Cardiovascular infections

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CATALANA



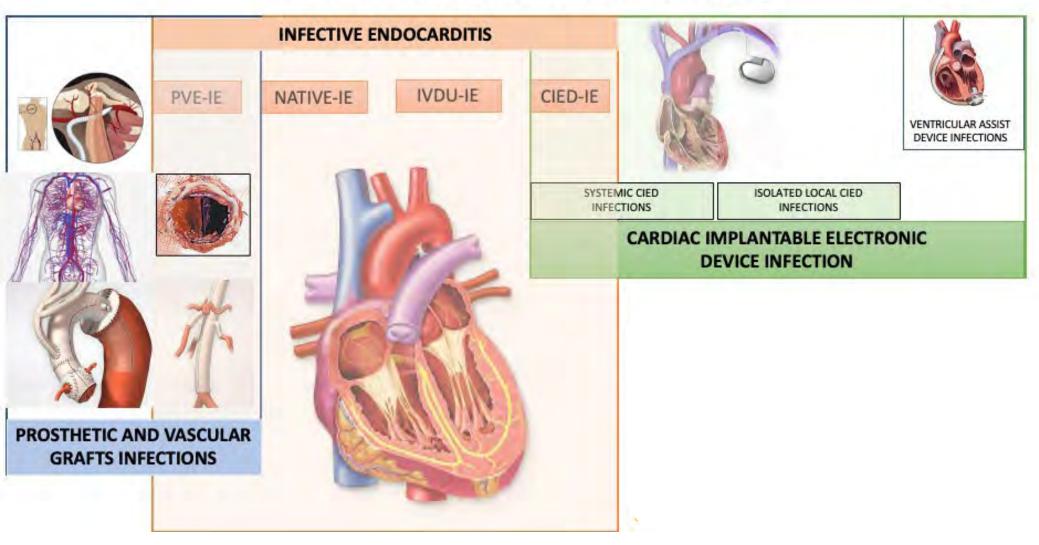






CARDIOVASCULAR INFECTIONS



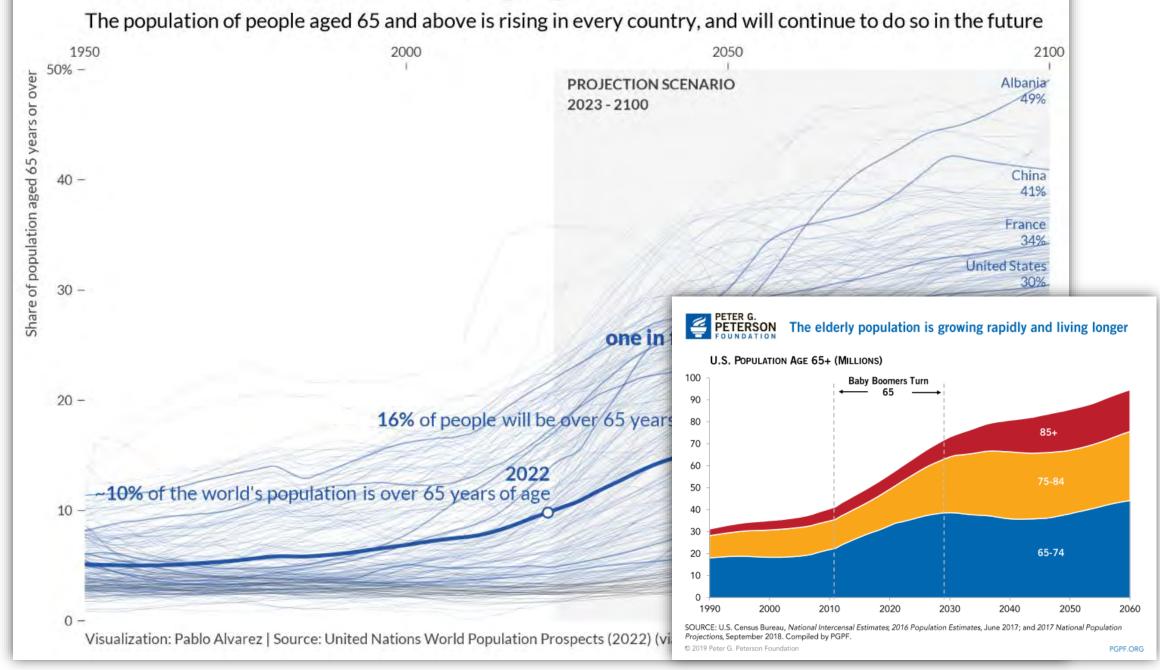


Abbreviations: PVE: prosthetic valve endocarditis; IVDU-IE: intravenous drug use related infective endocarditis; CIED IE: cardiac implantable electronic device infective endocarditis.

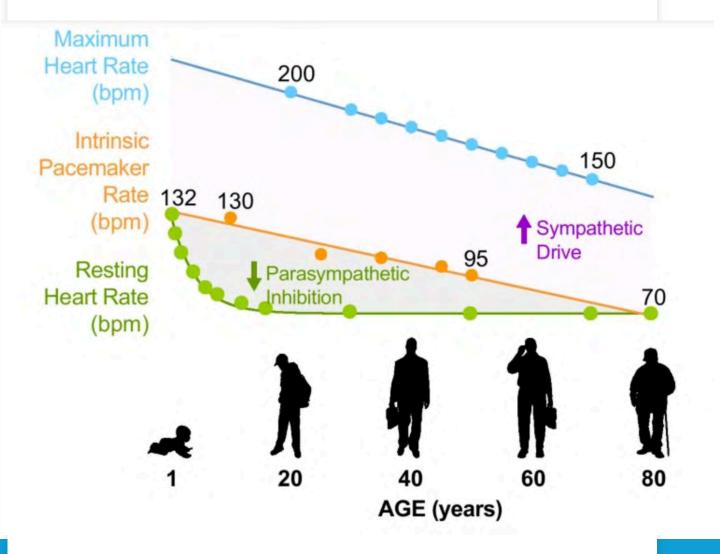


Infeccions dels dispositius d'electroestimulació cardiaca. A on estem?

The world's population is aging



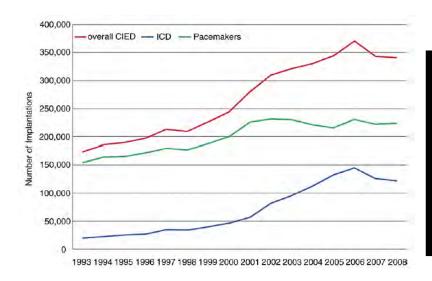
The world's population is aging



The burden of rising life expectancy is the growth in comorbidities, primarily cardiovascular diseases; therefore, the number of people requiring cardiac implantable electronic devices (CIEDs) has increased.

Trends in CIED infections

Number CIED implants



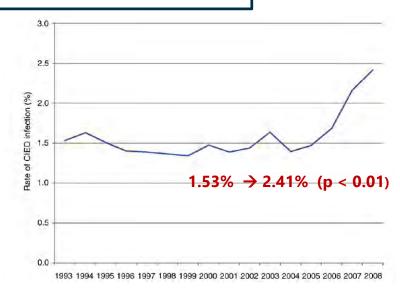
*CIED implantation increased by 96% from 1993 to 2008

Device complexity
Widening indications
Age / comorbidities
PPM > ICD > CRT

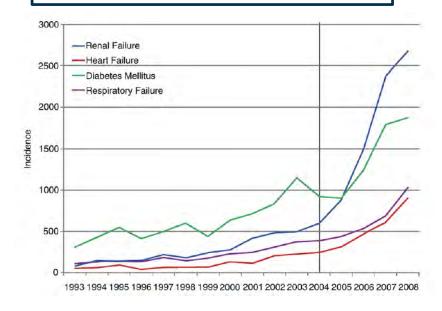


First-year post-implantation

Rate of CIED infection



Comorbidites in CIED infections



Comparison between ICE and EUROENDO cohorts

ICE registry 2000- 2006



registry
2016- 2018

ICE EURO-ENDO (2000-2006) (2016-2018) N=2781/3284 (85%) N=3116

IE Type		
- Native-IE	72%	59%
-	21%	31%
Prostnetic- IE		
- CIED-IE	7%	10%

¹Murdoch DR. Arch Intern Med 2009;169:463-73

²Habib G. EHJ 2019;5:202-207

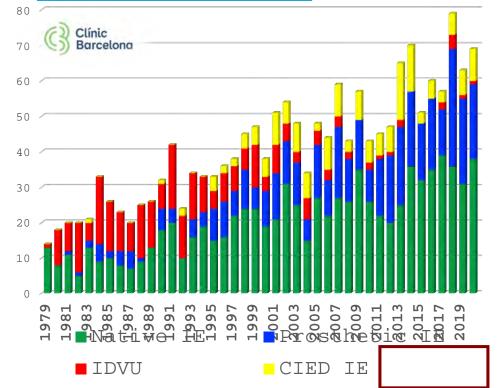
H. Clínic de Barcelona (1980-2020)

N = 1605

0.8 cases/1,000 admissions 6.3 cases/100,000 hab.

