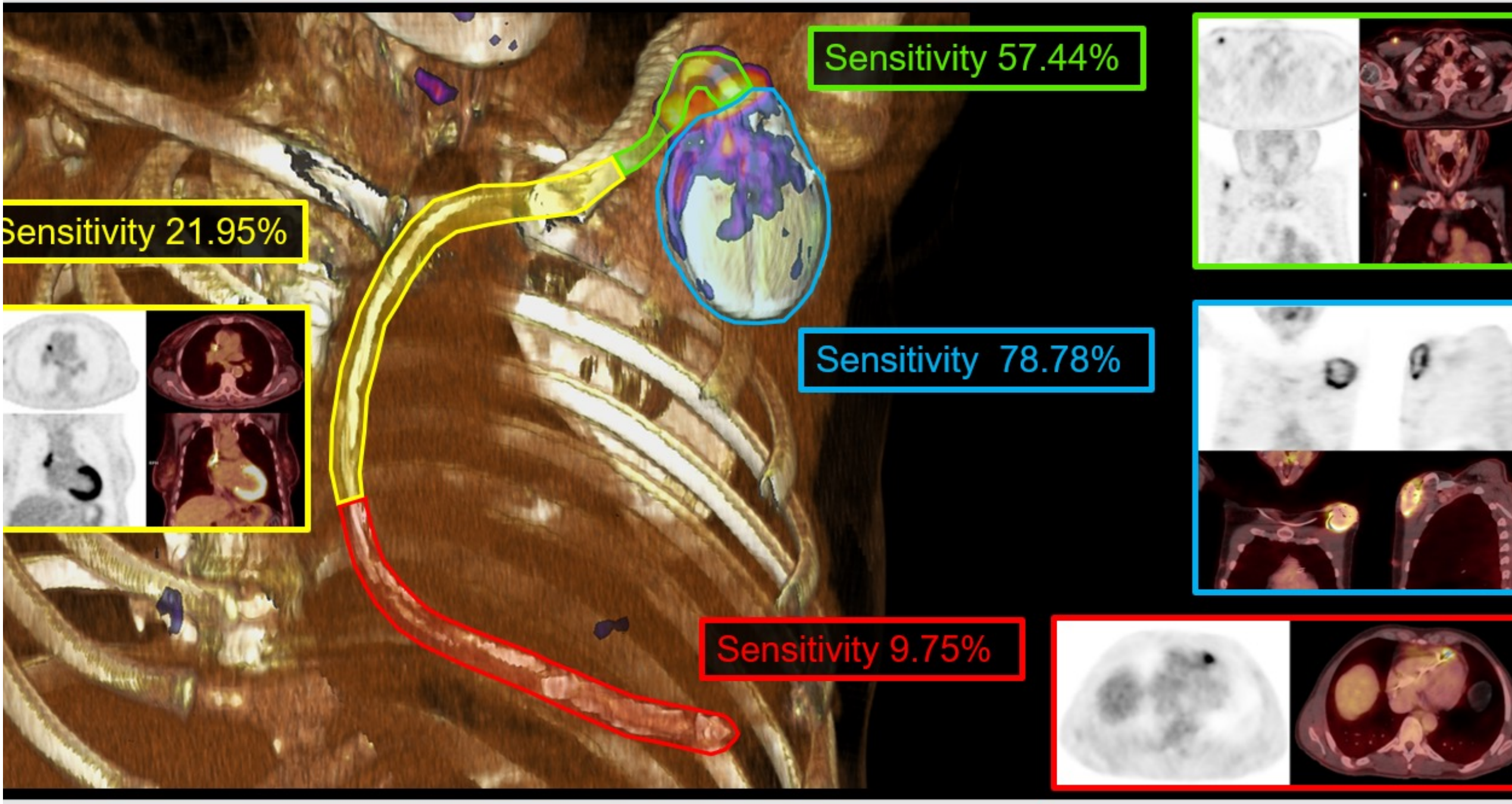
	Pocket infection	Infective endocarditis
Jerónimo et al	N=14	N=13
- Sensitivity (Sn)	72%	38.5%
- Specificity (Sp)	95.6%	98%
Cautela et al	N=15	N=13
- Sensitivity	86%	31%
- Specificity	100%	62%
Bensihmon en al	N=5	N=10
- Sensitivity	100%	60%
- Specificity	100%	100%

Sn 72-100%
Sp 96-100%

Sn 30-60%
Sp 62-100%

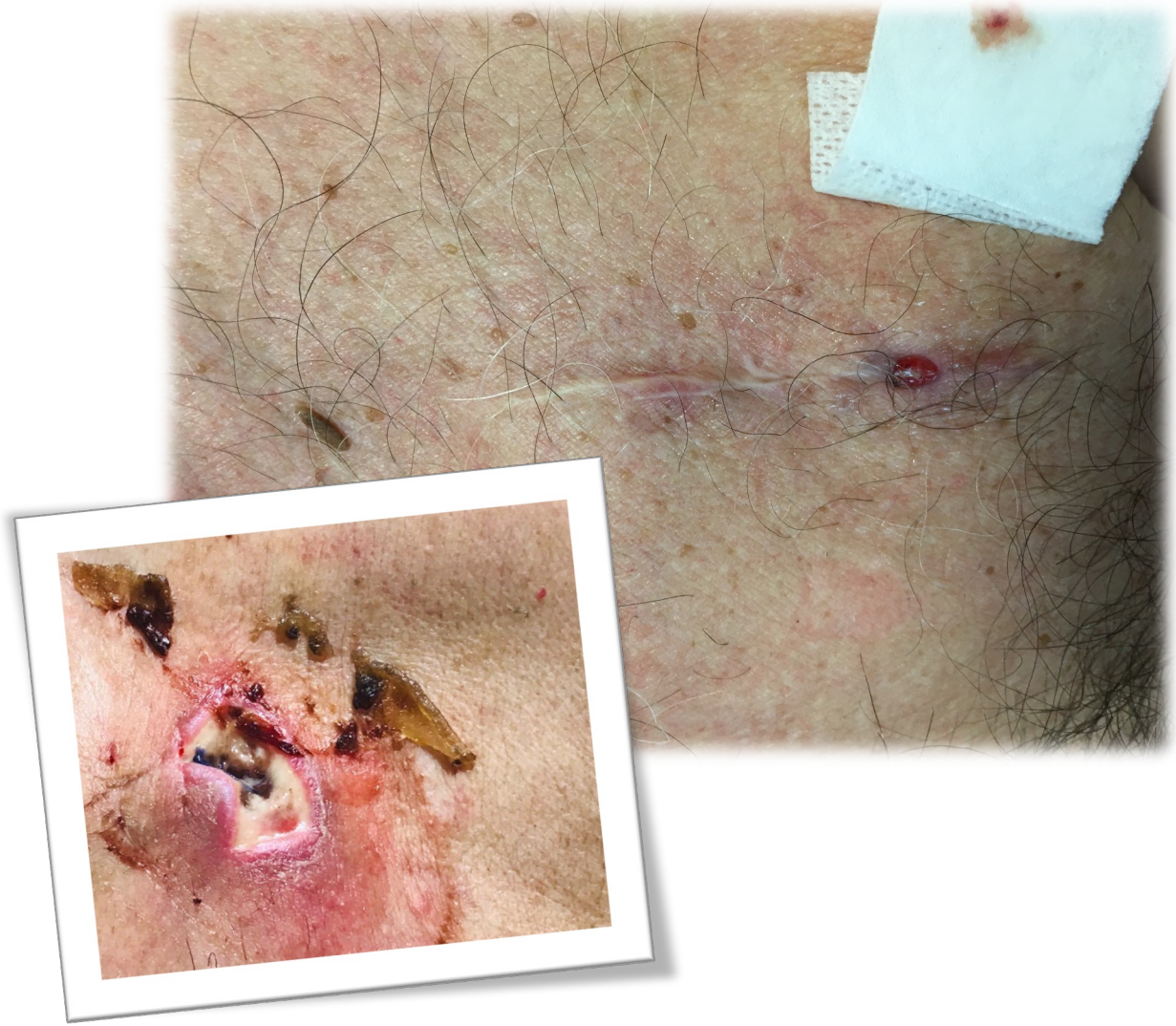
TEE/TTE: Transesophageal/Transthoracic Echocardiography

