

Pocket Guide to Diagnosis & Treatment of Vascular Graft Infections (VGI)



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DEFINITION

Infection confirmed, if ≥ 1 definitive criterion or ≥ 2 suggestive criteria fulfilled:

Investigation /sign	Definitive Criteria	Suggestive criteria
Local signs of infection	<ul style="list-style-type: none"> • Purulent wound secretion or sinus tract or abscess or • Wound dehiscence or graft on view • Aortoenteric fistula or • Intraoperative gross purulence 	<ul style="list-style-type: none"> • GI Bleeding
Histo-pathology	Evidence of infection in peiprosthetic tissue	
Micro-biology	<ul style="list-style-type: none"> • Positive culture from specimen taken at the immediate area around the graft¹ or • Continuous bacteremia² in the presence of a graft with no other infectious focus or • Positive sonication fluid culture of removed graft 	<ul style="list-style-type: none"> • Single positive culture
Imaging	<ul style="list-style-type: none"> • Abscess involving the graft and the surrounding tissue in CT/MRI or PET-CT • Failure of the graft to incorporate into surrounding soft tissue 	<ul style="list-style-type: none"> • Perigraft air or fluid in CT persisting for more than 8-12 weeks postoperatively • Lockal thickening of the intestinal wall (aortic VGI)

¹ For highly virulent organisms (e.g. *S. aureus*, *E. coli*) one positive culture needed, for low-virulent organisms (e.g. *S. epidermidis*) 2 or more positive cultures are needed to confirm infection

² ≥ 2 blood cultures with the same pathogen obtained at different times

CLASSIFICATION

	Peripheral VGI		Aortic VGI	
			Intrathoracic	Intraabdominal
Pathogenesis				
• perioperative			Intra- or postoperative contamination	
• contiguous	• Soft tissue infection	• Mediastinitis	• Aortoenteric fistula (duodenum > colon)	• Intraabdominal/pelvic abscess
		• Aortoesophageal fistula		
• hematogenous ¹		Primary or secondary bacteremia		
Clinical features	<p><u>Acute:</u> Acute pain, fever, rigors, prolonged wound discharge</p> <p><u>Chronic:</u> graft occlusion with distal ischemia, septic emboli, pseudoaneurysm, anastomotic rupture with hemorrhage</p>	Fever, chills, heart failure, („endocarditis-like“), chest pain, stroke/brain abscess (cerebral septic emboli), rupture with massive bleeding	Abdominal pain, intermittent polymicrobial bacteremia (fecal flora, erosion of the intestine), gastrointestinal bleeding (hematemesis, hematochezia oder melaena), peripheral ischemia/emboli, palpable abdominal or groin mass	
Causative micro-organisms	<p><i>Staphylococcus aureus</i>, coagulase-negative staphylococci, gram-negative bacteria (<i>Pseudomonas</i> spp.)</p>	<p><i>Staphylococcus aureus</i>, coagulase-negative staphylococci, <i>Cutibacterium</i> (formerly <i>Propionibacterium</i>) <i>acnes</i>, streptococci</p>	<p>Gram-negative bacteria (<i>Escherichia coli</i>, <i>Pseudomonas</i>), enterococci, anaerobes (<i>Bacteroides</i>, <i>Fusobacterium</i>, anaerobic cocci), <i>Candida</i></p>	

¹ The risk of hematogenous infection of VGI is highest in the early postoperative period (<2 months) and decreases over time because of partial endothelialization of the graft.

CLASSIFICATION according to biofilm maturity

	Acute infection (immature biofilm)	Chronic infection (mature biofilm)
Pathogenesis		
• Perioperative	<8 weeks after surgery (early)	≥8 weeks after surgery (delayed, late)
• Hematogenous <u>or</u> contiguous	<8 weeks of symptom duration	≥8 weeks of symptom duration
Surgical therapy	Retention and debridement of graft possible (see management algorithm)	Partial or complete excision/exchange of graft
Antimicrobial therapy	Biofilm-active (if available), consider suppressive treatment in difficult-to- treat infections	Biofilm-active (if available), consider suppressive treatment in difficult-to-treat infections and if no complete exchange is feasible/possible