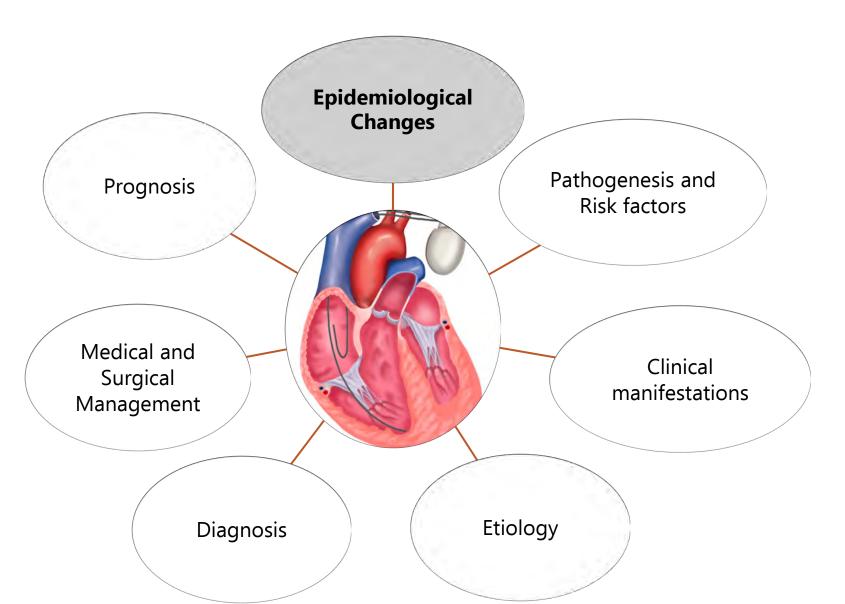


10% of all IE

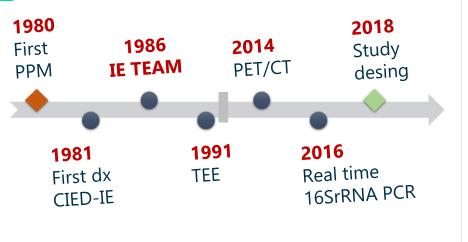


Mestres CA. 2015 Rev Esp

CIED INFECTIONS







Global analysis 40-year CIED-IE HCB cohort



Comparison between periods: **1981-2000** vs. **2001- 2020**

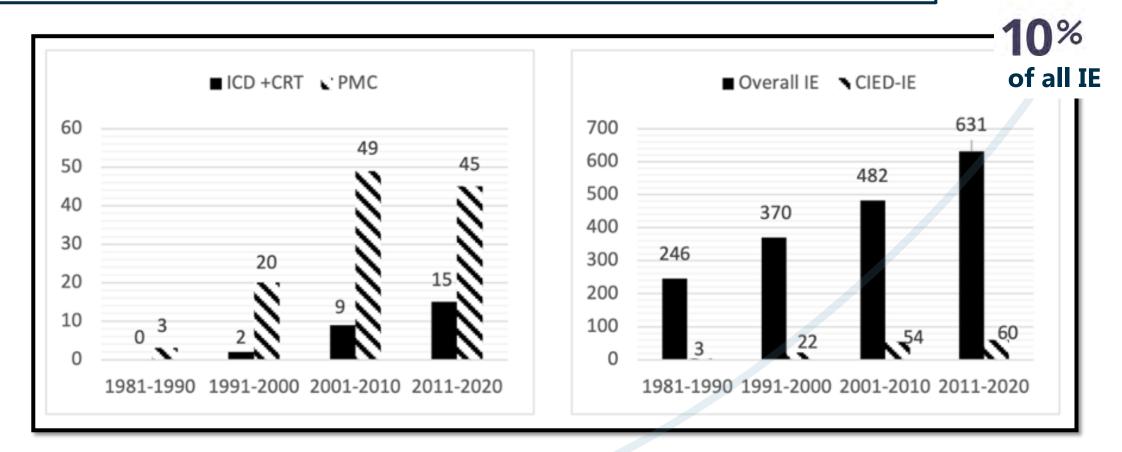
Comparison between the time presenting symptoms: early vs. late CIED-IE

Differences of CIED-IE depending on the **type of the device**

Survival analysis and predictors factors of one-year mortality



Proportion of CIED IE by type of CIED and compared with overall IE



TIME

40-year CIED IE cohort: comparison between periods

138 consecutive definite CIED IE

Nosocomial and
HA infections
Transfers
MR- CONS
E. faecalis

Variable	Total	1981-2000	2001-2020	P value
Variable	(N=138)	(N=25)	(N=113)	1 Value
Age, years (median, IQR)	70 (60-76)	63 (53-71)	71 (63-76)	<0.01
Nosocomial	19 (13.8%)	1 (4%)	18 (15.9%)	0.02
Transferred from other hospital	49 (35.5%)	2 (8%)	47 (41.6%)	<0.01
Charlson comorbidity index (Median IQR)	4.0 (3.0 – 6.0)	3.0 (2.0 – 4.0)	4.5 (3.0 – 6.0)	<0.01
Echocardiography				
Vegetation on device	138 (100%)	25 (100%)	113 (100%)	NA
Tricuspid valve vegetation	31 (22.5%)	7 (28%)	24 (21.2%)	0.49
¹⁸ FDG-PET/CT	29 (21%)	0	29 (25.7%)	<0.01
Microbiology				
S. aureus	46 (33.3%)	7 (28%)	39 (34.5%)	0.52
- MRSA	13 (9.4%)	1 (4%)	12 (10.6%)	0.18
Coagulase-negative Staphylococcus	62 (44.9%)	12 (48%)	50 (44.2%)	0.32
- MR-CoNS	15 (10.9%)	0	15 (13.3%)	<0.01
Enterococcus spp.	6 (4.3%)	0	6 (5.3%)	0.01

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40-year CIED IE cohort: comparison between periods

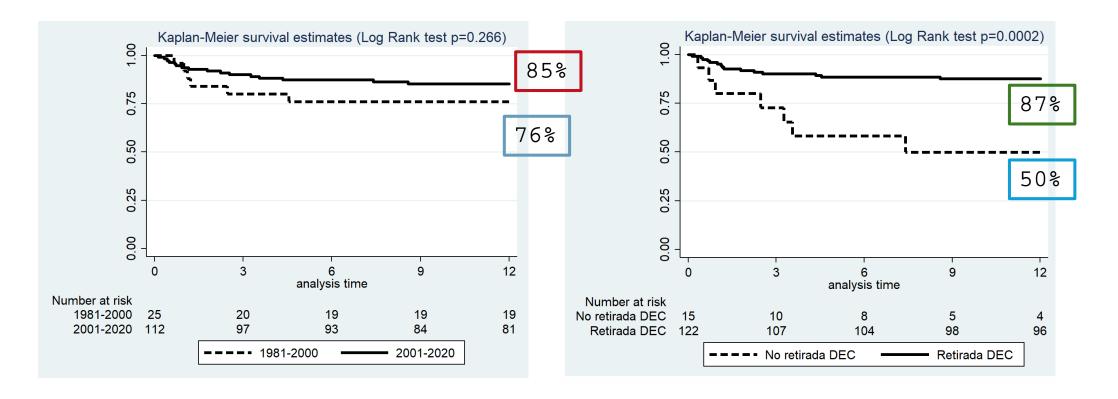
More complex infections

Variable	Total (N=138)	1981-2000 (N=25)	2001-2020 (N=113)	P value
Complications	75 (54.3%)	7 (28%)	68 (60.2%)	<0.01
Pulmonary embolism	12 (8.7%)	0	12 (10.6%)	<0.01
Treatment				
Removal of cardiac device system	123 (89.1%)	24 (96%)	99 (87.6%)	0.09
Interval diagnosis-removal	29.0	21.5	29.5	0.35
(median, IQR)	(20.0 – 42.0)	(18 – 46)	(23.0 – 42.0)	
Type of removal				
Traction	95 (77.2%)	19 (79.2%)	76 (76.8%)	0.79
Open surgery	28 (22.8%)	5 (20.8%)	23 (23.2%)	0.88
Reimplant	84 (68.3%)	16 (66.7%)	68 (68.7%)	0.85
In-hospital mortality	18 (13%)	5 (20%)	13 (11.5%)	0.32
One-year follow up				
Surgery	8 (5.8%)	3 (12%)	5 (4.4%)	0.26
Mortality	23 (16.7%)	6 (24%)	17 (15%)	0.33
Relapses	8 (5.8%)	2 (8%)	6 (5.3%)	0.65

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CIED-IE comparative survival between period 1981-2000 vs. 2001-2020

