

Aspetti Microbiologici: Classificazione dei dispositivi, patogenesi delle infezioni, problematiche diagnostiche

Corso Precongressuale A

Diagnostica delle Infezioni del torrente Circolatorio e dei Device Cardiovascolari: Percorsi, Buone Pratiche e Indicatori

Annibale Raglio
GLICADI



**51°
CONGRESSO
NAZIONALE
AMCLI**

**8-11 MARZO 2024
PALACONGRESSI RIMINI**



Disclosures

- No conflict of interest
- No disclosures to declare

Argomenti

Ruolo del Microbiologo Clinico

Tipologia dei Dispositivi Cardiovascolari Impiantabili

Tecniche diagnostiche

Esempi per Dispositivi Cardiovascolari Elettronici

Esempi per Protesi valvolari

Esempi per Protesi vascolari

RAGLIO D'ASINO

NON SALE AL CIELO



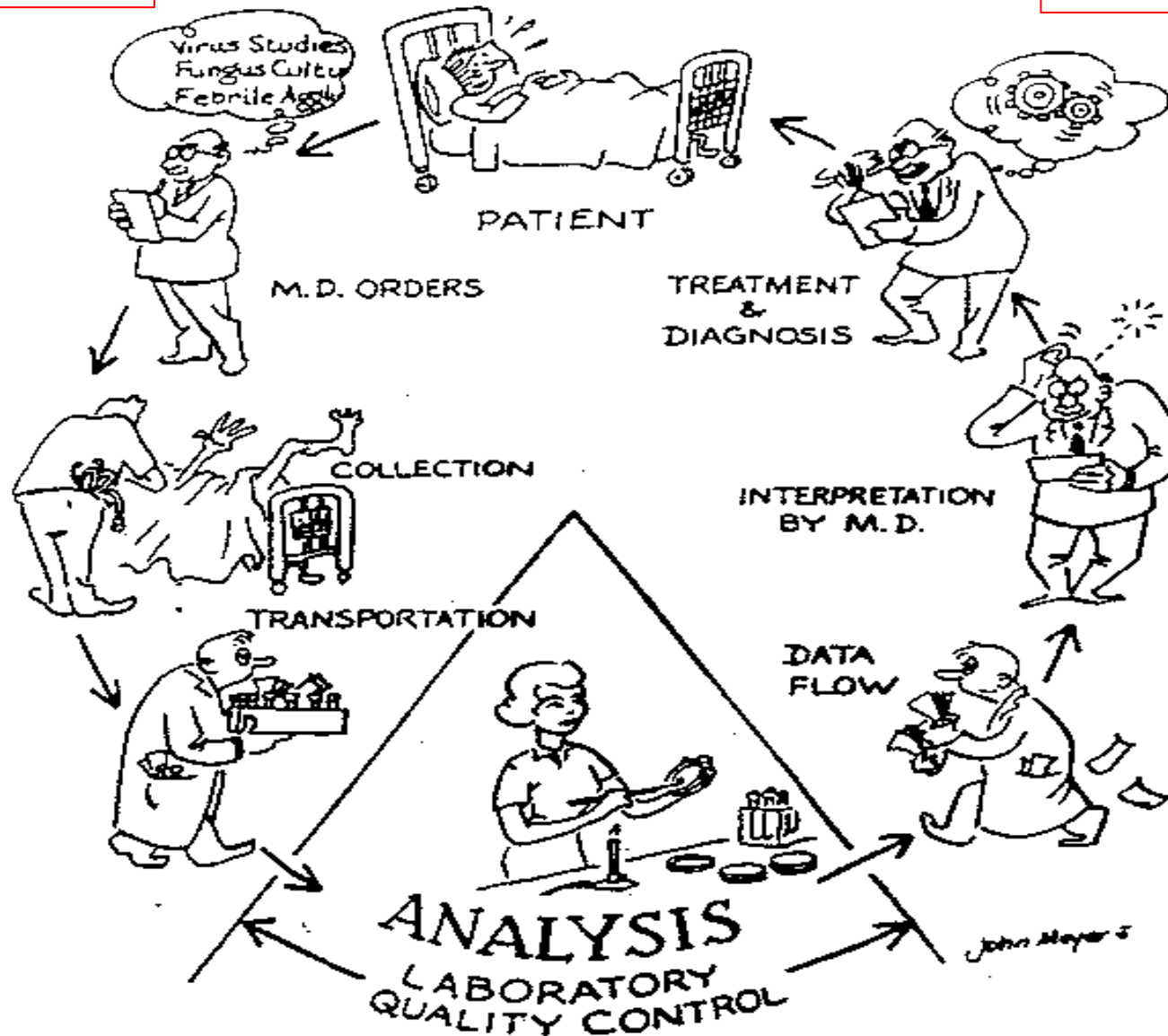
Iter dell'indagine microbiologica

Pre-Pre-
Analitica

Post-Post-
Analitica

Pre-
Analitica

Post-
Analitica



Raccolta e Condivisione Documenti, Protocolli, LG **DI RIFERIMENTO**

Pre-Pre Analitica	Redazione e implementazione di protocolli e Linee di indirizzo per la scelta del test più appropriato in funzione del quesito clinico
Pre Analitica	Formulazione del quesito clinico e scelta del test/esame;

Ch. Vascolari

Ing Clinica

Infettivologi

Infermieri

Cardiologi

Cardiochirurghi

Microbiologi



Contributo della microbiologia



Garbage in



Garbage out

Infezioni da Cateteri Vascolari: Aspetti Microbiologici e Percorso Diagnostico

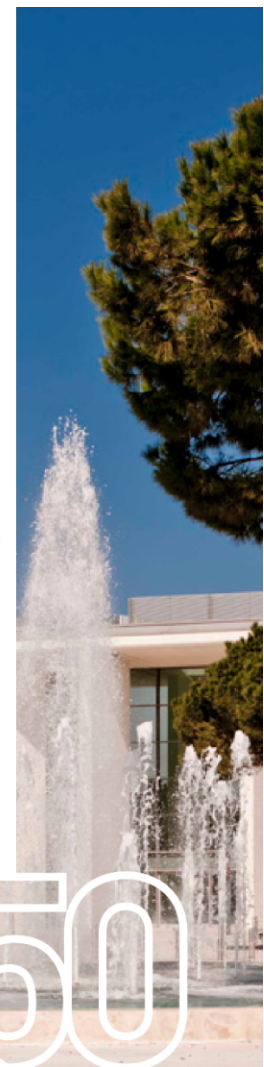
Sessione 9 **26-2-23**

LE INFEZIONI DEL TORRENTE
CIRCOLATORIO E DEI CATETERI
VASCOLARI: REVISIONE DEI
PERCORSI DIAGNOSTICI

Annibale Raglio per GLICADI

24-27 marzo 2023 Palacongressi Rimini

50



Cateteri vascolari



Port

Groshong

Broviac

PICC

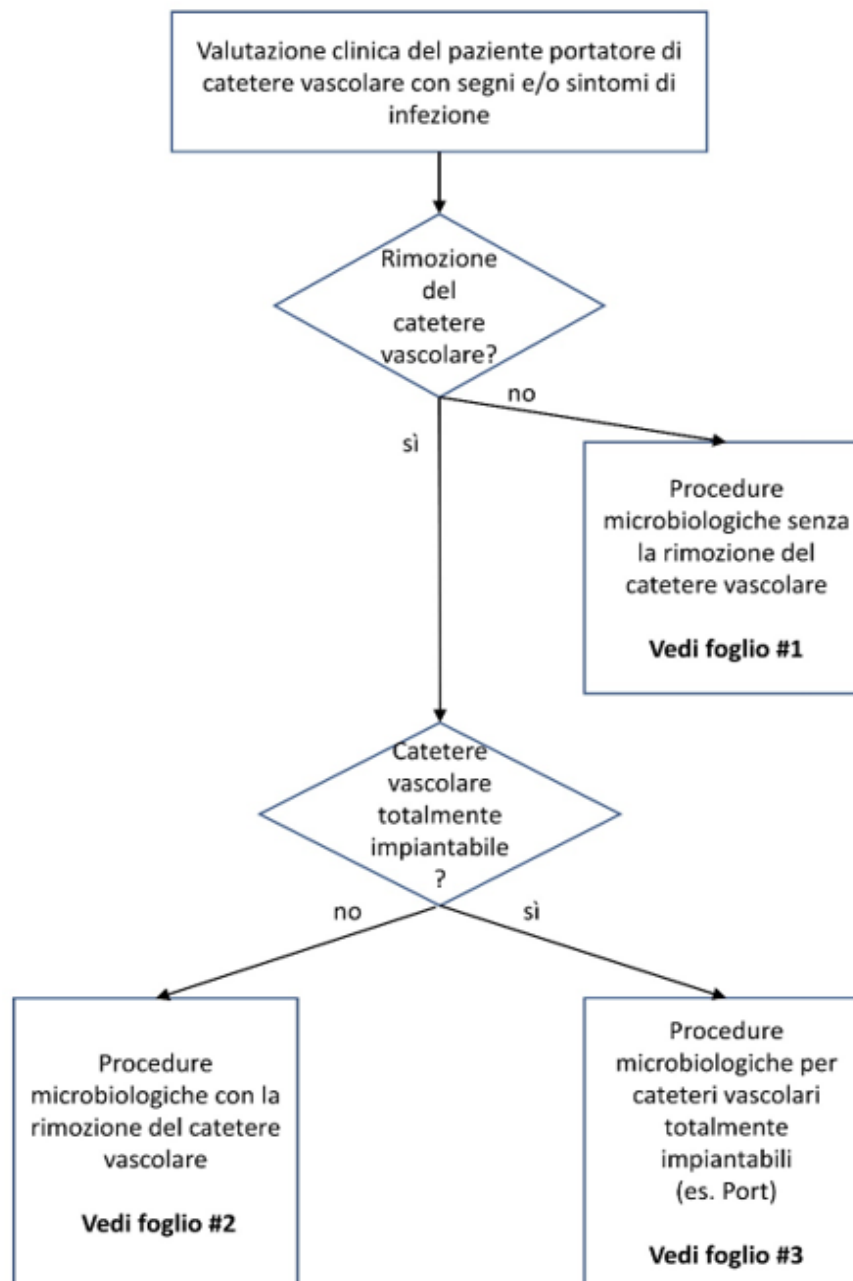
Med-line

.....

CVC impiantabili

CVC a lunga permanenza tunnellizzati

CVC a breve permanenza non tunnellizzati

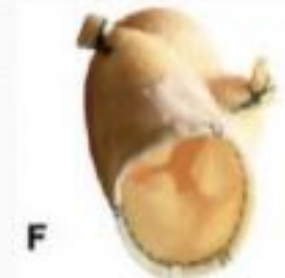




Types of Prosthetic Heart Valves

Types of Prosthetic Heart Valves

- **Mechanical**
 - Bileaflet (St Jude)(A)
 - Single tilting disc (Medtronic Hall)(B)
 - Caged-ball (Starr-Edwards) (C)
- **Biologic**
 - **Stented**
 - Porcine xenograft (Medtronic Mosaic) (D)
 - Pericardial xenograft (Carpentier-Edwards Magna) (E)
 - **Stentless**
 - Porcine xenograft (Medtronic Freestyle) (F)
 - Pericardial xenograft
 - Homograft (allograft)
 - **Percutaneous**
 - Expanded over a balloon (Edwards Sapiens) (G)
 - Self-expandable (Core Valve) (H)



Domanda 1

Quale tipo di valvola artificiale usano i tuoi chirurghi?

- Biologica
- Meccanica
- Entrambe Biologica e Meccanica
- Non so

Cosa vogliono sapere i chirurghi?

Quale è il miglior tipo di
valvola

Per evitare COMPLICAZIONI

Transcatheter Pulmonary Valve Implantation: A Comprehensive Systematic Review and Meta-Analyses of Observational Studies

Arka Chatterjee, MD; Navkaranbir S. Bajaj, MD, MPH; William S. McMahon, MD; Marc G. Cribbs, MD; Jeremy S. White, MD; Amrita Mukherjee, BDS, MPH; Mark A. Law, MD

B The difference of infection is pronounced when
P comparing Melody valves with homografts, but
P
N not for Contegra bovine valved conduit, suggesting
C possible tropism of micro-organisms to the bovine
P material used in making the Melody and Contegra
V
C valves.
I
R
≥
e

Conclusions—Our study provides favorable updated estimates of procedural and follow-up outcomes after transcatheter pulmonary valve implantation. Widespread adoption of pretesting has improved longer-term outcomes in these patients. (*J Am Heart Assoc.* 2017;6:e006432. DOI: 10.1161/JAHA.117.006432.)

Key Words: endocarditis • Melody valve • reintervention • transcatheter pulmonary valve

Definizione e Epidemiologia

- La definizione di infezione delle protesi valvolari è più semplice rispetto a quella di CIEDI. Si tratta di fatto di **un'endocardite della valvola protesica (PVE)**.
- La PVE è una malattia grave e pericolosa per la vita e la sua incidenza dipende da vari fattori
- PVE ad esordio **precoce entro 12 mesi** dall'intervento, **tardive dopo i 12 mesi**
- Rappresenta il **10-30% del totale dei casi di endocardite infettiva (EI)** con un'incidenza **dello 0,3–1,2% per paziente per anno** ma che può aumentare fino al **5% dopo i 10 anni dal posizionamento**.
- Nei pazienti con una valvola protesica il rischio cumulativo di EI era rispettivamente del **2,8% e del 4,5% a 5 e 10 anni**
- La **valvola aortica era coinvolta nel 66,5%**, la mitralica nel 40,7%, la tricuspide nel 2,9% e l'infezione multivalvolare si è avuta nel 7,2% dei pazienti con PVE
- Incidenza **minore** dopo 12 anni in pazienti con **valvola aortica meccanica rispetto ai soggetti con valvola aortica bioprotesica (1,4% vs 2,2%)**

2. Imaging positive for IE

a. Echocardiogram positive for IE:

- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F -FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

c. Definite paravalvular lesions by cardiac CT.