Hernández-Meneses M and Perissinotti A. et al, REC CI 2023



Hernández-Meneses M and Perissinotti A. et al, REC CI 2023

Clinical Case



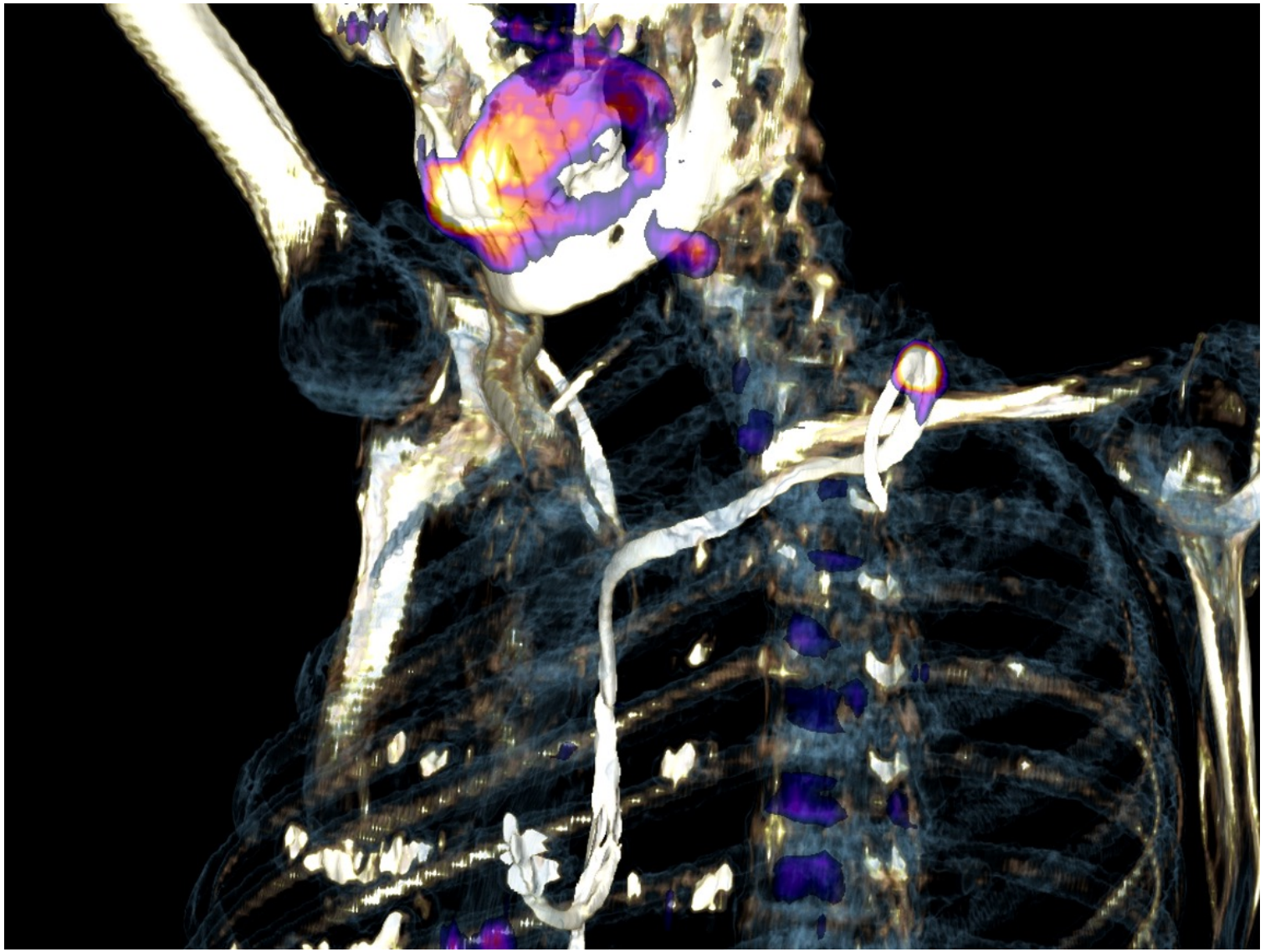
Clinical Case

Blood cultures negative

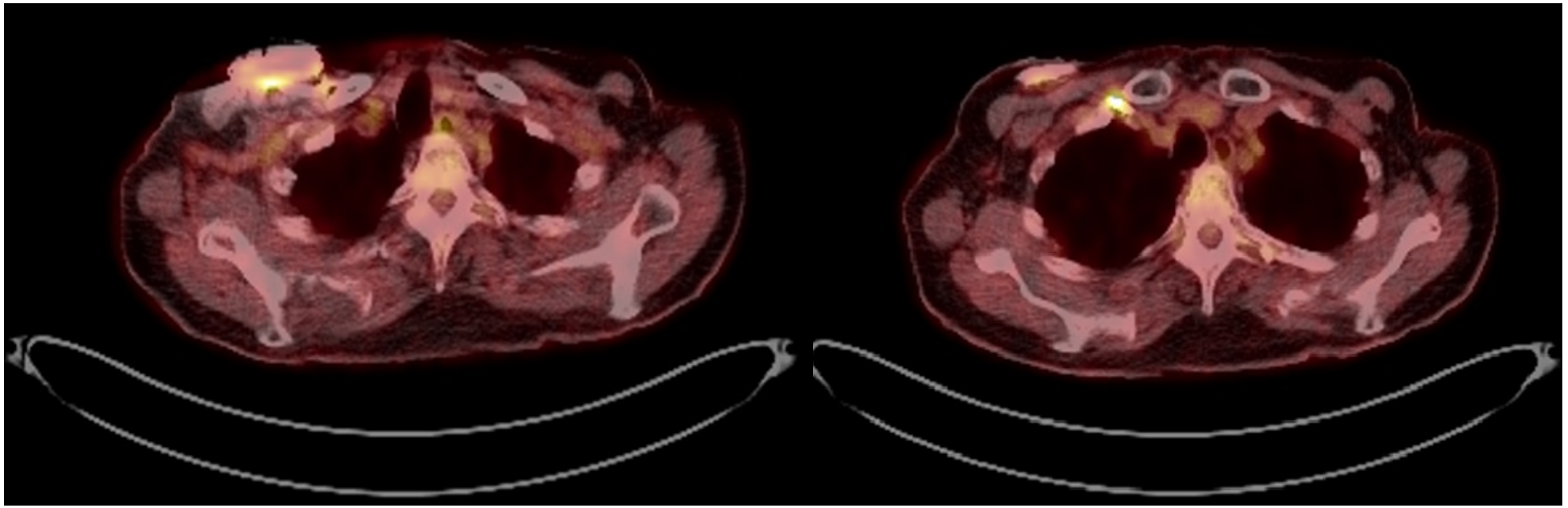
Chest X-Ray identified no pulmonary embolism

TTE and TEE were negative

Clinical Case

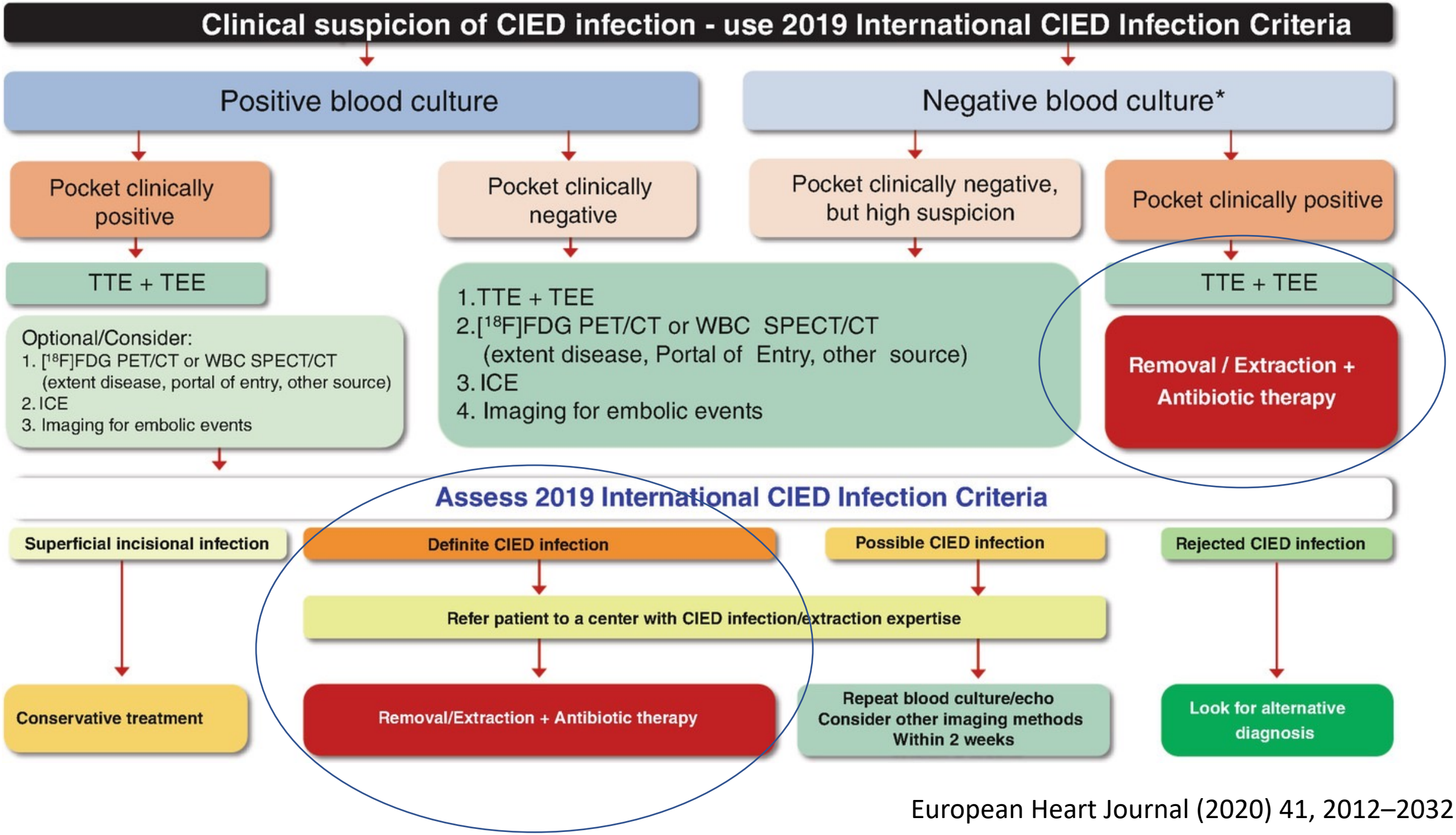


Clinical Case



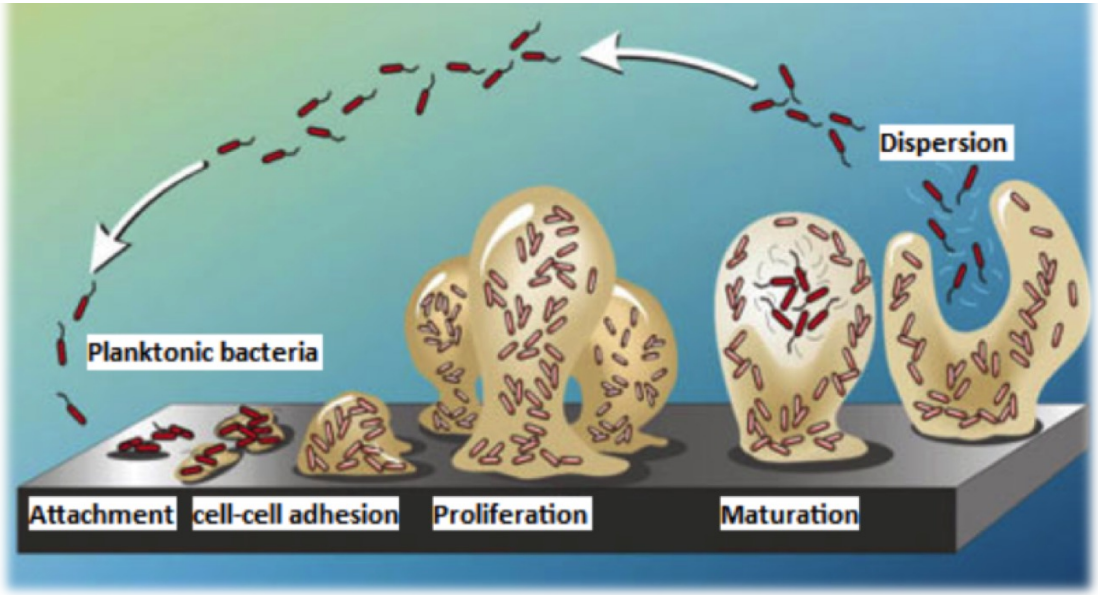
Pocket + SC lead CIED infection caused by *MRSA*

Biofilm-producing infection!!!



European Heart Journal (2020) 41, 2012–2032

Biofilm-producing infection!!!



Antimicrobial resistance

- Limited diffusion (extracellular matrix)

- Electrostatic repulsion (surface polymers)

- Sequestration (surface polymers)

- Bacteria in resting state.