Differences in survival between removal or not of the device

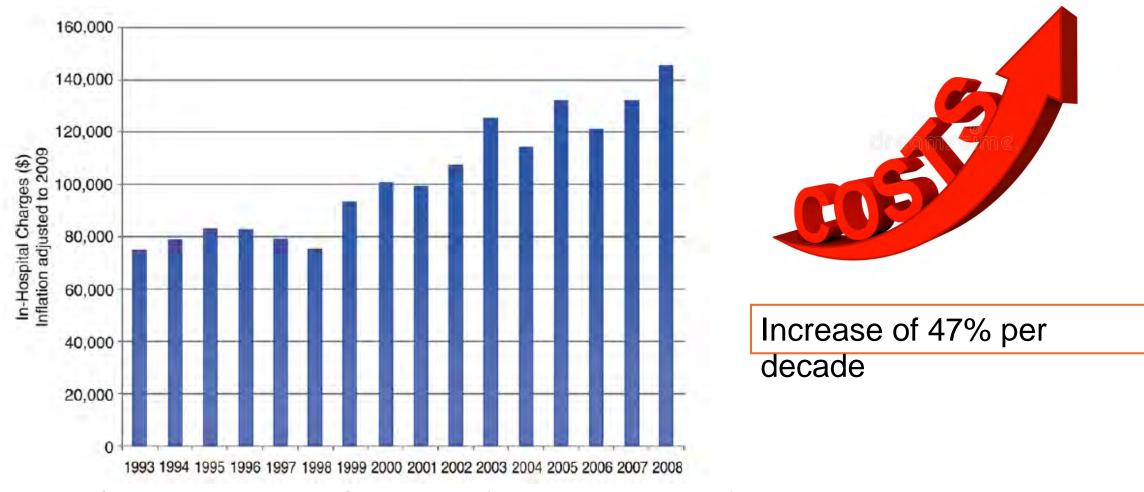


THELEASE TH the CIED implantation and CIED infection prevalence impact the Health-care system?



Update on the CIED infection burden

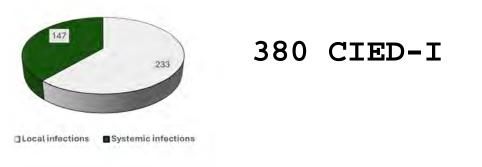
16-Year Trends in the Infection Burden for PM and ICD in the US: 1993 to 2008



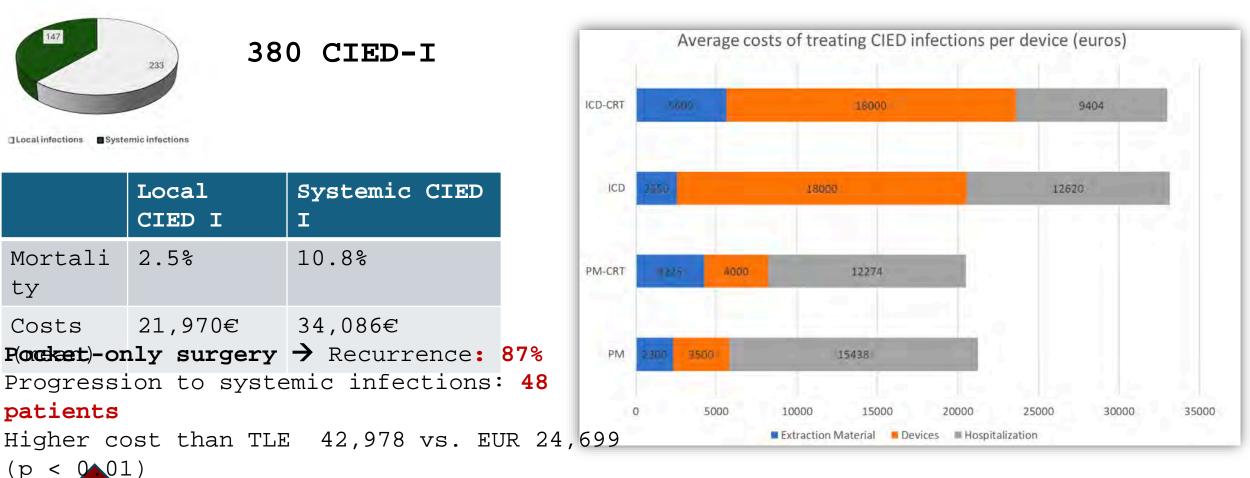
In-Hospital Charges Associated With CIED Infection (Inflation Adjusted to 2009)

Update on the CIED infection burden

Costs of CIED Infections According to the Therapeutic Approach



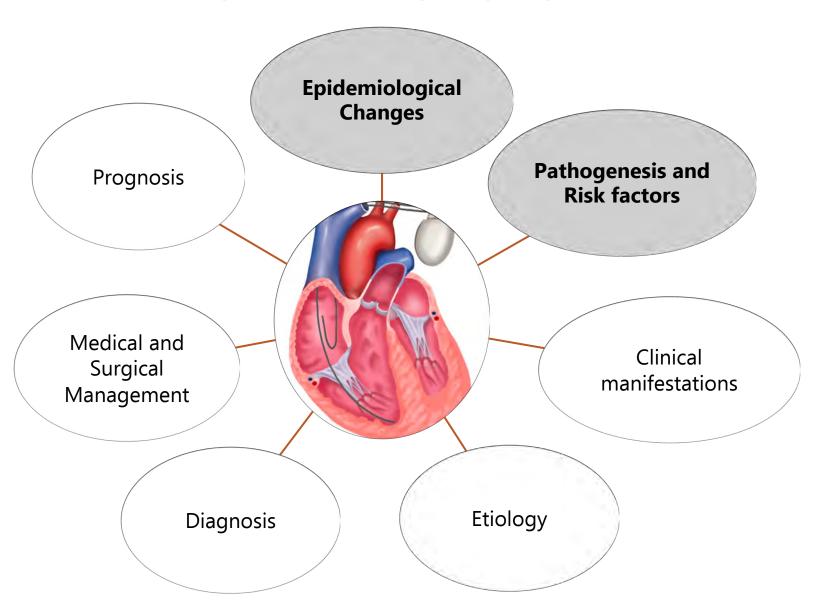
	Local CIED I	Systemic CIED			
Mortali ty	2.5%	10.8%			
	21,970€ aly surgery	34,086€ → Recurrence:	87%		
Progression to systemic infections: 48 patients					



(p < 0.01)Costs depends on type of treatment and length of hospitalization.

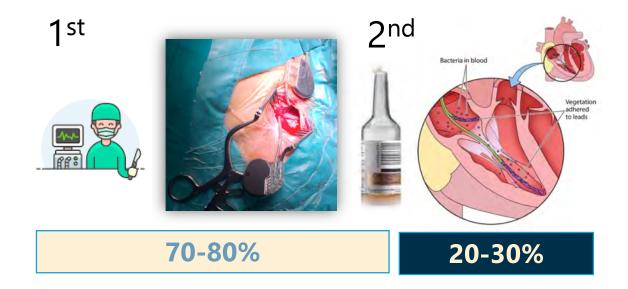
Complete device removal is always the most effective and cost-saving strategy

CIED INFECTIONS



Pathogenesis

Two major mechanisms



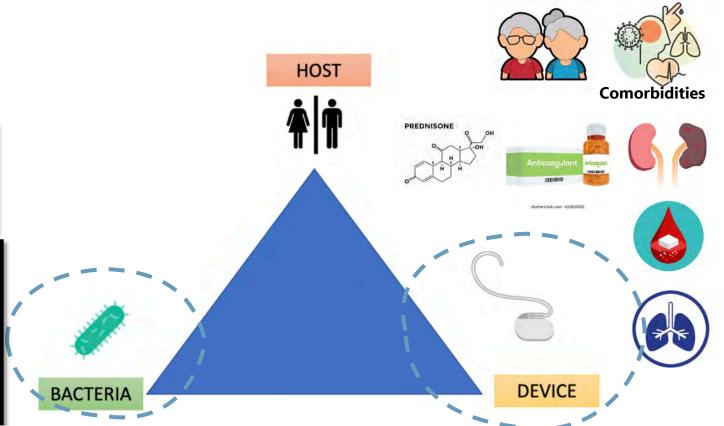


Device factors

- •>2 leads
- · ICD/CRT
- Heart disease/dysfunction

Procedural factors

- Early reintervention
- Temporary pacing
- Fever ≤ 24 hours before implantation
- Unrecognized bacteremia or focus of infection
- Prolonged procedure duration

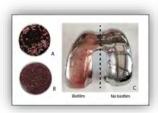


Risk factors **Evaluation of risk factors for CIED infection** Modifiable Non-modifiable Device-lead-related factors Procedure-related factors Device-lead-related factors Patient-related factors Procedure-related factors Patient-related factors Lead repositioning **Abdominal pocket** End-stage renal disease Device type: CRT or ICD Fever prior to implantation Prolonged procedure Device replacement/upgrade Corticosteroid use More than 2 leads Hematoma Skin disorders Renal failure Abandoned / complex route leads Prior procedure(s) Heparin bridging History of device infection **Dual chamber device** Inexperienced implanter Oral anticoagulants Presence of epicardial leads Temporary pacing wire Heart Failure NYHA > II Malignancy Diabetes mellitus Reassess indications for primary implantation, reoperation or re-implantation of a new device following lead extraction Administer preprocedural Reduce risk by taking action on modifiable risk factors antibiotic prophylaxis as recommended Replace Experienced OAC temporary Limit Follow operator Postpone uninterrupted Evaluate Ishortens pacing by number of outlined Limit procedure if Treat any need to use procedure Antiplatelets surgical field number of external pacing persons in fever or comorbidity duration & paused 1 w antibacterial Consider epicardial pacing, leadless preparation operating IV lines reduces lead or drugs in infection prior surgery /techniques envelopes dislodgement risk) room pacing, subcutaneous ICD non-dependent if possible patient

