

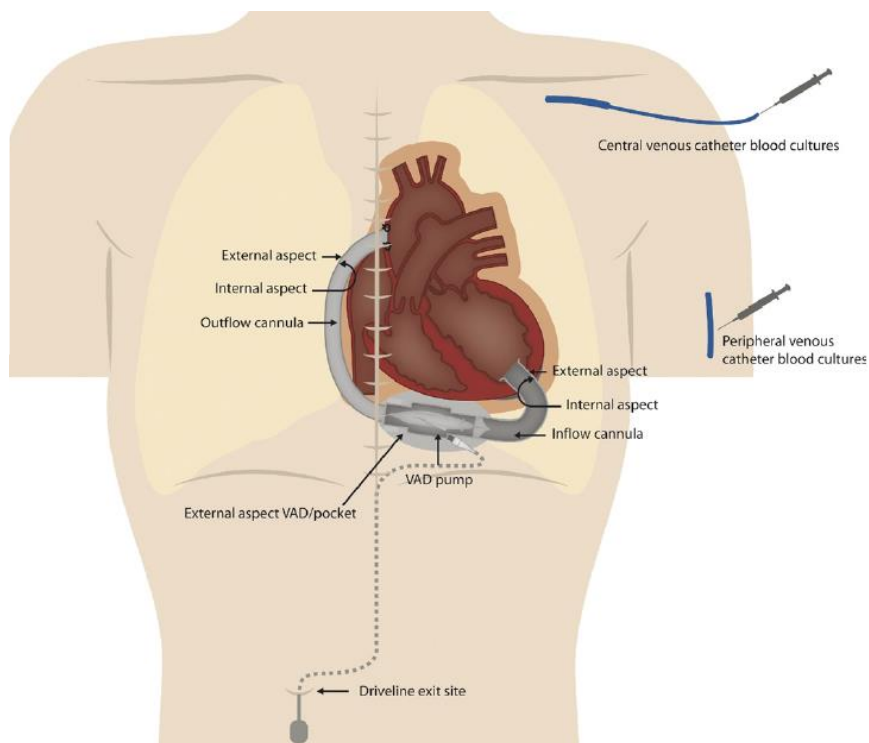
Pocket Guide to Diagnosis & Treatment of Ventricular Assist Device (VAD) Infections



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CLASSIFICATION OF VAD-INFECTIONS

- VAD - specific infection (pump, pocket, cannula, driveline)
- VAD - related infection (endocarditis, pancarditis)
- non VAD infection (pneumonia)
- VAD - related and non VAD mediastinitis
- VAD - related Bloodstream infection (BSI)
Time difference between CVC and PVC blood cultures
≤ 2hrs = BSI presumed VAD - related
> 2hrs = BSI presumed CVC - related



from Hannan M et al. Journal of Heart and Lung Transplantation, 2011

	VAD-specific infections	VAD-related infections	VAD-related bloodstream infections	other
Extra-vascular	<ul style="list-style-type: none"> • Driveline infection • Pocket infection 	<ul style="list-style-type: none"> • Pericarditis 		<ul style="list-style-type: none"> • CIED pocket infection • Mediastinitis
Intra-vascular	<ul style="list-style-type: none"> • Pump/cannula infection/outflow graft 	<ul style="list-style-type: none"> • Infective endocarditis 	<ul style="list-style-type: none"> • CIED lead infection • Catheter-related BSI 	<ul style="list-style-type: none"> • VAD-unrelated BSI

Abbreviations:

- VAD, ventricular assist device
- BSI, bloodstream infection
- CIED, cardiac implantable electronic device
- TEE, transesophageal echocardiography
- P/CVC, peripheral / central venous catheter
- US, ultrasound
- CT, computertomography
- PET/CT: 18-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography

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DEFINITIONS

Extravascular VAD (driveline, pocket) infections (A and B fulfilled)