To impair innate host defenses

- Antimicrobial peptides

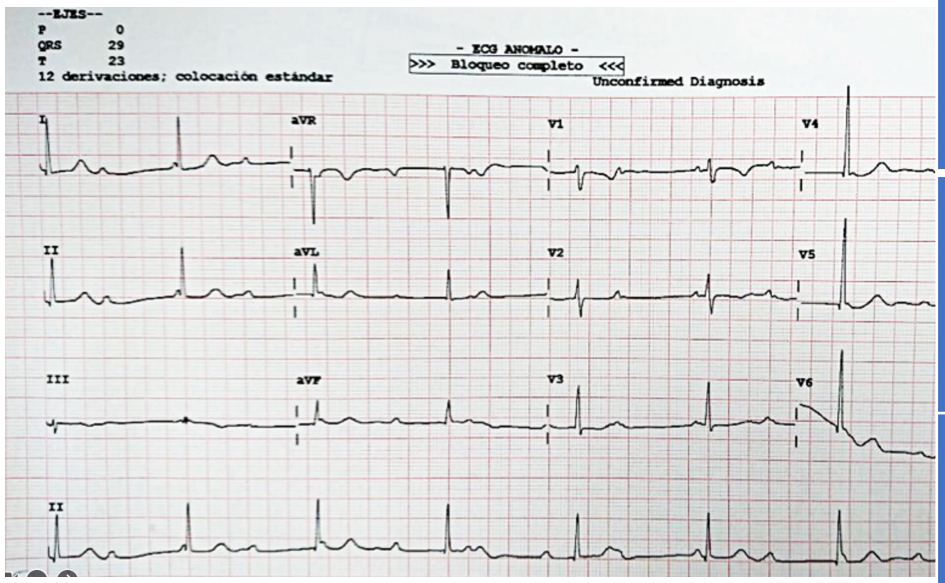
- Neutrophil phagocytosis (exo-polysaccharide/polymer)

↑↑↑ MIC x 10-1,000
⇒ Device removal !!!

Clinical Case

We decided to remove the device but…

We must implant a contralateral PCM



Guidelines	Immediate reimplantation (in a single time)	Early reimplantation after 72 h *	Reimplantation in 7-10 days	Reimplantation after 14 days
British [1] (2015)	Not recommended	Not recommended	If device was removed and negative blood cultures.	If valvular involvement
European [2] (2015)	Not recommended	Negative blood cultures*		If valvular involvement
AHA[3] (2010)	Not recommended	If device was removed and negative blood cultures.		If valvular involvemen

When is it safe to implant the new device???

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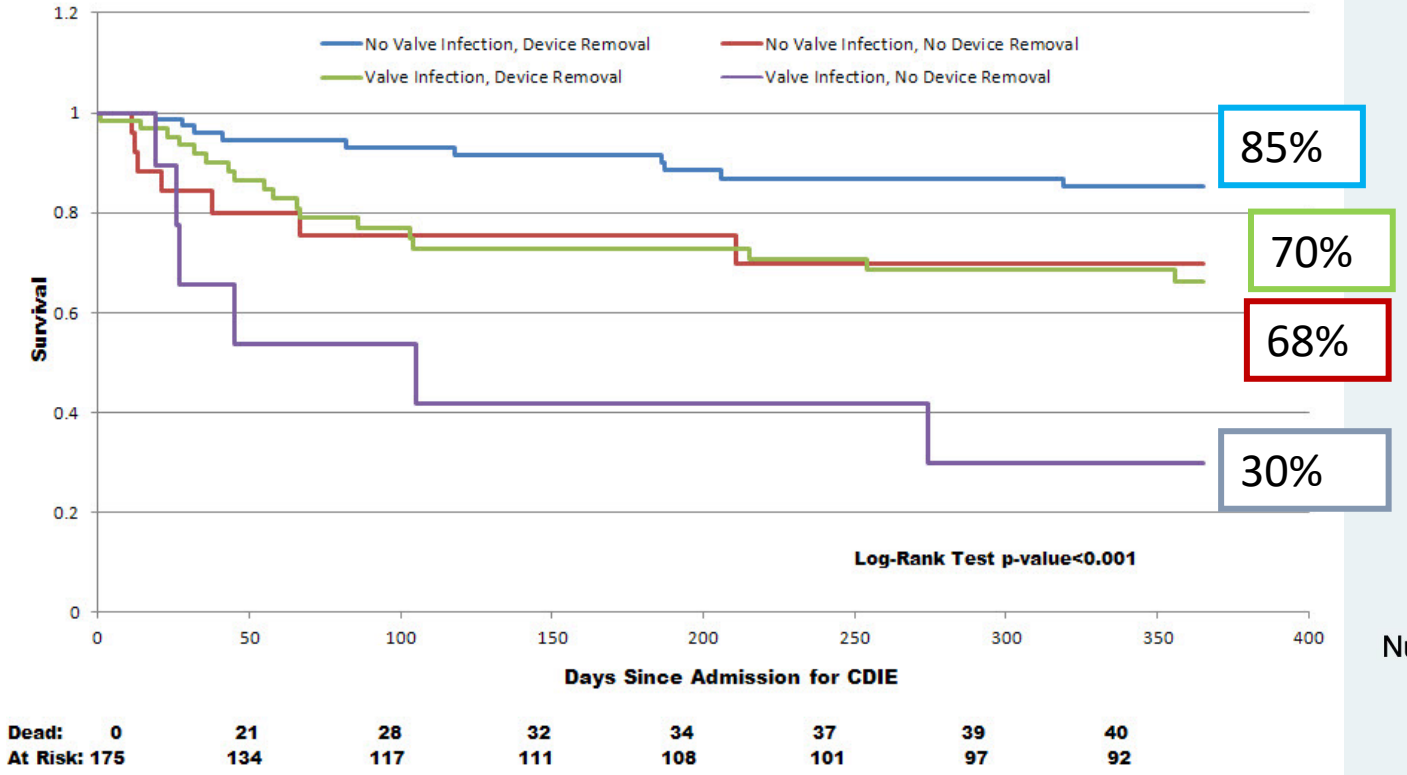
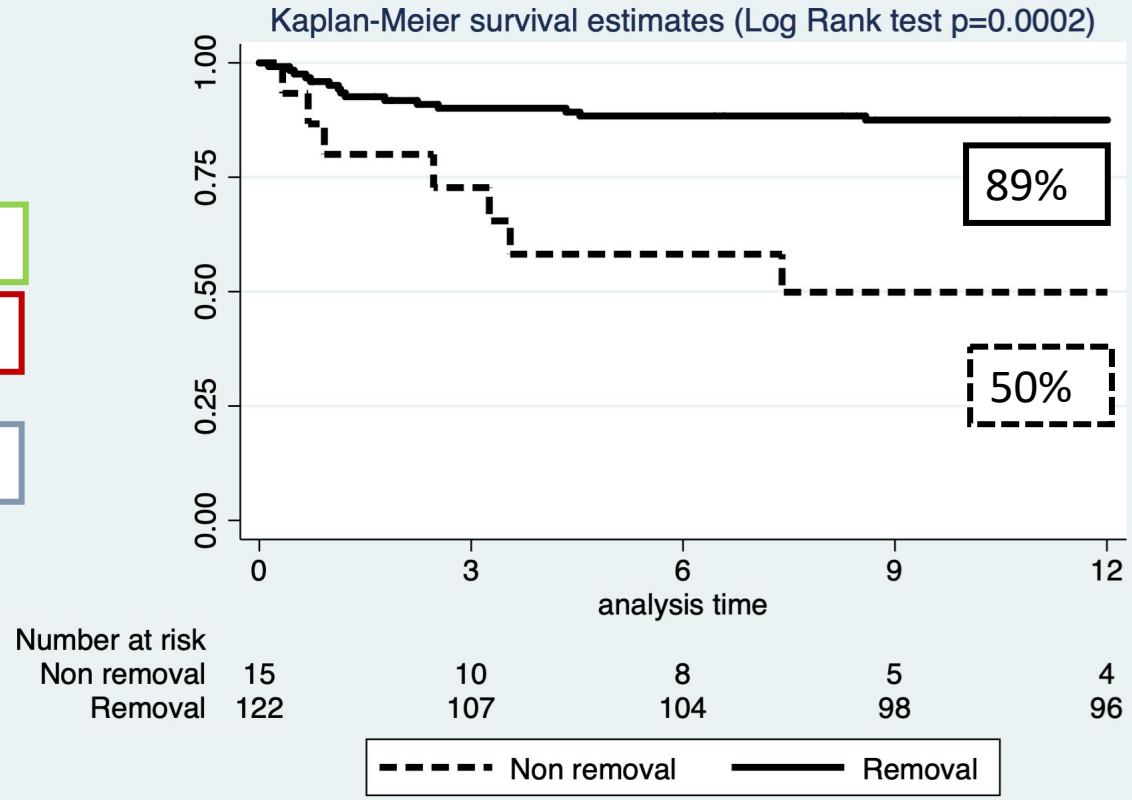
Complete device removal is the key for survival!