Positron Emission Tomography/Computed Tomography for Diagnosis of Prosthetic Valve Endocarditis Increased Valvular 18F-Fluorodeoxyglucose Uptake as a Novel Major Criterion

Saby, Raoult, Thuny, Marseille, France

Table 5

Diagnostic Value of the Modified Duke Criteria at Admission With (Duke-PET/CT) and Without the Implementation of the PET/CT Results

	Final Diagnosis		
	Definite PVE	Possible PVE	Rejected PVE
Duke			
Definite PVE	21 (70)	0 (0)	0 (0)
Possible PVE	8 (27)	22 (100)	10 (50)
Rejected PVE	1 (3)	0 (0)	10 (50)
Duke-PET/CT			
Definite PVE	29 (97)	10 (45)	2 (10)
Possible PVE	1 (3)	12 (55)	10 (50)
Rejected PVE	0	0	8 (40)

Values are n (% of each final diagnosis).

Journal of the American College of Cardiology 2013

an abnormal FDG uptake in PET/CT imaging as a **major criterion** for PHV endocarditis. This result should be used in patients with **PHV implanted for >1 month** and **must be interpreted in the clinical and the microbiological contexts.**

Take-home message

is **not** to consider **PET/CT** as a technique able to diagnose PVE **without other data**. It should be used with the global assessment of the patients with suspected PVE.

FDG PET/CT

- AHA
 - « More study is needed to define the utility of ^{18}F -fluorodeoxyglucose positron emission tomography/CT in the diagnosis and management of IE...»
- ESC
 - promising results for WBC SPECT/CT and ^{18}F -FDG PET/CT...
 - «...reduction in the rate of misdiagnosed possible IE...»
 - «it could be employed to monitor response to antimicrobial treatment...»

ESC modified criteria for IE suggest PET

AHA guidelines 2015 are more prudent

Table 10 Definitions of the 2023 European Society of Cardiology modified diagnostic criteria of infective endocarditis**Major criteria****(i) Blood cultures positive for IE**

- (a) Typical microorganisms consistent with IE from two separate blood cultures:
Oral streptococci, *Streptococcus gallolyticus* (formerly *S. bovis*), HACEK group, *S. aureus*, *E. faecalis*
- (b) Microorganisms consistent with IE from continuously positive blood cultures:
- ≥ 2 positive blood cultures of blood samples drawn >12 h apart.
 - All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥ 1 h apart).
- (c) Single positive blood culture for *C. burnetii* or phase I IgG antibody titre $>1:800$.

(ii) Imaging positive for IE:

Valvular, perivalvular/periprosthetic and foreign material anatomic and metabolic lesions characteristic of IE detected by any of the following imaging techniques:

- Echocardiography (TTE and TOE).
- Cardiac CT.
- $[^{18}\text{F}]\text{-FDG-PET/CT(A)}$.
- WBC SPECT/CT.

Minor criteria

- (i) **Predisposing conditions (i.e. predisposing heart condition at high or intermediate risk of IE or PWIDs)^a**
- (ii) **Fever defined as temperature >38°C**
- (iii) **Embolic vascular dissemination (including those asymptomatic detected by imaging only):**
 - Major systemic and pulmonary emboli/infarcts and abscesses.
 - Haematogenous osteoarticular septic complications (i.e. spondylodiscitis).
 - Mycotic aneurysms.
 - Intracranial ischaemic/haemorrhagic lesions.
 - Conjunctival haemorrhages.
 - Janeway's lesions.
- (IV) **Immunological phenomena:**
 - Glomerulonephritis.
 - Osler nodes and Roth spots.
 - Rheumatoid factor.
- (V) **Microbiological evidence:**
 - Positive blood culture but does not meet a major criterion as noted above.
 - Serological evidence of active infection with organism consistent with IE.

IE Classification (at admission and during follow-up)

Definite:

- 2 major criteria.
- 1 major criterion and at least 3 minor criteria.
- 5 minor criteria.

Possible:

- 1 major criterion and 1 or 2 minor criteria.
- 3–4 minor criteria.

Rejected:

- Does not meet criteria for definite or possible at admission with or without a firm alternative diagnosis.

[18F]-FDG-PET/CT, ¹⁸F-fluorodeoxyglucose positron emission tomography; CT(A), computed tomography (angiography); HACEK, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*; IE, infective endocarditis; Ig, immunoglobulin; PWID, people who inject drugs; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography; WBC SPECT/CT, white blood cell single photon emission tomography/computed tomography.

^aFor detailed explanation of predisposing conditions, please see [Section 3](#).

2023 Duke-ISCVID Criteria		
Major criterion: imaging	363 (91.0)	38 (19.4)
Major criterion: microbiology	313 (78.4)	98 (50.0)
Minor criterion: predisposing condition	281 (70.4)	106 (54.1)
Minor criterion: fever	291 (72.9)	116 (59.2)
Minor criterion: vascular phenomena	131 (32.8)	45 (23.0)
Minor criterion: immunologic phenomena	28 (7.0)	11 (5.6)

DOI: 10.1093/cid/ciae033

14

Minor criterion: microbiology	43 (10.8)	36 (18.4)
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All data are n (%) or median [IQR].

missing data in 34 patients, ## missing data in 40 patients, ### missing data in 40 patients, #### missing data in 429 patients (no fundoscopy performed)

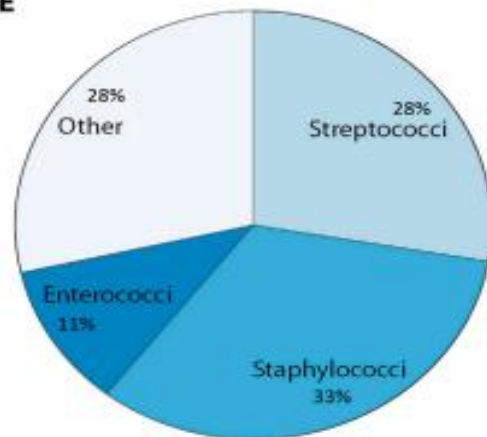
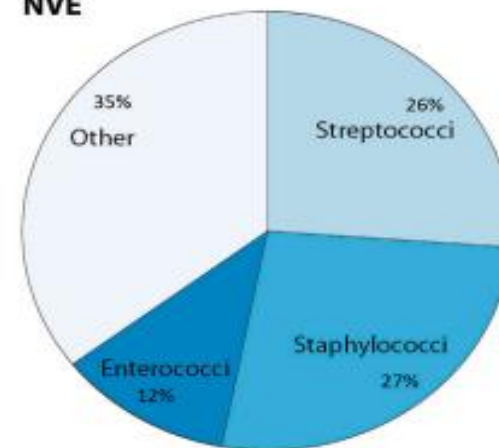
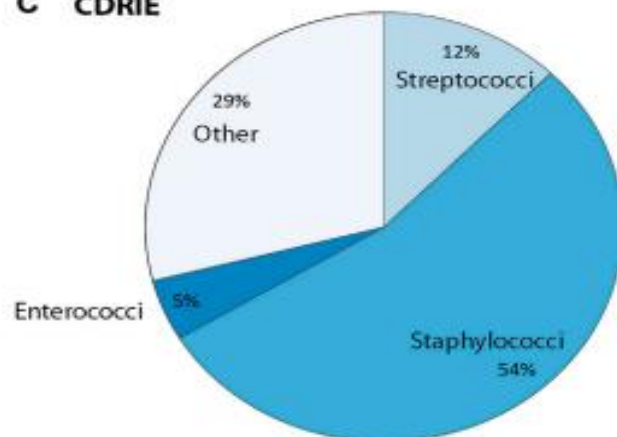
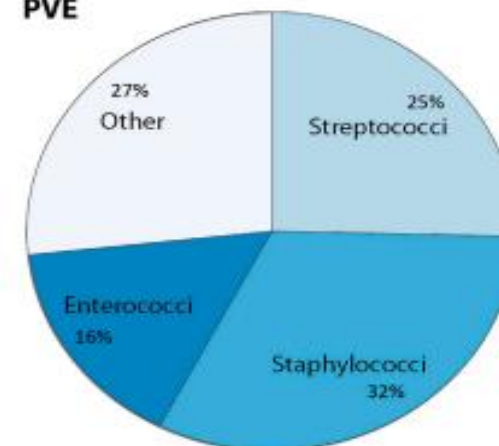
Abbreviations: IQR, interquartile range; HACEK, *Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, *Kingella*; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; [18F]FDG-PET/CT, [18F]fluorodeoxyglucose-positron emission tomography/computed tomography.

External Validation of the 2023 Duke - International Society for Cardiovascular Infectious Diseases Diagnostic Criteria for Infective Endocarditis CID 2024

Table 3 – Diagnostic accuracy of criteria sets compared to reference standard: “Full” Criteria

	Sensitivity (95% CI)	Specificity (95% CI)	Negative predictive value (95% CI)	Positive predictive value (95% CI)	P-value (sensitivity versus Duke- ISCVID sensitivity)	P-value (specificity versus Duke- ISCVID specificity)
Modified Duke Criteria	74.9 (70.4 - 79.1)	94.9 (90.8 - 97.5)	65.0 (59.2 - 70.6)	96.8 (94.1 - 98.4)	<0.001	0.16
2015 ESC Criteria	80.0 (75.7 - 83.8)	93.9 (89.6 - 96.8)	69.7 (63.8 - 75.2)	96.4 (93.8 - 98.1)	<0.001	1
2023 ESC Criteria	85.5 (81.6 - 88.8)	82.1 (76.1 - 87.2)	73.5 (67.2 - 79.2)	90.7 (87.3 - 93.4)	0.22	<0.001
Duke-ISCVID Criteria	84.2 (80.3 - 87.7)	93.9 (89.6 - 96.8)	74.5 (68.6 - 79.8)	96.6 (94.1 - 98.2)	-	-

Table footnote: diagnostic accuracy against adjudication panel as the reference standard. The “Full Criteria” include histology and microbiology results obtained from cardiac surgery. P-values based on Mc Nemar test statistics (29). The absolute numbers per classification/diagnosis combination are listed in supplemental table 1.

A All IE**B NVE****C CDRIE****D PVE****FIGURE 2**

Overview of causative bacteria in infective endocarditis (IE) concerning (A) all IE cases, (B) native valve endocarditis (NVE), and (C) cardiac device related-infective endocarditis (CDRIE) that is further subdivided into (D) prosthetic valve endocarditis (PVE). Other refers to either other cultured or unidentified microorganisms. The values in this graph were obtained using the following references (Cahill and Prendergast, 2016; Wang A. et al., 2018; DeSimone and Sohail, 2018; DeSimone and Sohail, 2018; Babeş et al., 2021; Doring et al., 2018; Teoh and Hannan, 2018; Slawinski et al., 2019; Mateos Gaitán et al., 2020; Khalil and Soufi, 2022).

Characteristics	IE episodes with embolic events	IE episodes without embolic events	$p \leq \dagger$
Microbiology			
<i>Staphylococcus aureus</i>	141 (28)	142 (15)	0.0001
Viridans group streptococci	66 (13)	151 (16)	NS
Coagulase-negative staphylococci	52 (10)	95 (10)	NS
<i>Enterococcus</i> species	45 (9)	137 (1)	0.004
<i>Streptococcus bovis</i>	44 (9)	98 (10)	NS
Polymicrobial	19 (4)	32 (3)	NS
Other microorganisms	16 (3)	45 (6)	NS
Other streptococci	16 (3)	43 (5)	NS
Fungi/yeasts	7 (1)	13 (1)	NS
HACEK	1 (0.2)	2 (0.2)	NS
Microbiology negative	92 (18)	199 (21)	NS

*Total cohort, N = 1456 episodes of infective endocarditis. Data reported as number, median (range, 5th to 95th percentile), or number (%). Abbreviations:

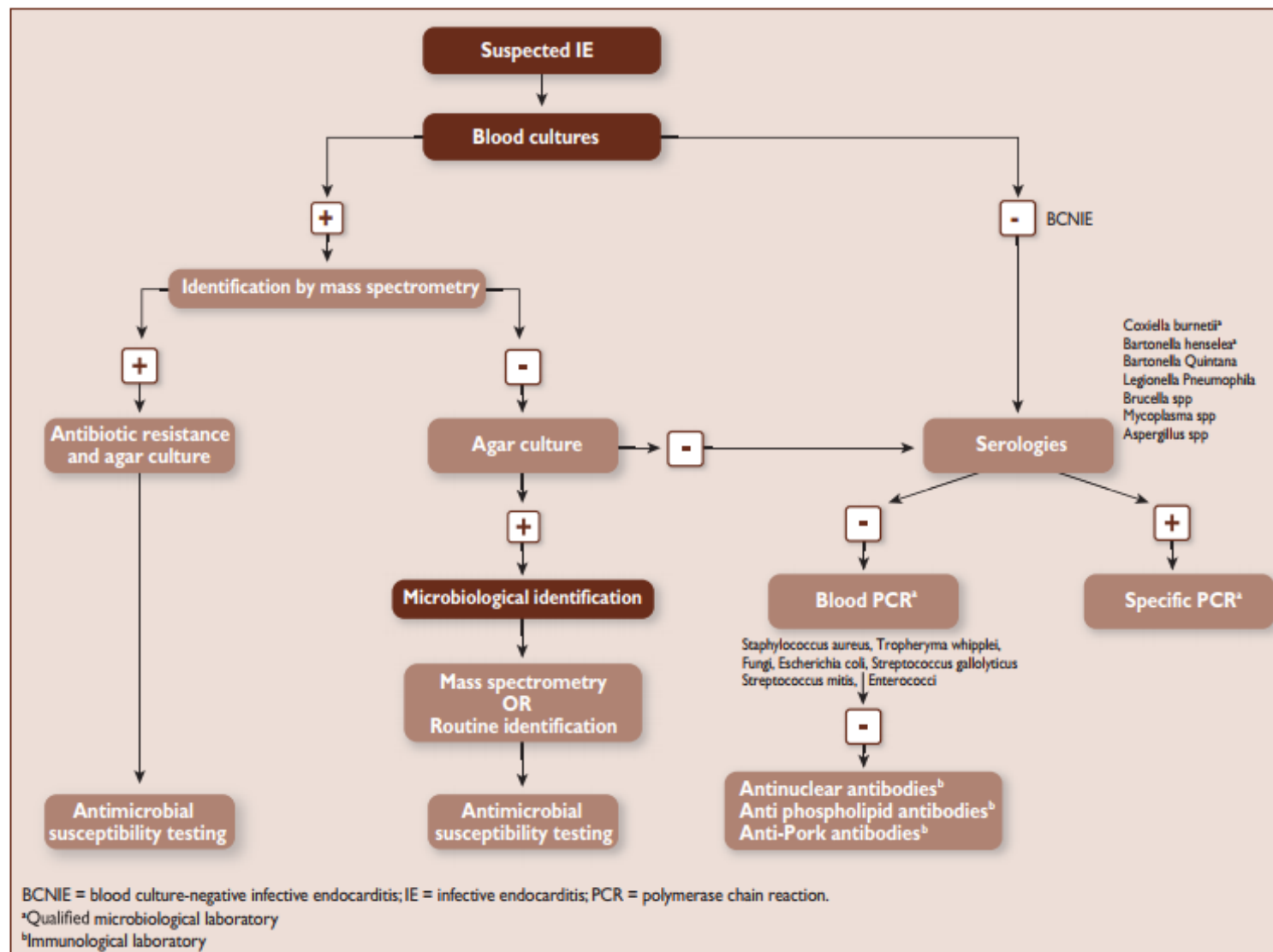


Figure 2 Microbiological diagnostic algorithm in culture-positive and culture-negative IE.

Blood culture-negative endocarditis

Improving the diagnostic yield using new diagnostic tools

Pierre-Edouard Fournier, MD, PhD^{a,b,*}, Frédérique Gouriet, MD, PhD^{a,b}, Jean-Paul Casalta, MD^b, Hubert Lepidi, MD, PhD^a, Hervé Chaudet, MD, PhD^a, Franck Thuny, MD^c, Frédéric Collart, MD, PhD^d, Gilbert Habib, MD, PhD^e, Didier Raoult, MD, PhD^{a,b}

Abstract

Blood culture-negative endocarditis (BCNE) may represent up to 70% of all endocarditis cases, depending on series. From 2001 to 2009, we implemented in our laboratory a multimodal diagnostic strategy for BCNE that included systematized testing of blood, and when available, valvular biopsy specimens using serological, broad range molecular, and histopathological assays. A causative microorganism was identified in 62.7% of patients.

In this study from January 2010 to December 2015, in an effort to increase the number of identified causative microorganisms, we prospectively added to our diagnostic protocol specific real-time (RT) polymerase chain reaction (PCR) assays targeting various endocarditis agents, and applied them to all patients with BCNE admitted to the 4 public hospitals in Marseille, France.

A total of 283 patients with BCNE were included in the study. Of these, 177 were classified as having definite endocarditis. Using our new multimodal diagnostic strategy, we identified an etiology in 138 patients (78.0% of cases). Of these, 3 were not infective (2.2%) and 1 was diagnosed as having *Mycobacterium bovis* BCG endocarditis. By adding specific PCR assays from blood and valvular biopsies, which exhibited a significantly greater sensitivity ($P < 10^{-2}$) than other methods, causative agents, mostly enterococci, streptococci, and zoonotic microorganisms, were identified in an additional 27 patients (14 from valves only, 11 from blood only, and 2 from both). Finally, in another 107 patients, a pathogen was detected using serology in 37, valve culture in 8, broad spectrum PCR from valvular biopsies and blood in 19 and 2, respectively, immunohistochemistry from valves in 3, and a combination of several assays in 38.

By adding specific RT-PCR assays to our systematic PCR testing of patients with BCNE, we increased the diagnostic efficiency by 24.3%, mostly by detecting enterococci and streptococci that had not been detected by other diagnostic methods, but also agents requiring specific management such as *Mycoplasma hominis* and *Tropheryma whipplei*.

Abbreviations: BCNE = blood culture-negative endocarditis, CIED = cardiovascular implantable electronic device, LCSF = LightCycler SeptiFast, PCR = polymerase chain reaction, RT-PCR = real time polymerase chain reaction.

Keywords: blood, diagnosis, endocarditis, serology, specific PCR, valve

Patients

- **918** patients admitted to Marseille public hospitals were diagnosed as having definite or possible endocarditis, according to the modified Duke criteria.^[8]
- **Blood cultures were positive in 635** patients (69.2%)
- Of the remaining **283** patients,
 - **177** (62.5%) were classified as having **definite endocarditis**,
 - **138 (48.7%) (77.9%)** in whom diagnostic strategy allowed the identification of an etiology,

Diagnostic procedures

Serology

- Indirect immunofluorescence assays to detect
 - C burnetii* (phase I IgG titer >1:800),
 - Bartonella quintana*, *B henselae* (IgG ≥ 1:800),
 - Legionella pneumophila* (total antibody titer ≥ 1:256)
- ELISA
 - Brucella melitensis* (titer ≥ 1:200)
 - Platellia *M pneumoniae* IgM kit
 - Mycoplasma pneumoniae* (titer ≥ 1:200)

When 1st rank tests were negative,

- Western blot *Bartonella* spp

Molecular Biology

- DNA Extraction from Blood, Valve (directly or suspension broth)
- PCR, RT-PCR, Sequencing 16 S-18S rRNA,

283 patients with definite or possible
blood culture-negative endocarditis

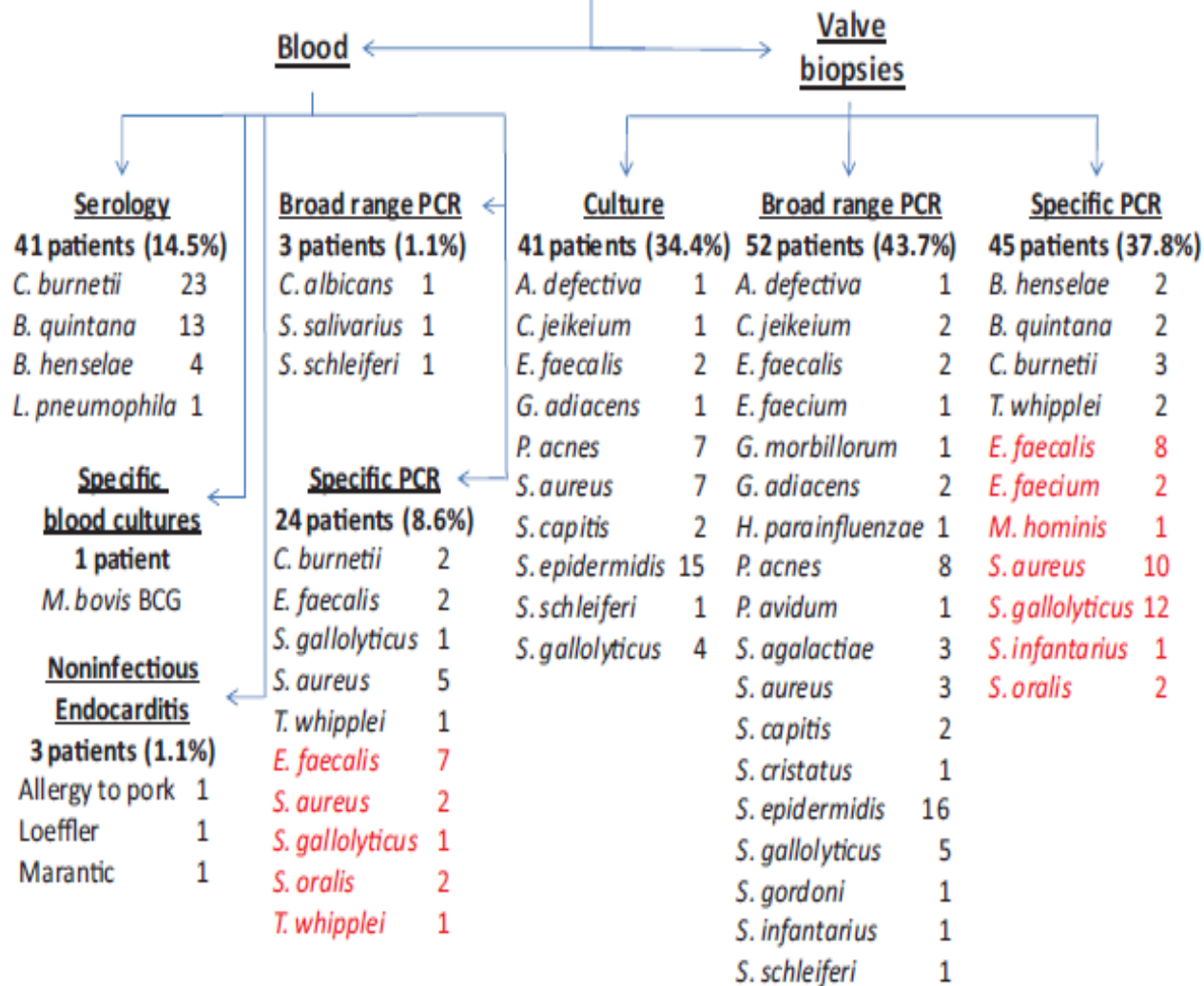


Figure 2. Distribution of identified etiological agents according to the diagnostic method used. The percentages of positive specimens per diagnostic method are indicated in parentheses. Etiological agents identified using newly added specific polymerase chain reaction (PCR) assays are indicated in red.

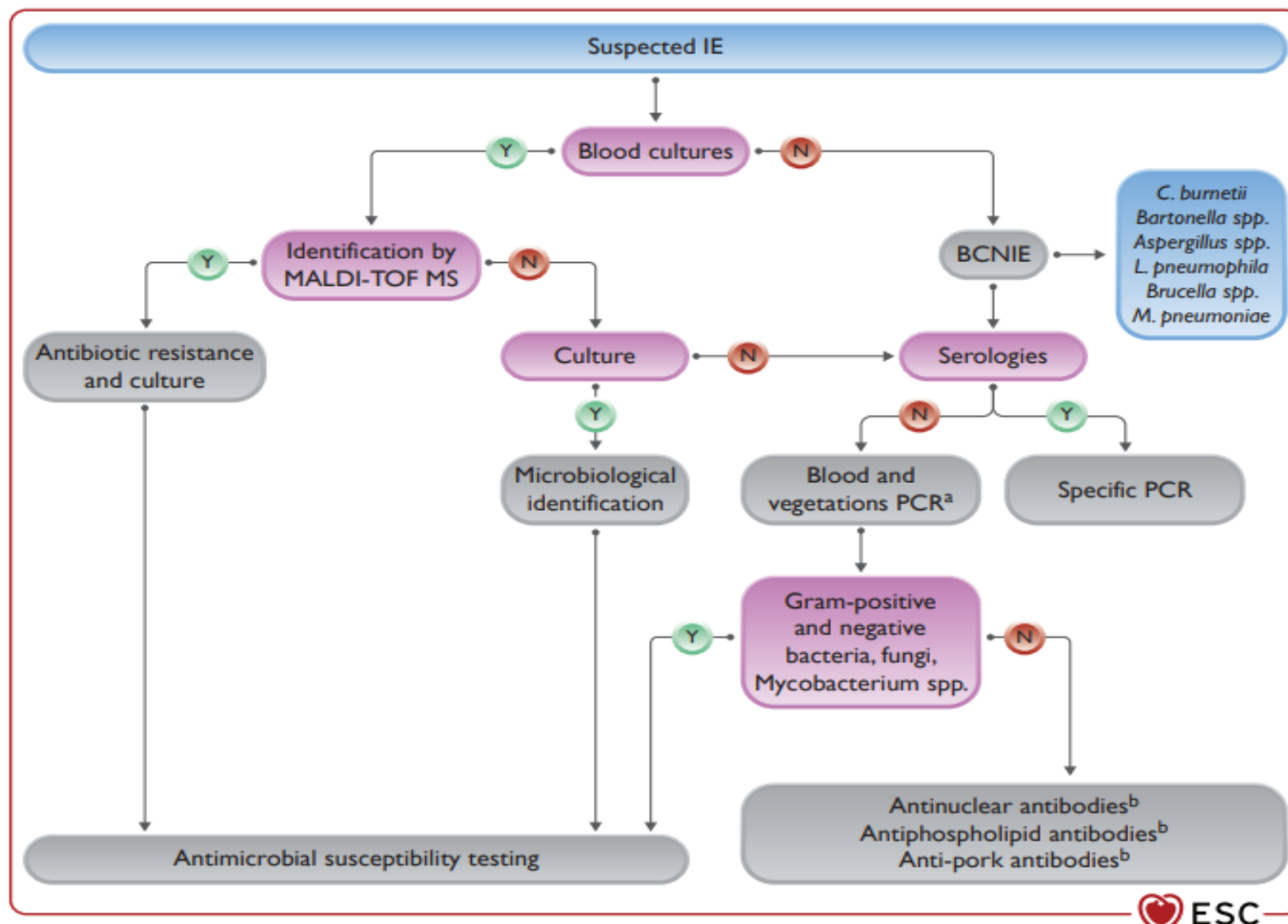


Figure 4 Microbiological diagnostic algorithm in culture-positive and culture-negative infective endocarditis. BCNIE, blood cultures negative endocarditis; IE, infective endocarditis; MALDI-TOF MS, matrix-assisted laser desorption ionization time-of-flight mass spectrometry; PCR, polymerase chain reaction.