Investigation/sign	Criteria
A) Microbiology	
Negative blood cultures	
B) At least 1 criterion fulfilled:	
Local signs of infection restricted to the LVAD entry or pump pocket site	Purulent wound secretion or sinus tract or abscess (clinical evidence or seen in ultrasound and/or CT/PET-CT)
Microbiology	Positive cultures from the skin/subcutaneous tissue

Systemic VAD infection (proven if ≥ 2 criteria, probable if ≥ 1 criterion fulfilled)

Investigation/sign	Criteria
A) Microbiology	
Positive blood cultures (time to positivity central/peripheral $<2h$) and no other focus	
B) Imaging (TEE, CT- or PET-Scan) (either):	
<ul style="list-style-type: none">Pump interior/cannula infection	<ul style="list-style-type: none">Intracardiac mass suspected to be vegetation adjacent to the deviceAbscess anatomically related to device ornew partial dehiscence of inflow (outflow) cannula
<ul style="list-style-type: none">VAD related endocarditis	<ul style="list-style-type: none">Vegetation on native valves orParavalvular abscess
C) Extravascular infection (driveline or pump pocket infection or mediastinitis)	

VAD-related bloodstream infection (A and B fulfilled)

Investigation	Criteria
A) Microbiology	Positive blood cultures (differential time to positivity central/peripheral $<2h$)
B) Imaging	Negative echocardiography and no other focus

CLASSIFICATION according to time of occurrence

	Acute infection (immature biofilm)	Chronic infection (mature biofilm)
Pathogenesis		
▪ Perioperative	<4 weeks after surgery (early)	≥4 weeks after surgery (delayed/low-grade)
▪ Hematogenous or contiguous	<3 weeks of symptom duration	≥3 weeks of symptom duration
Treatment strategy	Eradication	Suppression, treatment of infection exacerbation
Antimicrobial therapy	Biofilm-active (if available)	No biofilm-active antibiotics, suppression

DIAGNOSTIC WORK-UP

All patients with suspected LVAD infection:

- C-reactive protein (CRP) and white blood cell count
- Echocardiography (transesophageal, TEE)
- Blood cultures:
 - At least 3 sets within 24h
 - 2 from peripheral sites
 - If central line in place: 1 central and peripheral culture at same time
- Chest X-ray or CT or PET-CT* or leukocyte scintigraphy**

Specific situations:

- If local infection: aspiration of pus at driveline exit site/pocket abscess, swab of driveline exit site
- Sonication of retrieved hardware/catheter, if removed
- In culture-negative infections consider molecular diagnostics (e.g. PCR, NGS)