MEDIC-Prospective cohort study, 2000-2006



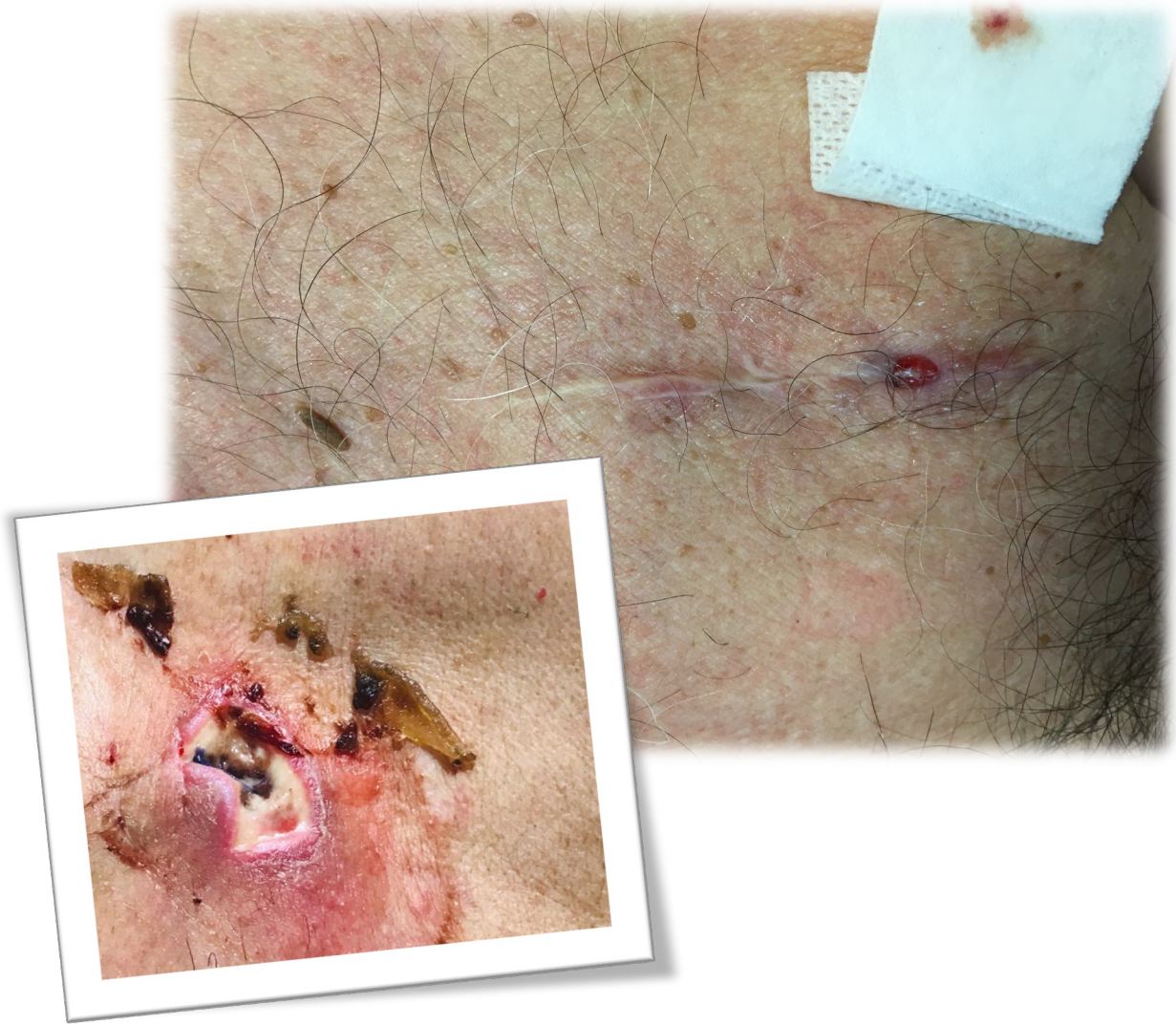
Athan E et al. JAMA 2012

Hospital Clinic Barcelona-Spain, 1981 - 2020



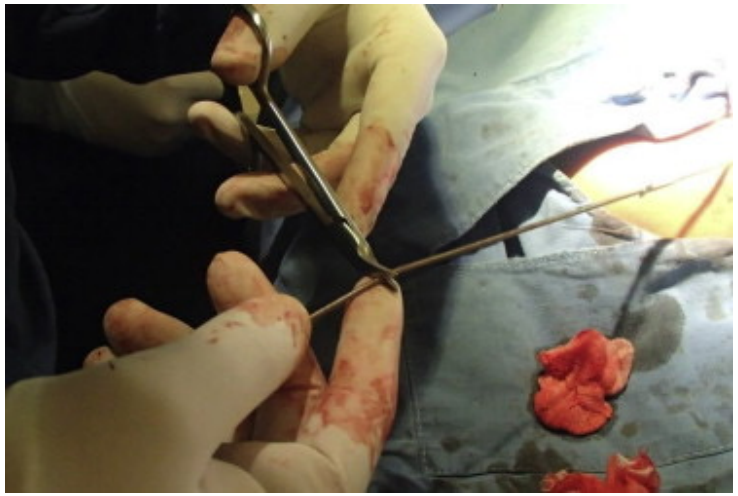
Hernández-Meneses M et al. OFID 2022

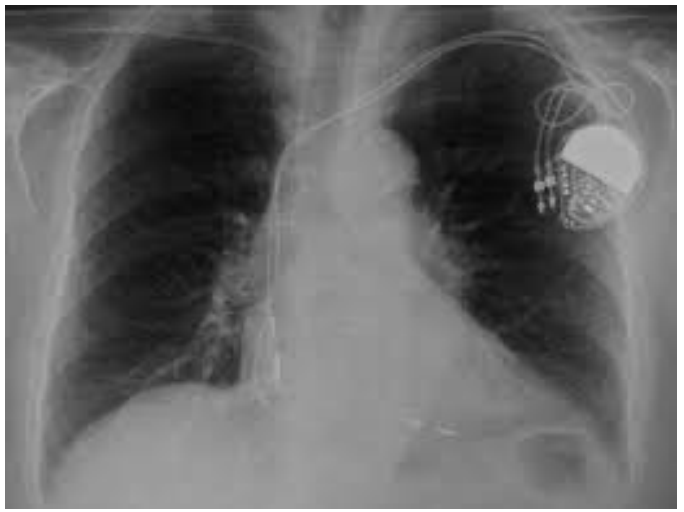
Clinical Case



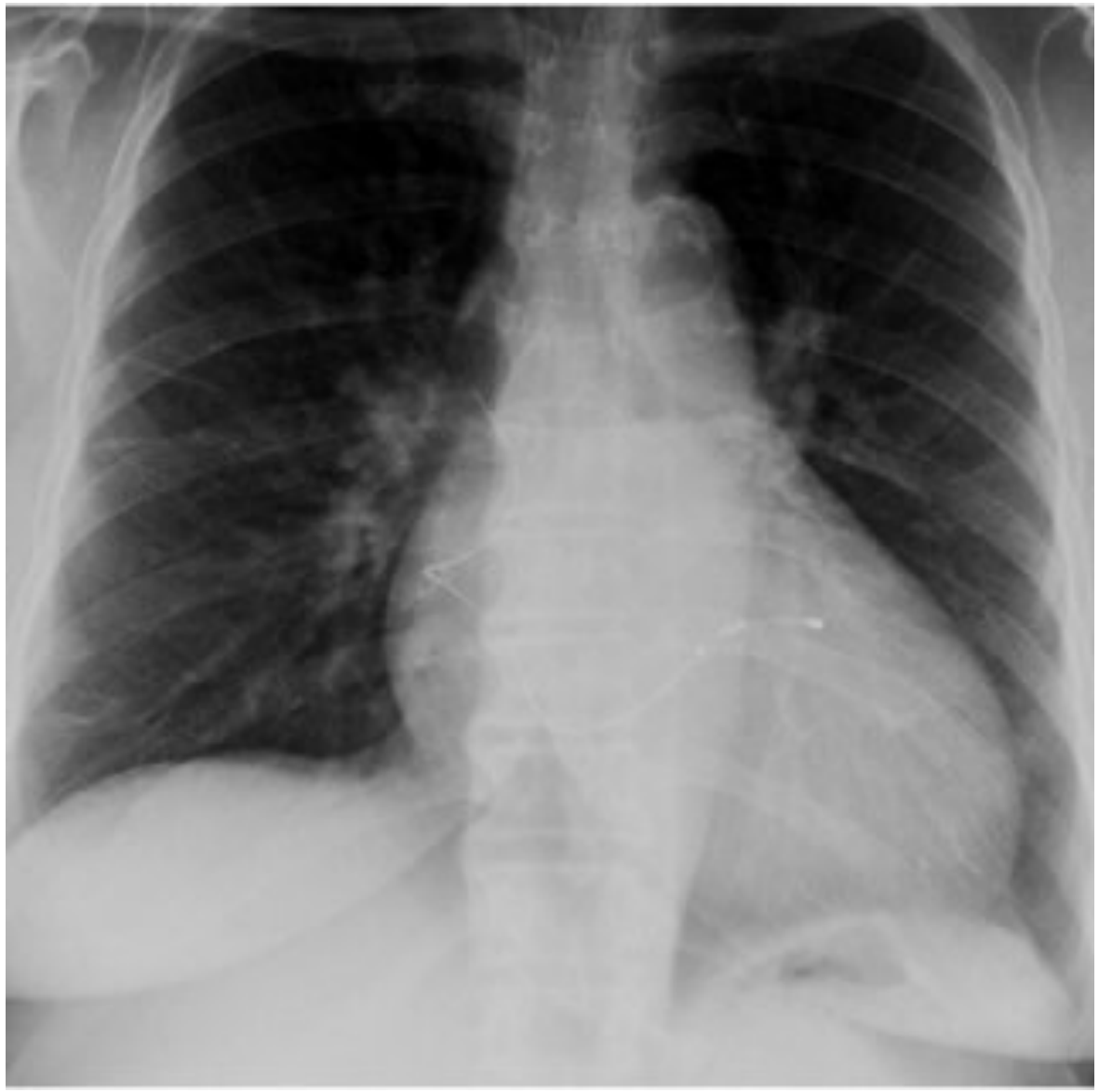
Clinical Case

Since blood cultures were negative, meropenem was stopped.
He was on **daptomycin for seven days** and finally the removal was scheduled.





17/01/2019 → The device and one lead were removed, unfortunately the other lead broke and **more than 4 cm of the fragment was abandoned at the place**.



Clinical Case

MICROBIOLOGIA

MOSTRA: Mostra genèrica. Cultiu CAPSULA MCP 182245399-

Estudi de bacteris i fongs

Cultiu

1 S'aïllen escasses colònies de: Staphylococcus aureus

Soca resistent a l'oxacil.lina i a tots els antibiòtics betalactàmics.
Recomanem aplicar mesures d'aïllament.

Antibiograma

	1(CMI:µg/ml)
Clindamicina	R (>1)
Cotrimoxazol	S (<=0,5/9,)
Eritromicina	R (>4)
Gentamicina	S (<=1)
Levofloxacina	R (>4)
Linezolid	S (2)
Oxacil.lina	R (>2)
Penicilina	R (>0,25)
Rifampicina	S
Vancomicina	S (1)

What should we do when the device can not be removed?

16S rRNA PCR/sequencing was also positive

What to do with the retained leads and/or devices?

=Chronic oral suppression (CAS)

Mayo Clinic cohort study, 2005-2015

CAS therapy 7%

RELAPSES: 18%
IN-HOSPITAL MORTALITY: 25%
ONE-YEAR MORTALITY: 44%

Survival 1.43 years (IC 95%, 0.27-2.14)

CAS-Toxicity (rash 9%, C. difficile 6%, pancreatitis 3%)

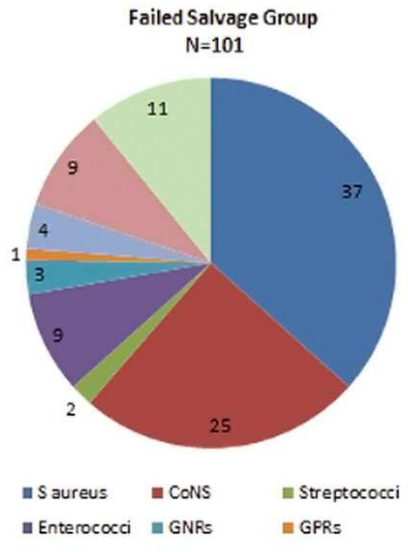
18% developed CIEDI **relapse:**

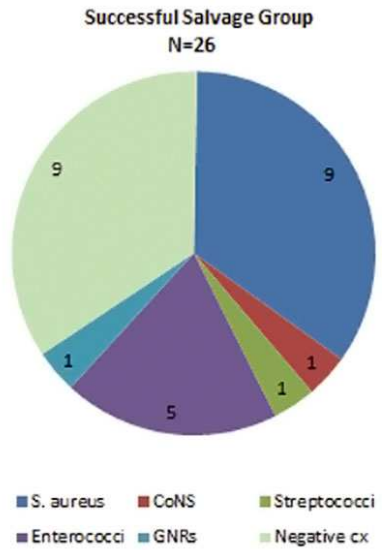
- 100% → alternative AB therapy
- 33% → underwent extraction due to relapse
  - 50% → expired due to CIED extraction surgery.