^aQualified microbiological laboratory. ^bImmunological laboratory.

Table 9 Investigation of rare causes of blood culture-negative infective endocarditis

Pathogen	Diagnostic procedures
<i>Brucella</i> spp.	Serology, blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
<i>C. burnetii</i>	Serology (IgG phase I >1:800), tissue culture, immunohistology, and 16S rRNA sequencing of tissue
<i>Bartonella</i> spp.	Serology (IgG phase I >1:800), blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
<i>T. whipplei</i>	Histology and 16S rRNA sequencing of tissue
<i>Mycoplasma</i> spp.	Serology, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
<i>Legionella</i> spp.	Serology, blood cultures, tissue culture, immunohistology, and 16S rRNA sequencing of tissue
Fungi	Serology, blood cultures, 18S rRNA sequencing of tissue
Mycobacteria (including <i>Mycobacterium chimaera</i>)	Specific blood cultures, 16S rRNA sequencing of tissue

Domanda 3

Quanti centri sono in grado di fare una Diagnosi Microbiologica in accordo alle Linee-guida ESC 2023 o Duke ISCVID?

- Nessuno
- Pochi: uno o due centri di riferimento
- Più di dieci
- Non lo so



Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: <http://www.elsevier.com/locate/jic>



Case report

Metagenomic analysis for detecting pathogens in culture-negative infective endocarditis



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- Culture-negative IE is still a major clinical problem and a diagnostic challenge.
- Metagenomic analysis using next generation sequencing has been used to detect pathogens
- However, **there are very few reports of the use of metagenomic analysis**

Piccola esperienza del 2010, OORR BG

Preparation & PCR

sample pre treatment

enrichment of bacteria & fungi DNA

PCR



≈ 35 min



60 min



≈ 10 min



100 min



≈ 30 min



90 min

Hands on time
75 min

Process time
250 min

Sequencing

PCR cleaning
(QiaQuick)

sequencing PCR

Seq PCR cleaning
(Dye Ex Spin Kit)

sequencing



< 10 min



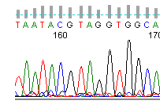
≈ 20 min



180 min



< 10 min



≈ 20 min



80 min

Hands on time
60 min

Process time
260 min

Total hands on time ≈
2 h 15 min

Total process time ≈ 8
h 30 min

Risultati

- 13 valvole esaminate
- Colture positive per StaCon, Streptococchi
- 16 s RNA: Sempre NEGATIVO

»Problema di Estrazione

»Limite rilevazione 40 UFC/ml

Heart Valves Microbiological Diagnosis

- Homogenize by
 - balls
 - Sonication?
 - Dithiothreitol?
- Culture in BC Vials
- Broad Range PCR and Specific PCR
 - Critical point the Extraction of DNA

New Perspectives for Prosthetic Valve Endocarditis: Impact of Molecular Imaging by FISHseq Diagnostics

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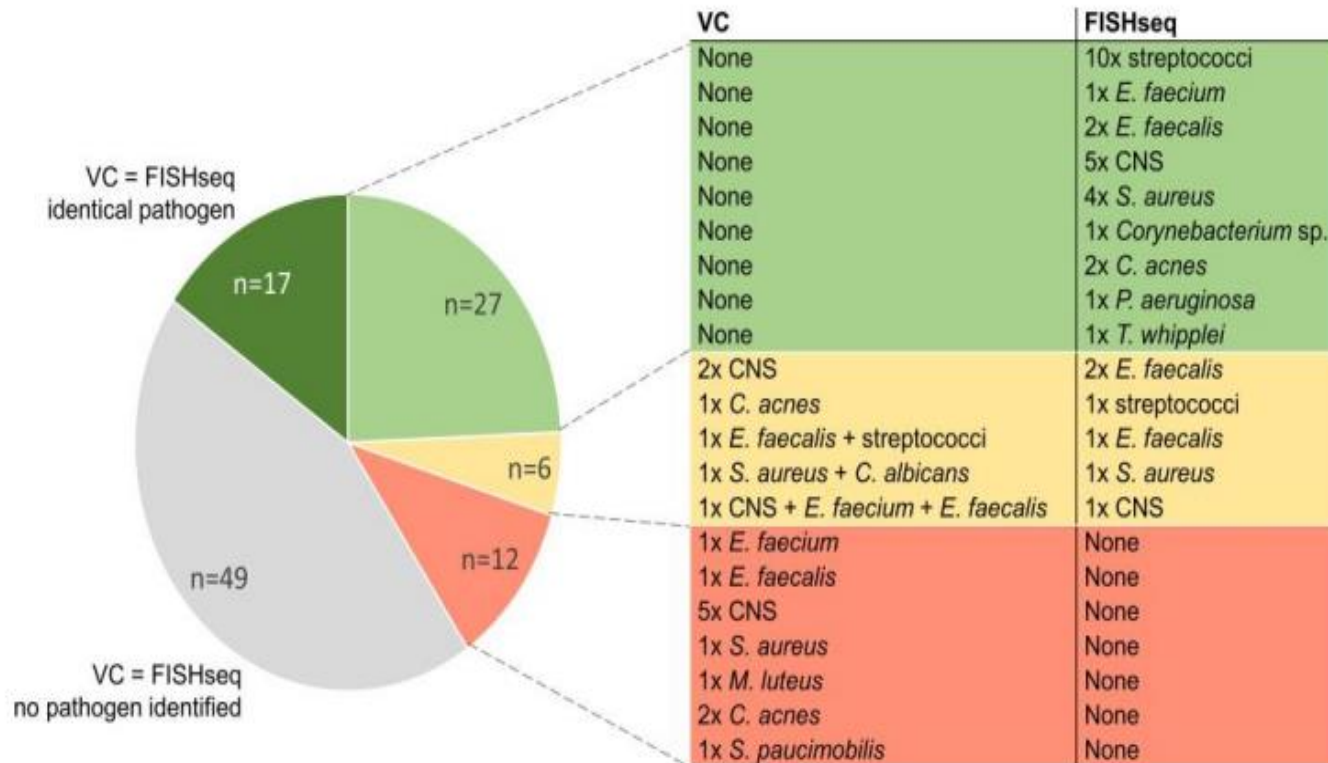


Figure 2. Pathogen detection: VC versus FISHseq (N = 111). In 59.5% (n = 66), VC and FISHseq results were identical, either identifying the same pathogen or detecting no pathogen on the prosthetic valve. VC remained negative in 24.3% (n = 12), whereas FISHseq detected typical prosthetic valve endocarditis pathogens, like streptococci, CNS, *Staphylococcus aureus*, or rare species like *Tropheryma whipplei*. Despite positive VC, FISHseq identified no pathogens in 12 cases. Interestingly, 9 of these cases grew species known as skin flora or contaminants. Abbreviations: CNS, coagulase negative staphylococci; FISHseq, fluorescence in situ hybridization combined with 16S rRNA gene polymerase chain reaction and sequencing; VC, valve culture.

Pacemaker, Defibrillators, Risincronizzatori

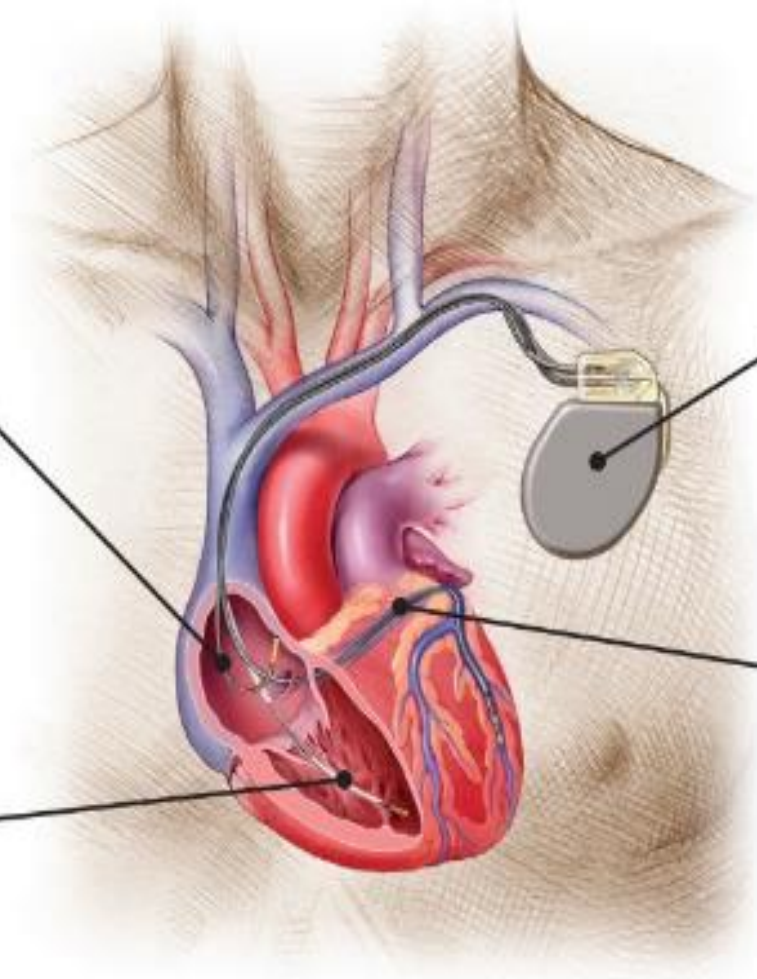


Lead
in right
atrium

Implanted
CRT-D

Lead
in right
ventricle

Lead
within
coronary
sinus vein



An implanted CRT-D system.

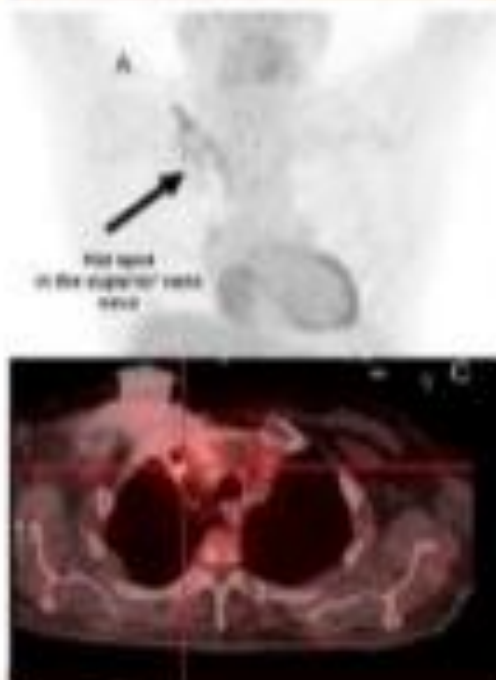
Le complicanze legate all'impianto di un pacemaker, sono per la maggior parte, legate alla tasca sottocutanea ed agli elettrocateteri.

CIED infections

CIED- IE



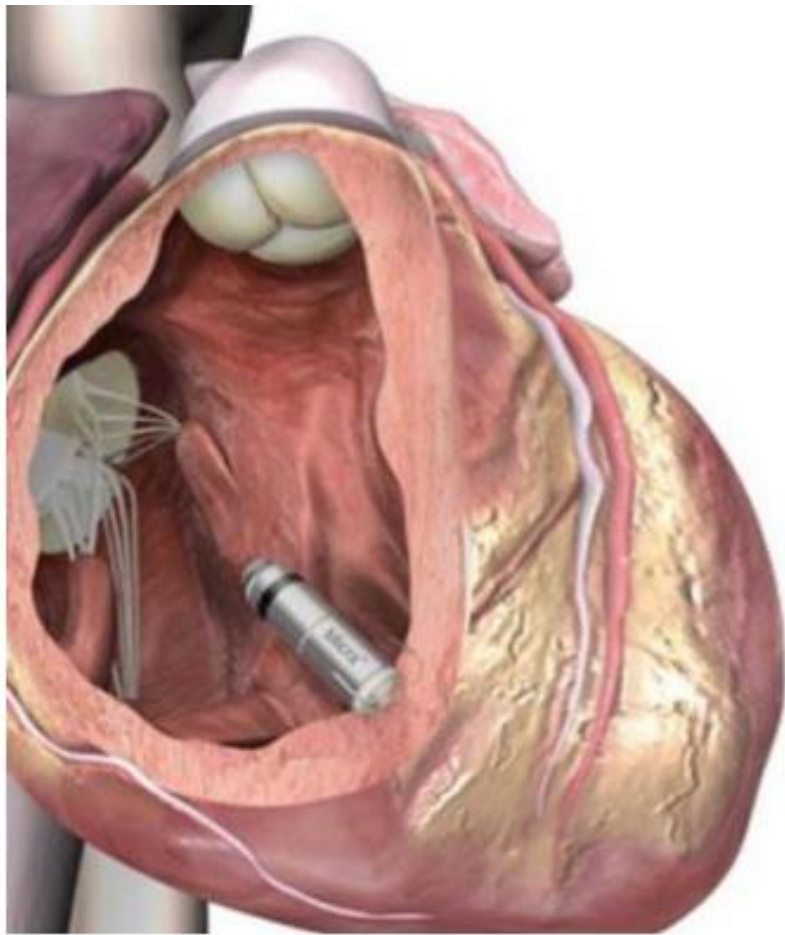
CIED-LI



CIED-Generator
Pocket Infection (GPI)



Implantable Cardiac Electronic Device Infection



SALUTE E SICUREZZA

Elettrostimolazione cardiaca: il pacemaker senza fili

European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections—endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

- **It is difficult to give a precise rate of CIED infections** because of divergent definitions, varied populations, and the range of rates in retrospective and prospective studies.
- In the Danish registry including 46 299 consecutive patients who underwent pacemaker implantation between 1982 and 2007, the incidence of infection was **4.82/1000 device-years after a primary implantation**, and **12.12/1000 device-years after replacement**.
- Greenspon et al. found that the incidence of CIED infection in the **USA increased from 1.53% in 2004 to 2.41% in 2008**
- a National Inpatient Sample database study showed an **increase from 1.45% to 3.41% (P < 0.001)** from 2000 through 2012, particularly for CRT devices.