Biofilm: the major cause of medical device-associated infections







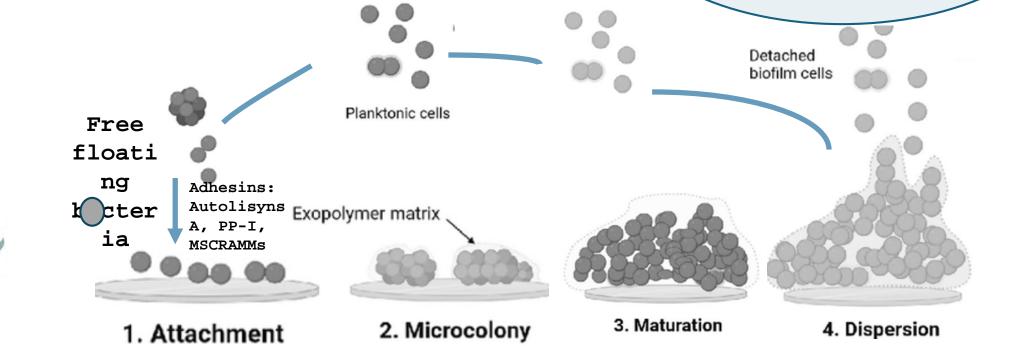












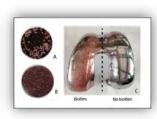


Cardiac implantable electronic device

Biofilm: the major cause of medical device-associated infections

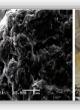








Planktonic cells







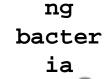


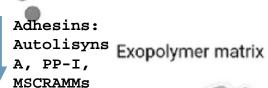










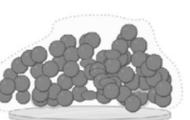








Detached biofilm cells







4. Dispersion

Treatment Avoid the spread of infection. Prevent complicatio

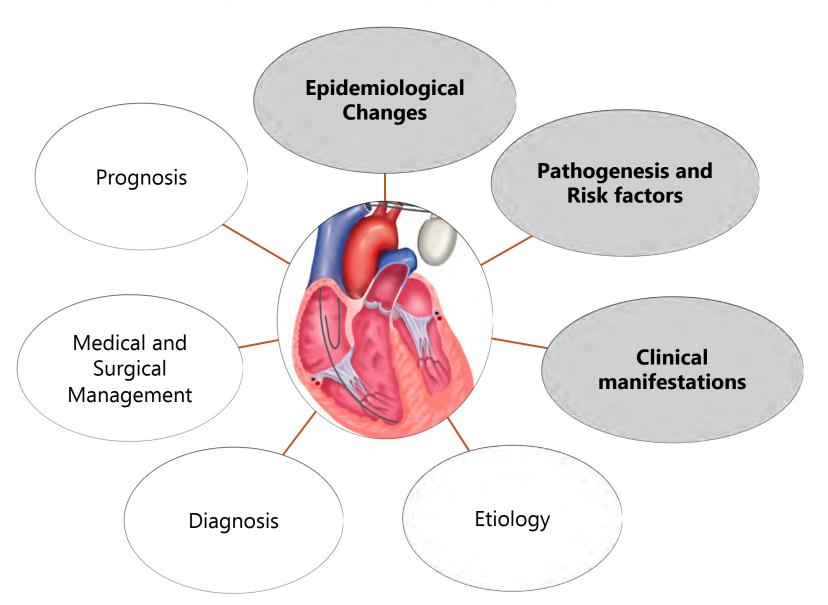
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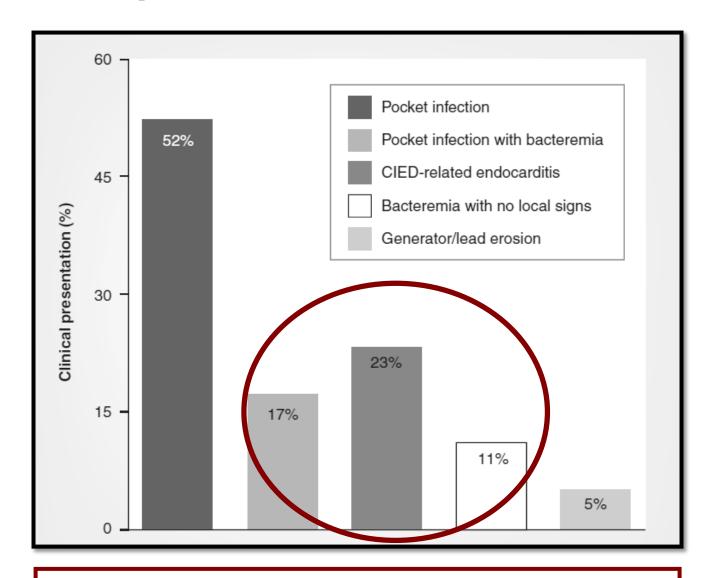
1. Attachment



CIED INFECTIONS



Clinical presentation of CIED infections

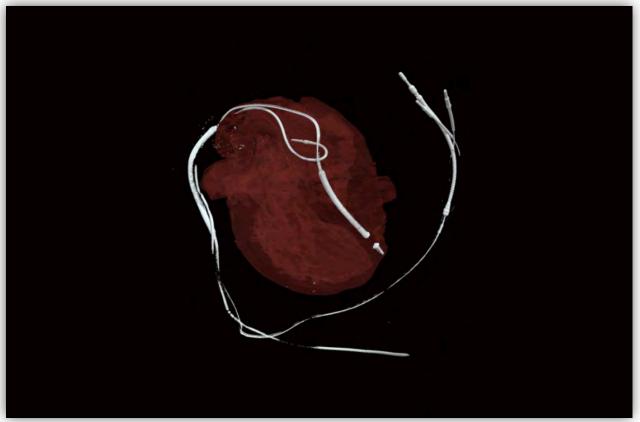


>50% CIED infections are high risk infections!



Clinical presentation of CIED infections





70-80% from local source - pocket 20-30% hematogenous spread

Staphylococcus aureus bacteriemia in CIED patients

3m - early infecti



Population: 87 257 Danish patients (18-99) y/o undergoing first cardiac implantable electronic device (CIED) implantation between 2000 and 2020 Pacemaker n= 66 180; ICD n= 13 504; CRT-P/D 7573.

Median age 75 [IQR 66-82], 62.6 % male sex

METHODS

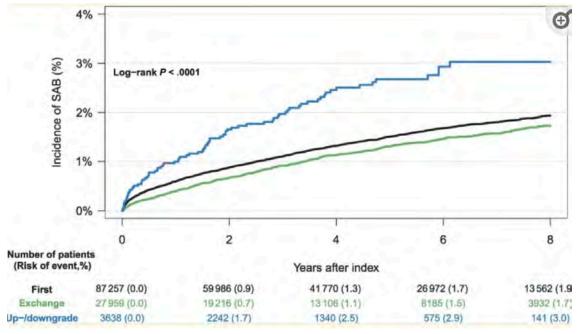
Nationwide Danish register study, crosslinking administrative registers and clinical quality databases. Study cohort obtained from *The Danish Pacemaker* and *ICD Register*. Primary outcome identified from *The National Danish* Staphylococcus aureus Bacteraemia Database



Primary Outcome Measure: Firsttime Staphylococcus aureus bacteremia after CIED implantation



Secondary Outcome Measure: Identification of risk factors associated with SAB



1,366 patients (1.6%)

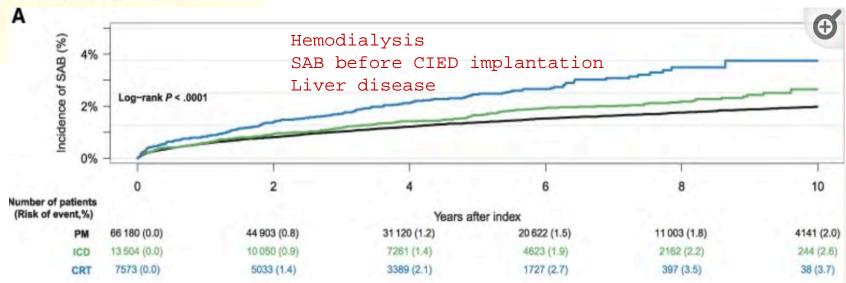
developed **SAB** 10-year absolute risk

of SAB: **PM**: 2.0%

(1.98-2.18)