MEDIC cohort study, 2009-2012

CAS therapy 29%

RELAPSES: 22%
IN-HOSPITAL MORTALITY: 30%
ONE-YEAR MORTALITY: -



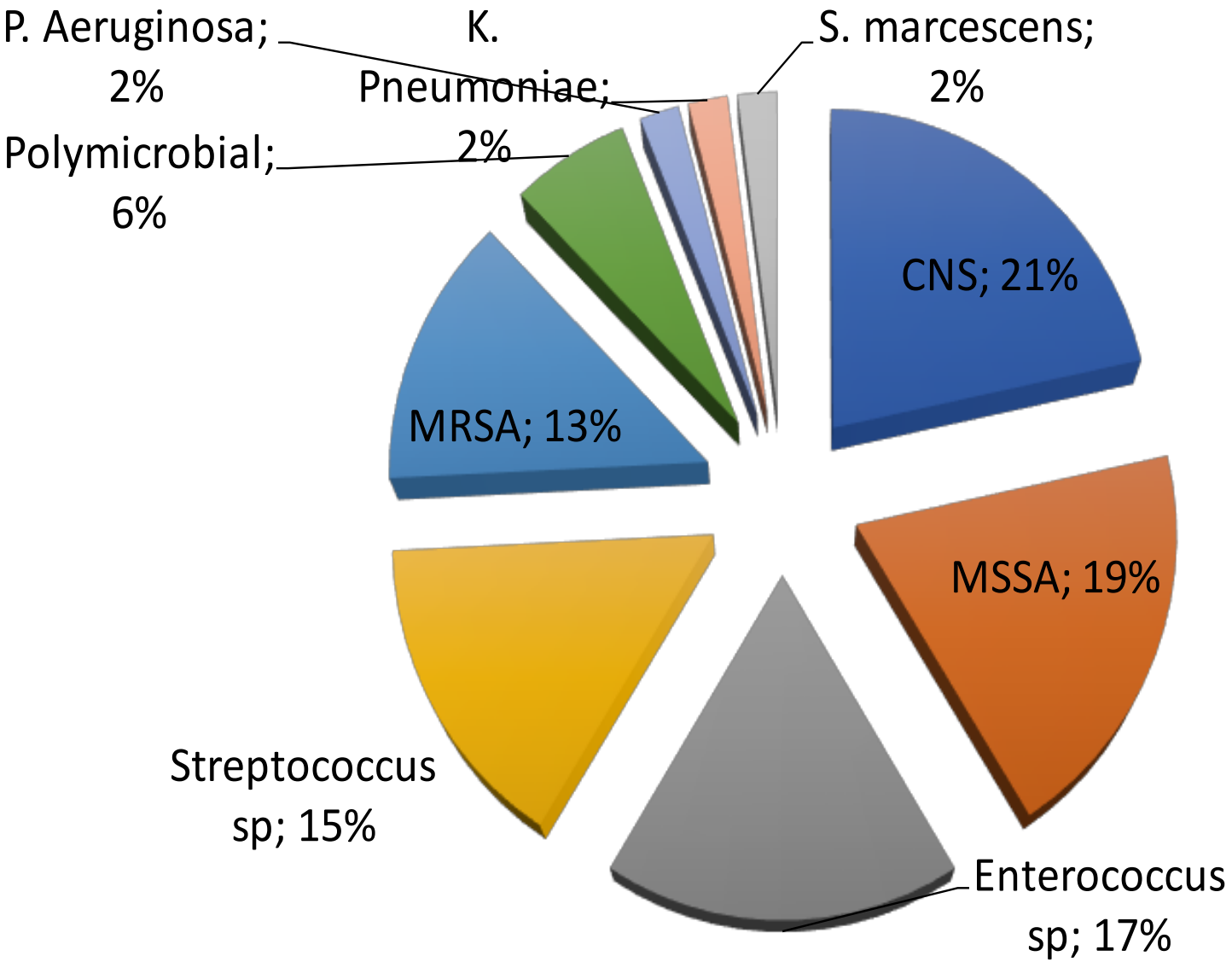


Antibiotics Duration? Follow-up?

E. M. Tan et al, CID, 2017

J.E Peacok et al, Pacing Clinic Electrophysiol, 2018

Antibiotics schemas?, Duration?, Follow-up?



Type of CAS

- Penicillin 22%
- Cotrimoxazole 22%
- Amoxicillin 22%
- Minocycline 14%
- Cephalexin 14%
- Dicloxacillin 3%

E. M. Tan et al, CID, 2017

Clinical Case

What should we do when the device can not be removed ?????

Linezolid 600 mg/bid, and switch to tedizolid if cytopenias

Test for doxycycline or minocyclin

Dalbavancin weekly

Cotrimoxazole bid

He completed seven days of ev **daptomycin** **treatment before the new one PCM was implanted**

He was started on suppressive antibiotic treatment **cotrimoxazole 800/160 bid**

Clinical Case – follow up

The patient stopped the antibiotic treatment by his-own and one months later…

New admission → fever

Estudi de bacteris i fongs

Cultiu

1 S'aïllen escasses colònies de: Staphylococcus aureus

Soca resistent a l'oxacil.lina i a tots els antibiòtics betalactàmics.
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Oxacil.lina	R (>2)
Penicilina	R (>0,25)
Rifampicina	S
Vancomicina	S (1)

Continuous *MRSA* Bacteremia

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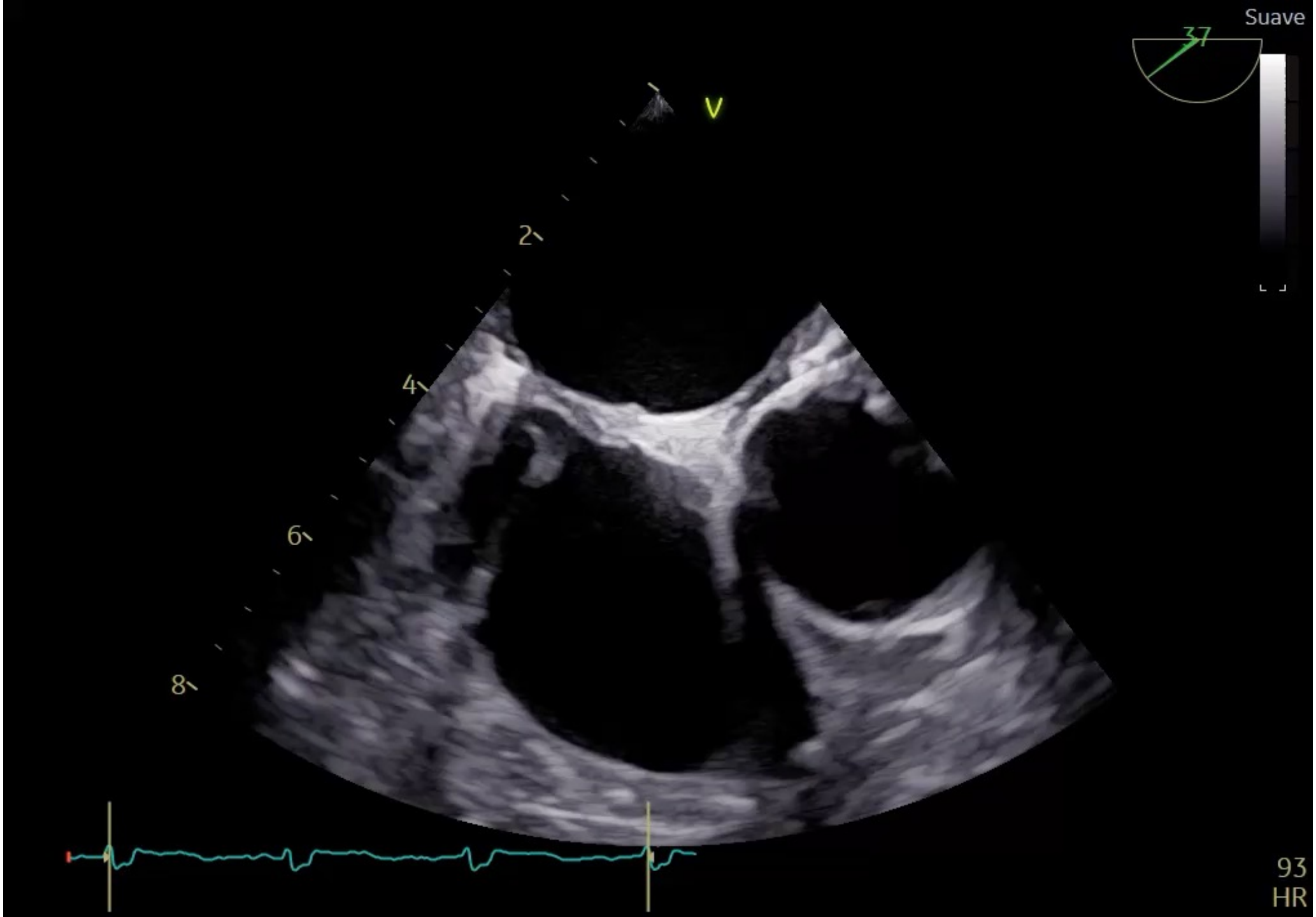

Suave
37
V
2
4
6
8
93
HR

Clinical Case

CIED-lead infective endocarditis “lead-carditis” due to MRSA

Chest X-RAY and 18 FDG-PET/CT were performed without showing septic metastasis

CIED infective endocarditis due to MRSA

Which therapy would you start and for how long?

Vancomycin plus rifampicin and gentamicin two weeks, following by vancomycin alone.

Daptomycin alone for four weeks

Daptomycin plus fosfomycin, following by daptomycin alone to complete four weeks

Daptomycin plus ceftaroline, following by daptomycin alone to complete four weeks

Clinical Case

CIED-lead infective endocarditis “lead-carditis” due to MRSA

He was started on **daptomycin and ceftaroline** until bacteremia was cleared and for ten more days. He finished four weeks of treatment with daptomycin.

He underwent open surgery to **abandoned lead removal**.
The new device implanted one moth ago was also replaced.