European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections—endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

- recent cross-over cluster PADIT- and randomized WRAP-IT trials, **incidence were only 0.6–1.3%**, as compared to retrospective studies, reporting significantly **higher rates (2.3–3.4%) in the first year after implantation**

Pathogenesis and microbiology of cardiac implantable electronic device infections

- Cardiac implantable electronic device infections occur **via two major mechanisms**.
- The most common is **contamination of leads and/or pulse generator** during implantation or subsequent manipulation. Device erosion late after interventions may either be due to, or result in **pocket infection**. In either case, contamination and subsequent bacterial colonization result in **pocket infection which can spread along the intravascular parts of the leads and progress to systemic infection**.
- **The second mechanism is a bloodstream infection**. Direct lead seeding can occur during bacteraemia caused by a distant infectious focus, such as a local septic thrombophlebitis, osteomyelitis, pneumonia, surgical site infection, contaminated vascular catheters or bacterial entry via the skin, mouth, gastrointestinal, or urinary tract

Pathogenesis and microbiology of cardiac implantable electronic device infections

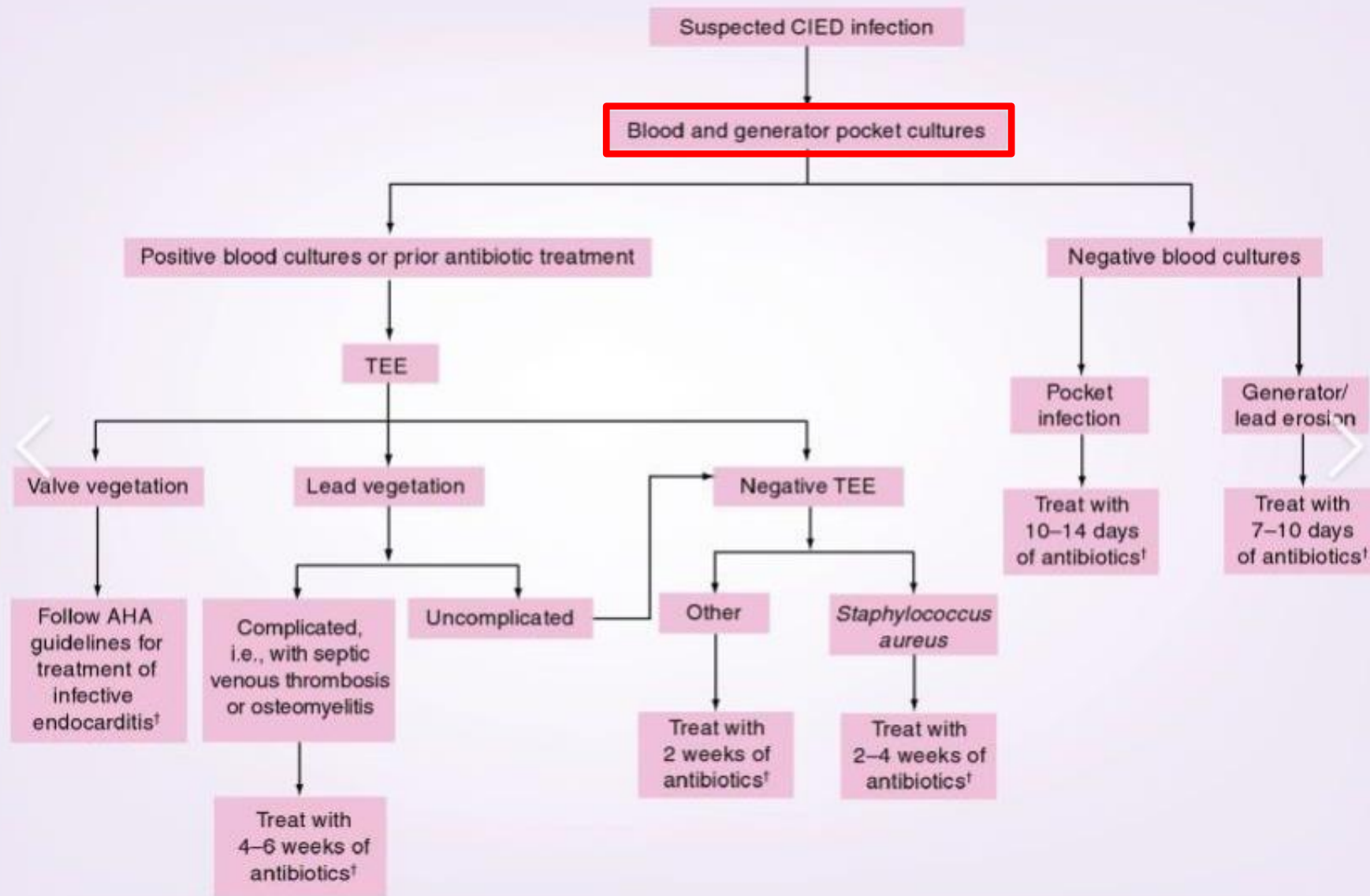
- Factors, which play a role in the pathogenesis of CIED infections, can be related to the host, the device, or the microorganism.
- The patient's own skin flora can be introduced into the wound at the time of skin incision and thereby contaminate the device.
- Contamination may also occur before implantation via the air in the operating room (both host and staff) or via the hands of anyone handling the device.

Pathogenesis and microbiology of cardiac implantable electronic device infections

- From a pathophysiological standpoint, device-related factors are those affecting bacterial adherence to the generator or lead and the **biofilm formation** on these surfaces. **Bacterial adherence is facilitated by irregular and hydrophobic surfaces.**
- Of the commonly used polymers, polyvinylchloride and silicone allow better adherence than polytetrafluoroethylene, while **polyurethane allows less adherence than polyethylene.**
- Metals also differ in their propensity for bacterial adherence—e.g. **titanium has less propensity for bacterial adherence than steel**

Table 2 Pathogens isolated in patients undergoing interventions for device infection from three large patient cohorts in North America, Europe, and Asia

Pathogen	Percentage of isolates		
	North America ¹⁶	Europe ¹⁷	Asia ¹⁸
Coagulase-negative staphylococci		69	45.2
Methicillin-resistant	18.8		
Methicillin-sensitive	18.8		
<i>S. aureus</i>		13.8	4.1
Methicillin-sensitive	15.8		
Methicillin-resistant	15.0		
<i>Streptococcus</i> spp.	2.5		
<i>Enterococcus</i> spp.			
Vancomycin-sensitive	2.8		
Vancomycin-resistant	1.4		
<i>Cutibacterium</i> spp. (previously <i>Propionibacterium</i> spp.)		2.5	
<i>Corynebacterium</i>		5	
Gram-negative bacteria	8.9	6.1	9.1
Enterobacteriaceae		3	3.2
Non-fermentative bacilli, incl. <i>Pseudomonas</i> spp.		1.5	5.9
Anaerobes	1.6		
Fungi	0.9	1	0.9
Mycobacteria	0.2		



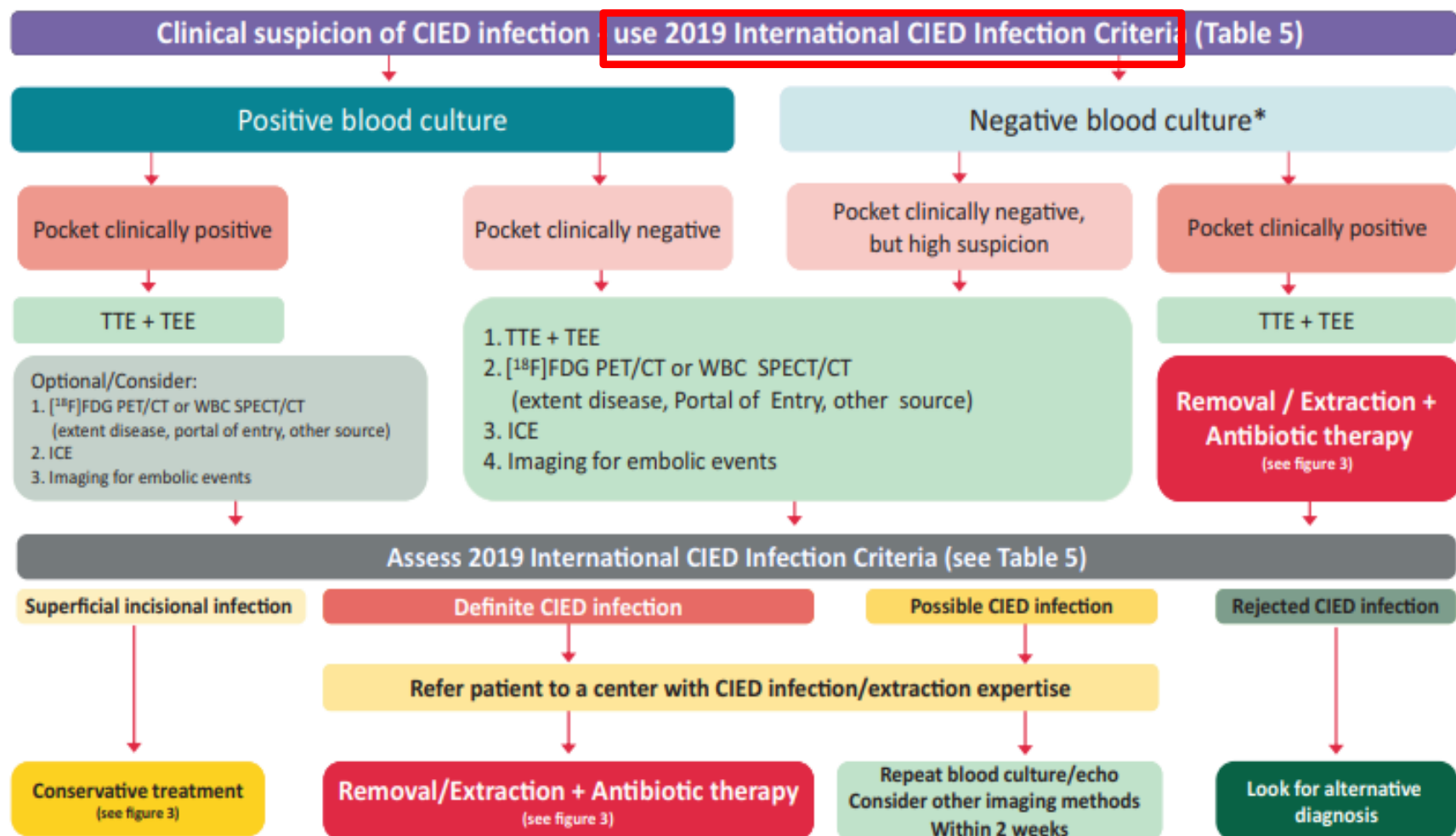


Figure 2 Diagnostic algorithm for diagnosis of suspected CIED infections. *, ensure sufficient number of blood cultures collected and absence of confounding antibiotic therapy prior to cultures. CIED, cardiac implantable electronic device; $[^{18}\text{F}]$ FDG PET/CT, fluorodeoxyglucose positron emission tomography—computed tomography; ICE, Intracardiac echocardiography; IE, infective endocarditis, TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography; WBC SPECT/CT, white blood cell single-photon emission computed tomography—computed tomography.