DIAGNOSTIC WORK-UP

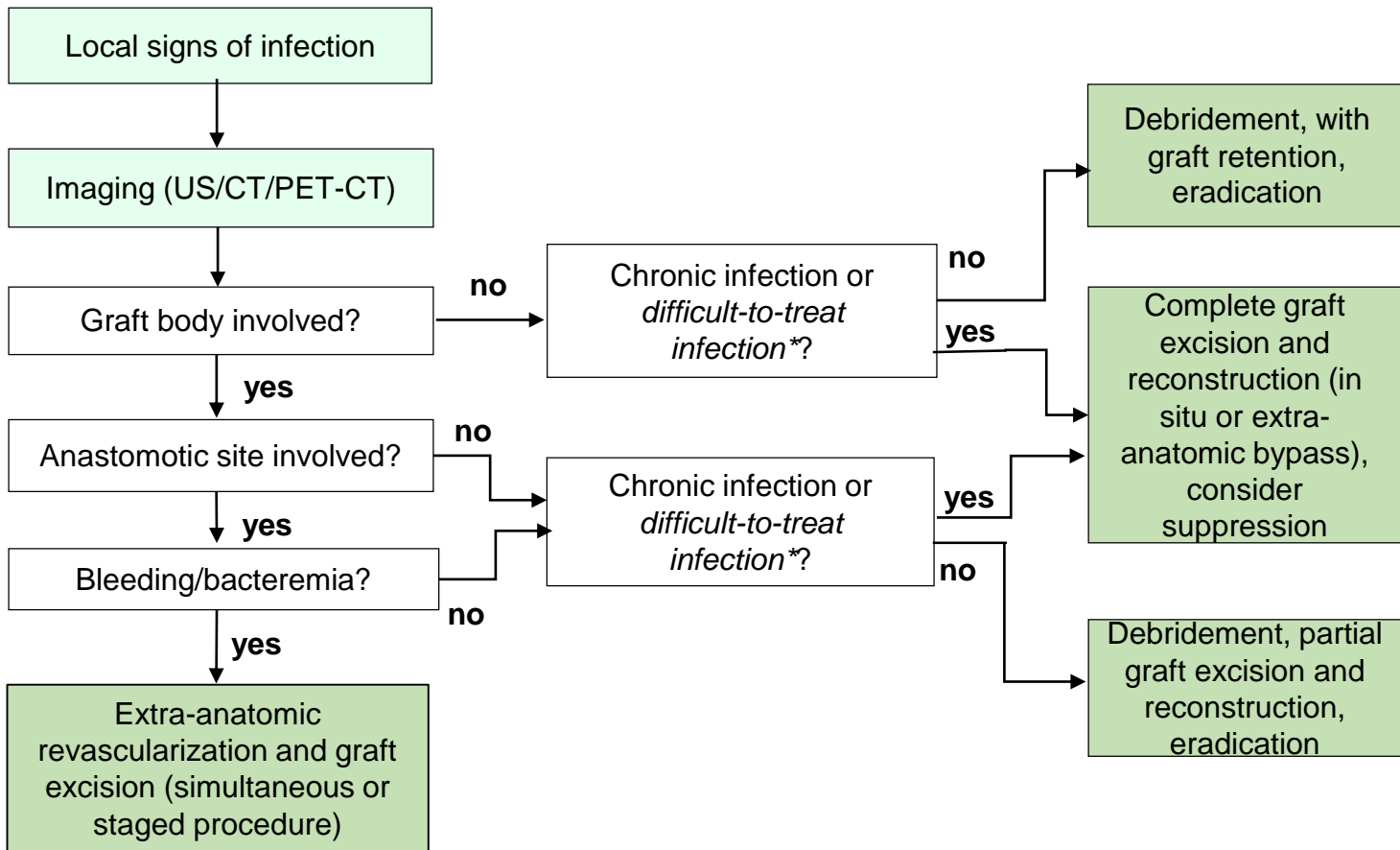
All patients with suspected VGI infection:

- C-reactive protein (CRP) and white blood cell count
- Blood cultures (at least 3 sets)
- Imaging¹ :
 - Peripheral VGI: ultrasound, computed tomographic angiography (CTA)
 - Aortic VGI: CTA (also in combination with positron-emission tomography, PET/CTA) or MRI
- **Specific situations:**
 - Preoperative setting: aspiration of perigraft fluid for culture, (avoid superficial swabs as they yield skin colonisation)
 - Intraoperative setting: perigraft tissue culture, sonication of retrieved synthetic graft, if removed
 - Aortic VGI: test for occult blood in stool, consider endoscopy if aortoenteric fistula suspected (sensitivity low, 55%)