The 2015 guidelines of the American (AHA) and European (ESC) cardiology societies for the treatment of IE recommend the use of **vancomycin-based guidelines for IE by MRSA**, which have **suboptimal efficacy** and are not exempt from **toxicity**.

Antibiotic treatment
Staphylococcus spp. Native valves
Pas d'aminosides

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Native valves				
Methicillin-susceptible staphylococci				
(Flu) cloxacillin or **oxacillin**	12 g/day i.v. in 4-6 doses	4-6	I	B
Alternative therapy				
Cotrimoxazole WITH Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses) 1800 mg/day IV in 3 doses	1 i.v. + 5 oral intake 1	IIb	C
Penicillin-allergic patients or methicillin-resistant staphylococci				
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses	4-6	I	B
Alternative therapy				
Daptomycin	10 mg/kg/day i.v. once daily	4-6	IIa	C
Alternative therapy				
Cotrimoxazole WITH Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 doses) 1800 mg/day IV in 3 doses	1 i.v. + 5 oral intake 1	IIb	C

Antibiotic treatment
Staphylococcus spp. Prosthetic valves

Antibiotic	Dosage and route	Duration (weeks)	Class	Level
Prosthetic valves				
Methicillin-susceptible staphylococci				
(Flu) cloxacillin or **oxacillin**	12 g/day i.v. in 4–6 doses	≥6	I	B
WITH **Rifampin**	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥6		
AND **Gentamicin**	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2		
Penicillin-allergic patients and methicillin-resistant staphylococci				
Vancomycin	30–60 mg/kg/day i.v. in 2–3 doses	≥6	I	B
WITH Rifampin	900–1200 mg i.v. or orally in 2 or 3 divided doses	≥6		
AND Gentamicin	3 mg/kg/day i.v. or i.m. in 1 or 2 doses	2		

But treatment have not changed among years!!

Guidelines IDSA 2011
MRSA bacteremia

Identify the source and extent of the infection with **elimination** and/or debridement of other sites of infection should be conducted (A-II).

Echocardiography is recommended for all adult patients with bacteremia. Transesophageal echocardiography (TEE) is preferred over transthoracic echocardiography (TTE)

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

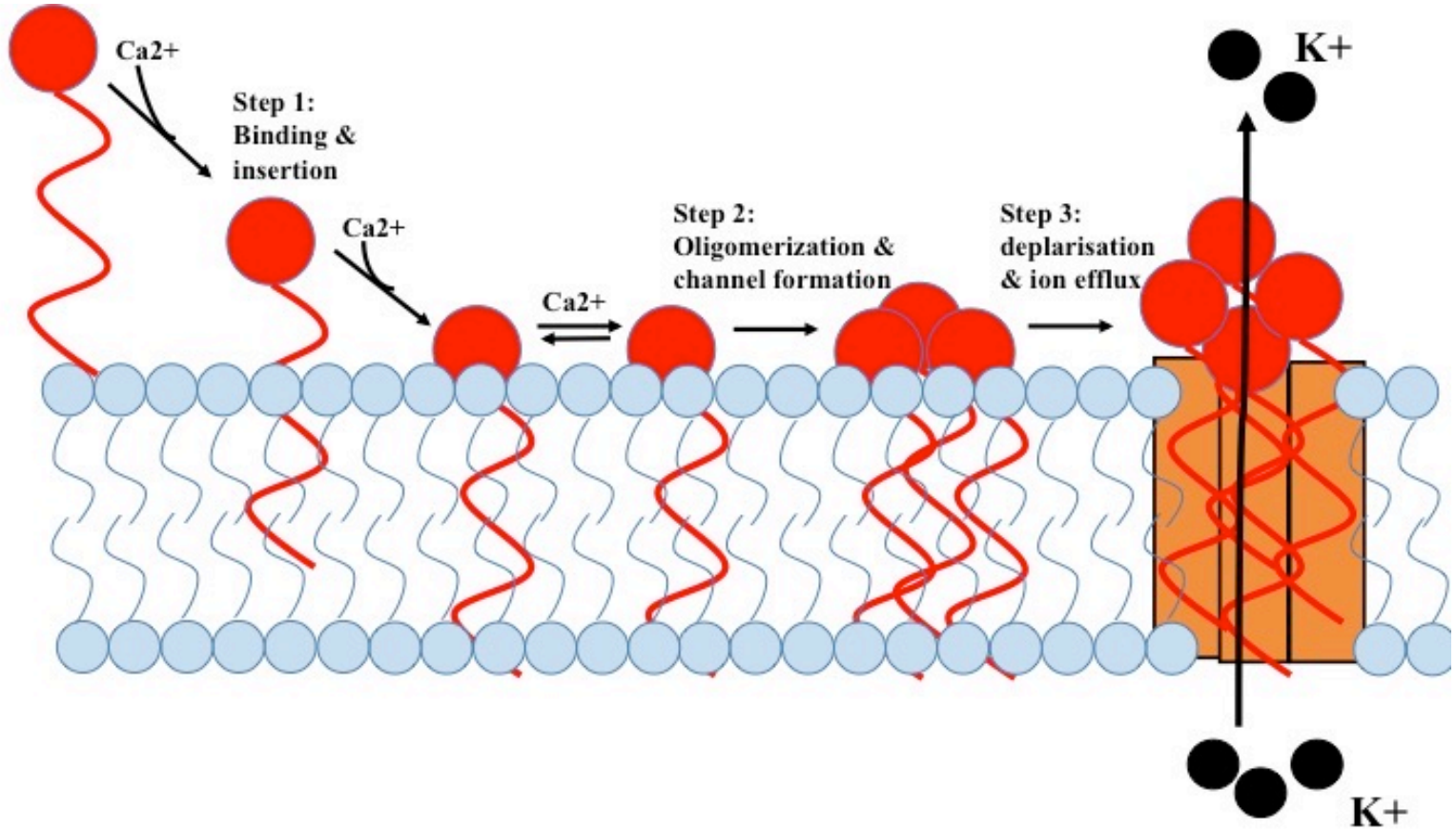
Bacteremia and Infective Endocarditis, Native Valve

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 complicated bacteremia (defined as patients with positive blood culture results who do not meet criteria for uncomplicated bacteremia), 4–6 weeks of therapy is recommended, depending on the extent of infection. Some experts recommend higher dosages of daptomycin at 8–10 mg/kg/dose IV once daily (**B-III**).

Liu C. et al, Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary. Clin Infect Dis. 2011 Feb 1;52(3):285-92.

Daptomycin MoA

Lipopeptide antibiotic active against *Staphylococci*, which has **rapid bactericidal activity**, although cases of microbiological failure in monotherapy have been described. In *S. aureus*, the synergy between daptomycin and antibiotics that act on the bacterial wall, such as β-lactam antibiotics and fosfomycin, has been described.



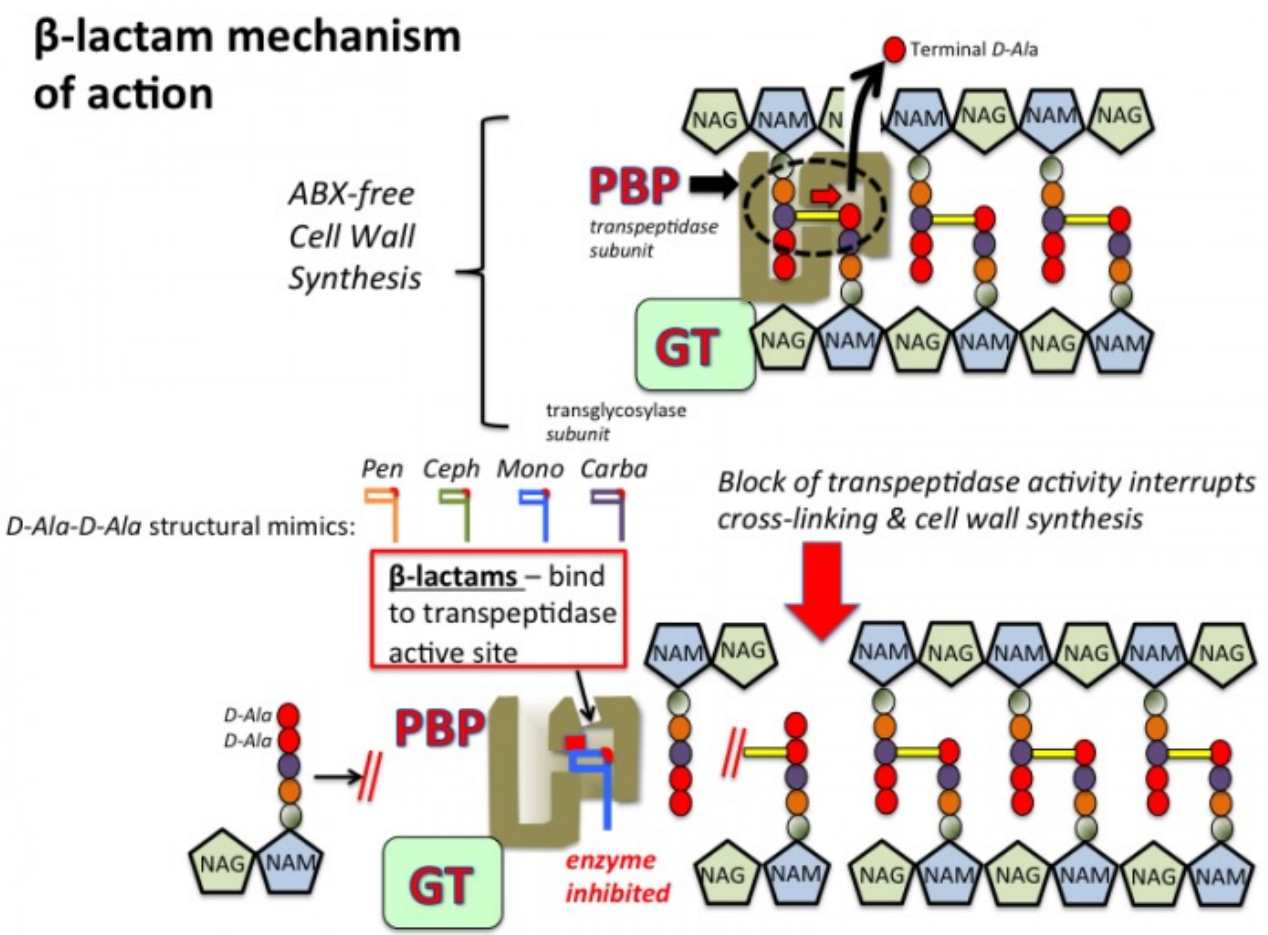
Rapid bactericidal activity

MoR

Lysine --> Electrostatic repulsión

Ceftaroline MoA

Cephalosporin with activity against PBP 2a and very active against *methicillin-resistant Staphylococci*