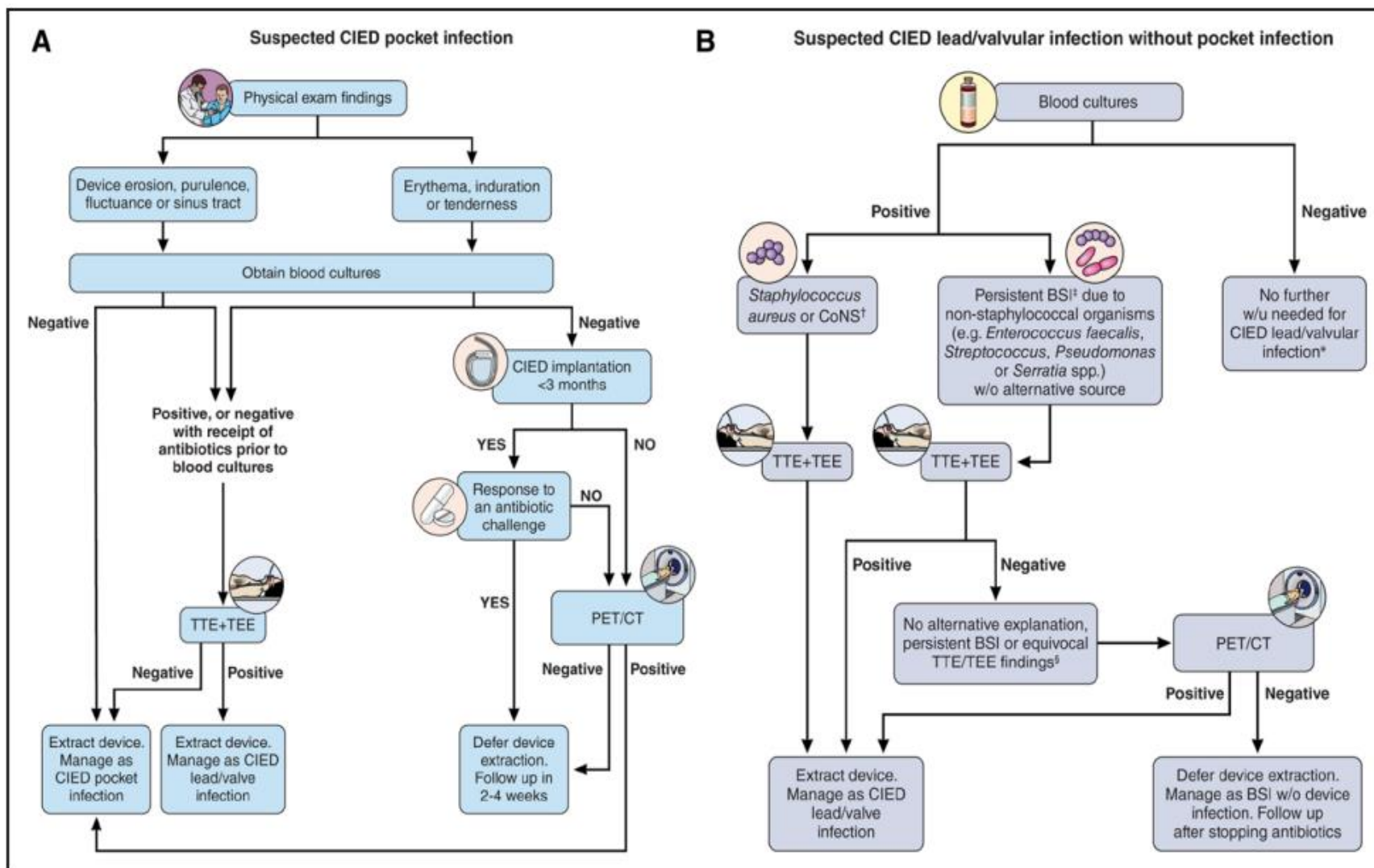


Figure 3. Diagnosis and management algorithms for suspected CIED pocket infection (A) and suspected CIED lead/valvular infection without pocket infection (B).

BSI indicates bloodstream infection; CIED, cardiovascular implantable electronic device; CoNS, coagulase-negative staphylococci; PET/CT, positron emission tomography/computerized tomography scanning; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; w/o, without; and w/up, work up.

Table 5 Recommendations for diagnosis of CIED infections and/or infective endocarditis: the Novel 2019 International CIED Infection Criteria



Consensus statement	Statement class	Scientific evidence coding	Reference
<p>'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</p> <p>'Definite' CIED/IE = presence of either 2 major criteria or 1 major + 3 minor criteria</p> <p>'Possible' CIED/IE = presence of either 1 major + 1 minor criteria or 3 minor criteria</p> <p>'Rejected' CIED/IE diagnosis = patients who did not meet the aforementioned criteria for IE</p>			
Major criteria		E	59
Microbiology	<div><p>A. Blood cultures positive for typical microorganisms found in CIED infection and/or IE (<i>Coagulase-negative staphylococci</i>, <i>S. aureus</i>)</p><p>B. Microorganisms consistent with IE from 2 separate blood cultures:</p><ul style="list-style-type: none">a. Viridans streptococci, <i>Streptococcus gallolyticus</i> (<i>S. bovis</i>), HACEK group, <i>S. aureus</i>; orb. Community-acquired enterococci, in the absence of a primary focus<p>C. Microorganisms consistent with IE from persistently positive blood cultures:</p><ul style="list-style-type: none">a. ≥ 2 positive blood cultures of blood samples drawn >12 h apart; orb. All of 3 or a majority of ≥ 4 separate cultures of blood (first and last samples drawn ≥ 1 h apart); orc. Single positive blood culture for <i>Coxiella burnetii</i> or phase I IgG antibody titre $>1:800$</div>		

Table 5 Recommendations for diagnosis of CIED infections and/or infective endocarditis: the Novel 2019 International CIED Infection Criteria

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<p>'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</p> <p>'Definite' CIED/IE = presence of either 2 major criteria or 1 major + 3 minor criteria</p> <p>'Possible' CIED/IE = presence of either 1 major + 1 minor criteria or 3 minor criteria</p> <p>'Rejected' CIED/IE diagnosis = patients who did not meet the aforementioned criteria for IE</p>			
Imaging positive for CIED infections and/or IE	<p>D. Echocardiogram (<i>including ICE</i>) positive for:</p> <p>a. CIED infection:</p> <p>i. Clinical pocket/generator infection</p> <p>ii. Lead-vegetation</p> <p>b. Valve IE</p> <p>i. Vegetations</p> <p>ii. Abscess, pseudoaneurysm, intracardiac fistula</p> <p>iii. Valvular perforation or aneurysm</p> <p>iv. New partial dehiscence of prosthetic valve</p> <p>E. [¹⁸F]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</p> <p>F. Definite paravalvular leakage by cardiac CT</p>		

Table 5 Recommendations for diagnosis of CIED infections and/or infective endocarditis: the Novel 2019 International CIED Infection Criteria

Consensus statement	Statement class	Scientific evidence coding	Reference
<p>'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</p> <p>'Definite' CIED/IE = presence of either 2 major criteria or 1 major + 3 minor criteria</p> <p>'Possible' CIED/IE = presence of either 1 major + 1 minor criteria or 3 minor criteria</p> <p>'Rejected' CIED/IE diagnosis = patients who did not meet the aforementioned criteria for IE</p>			
Minor criteria		E	59
<p>a. Predisposition such as predisposing heart condition (e.g. new onset tricuspid valve regurgitation) or injection drug use</p> <p>b. Fever (temperature >38°C)</p> <p>c. Vascular phenomena (including those detected only by imaging): major arterial emboli, septic pulmonary embolisms, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions</p> <p>d. Microbiological evidence: positive blood culture which does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE or pocket culture or leads culture (extracted by non-infected pocket)</p>			

Based on merging of the modified Duke and ESC 2015 Guidelines criteria, see text.^{59,60} Green text refers to CIED-related infection criteria.

CIED, cardiac implantable electronic device; CT, computerized tomography; E, expert opinion; ICE, intracardiac echocardiography; IE, infective endocarditis; M, meta-analysis; O, observational studies; R, randomized trials; SPECT, single-photon emission tomography; WBC, white blood cell.

Table 6 Recommendations for diagnosis of CIED infections by clinical findings and microbiology

Consensus statement	Statement class	Scientific evidence coding	References
At least three sets of blood cultures should be acquired in case of clinically suspected CIED endocarditis		E, O	19,65
Samples from the pocket should be cultured but only if acquired during removal and not passing through the sinus		E, O	19,65
Suspect CIED infections in case of vertebral osteomyelitis and/or embolic pneumonia (clinical signs and symptoms of CIED systemic infections may be difficult to recognize as only fever may be present)		E, O	61,65
Cultures of extracted CIED should be performed		E, O	66
PCT may be useful in case of infective endocarditis and embolism and/or in case of <i>S. aureus</i> CIED-related infective endocarditis		E, O	64
Increased incubation time (10–14 days) for slowly-growing microorganism may be considered in case of CIED-related infective endocarditis and persistent negative blood cultures		E	67
The usefulness of sonication of CIED to enhance microbial detection during removal/extraction is still under evaluation but may be used with caution when interpreting results		E, O	68–70
Cultures from the sinus of the CIED pocket or from parts of the device exposed		E	19

Identification of the causative microorganisms

- Therefore, every effort should be made to obtain cultures prior to the institution of antibiotic therapy.
- **Blood cultures should be repeated** in patients with CIED and fever without clear signs of local infections and infective endocarditis.
- **Three sets of blood cultures** should be taken (at least 30 min in between) prior to starting antibiotic therapy (Table 6).
- **Multiple blood cultures at different time intervals** enable a distinction between transient and persistent bacteraemia and increases sensitivity.
- In stable patients, a 2–3 days washout period free from antibiotic therapy may increase precision of microbiological diagnosis.
- In unstable patients with sepsis or septic shock, early empiric antibiotic therapy should be administered following two sets of blood cultures

Identification of the causative microorganisms

- An **aseptic technique for blood culture is mandatory** since bacteria mostly considered as skin contaminants often are the causative agents of CIED infections
- **Increased incubation time (10–14 days)**
- and the **use of biomolecular methods (DNA amplification and/or gene sequencing)** to detect fastidious or atypical pathogens may be considered for CIED endocarditis and persistent negative blood cultures

Identification of the causative microorganisms

- **Swabs** collected from the chronic draining sinus or fistula for culture **are discouraged** (Table 6).
- Instead, **tissue or fluid collected from the pocket via an adjacent intact portion of the skin (via a sterile needle or syringe) is encouraged** avoiding passing through the sinus. This approach should only be used to make a bacterial diagnosis, not to determine the presence of a pocket infection

Identification of the causative microorganisms

- During an extraction procedure, distal and proximal lead fragments, lead vegetation if present and generator pocket tissue should be sent for culture (Table 6).
- Gram stain is still encouraged and biomolecular methods are increasingly used and may be more specific
- Culture media suggested are chocolate agar incubated in 5% CO₂ for 48–72 h, MacConkey agar incubated for 48 h, blood agar in anaerobic condition for 48–72 h, and Sabouraud agar incubated for 5 days.⁷
- In case of pus, but no growth after 3 days, consider slow-growing microorganisms including *C. acnes* and increase incubation duration

Identification of the causative microorganisms

- Sonication for the recovery of bacteria from CIED leads and tissue, may be useful in patients with clinical signs of infection although the method merits further investigational study

Diagnosi preoperatoria

- 1. Eseguire emocromo completo, velocità di eritrosedimentazione (VES) e
- Proteine C-reattive (CRP) e livelli di procalcitonina.
- 2. Eseguire 3 set di emocoltura prima di iniziare la terapia antibiotica empirica.
- ● I campioni di sangue devono essere coltivati in aereobiosi e anaerobiosi e anche per la ricerca di Candida.
- **3. Raccogliere in idonei contenitori anche per mantenere microrganismi anaerobi, eventuali secrezioni o raccolte della tasca per vetrino colorato con Gram, semina diretta su agar e in flaconi per emocoltura sia in aerobiosi che in anaerobiosi**

Diagnosi intraoperatoria

- 1. Raccogliere campioni delle eventuali raccolte o secrezioni o tessuto della tasca del generatore, il dispositivo stesso e gli elettrodi.
 - Se si sospetta, prendere in considerazione colture per miceti e micobatteri
- 2. Raccogliere le secrezioni in idonei contenitori anche per mantenere microrganismi anaerobi
- 3. Utilizzare le secrezioni e/o parte del tessuto per vetrino colorato con Gram, semina diretta su agar e in flaconi per emocoltura sia in aerobiosi che in anaerobiosi i campioni liquidi, mentre i campioni di tessuto possono essere incubati in flaconi a bocca più larga.
- 4. Eseguire Sonicazione del dispositivo, degli elettrodi e del tessuto.
 - Collocare il dispositivo o gli elettrodi o il tessuto estratto in un barattolo / contenitore sterile da 50 a 100 ml di soluzione salina sterile prima di inviarlo al laboratorio di microbiologia.

- **Local infection:** infections were considered local when patients showed no systemic symptoms (fever, shock, embolisms, or remote infectious complications), blood cultures were negative, and there were signs of infection in the region of the generator pocket, such as pain, erythema, and purulent material.
- **Systemic infection:** infections were considered systemic when patients showed systemic symptoms and blood cultures were repeatedly positive. Negative blood cultures required the presence of vegetation in the lead or right-sided cardiac structures.

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)

Jonathan A. T. Sandoe^{1*}, Gavin Barlow², John B. Chambers³, Michael Gammage⁴, Achyut Guleri⁵, Philip Howard¹, Ewan Olson⁶, John D. Perry⁷, Bernard D. Prendergast⁸, Michael J. Spry⁹, Richard P. Steeds¹⁰, Muzahir H. Tayebjee¹ and Richard Watkin¹¹

- If culture of pocket-site tissue is negative despite convincing evidence of infection, microbiologists may wish
 - to consider **prolonged incubation of media**
 - or, preferably, referral of tissue for amplification and **sequencing of bacterial 16S ribosomal RNA genes** to detect atypical causes not detected by routine culture.
 - The **use of sonication** for the recovery of bacteria from ICEDs may have a useful role to play in patients with clinical signs of infection and this merits further study.

Molecular Approach to Diagnosis of Cardiovascular Implantable Electronic Device Infection

Zerelda Esquer Garrigos, M Rizwan Sohail, Kerryl E Greenwood-Quaintance, Scott A Cunningham, Prakhar Vijayvargiya, Madiha Fida, Paul A Friedman, Jayawant Mandrekar, Daniel C DeSimone, Larry M Baddour ... Show more

Clinical Infectious Diseases, ciz266, <https://doi.org/10.1093/cid/ciz266>

Published:

04 April 2019

Article history

SF culture fails to identify a causative organism in ~50% of cases.