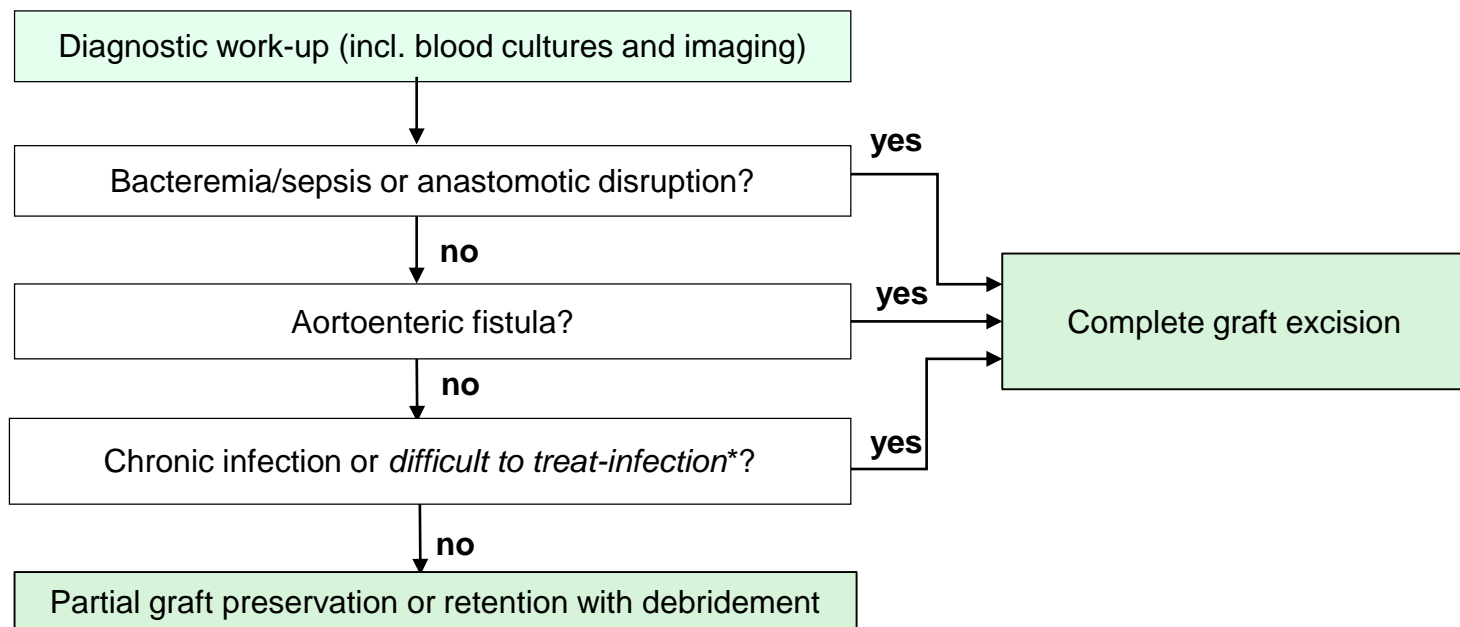
¹ **CT**: sensitivity 85-100%, specificity 85-94%, **MRI**: sensitivity 68-85%, specificity 97-100%, **PET**: sensitivity 78-96%, specificity 70-93% (Wilson WR et al on behalf of the American Heart Association, *Circulation* 2016)

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 vascular graft infections. For individual recommendations contact our Consultation Portal at: cp.pro-implant-foundation.org

MANAGEMENT ALGORITHM PERIPHERAL VGI



MANAGEMENT ALGORITHM AORTIC VGI*



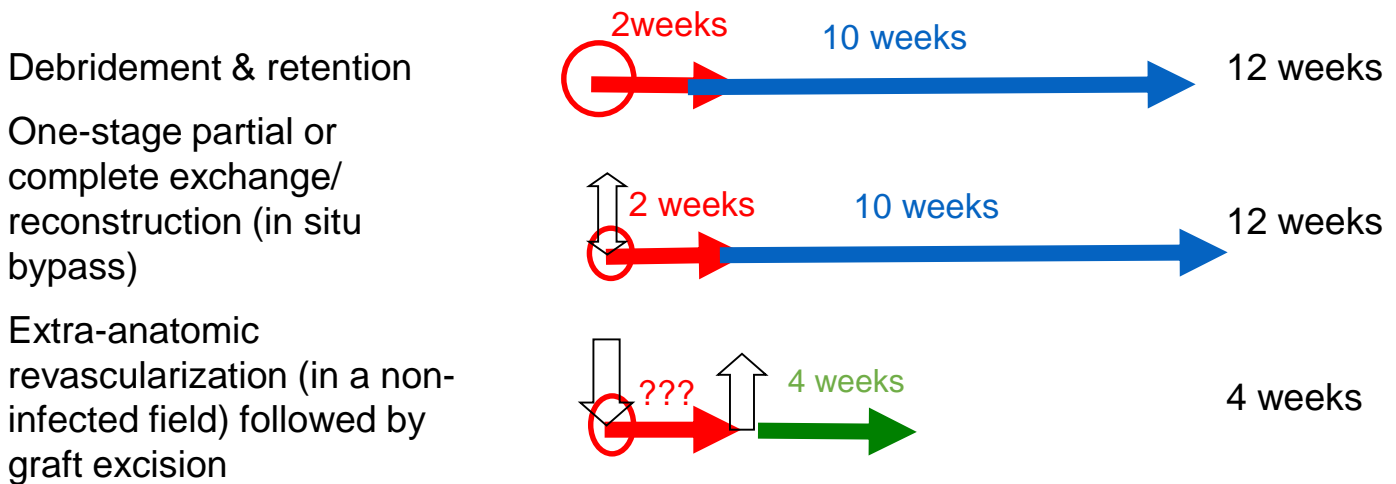
* If the surgical treatment is less invasive than suggested by the algorithm, consider long-term suppressive treatment to prevent relapse