Resistance to beta-lactams→ Changes in PBP2A

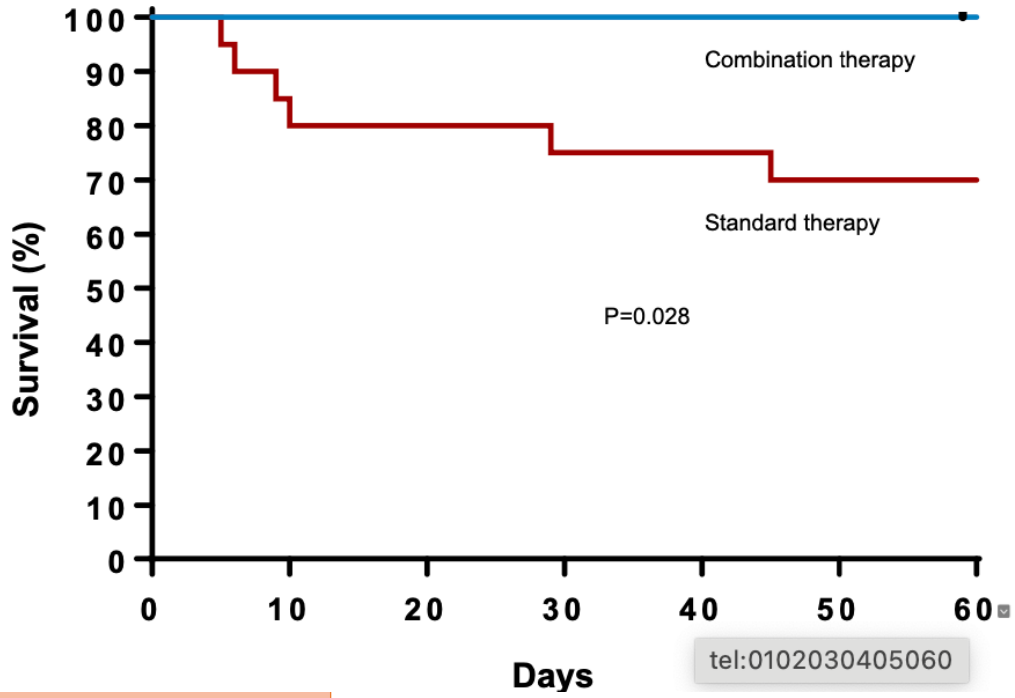
In vitro →The combination of **daptomycin and ceftaroline** has been effective in bacteremia caused by methicillin-resistant *S. aureus (MRSA).*

Outcomes. Primary outcomes examined were duration of bacteremia and in-hospital mortality. Secondary outcomes were later (60 and 90 day) mortality and length of hospital stay. **Serum interleukin-10 measurement.**

DAP + CTL 17
VAN 23
DAP 2

TABLE 4 Study outcomes

Outcome	Values by treatment type: Combination therapy	Monotherapy	*P* value
Mortality, *n* (%)			
In hospital	0 (0)	6 (26)	0.02
30 day	0 (0)	6 (26)	0.02
90 day	0 (0)	7 (30)	0.03
Bacteremia duration, median (IQR) days	3 (1.5, 5.5)	3 (1, 5.3)	0.56
Length of stay, median (IQR) days	11 (6, 14)	12 (8, 23)	0.24



It was observed an unanticipated in-hospital mortality difference of 0% (0/17) for combination therapy and 26% (6/23) for monotherapy (*P* □ 0.029), causing us to halt the study.

Geriak et al. AAC. May 2019

Potential mechanisms underlying advantages of combined therapy

- Beta-lactam reduction of cell wall cross-linking, **enhancing DAP to access to the cell membrane**
- **Synergy** of Beta-lactam with **endogenous cationic** host defense **peptides** against MRSA
- **Increased NLRP3 inflammasome** activation and IL1B-mediated bacterial clearance induced by altered peptoglycan syntetized by MRSA

Ceftobiprole

5th-generation, broad-spectrum cephalosporin blooks the transpeptidase activity of PBPs including PBP2a

S. aureus (MRSA, VISA)

CoNS (MRSE, VISE)

S. Pneumoniae MIC_{90} <0.5 mg/L

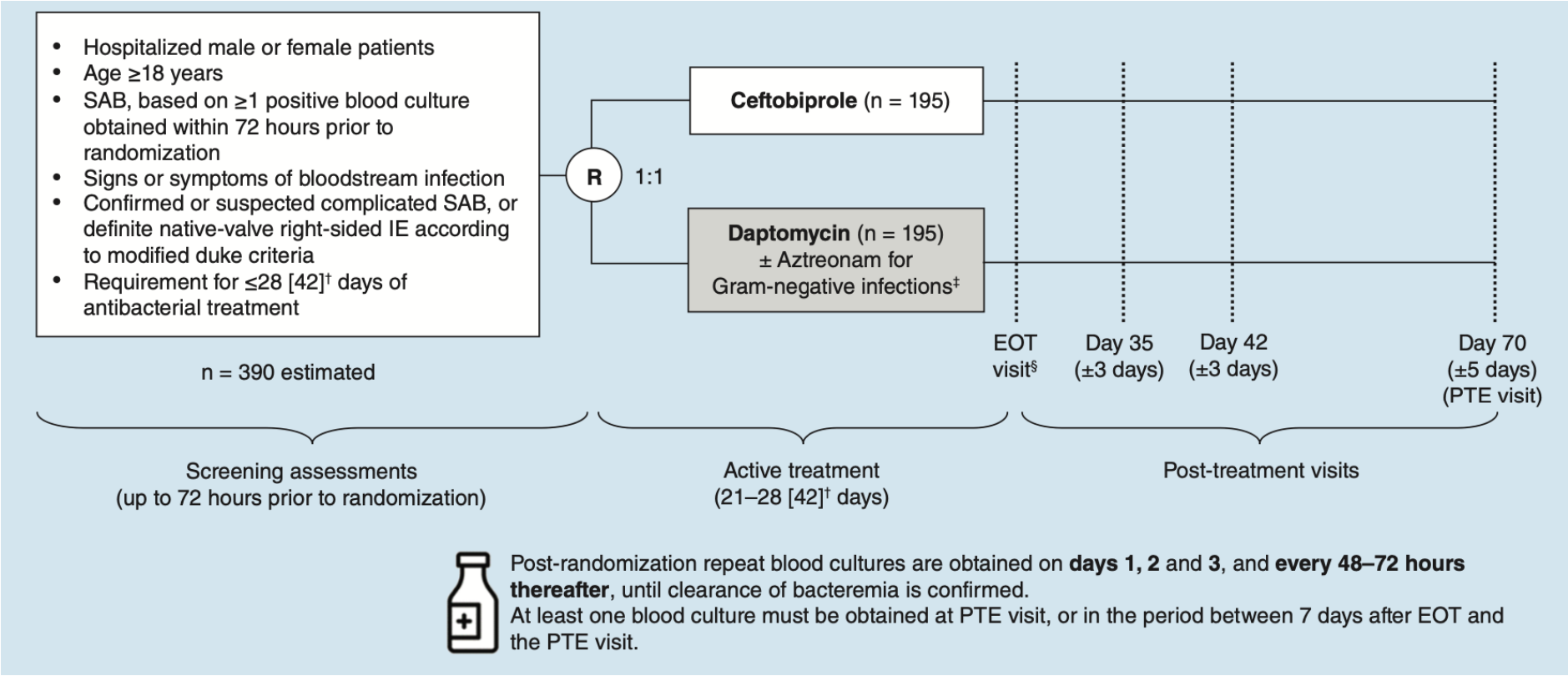
S. Betahemolytic MIC_{90} <0.5 mg/L

Moderate activity *E. faecalis* MIC_{90} 4 mg/L

P. Aeruginosa

Other gram negatives/anaerobic

FASE III TRIAL



This double-blind study will establish whether ceftobiprole < to daptomycin complicated SAB, including IE.

If noninferiority is established, ceftobiprole → important new treatment option against SAB (MSSA or MRSA).

Hamed et al. Future Microbiol 2020 Jan

CEFTAROLINA vs CEFTOBIPROL

MIC distributions, mode MICs and geometric mean MICs of ceftaroline and ceftobiprole for staphylococci

Organism (*n*)	Agent	MIC (mg/L)													Geometric mean MIC (mg/L)			
		0.002	0.004	0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	2008	2013	2017	2018
Bacteraemia																		
S. aureus (1884)																		
MRSA (234)	ceftaroline	—	—	—	—	—	—	—	6	81	137	10	—	—	0.54	0.35	0.48	0.48
	ceftobiprole	—	—	—	—	—	—	—	—	8	140	86	—	—	1.51	0.95	1.13	1.19
MSSA (1650)	ceftaroline	—	—	—	—	—	8	140	**1361**	111	30	—	—	—	0.3	0.22	0.25	0.25
	ceftobiprole	—	—	—	—	—	5	12	330	1182	113	8	—	—	0.95	0.66	0.68	0.68
CoNS (813)																		
methicillin- resistant CoNS (574)	ceftaroline	1	—	1	—	—	3	57	**276**	121	59	55	1	—	0.39	0.35	0.39	0.37
	ceftobiprole	—	—	—	1	—	—	—	6	118	**287**	107	54	1	1.2	0.92	1.15	1.17
methicillin- susceptible CoNS (239)	ceftaroline	—	—	—	6	29	**105**	80	18	1	—	—	—	—	0.09	0.08	0.07	0.07
	ceftobiprole	—	—	—	2	5	18	45	**131**	33	4	1	—	—	0.3	0.18	0.2	0.19