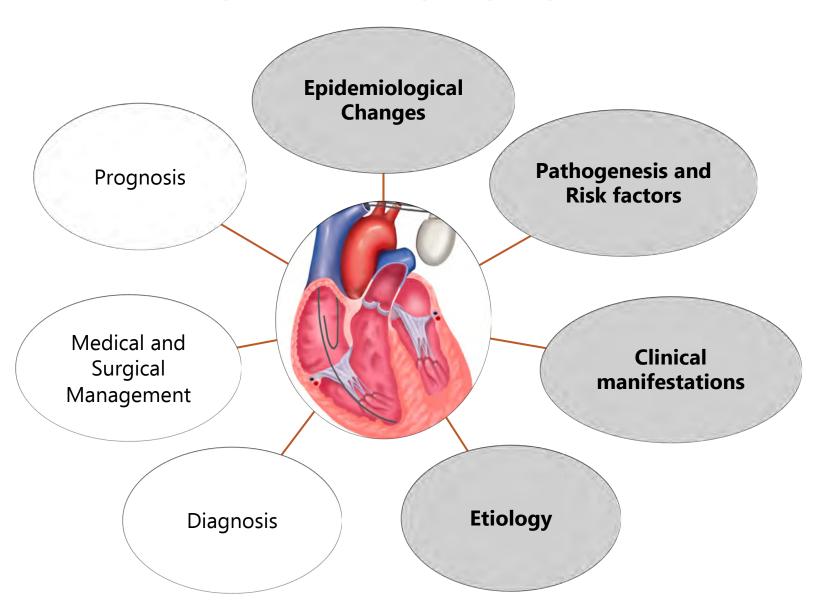
ICD: 2.6% (2.2%-3.1%)

CRT: 3.7% (3.0%-4.5%)

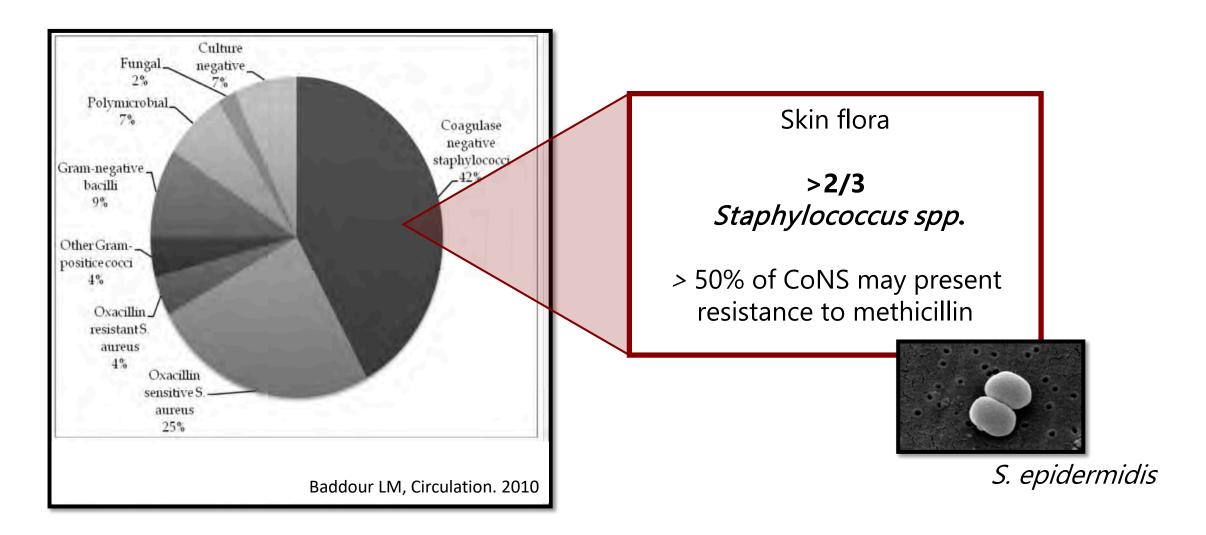


Bengtsen KH, OFID. 2024 Sep 9;11(9):ofae515.

CIED INFECTIONS



Etiology of <u>CIED infections</u>



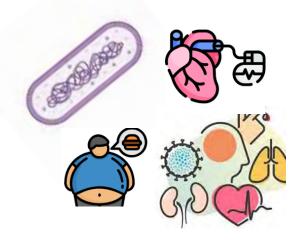
Etiology of CIED Infective endocarditis

	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		200 700 4			200	2.00
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)	9.3
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)	0.03
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)	0.00
Enterococcus spp.	230 (12.7)	142 (13.2)	5 (9.6)	77 (15.3)	6 (3.6)	0.00
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	Control of the contro	Secret Lines	1,004	-7-04/775		

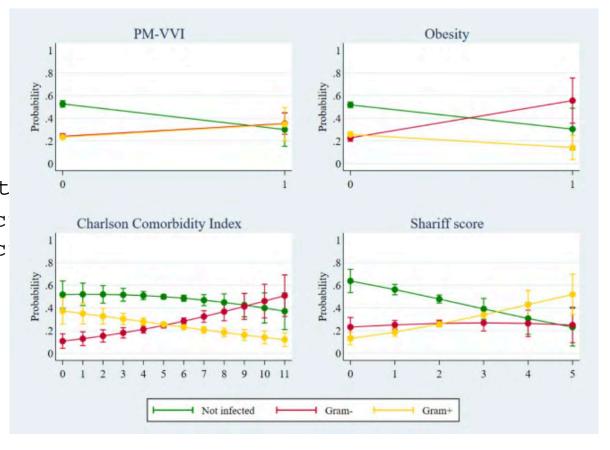
Gram-negative CIED infection: CarDINe Study



Multicentric observational st 236 p 59 with GNB-CIED infec 59 with GPB-CIED infec 118 without infection

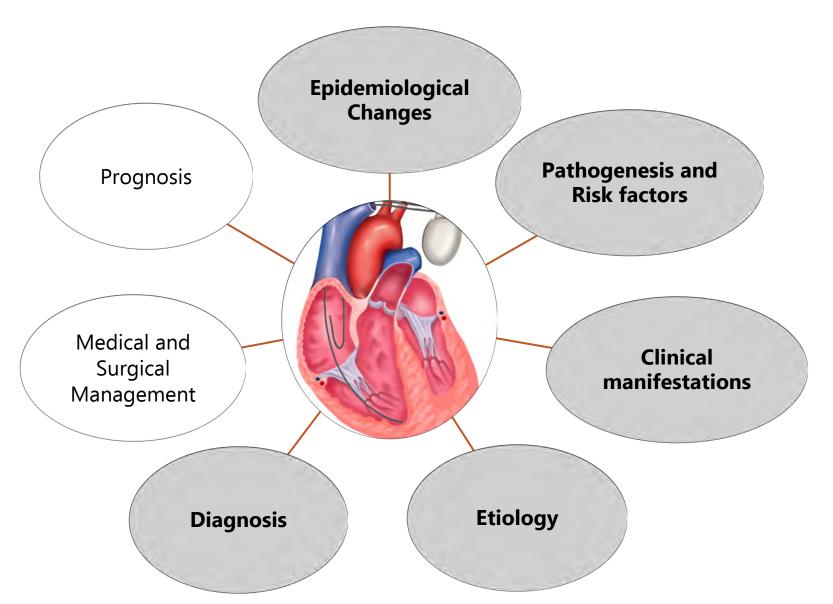


Risk factors for GNB-CIED infection



Increased mortality (180 days): HR 1.842 (P = 0.067)

CIED INFECTIONS



Circulation

AHA SCIENTIFIC STATEMENT

Update on Cardiovascular Implantable Electronic Device Infections and Their Prevention, Diagnosis, and Management: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovascular Infectious Diseases

Larry M. Baddour, MD, FAHA, Chair; Zerelda Esquer Garrigos, MD; M. Rizwan Sohail, MD; Eva Havers-Borgersen, MD; Andrew D. Krahn, MD; Vivian H. Chu, MD; Connie S. Radke, MSN, NP; Jennifer Avari-Silva, MD, FAHA; Mikhael F. El-Chami, MD; Jose M. Miro, MD, PhD; Daniel C. DeSimone, MD, Vice Chair; on behalf of the American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young (Young Hearts); and Council on Clinical Cardiology

Baddour LM. Circulation. 2024 Jan 9;149(2):e201-e216.

J Antimicrob Chemother 2015; **70**: 325–359 doi:10.1093/jac/dku383 Advance Access publication 29 October 2014 Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE)

Sandoe JA. J Antimicrob Chemother. 2015 Feb;70(2):325-59.