A total of 278 SF samples corresponded to infected cases, of which 160 were culture positive and 118 culture negative. The remaining 44 were from noninfected cases, of which 2 were culture positive. Compared with SF culture, the sensitivity of 16S rRNA PCR/sequencing was higher (64% vs 57.5%, $P = .003$). **16S rRNA PCR/sequencing detected a potential pathogen in 28 of 118 culture-negative cases, identifying staphylococci in the majority (18/28).**

RESEARCH ARTICLE

Open Access

The oral cavity is not a primary source for implantable pacemaker or cardioverter defibrillator infections

Jörg Eberhard^{1†}, Nico Stumpp^{1†}, Fadi Ismail¹, Ulrike Schnaidt¹, Wieland Heuer¹, Maximilian Pichlmaier², Christian Kühn², Axel Haverich² and Meike Stiesch¹

Methods: A metagenomic approach was used to analyze the bacterial diversity on the surfaces of non-infected and infected pacemakers. The DNA from surfaces swaps of 24 non-infected and 23 infected pacemaker were isolated and subjected to bacterial-specific DNA amplification, single strand conformation polymorphism- (SSCP) and sequencing analysis. Species-specific primer sets were used to analyze for any correlation between bacterial diversity on pacemakers and in the oral cavity

Results: In 17 cases bacterial DNA was found on pacemakers with no clinical signs of infections. On the basis of the obtained sequence data, the phylotypes *Propionibacterium acnes*, *Staphylococcus* and an uncultured bacterium were identified. *Propionibacterium acnes* and *Staphylococcus epidermidis* were the only bacteria detected in pacemaker (n = 25) and oral samples (n = 11).

Conclusion: The transmission of oral bacteria to the lead or device of implantable pacemaker or cardioverter defibrillators is unlikely relevant for the pathogenesis of pacemaker or cardioverter defibrillators infections.

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

ABSTRACT: The American Heart Association sponsored the first iteration of a scientific statement that addressed all aspects of cardiovascular implantable electronic device infection in 2010. Major advances in the prevention, diagnosis, and management of these infections have occurred since then, necessitating a scientific statement update. An 11-member writing group was identified and included recognized experts in cardiology and infectious diseases, with a career focus on cardiovascular infections. The group initially met in October 2022 to develop a scientific statement that was drafted with front-line clinicians in mind and focused on providing updated clinical information to enhance outcomes of patients with cardiovascular implantable electronic device infection. The current scientific statement highlights recent advances in prevention, diagnosis, and management, and how they may be incorporated in the complex care of patients with cardiovascular implantable electronic device infection.

- To enhance device culture sensitivity, vortexing sonification of explanted devices has been used for more than a decade in cases of prosthetic joint infection, and the technique is widely available among clinical laboratories
- Culture methods may not be adequate in some cases of CIEDI, most often due to recent antimicrobial exposure
- includes 16S rRNA gene polymerase chain reaction/sequencing of sonicate fluid.
- NGS is clearly of interest in defining pathogens in culture-negative CIEDI cases, and additional investigations are needed to better define its role

Esperienza CIED Bergamo

Impiantati/anno

- 300 Pacemaker
- 110 Defibrillatori

Infezioni

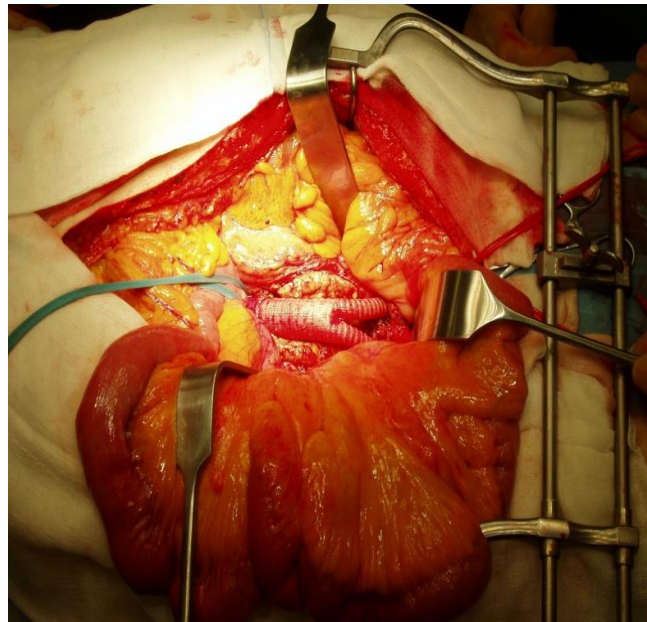
7 (1,7%)

Ma gestite dal Team
Esperto per le Estrazioni
di Brescia

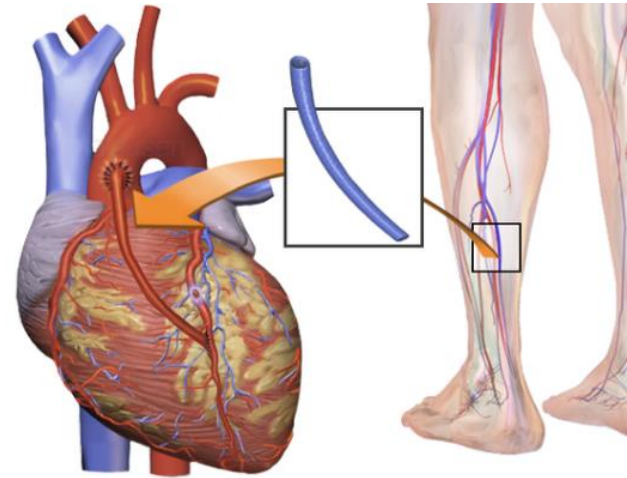
Le Protesi Vascolari



Protesi grosso calibro >7 mm



Protesi piccolo calibro <6 mm



Vascular prostheses include vascular grafts (VGs), generally implanted surgically, and vascular endografts (VEs) (or stent-grafts) implanted by endovascular procedure

Vascular prostheses

vascular grafts (VGs), generally implanted surgically, and
vascular endografts (VEs) (or stent-grafts) implanted by endovascular procedure

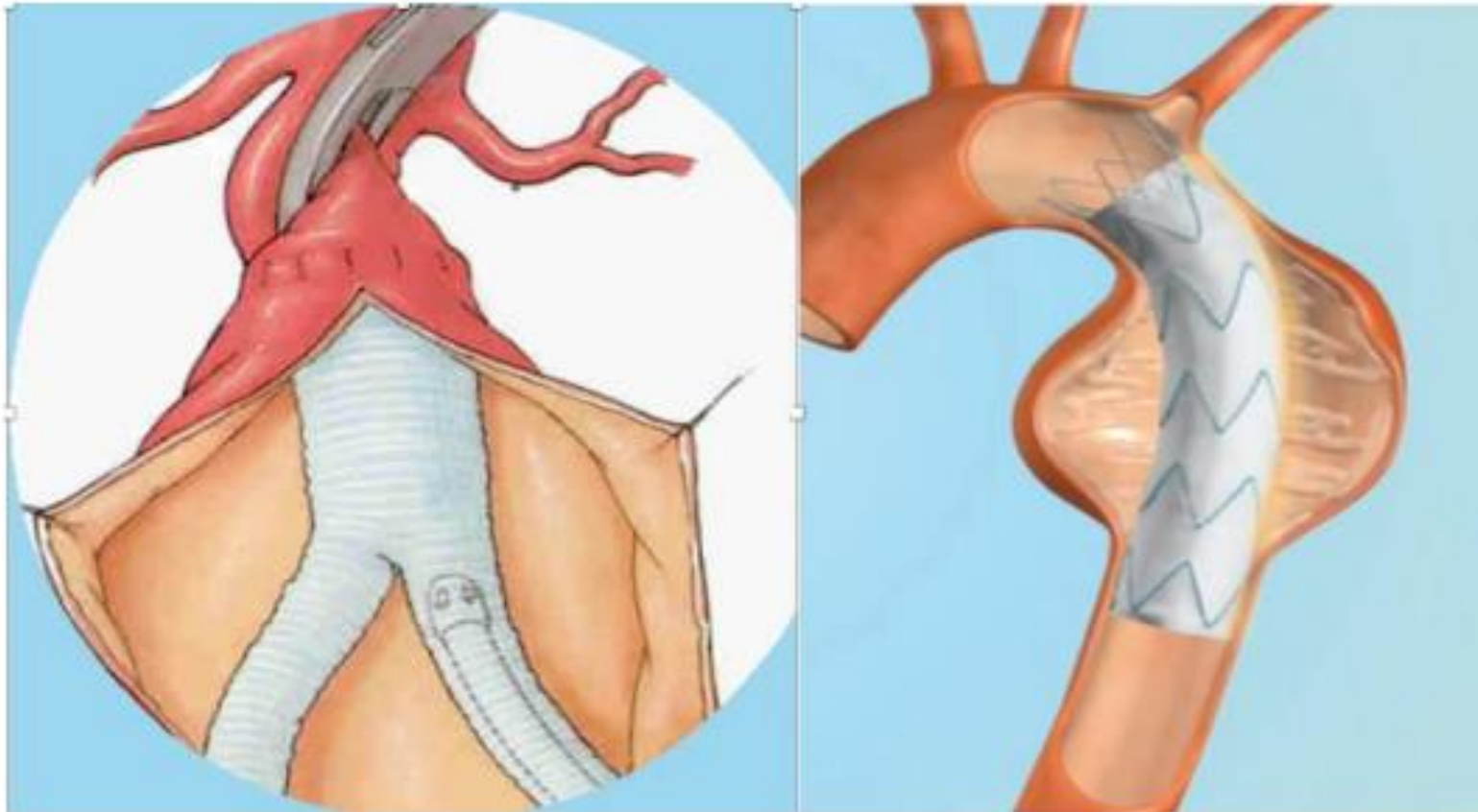


Figure 1. Vascular graft and vascular endograft. On the **(left)**: vascular graft; on the **(right)**: vascular endograft.

- VGs may be classified into **biological grafts**, which are composed of actual tissues, most often blood vessels (e.g., autologous grafts derived from the patient's own vessel); allografts (from human vessels); xenografts (generally of bovine origins); and **synthetic grafts** made from either poly-ethylene-terephthalate (PET, or Dacron), a textile material, or expanded polytetrafluoroethylene (ePTFE), a non-textile material

FATTORI IMPORTANTI NEL DETERMINARE IL DESTINO DELLE PROTESI VASCOLARI

Fattori legati alla protesi

- tipo e qualità del materiale
- disegno tecnologico della protesi
- fattori tecnici collegati all'impianto della protesi

Vasi e tessuti naturali

Sono state provate numerose protesi fatte con tessuti umani (auto- e omograft) e animali (eterograft) , incluse:

- a) **arterie crio-preserved** di cadavere umano;
- b) **carotidi bovine** modificate chimicamente;
- c) **vene ombelicali umane**, fissate;
- d) **vasi fibrosi** fabbricati su di un mandrino rotante.

Il destino di queste protesi non è sempre buono.

Le pareti, ad eccezione di quelle dei vasi omologhi, sono "morte", e vengono rapidamente rimpiazzate con tessuto fibrotico scadente.

I bypass che rimangono pervi spesso mostrano dilatazioni localizzate (aneurismi) e a volte vanno incontro a rottura.

Materiali Sintetici Utilizzati

DACRON® (polietilentereftalato)

Risultati: successo a lungo termine con il 90% degli impianti in larghi vasi

PTFE (politetrafluoroetilene)

Risultati: pervietà a lungo termine in vasi di medio calibro, come seconda scelta rispetto ai sostituti biologici

The background of the slide is a close-up photograph of several pink peony flowers. The petals are layered and have a delicate, ruffled texture. The lighting is soft, highlighting the various shades of pink from light to deep magenta.

Dacron

PTFE

Bioprotesi da Vena ombelicale umana

Bioprotesi di derivazione animale

Protesi eparinate

Protesi endotelizzate

Vena autologa

Arteria omologa crio-preservata

Bio-compound

CARATTERISTICHE DI UNA BIOPROTESI OTTIMALE

- resistenza alle infezioni
- biocompatibilità (atossica, aflogistica, non carcinogena, non immunogena) e biostabilità
- emostatica ma non trombogena con adeguata porosità per una buona bio-integrazione (queste caratteristiche sono garantite in una arteria dall'endotelio che agisce come organo secretivo e come barriera a permeabilità selettiva.
- proprietà meccaniche adeguate (resistenza parietale, resistenza al kinking)
- buona "suturabilità"
- bio-attività intesa come capacità di reagire appropriatamente agli stimoli fisiologici (capacità di vasocostrizione in risposta agli stimoli nervosi o biochimici)

Protesi vascolari in generale: problematiche

- A. Invecchiamento relativamente rapido delle protesi biologiche autologhe ed omologhe (iperplasia fibrosa lungo le linee di sutura, sclerosi della parete, calcificazione)**
- B. Degradazione delle protesi biologiche trattate (eterograft bovini, vena ombelicale umana) e delle protesi in Dacron**
- C. Infezioni della protesi, specie le sintetiche e le biologiche trattate**
- D. Dilatazione e rottura dei graft "leggeri" in poliestere**
- E. Lacerazioni a livello dei punti di sutura alle anastomosi**
- F. Trombosi in ogni tipo di graft**



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Perspective

Diagnosis and treatment of vascular graft and endograft infections: a structured clinical approach



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A vascular graft or endograft infection (VGEI) is a severe infectious disease and is accompanied by high morbidity and mortality rates. Diagnosis can be challenging due to the often difficult to reach anatomical sites for microbiologic diagnosis and the possibility of false-positive imaging. In addition, antimicrobial and surgical treatment is challenging due to the polymicrobial nature of the infection, the presence of biofilm, and the extensiveness of surgery to achieve curation. To handle these infections, a dedicated and experienced multidisciplinary team is key







Epidemiologia

- Le infezioni delle VG e VE hanno un rischio relativamente basso e
- hanno un'incidenza dell'1% se localizzate a livello addominale ma del 6% se localizzate a livello toracico.