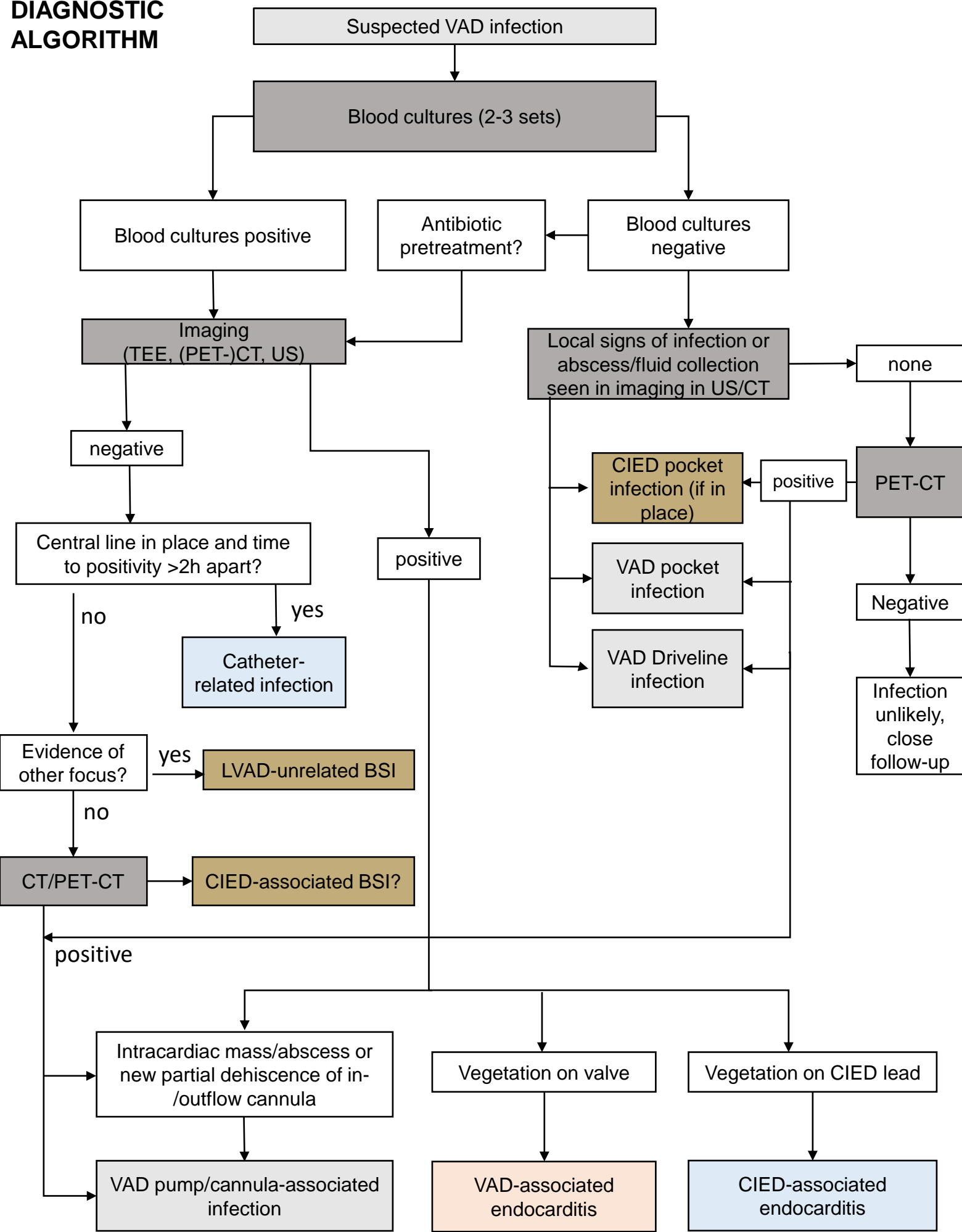
*18-FDG-PET/CT: sensitivity of 90-100% and specificity of 67-80% were reported for qualitative (visual) analysis¹⁻³. False-positive results may occur within approx. 6 months after implantation.

**Leukocyte scintigraphy if no PET/CT available (less sensitive but more specific than PET-CT³) and at least 3-6 months after surgery.

¹Dell'Aquila et al, Ann Thoracic Surg, 2016, ²Dell'Aquila et al, European Heart Journal - Cardiovascular Imaging, 2018, ³De Vaugelade et al, Journal of Nuclear Cardiology, 2018

Note: many of the recommendations are based on expert opinion because rigorous clinical data are not available and the likelihood that clinical trials will be conducted to answer some of these questions is low. Our goal was to develop guidelines that offer a practical and useful approach to assist practicing clinicians in the management of VAD-infections. For individual recommendations contact our Consultation Portal at: cp.pro-implant-foundation.org