ESC GUIDELINES

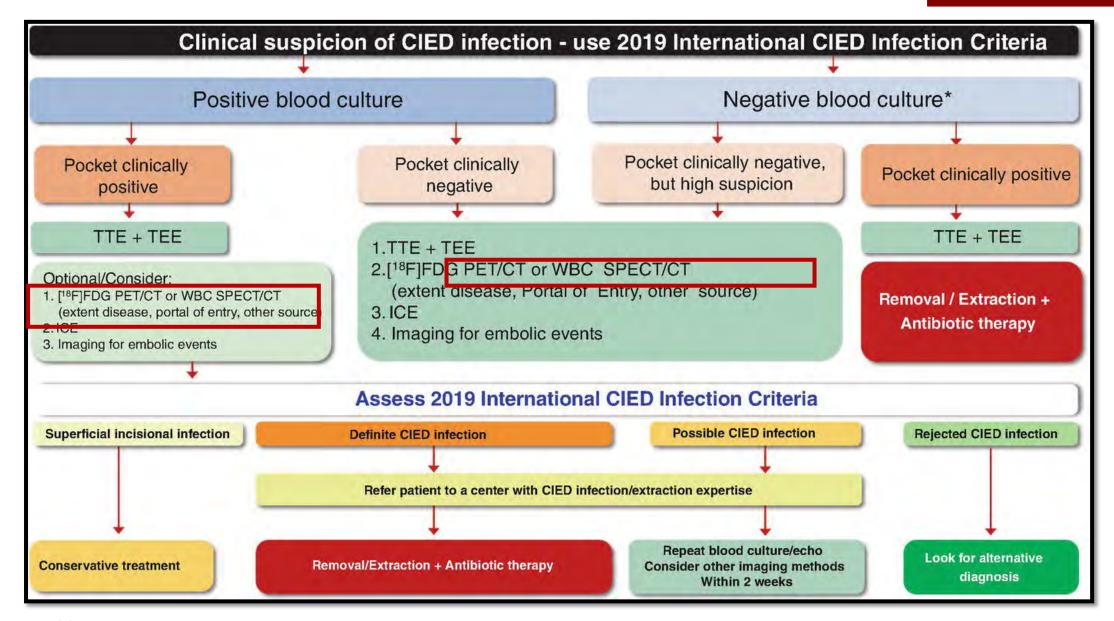
2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

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Authors/Task Force Members: Victoria Delgado **, (Chairperson) (Spain), Nina Ajmone Marsan **, (Task Force Co-ordinator) (Netherlands), Suzanne de Waha*, (Task Force Co-ordinator) (Germany), Nikolaos Bonaros (Austria), Margarita Brida (Croatia), Haran Burri (Switzerland), Stefano Caselli (Switzerland), Torsten Doenst (Germany), Stephane Ederhy (France), Paola Anna Erba ** (Italy), Dan Foldager (Denmark), Emil L. Fosbøl (Denmark), Jan Kovac (United Kingdom), Carlos A. Mestres (South Africa), Owen I. Miller (United Kingdom), Jose M. Miro ** (Spain), Michal Pazdernik (Czech Republic), Maria Nazarena Pizzi (Spain), Eduard Quintana ** (Spain), Trine Bernholdt Rasmussen (Denmark), Arsen D. Ristić (Serbia), Josep Rodés-Cabau (Canada), Alessandro Sionis (Denmark)
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Delgado V. Eur Heart J. 2023 Oct 14;44(39):3948-4042



Innovations in Imaging: ¹⁸F-Fluorodeoxyglucose PET/CT for Assessment of Cardiovascular Infection and Inflammation

Pathology		Sensitivity	Specificity	Summary	
	Infective endocarditis	PVE	86% (7)	84% (7)	Combining ¹⁸ F-FDG PET with CT angiography improves diagnostic performance and helps detect peri-prosthetic and peripheral complications
		NVE	31-36% (7)	98-99%(7)	Emerging use – limited sensitivity due to small vegetations; may have a role in assessing extracardiac infection
		Transcatheter valve infection	83% (34)	-	Increasing utility in TAVI, particularly when combined with CT angiography
	Cardiac implan infection	ted electronic device	Pocket infection: 96% (38); Lead involvement: 97% (38)	Pocket infection: 97% (38); Lead involvement: 83% (38)	Utility is superior for pocket infection compared to lead involvement
	LVAD infection		95% (50)	91% (50)	Promising role of ¹⁸ F-FDG PET/CT as many components of the LVAD are not assessed by echocardiography
Cardiovascular Inflammation	Cardiac sarcoidosis		84%(62)	83%(62)	Quantification of inflammation may provide added value for diagnosis and monitoring of disease progression and response to therapy
	Large vessel vasculitis		76% (83)	93% (83)	Role in patients with symptoms of large vessel vasculitis or fever/inflammation of unknown origin

Abbreviations: ¹⁸F-FDG, ¹⁸F-Fluorodeoxyglucose; CT, computed tomography; LVAD, left ventricular assist device; NVE, native valve endocarditis; PET, positron emission tomography; PVE, prosthetic valve endocarditis; TAVI, transcatheter-aortic valve implantation

PET's usefulness is not well characterized

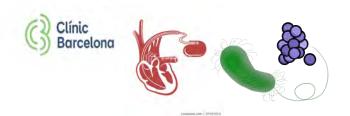
	Local	Systemic infection		
	infection			
Mahmood⁵	N=66	N=78		
Sensitivity	96%	76%		
Specificity	97%	83%		
Jerónimo ⁶	N=14	N=13		
Sensitivity	72%	38.5%		
Specificity	95.6%	98%		
Bensihmon ⁷	N=5	N=10		
Sensitivity	100%	60%		
Specificity	100%	100%		
Cautela ⁸	N=15	N=13		
Sensitivity	86%	31%		
Specificity	100%	62%		
	Sn 72-100%	Sn 30-60%		
	Sp 96-100%	Sp 62-100%		

The topographical lead segment has <u>not</u> been studied.

PROGNOSIS

What's new on CIED infections and PET/CT

Retrospective case-control study (2014 – 2021) \rightarrow 54 cases and 54 controls*









Cases (definite CIED infection diagnosis)

- Local infection (pocket +/- SC lead) → local signs of infection and/or device positive cultures
- Systemic infection (EV-lead or IE) → positive blood or lead cultures w/wo vegetations on TEE

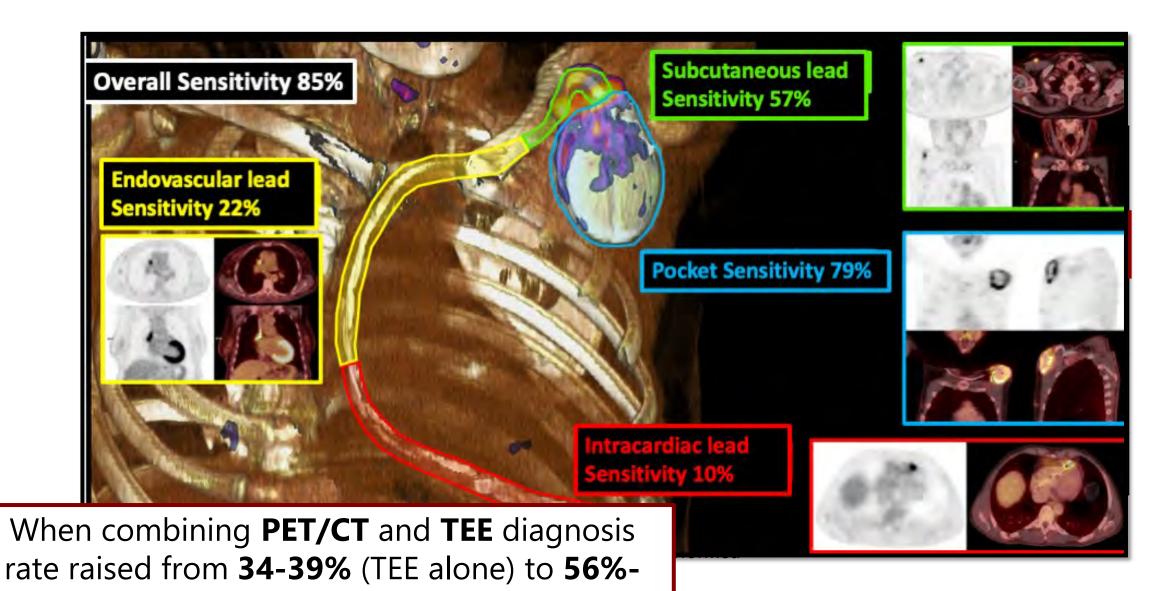
Controls (patients without CIED infection)PET done for other reasons (neoplasms)

* Matched by gender, similar age, calendar year and CIED type

Primary endpoint → PET accuracy (Sn, Sp, PPV, NPV) on each topographical region **Secondary endpoints** → Comparison with TEE, SUVmax (ROC curve), time between device implantation and PET and time since ATB and PET, bone marrow and spleen uptake, role in the follow up.