- in thoracic VEGIs, mainly gram-positive bacteria, like those found in infective endocarditis, can be found (Staphylococcus aureus, Coagulase-negative Staphylococcus, Enterococcus, and Streptococcus).
- On the other hand, Gram-negative bacteria and polymicrobial infections can be isolated in abdominal VGEIs

Review

Infection of Vascular Prostheses: A Comprehensive Review

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- Several infectious microorganisms are involved in VGEI development, but the most frequent type, responsible for over **75% of infections**, is ***Staphylococcus aureus*** and, in particular, the most severe infections are those with methicillin-resistant *Staphylococcus aureus* (**MRSA**). On the other hand, **gram-negative** bacteria infections, such as ***Pseudomonas aeruginosa***, ***Escherichia coli***, ***Klebsiella***, ***Enterobacter***, or ***Proteus***, although less frequent, are associated with a more serious course

Table 1

Management of Aortic Graft Infection Collaboration (MAGIC) criteria for VGEI diagnosis [[Anagnostopoulos et al., 2021](#)].

Clinical/surgical	Radiology	Laboratory
<p><i>Major</i></p> <ul style="list-style-type: none"> • Pus around graft or in aneurysm sac at surgery • Open wound with exposed graft or communicating sinus • Graft insertion in an infected site, e.g., fistula, mycotic aneurysm or infected pseudoaneurysm 	<p><i>Major</i></p> <ul style="list-style-type: none"> • Perigraft fluid on CT scan ≥ 3 months after insertion • Perigraft gas on CT scan ≥ 7 weeks after insertion • Increase in perigraft gas volume demonstrated on serial imaging 	<p><i>Major^a</i></p> <ul style="list-style-type: none"> • Organisms recovered from an explanted graft • Organisms recovered from an intra operative specimen • Organisms recovered from a percutaneous, radiologically guided aspirate or perigraft fluid
<p><i>Minor</i></p> <ul style="list-style-type: none"> • Localized clinical features of VGEI, e.g., erythema, warmth, swelling, purulent discharge, pain • Fever $\geq 38^{\circ}\text{C}$ with VGEI as the most likely cause. 	<p><i>Minor</i></p> <ul style="list-style-type: none"> • Other, e.g., suspicious perigraft gas/fluid/soft tissue inflammation; aneurysm expansion; pseudoaneurysm formation; focal bowel wall thickening; discitis/ osteomyelitis; suspicious metabolic activity on fluorodeoxyglucose-positron emission tomography/ CT; radiolabeled leukocyte uptake 	<p><i>Minor</i></p> <ul style="list-style-type: none"> • Blood culture results positive and no apparent source except VGEI aneurysm sac at surgery^a • Abnormally elevated inflammatory markers with VGEI as most likely cause, e.g., ESR, C-reactive protein, white cell count

^a If microbiologic investigations identify organisms that are potential contaminants (e.g., coagulase-negative staphylococci, propionibacteria, corynebacteria, and other skin commensals), a minimum of (i) two intraoperative specimens; (ii) two blood cultures; or (iii) one intraoperative specimen plus one blood culture must have positive results for an indistinguishable organism in each sample (based on antibiograms or a recognized typing method).CT, computed tomography; ESR, erythrocyte sedimentation rate; VGEI, vascular graft or endograft infection.

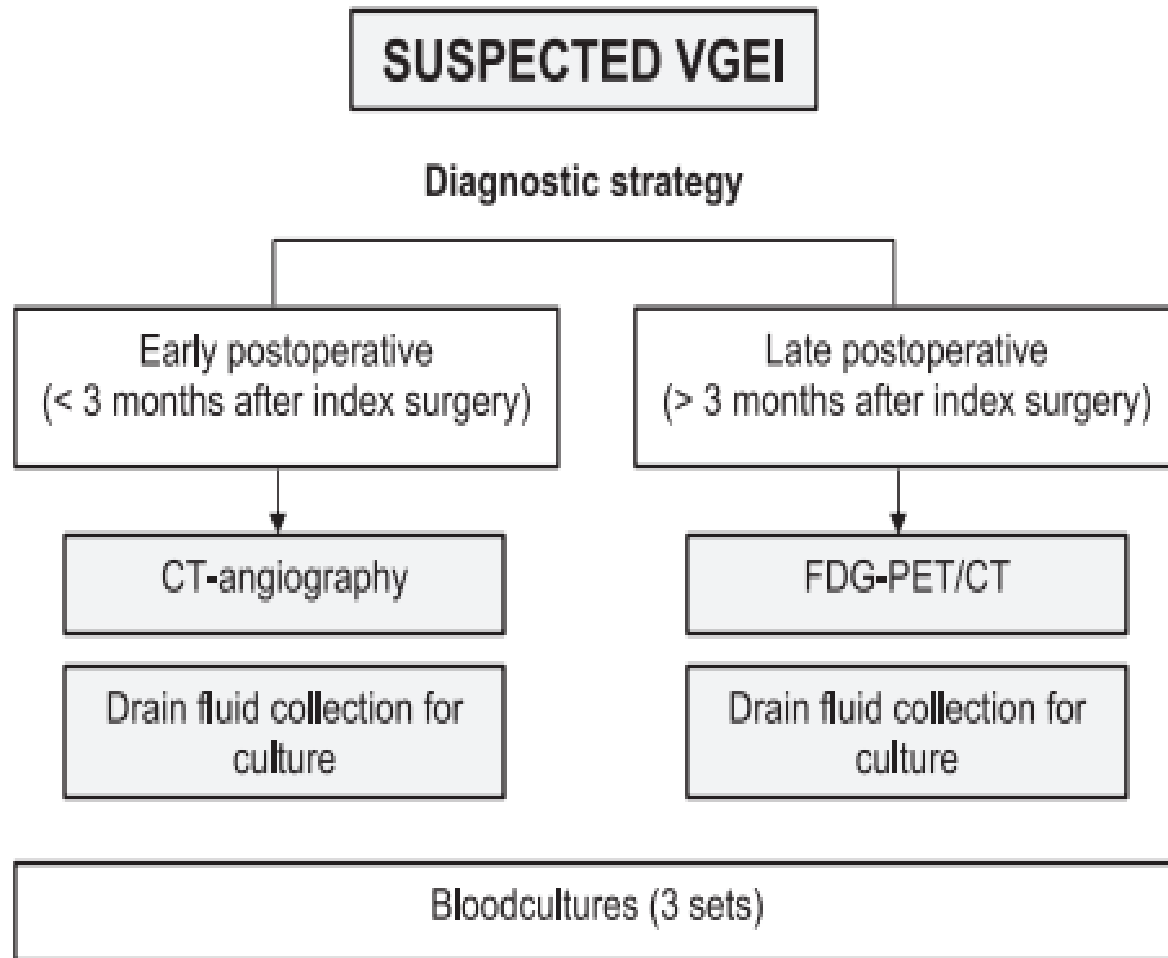


Figure 1. Diagnostic strategy.

CT, computed tomography; FDG, fluorodeoxyglucose; PET, positron emission tomography; VGEI, vascular graft or endograft infection.

- the microbiologic yield of blood cultures is generally low (~30%) and does not always reflect the complete spectrum of causative microorganisms isolated from intraoperative material (Bisharat and Minuhin, 2012; Legout et al., 2012a)
- In cases when blood culture results are positive, we recommend follow-up blood cultures at 1-day intervals after the start of antimicrobial treatment until follow-up blood culture results are negative.
- A culture of a sinus tract or superficial wound is discouraged, as the results cannot differentiate between skin colonization and infection

- In cases when surgery is feasible, the **entire explanted vascular graft should be sent to the microbiology** laboratory in a sterile container
- If **sonication methods** are available at the treating center, the vascular graft can be sonicated to increase the culture yield of biofilm-embedded bacteria (Fournier et al., 1998; Kokosar Ulcar et al., 2018).
- In addition, multiple (**>3**) **tissue biopsy specimens near the vascular graft must be obtained** (with uncontaminated surgical instruments) and immediately transferred into a sterile container (i.e., they should not be left on the sterile surgical field); these should be sent immediately to the microbiology laboratory

- Pus must be aspirated in a syringe and capped with as little air as possible (to ensure the reliability of anaerobic cultures)
- When a part of the vascular graft cannot be removed, a separate sample/ring of the vascular graft can be collected at the site/border of the part that remains in situ.
- The culture results from this part of the vascular graft may be used to decide whether lifelong antimicrobial suppressive therapy is necessary

VGEI

Surgical strategy

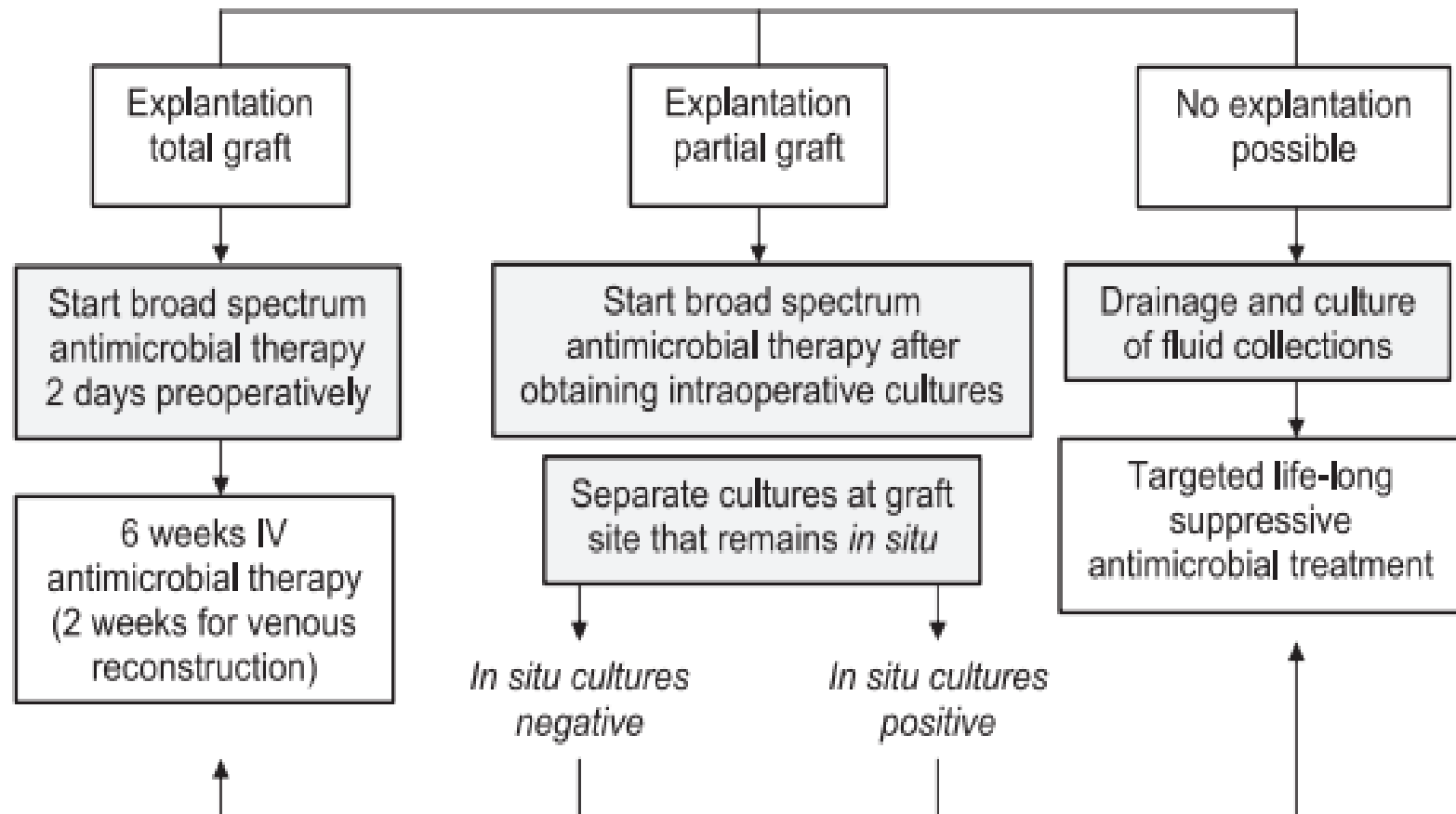


Figure 2. Surgical and antimicrobial strategy.

IV, intravenous; VGEI, vascular graft or endograft infection.

- In cases when **all culture results are negative** (possibly due to previous antimicrobial treatment or to the presence of fastidious—i.e., difficult-to-culture—microorganisms), **molecular techniques and/or serology** can be performed in patients in whom a VGEI is highly suspected.
- It is important to note that **molecular techniques remain (in most cases) less sensitive than microbiologic cultures, and phenotypic resistance of bacteria cannot be determined.**
- Examples of causative microorganisms diagnosed by **serology, molecular techniques, or special culture methods are *Coxiella burnetii*, *Tropheryma whipplei*, *Bartonella henselae*, and mycobacteria**



GRAZIE PER L'ATTENZIONE