DIAGNOSTIC ALGORITHM



TREATMENT OF VAD-SPECIFIC INFECTIONS

Infection	Surgery	Antimicrobial treatment	
		Acute infection	Chronic infection
Local VAD infections			
Pocket infection	Surgical debridement, wrapping with omental or latissimus dorsi flap	6 weeks of biofilm-active treatment* (eradication)	2-4 weeks, consider suppressive treatment**
Driveline infection	<ul style="list-style-type: none"> • Surgical debridement or percutaneous drainage, if abscess. • Driveline relocation • Consider listing for high urgent transplantation 	6 weeks of biofilm-active treatment* (eradication)	2-4 weeks of antibiotic treatment, consider local use of antibiotics
Systemic VAD infections			
Pump/cannula infections	<ul style="list-style-type: none"> • Surgical debridement • Pump exchange after temporary intravascular VAD support • Consider listing for high urgent transplantation 	12 weeks of biofilm-active treatment* (eradication)	4-6 weeks, consider suppressive treatment**

* Attention to drug interactions between rifampin and comedication (particularly warfarin or other vitamin k antagonists) is required.

** Consider suppression (until transplantation or lifelong), if bacteremia persists despite removal of device (CIED/catheter) and adequate treatment or if relapse occurs after adequate treatment

TREATMENT OF VAD-RELATED INFECTIONS

Infection	Surgery	Antimicrobial treatment
Bloodstream infections		
Catheter-related infection	Removal of catheter	According to guidelines for catheter-related BSI
Endocarditis		
CIED-lead vegetation	Removal/exchange of CIED	According to CIED Pocket Guide, consider suppressive treatment
VAD-related endocarditis	No surgery (consider listing for high urgent transplantation)	≥6 weeks of antimicrobial therapy followed by suppressive treatment*

TREATMENT OF OTHER INFECTIONS

Infection	Surgery	Antimicrobial treatment
VAD-unrelated BSI	None	Treatment according to primary focus

ANTIMICROBIAL TREATMENT

Empirical intravenous treatment

Ampicillin/sulbactam 3-4x3g **or** amoxicillin/clavulanic acid 3-4x2.2g (higher dose, if systemic infection)
+ vancomycin 2x15mg/kg **or** daptomycin 1x10mg/kg

→ if patient septic or polymicrobial infection possible: **add** gentamicin 1x240mg i.v.

→ if patient is allergic to penicillin: cefazolin 4x2 (**or** meropenem 3x2g, if anaphylaxis)

→ if fungal infection suspected: **add** caspofungin 1x70mg (reduce dose to 50mg from day 2, if patient weighs <80kg)

Local/extravascular infections

	Intravenous treatment	Suppression (oral)	Eradication (oral)
<i>Staphylococcus spp.</i> <ul style="list-style-type: none"> Oxacillin-susceptible Anaphylactic reaction to penicillins or methicillin-resistant 	Flucloxacillin 4x2g or Cefazolin 3x2g Vancomycin 2x15mg/kg or Daptomycin 1x 6-8mg/kg	Cotrimoxazol 2x960mg or Clindamycin 3x600mg or Doxycyclin 2x100mg or Amoxicillin/clavulanic acid 3x1g	Rifampin ¹ 2x450mg plus Levofloxacin 2x500mg or Cotrimoxazol 3x960mg or Doxycyclin 2x100mg
<i>Streptococcus spp.</i> <ul style="list-style-type: none"> Penicillin-susceptible Anaphylactic reaction to penicillin or penicillin-resistant 	Penicillin G 4x5 Mio E or Ceftriaxon 1x2g Vancomycin 2x15mg/kg or Daptomycin 1x 6-8mg/kg	Amoxicillin 3x1g or Clindamycin 3x600mg or Levofloxacin 2x500mg	Amoxicillin 3x1g or Clindamycin 3x600mg or Levofloxacin 2x500mg
<i>Enterococcus spp.</i> <ul style="list-style-type: none"> Penicillin- and gentamicin (HL)-susceptible Anaphylactic reaction to penicillins or penicillin-resistant 	Amoxicillin 4x2g ² (plus gentamicin 1x3 mg/kg, if device in situ) Vancomycin 2x15mg/kg or Daptomycin 1x10mg/kg (plus gentamicin 1x3 mg/kg, if device in situ)	Amoxicillin 3x1g or Linezolid 2x600mg	Amoxicillin 3x1g or Linezolid 2x600mg
Enterobacteriaceae <ul style="list-style-type: none"> Anaphylactic reaction to penicillin/cephalosporins 	Ceftriaxon 1x2g or Piperacillin/tazobactam 3x4.5g Ciprofloxacin 2-3x400mg or meropenem 3x1g	Cotrimoxazol 2x960mg or Ciprofloxacin 2x750mg	Ciprofloxacin 2x750mg (if resistant to ciprofloxacin, consider long-term suppression)