* **Difficult-to-treat infections** caused by pathogens resistant to **biofilm-active antimicrobials**:

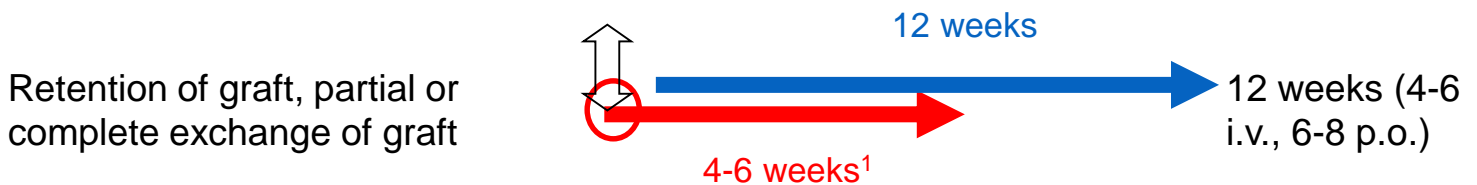
- Rifampin-resistant staphylococci
- Ciprofloxacin-resistant gram-negative bacteria
- Fungi (*Candida spp.*)

SURGICAL PROCEDURES FOR VGI INFECTIONS

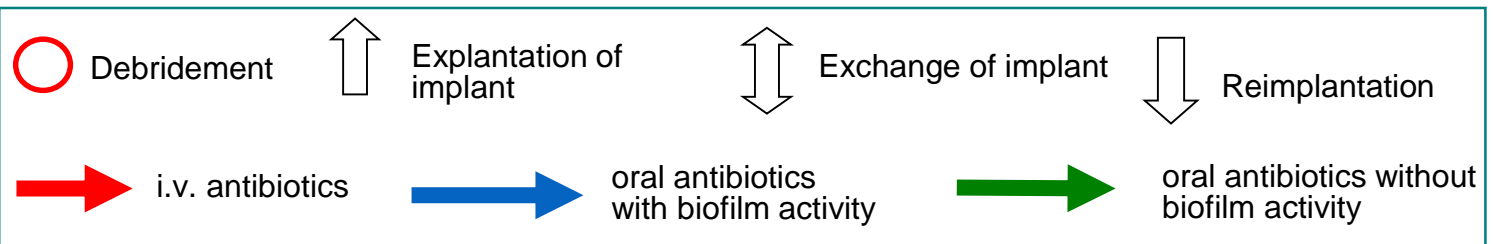
Peripheral VGI



Aortic VGI



¹ analogous to prosthetic valve endocarditis: 4-6 weeks for *S. aureus*, enterococci, gram-negative bacteria; 4 weeks for streptococci (2 weeks in combination with gentamicin in high susceptibility to penicillin)



Soft tissue management:

- The use of **vascularized tissue flaps** to provide coverage of infected grafts is beneficial in terms of sound dead space management, improved healing time, enhanced delivery of oxygen, antimicrobials and phagocytes.
- Avoid long use of negative pressure wound therapy if graft in situ

INDICATIONS FOR SUPPRESSIVE TREATMENT

- Difficult-to-treat infections and implant in infected area (no biofilm-active agent available)
- Remaining graft in case of chronic infection
- Relapsing infection

ANTIMICROBIAL TREATMENT

Empirical intravenous treatment

- **Peripheral VGI:** Ampicillin/sulbactam 3x3g or amoxicillin/clavulanic acid 3x2.2g + vancomycin 2x15mg/kg or daptomycin 1x10mg/kg
 - **Aortic VGI:** Piperacillin/tazobactam 3-4x4.5g i.v. + 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 or aortic VGI)
 → if fungal infection suspected: **add** caspofungin 1x70mg