What's new on CIED infections and PET/CT

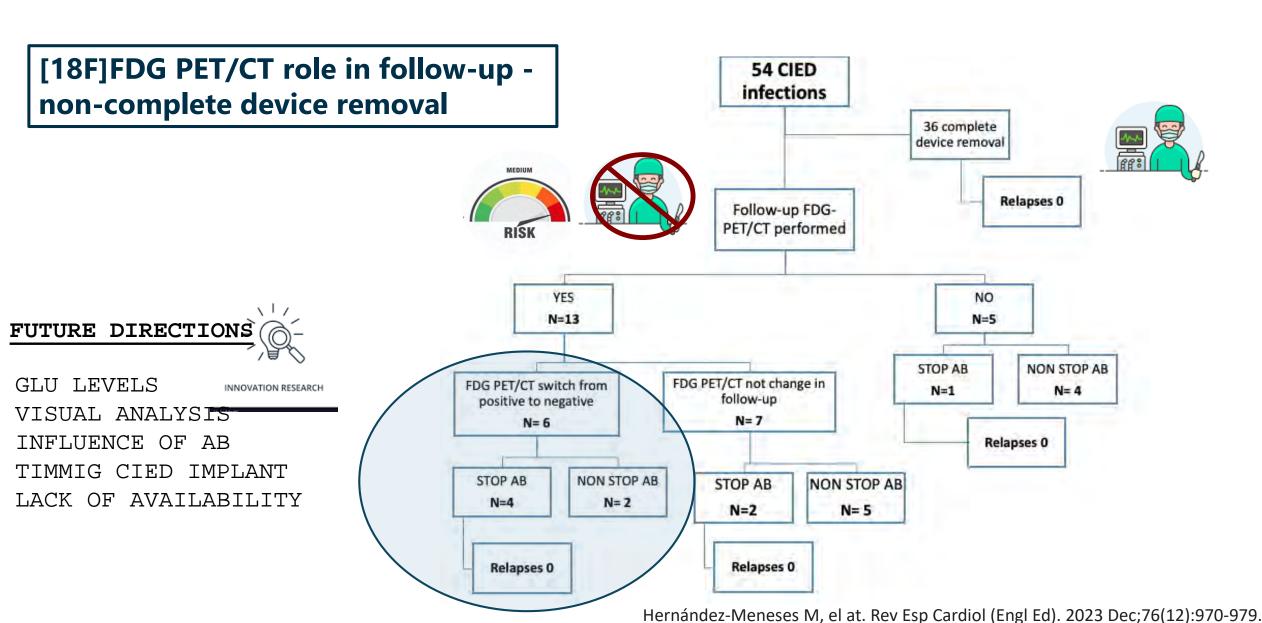
67% (both).



lez-Meneses M, el at. Rev Esp Cardiol (Engl Ed). 2023 Dec;76(12):970-979.

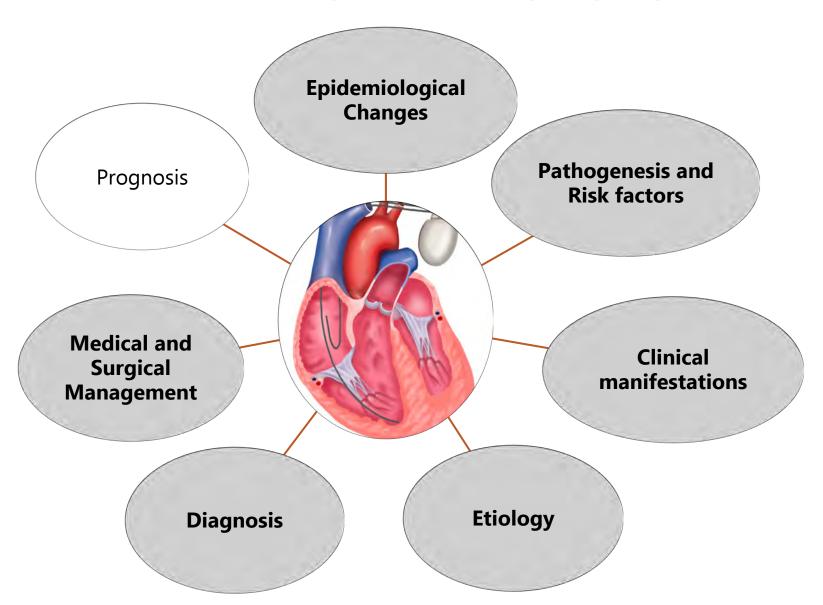


What's new on CIED infections and PET/CT

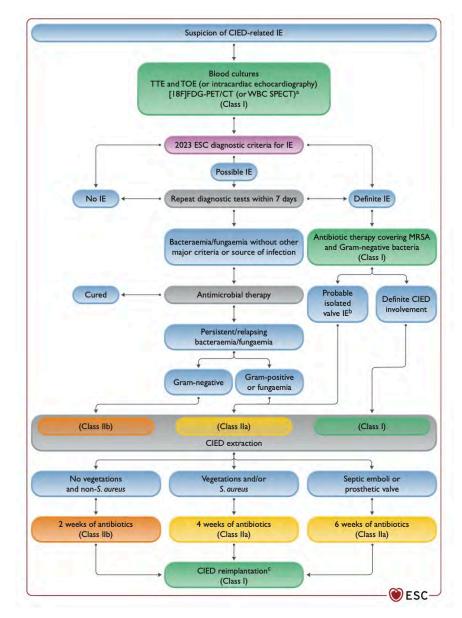


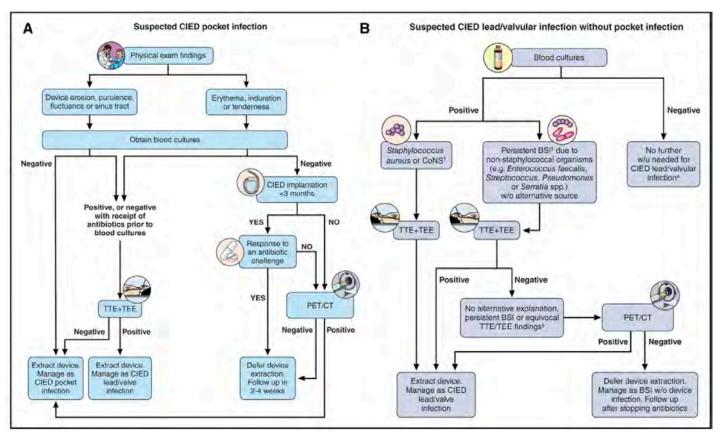


CIED INFECTIONS



What's new in CIED infection management?



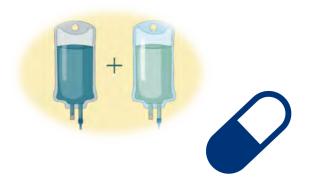


Baddour LM. Circulation. 2024 Jan 9;149(2):e201-e216.

Delgado V. Eur Heart J. 2023 Oct 14;44(39):3948-4042

Medical and surgical management





Antibiotics + Device Removal



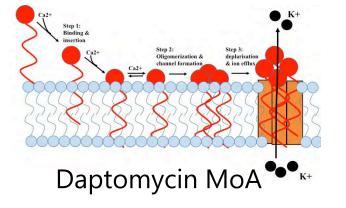


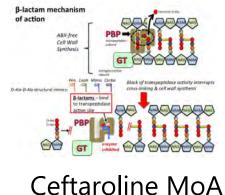
But AB treatments have not changed over 20 years!!

Guidelines AHA, ESC and EHRA consensus

Vancomycin/gentamicin-based AB suboptimal efficacy toxicity.

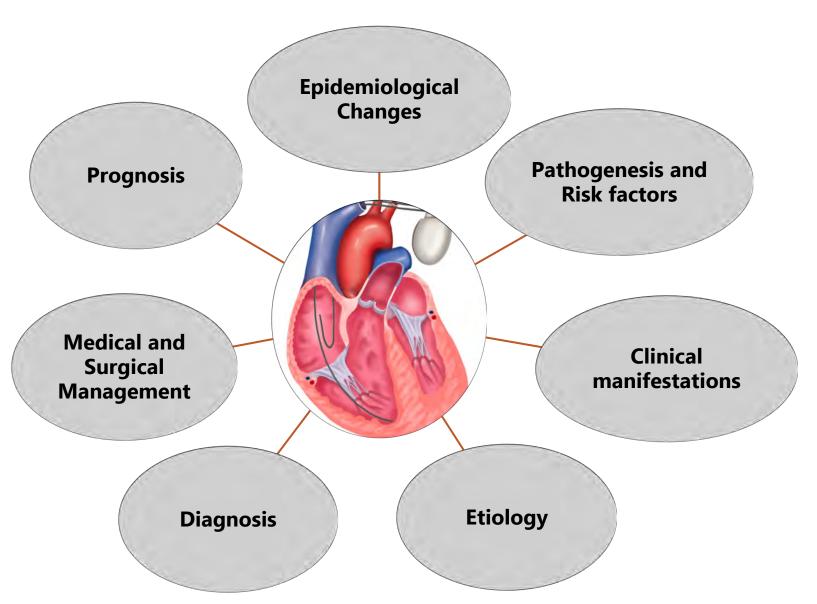
New antibiotics have not been studied:







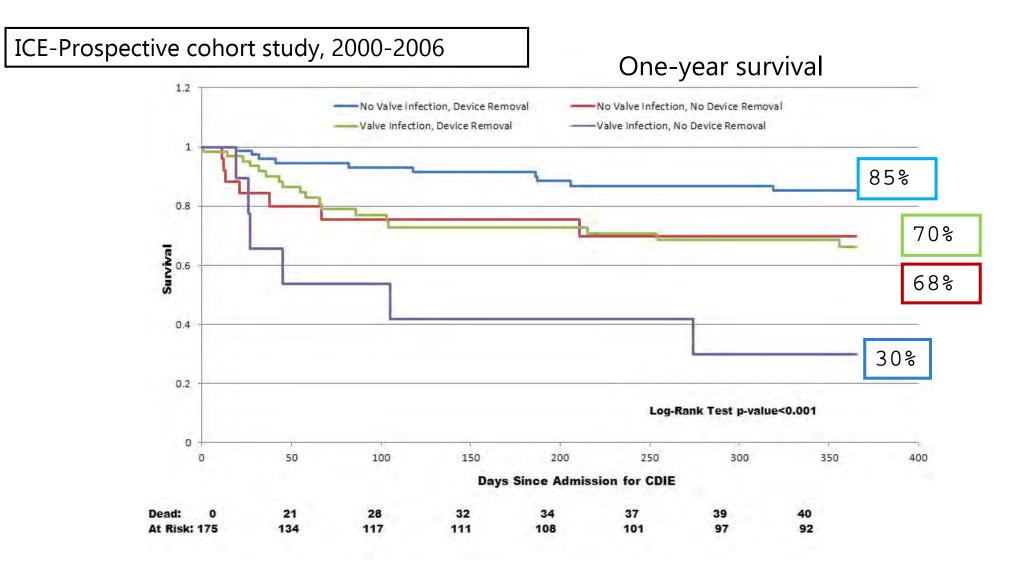
CIED INFECTIONS



Prognosis in CIED infections







Non-complete device removal?