¹ Attention to drug interactions between rifampin and other drugs metabolized through CYP-3A4 and CYP-2C9 (particularly warfarin) is required.

² or ampicillin 6x2g i.v.

Systemic VAD infections

	Intravenous treatment (suppression)	Intravenous treatment (eradication)
<i>Staphylococcus spp.</i> <ul style="list-style-type: none"> Oxacillin-susceptible Anaphylactic reaction to penicillins or methicillin-resistant¹ 	Flucloxacillin 6x2g or Cefazolin 3x2g Vancomycin ² 2x15mg/kg or Daptomycin 1x 8-10mg/kg	Add Rifampin ³ 2x450mg p.o. to regimen in the left column
<i>Streptococcus spp.</i> <ul style="list-style-type: none"> Penicillin-susceptible Anaphylactic reaction to penicillins or penicillin-resistant 	Penicillin G 4x5 Mio E or Amoxicillin 6x2g or Ceftriaxon 1x2g Vancomycin ² 2x15mg/kg or Daptomycin 1x 8-10mg/kg	Add Gentamicin ² 1x 3mg/kg to regimen in the left column
<i>Enterococcus spp.</i> <ul style="list-style-type: none"> Penicillin- and gentamicin (HL)-susceptible Penicillin- susceptible and gentamicin (HL)-resistant (only <i>E. faecalis</i>) Anaphylactic reaction to penicillins or penicillin-resistant enterococci 	Amoxicillin or ampicillin 6x2g plus Gentamicin ² 1x3mg/kg Amoxicillin or Ampicillin 6x2g plus Ceftriaxon 2x2g Vancomycin ² 2x15mg/kg or Daptomycin 1x10mg/kg plus Gentamicin ² 1x3mg/kg or Fosfomycin 3x5g	Amoxicillin or ampicillin 6x2g plus Gentamicin ² 1x3mg/kg Amoxicillin or ampicillin 6x2g plus Ceftriaxon 2x2g Vancomycin ² 2x15mg/kg or Daptomycin 1x10mg/kg plus Gentamicin ² 1x3mg/kg or Fosfomycin 3x5g
Enterobacteriaceae <ul style="list-style-type: none"> Anaphylactic reaction to penicillins/cephalosporins 	Ceftriaxon 1x2g plus Gentamicin ² 1x3mg/kg Ciprofloxacin 2-3x400mg or meropenem 3x1g	Replace gentamicin with Ciprofloxacin 2x750mg p.o. to regimen in the left column
<i>Candida spp.</i>	Amphotericin B (liposomal) 1x 3-5mg/kg or Caspofungin 1x50-70 mg or Anidulafungin 1x200 mg	Fluconazol 1x400-800mg p.o. (consider suppression for ≥1 year)

¹ In MRSA according to MIC for vancomycin: if ≤0.5mg/L: vancomycin, if ≥1mg/l: daptomycin

² Adjustment according to trough level: gentamicin: target <1 mg/l; vancomycin: target 15-20mg/l)

³ Check drug interactions between rifampin and other drugs (particularly warfarin, vit k antagonists)

MANAGEMENT OF BACTEREMIA IN VAD-RECIPIENTS

(extrapolated and modified after DeSimone et al. Heart Rhythm 2016 (for CIED))