Targeted treatment for peripheral VGI

	Intravenous treatment	Oral treatment (biofilm-active)	Oral treatment (suppressive)
<i>Staphylococcus spp.</i> • Oxacillin-susceptible • Anaphylactic reaction to penicillins or methicillin-resistant	Flucloxacillin 4x2g or Cefazolin 3x2g Vancomycin 2x15mg/kg or Daptomycin 1x 6-8mg/kg	Rifampicin 2x450mg plus Levofloxacin 2x500mg or Cotrimoxazol 3x960mg or Doxycyclin 2x100mg	Cotrimoxazol 2x960mg or Clindamycin 3x600mg or Doxycyclin 2x100mg or Amoxicillin/clavulanic acid 3x1g
<i>Streptococcus spp.</i> • 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> • Penicillin- and gentamicin (HL)-susceptible • Anaphylactic reaction to penicillins or penicillin-resistant	Amoxicillin 4x2g ³ (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 • Anaphylactic reaction to penicillin	Ceftriaxon 1x2g or Piperacillin/tazobactam 3x4.5g Ciprofloxacin 3x400mg or meropenem 3x1g	Ciprofloxacin 2x750mg (if resistant to ciprofloxacin, consider long-term suppression)	Cotrimoxazol 2x960mg or Ciprofloxacin 2x750mg

Targeted treatment for aortic VGI:

	Intravenous treatment after device removal	Oral treatment (biofilm-active)	Oral treatment (suppressive)
<i>Staphylococcus</i> spp. <ul style="list-style-type: none"> Oxacillin-susceptible Anaphylactic reaction to penicillins or methicillin-resistant¹ 	Rifampicin 2x450mg p.o. plus <ul style="list-style-type: none"> Flucloxacillin 6x2g or Cefazolin 3x2g Vancomycin² 2x15mg/kg or Daptomycin 1x 8-10mg/kg 	Rifampicin 2x450mg plus <ul style="list-style-type: none"> Levofloxacin 2x500mg or Cotrimoxazol 3x960mg or Doxycyclin 2x100mg 	<ul style="list-style-type: none"> Cotrimoxazol 2x960mg or Clindamycin 3x600mg or Doxycyclin 2x100mg or Amoxicillin/clavulanic acid 3x1g
<i>Streptococcus</i> spp. <ul style="list-style-type: none"> Penicillin-susceptible Anaphylactic reaction to penicillins or penicillin-resistant 	<ul style="list-style-type: none"> Gentamicin² 1x 3mg/kg plus Penicillin G 4x5 Mio E or Amoxicillin 6x2g or Ceftriaxon 1x2g Vancomycin² 2x15mg/kg or Daptomycin 1x 8-10mg/kg 	<ul style="list-style-type: none"> Amoxicillin 3x1g or Clindamycin 3x600mg or Levofloxacin 2x500mg 	<ul style="list-style-type: none"> Amoxicillin 3x1g or Clindamycin 3x600mg or Levofloxacin 2x500mg
<i>Enterococcus</i> spp. <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 	<ul style="list-style-type: none"> Amoxicillin 6x2g³ plus Gentamicin² 1x3mg/kg Amoxicillin 6x2g³ plus Ceftriaxon 2x2g Vancomycin² 2x15mg/kg or Daptomycin 1x10mg/kg plus Gentamicin² 1x3mg/kg or Fosfomycin 3x5g 	<ul style="list-style-type: none"> Amoxicillin 3x1g or Linezolid 2x600mg 	<ul style="list-style-type: none"> Amoxicillin 3x1g or Linezolid 2x600mg
Enterobacteriaceae <ul style="list-style-type: none"> Anaphylactic reaction to penicillins 	<ul style="list-style-type: none"> Ceftriaxon 1x2g plus Gentamicin² 1x3mg/kg Ciprofloxacin 3x400mg or meropenem 3x1g 	Ciprofloxacin 2x750mg (if resistant to ciprofloxacin, consider long-term suppression)	<ul style="list-style-type: none"> Cotrimoxazol 2x960mg or Ciprofloxacin 2x750mg
<i>Candida</i> spp.	<ul style="list-style-type: none"> Amphotericin B (liposomal) 1x 3-5mg/kg or Caspofungin 1x70 mg or Anidulafungin 1x200 mg 		<ul style="list-style-type: none"> 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 or ampicillin 6x2g i.v.