Mayo Clinic cohort study, 2005-2015

660 CIED infections

48 (7%) non-complete removal

Chronic antimicrobial suppresion (CAS) therapy 7%

RELAPSES: 18%

IN-HOSPITAL MORTALITY: 25%

ONE-YEAR MORTALITY: 44%

CAS-Toxicity

(rash 9%, C. diff

pancreatitis 3%)

18% developed CIED relapse:

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

MEDIC cohort study, 2009-2012

443 CIED infections.

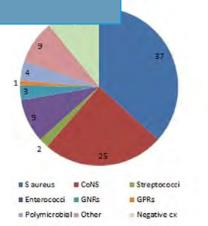
RFI ADSFS: 22%

127 (29%) non-complete removal

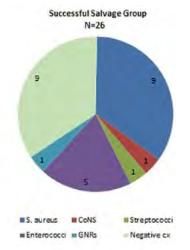
Chronic antimicrobial suppresion (CAS) therapy **29%**

Antibiotics Duration? Follow-up?

ORTALITY: 30% TALITY: -



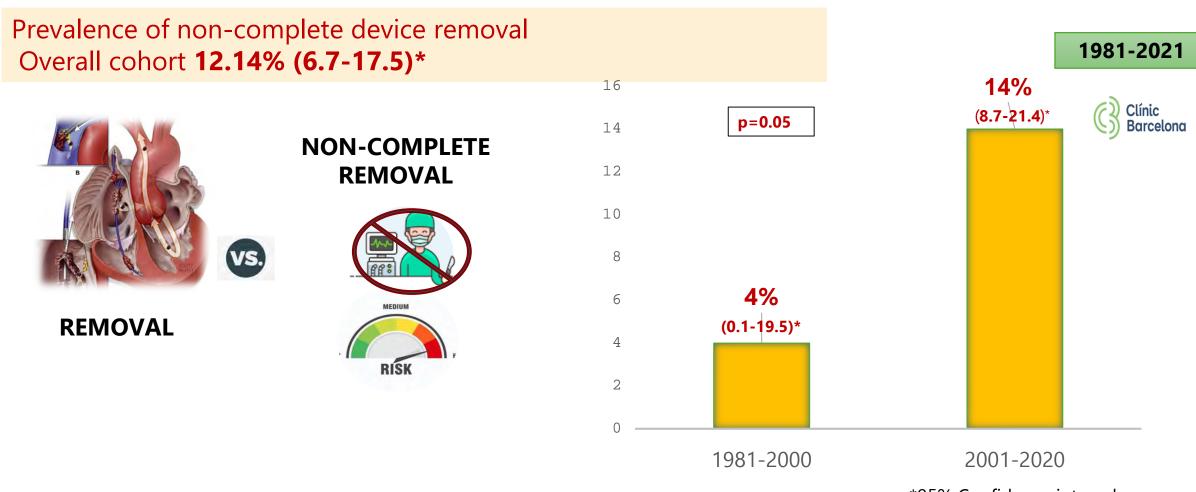
Group



Non-complete device removal cohort



Comparison between complete vs. non-complete device removal



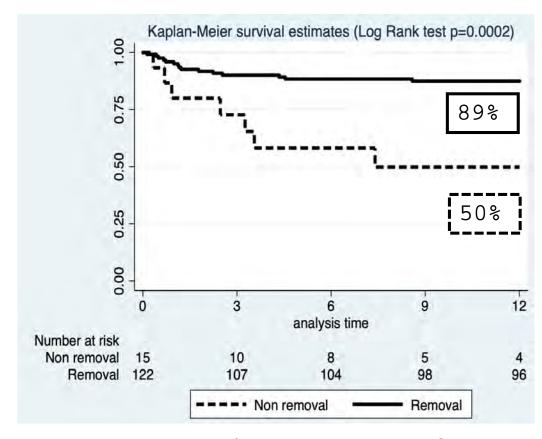
*95% Confidence interval

Non-complete device removal cohort

Predictors for non-complete device removal

	Univariate			Multivariate		
	OR	CI 95%	р	OR	CI 95%	р
2001-2020 vs. 1981-2000	0.58	(0.12,	0.12	-	-	-
		2.71)				
Age	1.12	(1.05,	<0.01	1.15	(1.05,	<0.01
		1.21)			1.25)	
Charlson index	1.18	(0.99,	0.05	1.15	(0.97, 1.39)	0.11
		1.41)				
PPM vs ICD+CRT	1.82	(0.39,	0.45	-	-	-
		8.49)				
Transferred from another	0.72	(0.24,	0.56	-	-	-
hospital		2.18)				
> 2 leads vs <= 2 leads	0.57	(0.07,	0.60	-	-	-
		4.66)				
Concomitant pocket infection	0.55	(0.17,	0.33	-	-	-
		1.81)				
Concomitant tricuspid	0.19	(0.02,	0.12	0.23	(0.03,	0.20
vegetation		1.52)			2.03)	
CoNS CIED-IE	0.34	(0.11,	0.08	0.60	(0.11,	0.54
		1.12)			3.15)	
S. aureus CIED-IE	3.32	(1.17,	0.02	4.35	(1.93,	<0.01





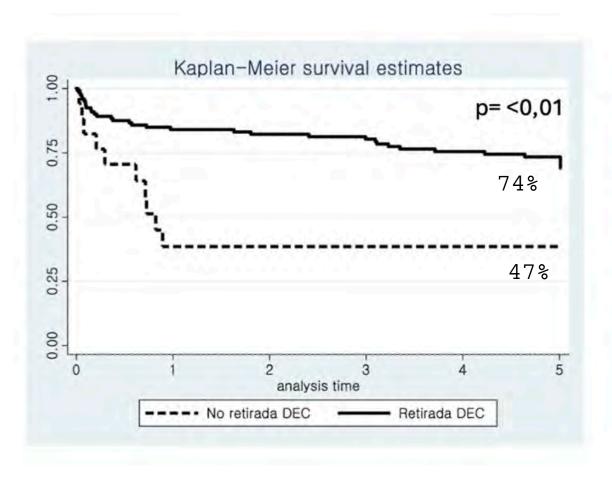
Hernández-Meneses M et al. OFID 2022

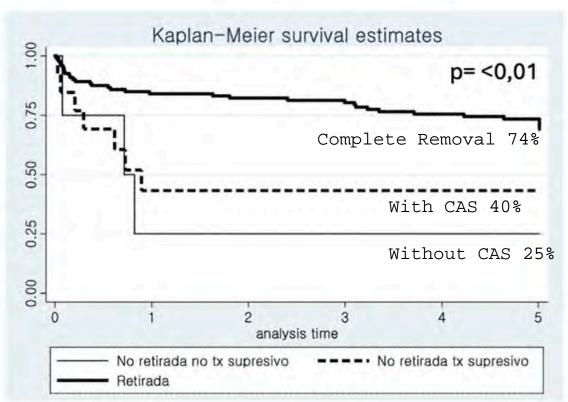
Hernandez-Meneses et al. Manuscript on preparation

Non-complete device removal cohort



Five-year survival of non-removal CIED IE





Take home messages

- The rise in CIED implants leads to more infections, especially in older, comorbid populations with longer life expectancy. CIED IE also increased. More healthcare-associated infections, more transfers from other centers, and higher rates of resistant pathogens (staphylococci, enterococci). Despite this, one-year survival has improved.
- Staphylococci (primarily CONS) are the most frequent cause. Obesity, comorbidities, and ventricular stimulation may be risk factors for Gram-negative infections, though this data should be interpreted cautiously.
- New Guidelines: Limited changes, but PET/CT is highlighted for pocket infections. There is limited published evidence on molecular biology use, but it has proven efficacy. Combining PET/CT with TEE increases the diagnosis of systemic lead infections. PET/CT is key for local infections, and TEE is crucial for intracardiac leads. PET/CT disappearance of uptake during follow-up could help safely stop CAS when device removal is incomplete.
- Complete device removal is critical for survival requiring undated quidelines

Thank you

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