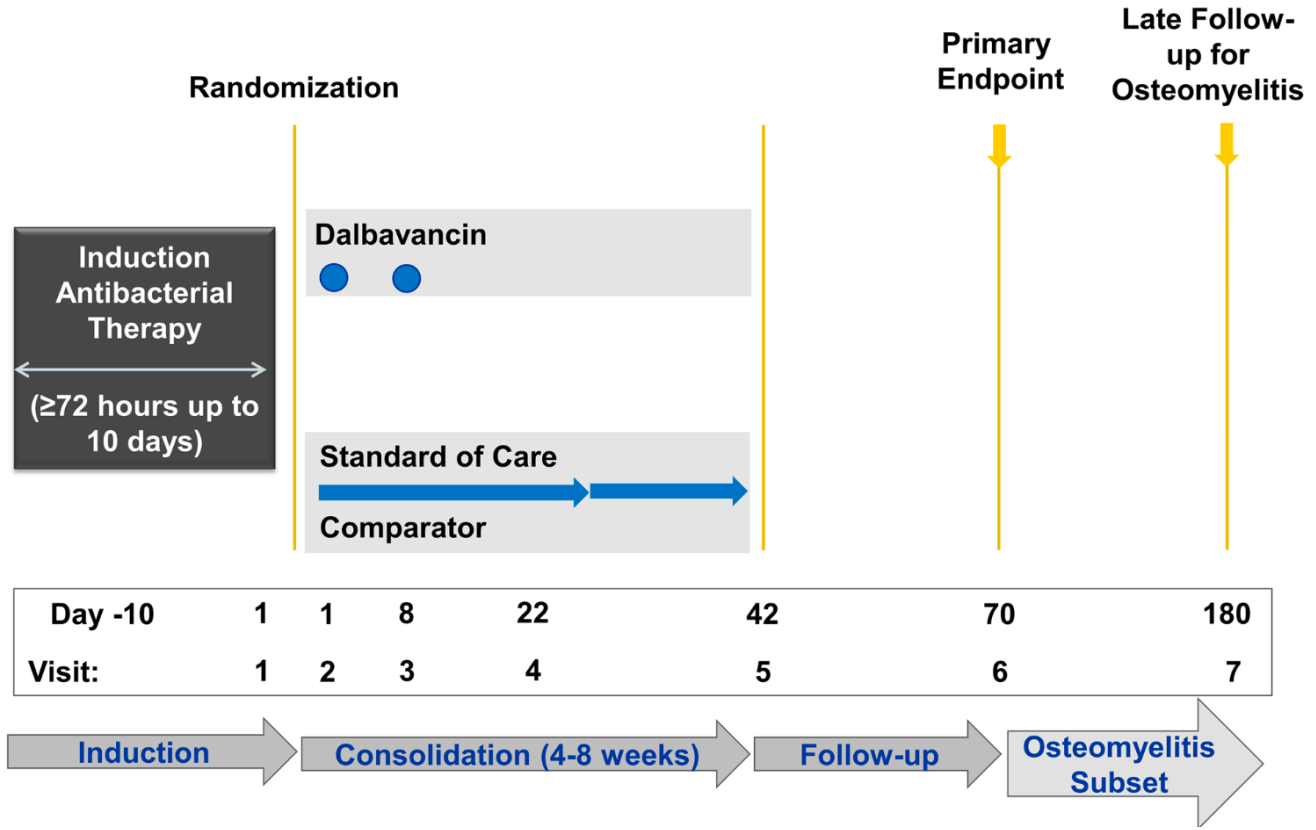
Ann Cardiol Angeiol (Paris) 2008 Apr;57(2):88-92.

Dalbavancin

Lypoglycopeptide. Block peptidoglycan syntesis. Time-dependent bactericidal activity, with a maximum when the concentration is four times higher than MIC. Long-active

Staphylococcus including
MRSA/MRSE
S pneumoniae
Enterococcus sp.
susceptible to vancomycin
Gram positive bacilli with
MIC_{90} of 0.12 mg/dl

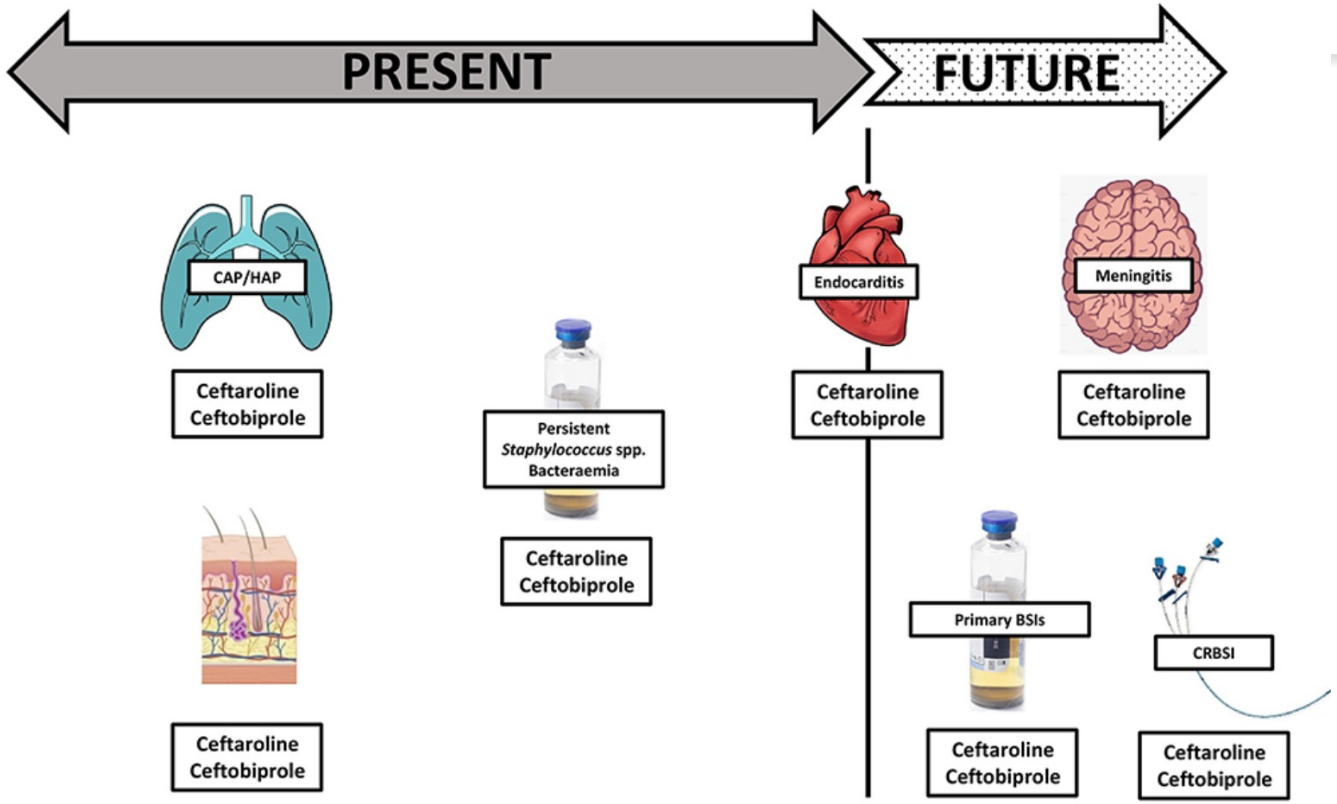
DOTS): study protocol for a phase 2b, multicenter, randomized, open-label clinical trial



Turner et al.Trials. 2022 May

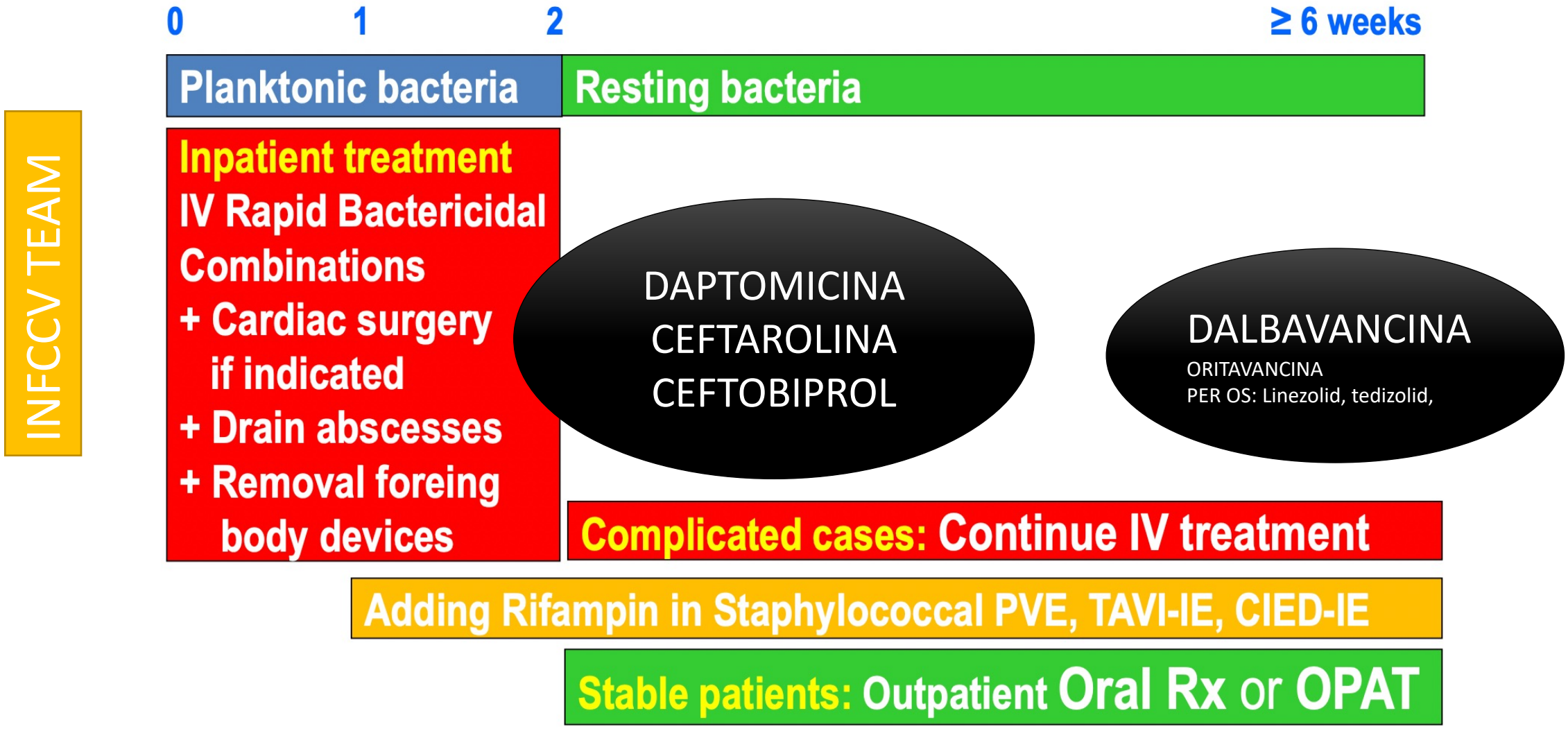
TAKE HOME MESSAGES →

THE CHALLENGE OF MDR and XDR GPC



Gram-positive spectrum only	Gram-positive and aerobic Gram-negative rods	Gram-positive, Gram-negative and *Bacteroides fragilis*
Dalbavancin	Ceftaroline	Moxifloxacin
Daptomycin	Ceftobiprole	PZ-601
Linezolid	Iclaprim	PTK 0795
Oritavancin	Gemifloxacin	Tigecycline
Quinupristin–dalfopristin		Tomopenem
Telavancin		

Future Antibiotic Treatment of Endocarditis



OPAT = Outpatient parenteral antibiotic therapy

Miro JM, SEICAV Madrid Nov. 16th 2019

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Thank you for your attention. Questions?

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