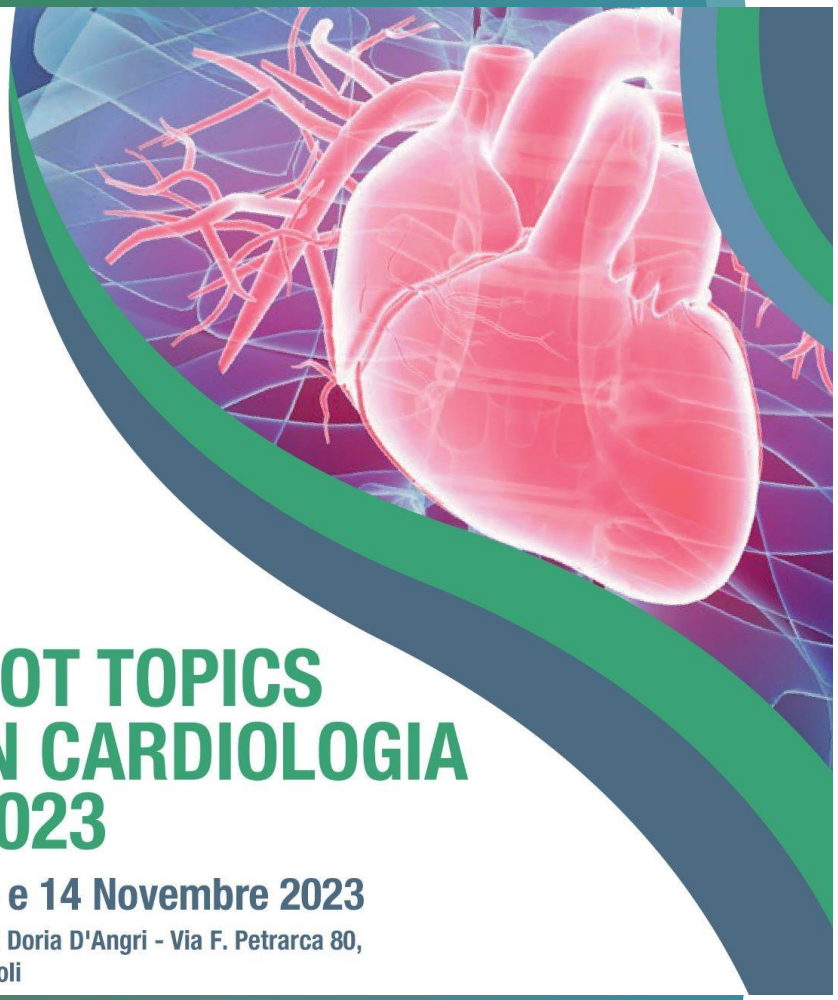


HOT TOPICS
IN CARDIOLOGIA
2023

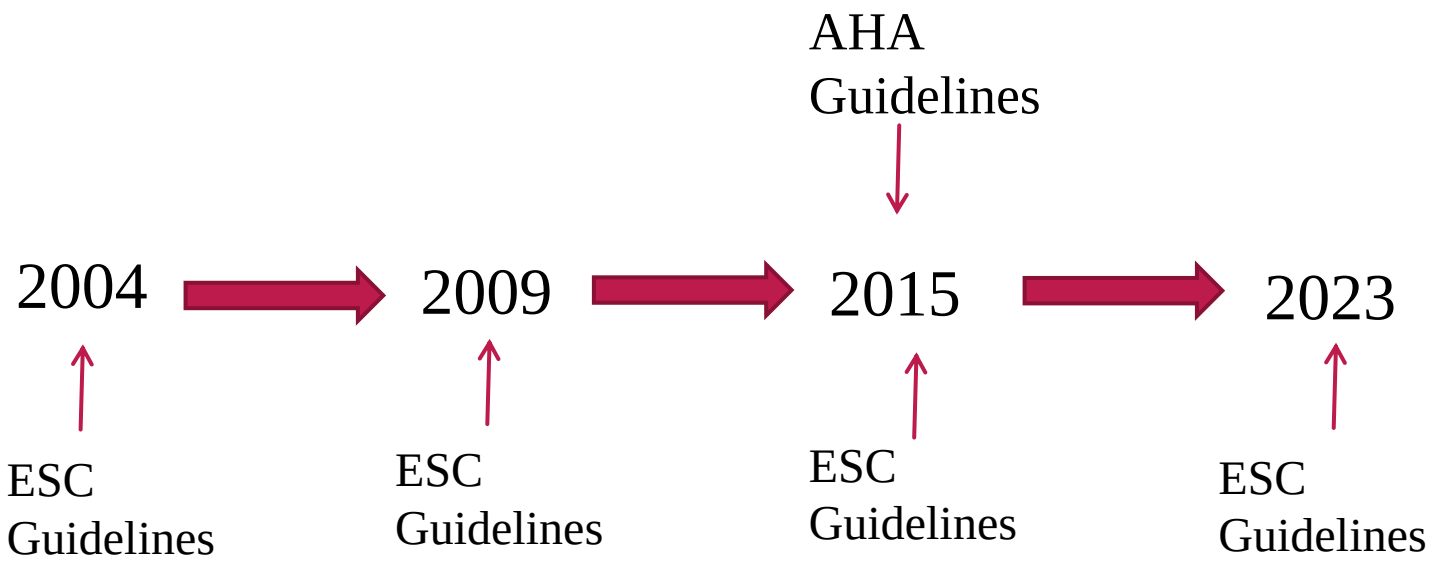
13 e 14 Novembre 2023

Villa Doria D'Angri - Via F. Petrarca 80,
Napoli

GUIDELINES ESC 2023: ENDOCARDITI INFETTIVE

Tiziana Ascione
Malattie Infettive
AORN Cardarelli
Napoli

Diagnosis and Management of Endocarditis has been changing



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European Heart Journal (2023) **00**, 1–95
https://doi.org/10.1093/eurheartj/ehad193

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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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Classes of recommendations

	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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Table 7 Members of the Endocarditis Team

	Heart Valve Centre
Core members	• Cardiologists. • Cardiac imaging experts. • Cardiovascular surgeons. • Infectious disease specialist (or internal medicine specialist with expertise in infectious diseases). • Microbiologist. • Specialist in outpatient parenteral antibiotic treatment.
Adjunct specialities	• Radiologist and nuclear medicine specialist. • Pharmacologist. • Neurologist and neurosurgeon. • Nephrologist. • Anaesthesiologists. • Critical care. • Multidisciplinary addiction medicine teams. • Geriatricians. • Social worker. • Nurses. • Pathologist.

Core Members Team

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2.1. What is new

Table 3 New recommendations

Table 4 Revised recommendations

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New recommendation

• Increased level of recommendation and a clearer definition of prevention and prophylaxis of endocarditis in higher-risk patients.

• An increasing role of nonechocardiographic, advanced cardiac imaging techniques in the diagnosis of endocarditis.

• More precisely defined indications for surgery and the timing for surgery, as well as a couple of new surgical recommendations.

• More precisely defined criteria for diagnosing and managing cardiac electronic implantable device (CIED)–associated endocarditis.

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Table 5 General prevention measures to be followed in patients at high and intermediate risk of infective endocarditis

Patients should be encouraged to maintain twice daily tooth cleaning and to seek professional dental cleaning and follow-up at least twice yearly for high-risk patients and yearly for others.
Strict cutaneous hygiene, including optimized treatment of chronic skin conditions.
Disinfection of wounds.
Curative antibiotics for any focus of bacterial infection.
No self-medication with antibiotics.
Strict infection control measures for any at-risk procedure.
Discouragement of piercing and tattooing.
Limitation of infusion catheters and invasive procedures. when possible. Strict adherence to care bundles for central and peripheral cannulae should be performed.

Prevention

The guidelines identify patients at **high risk for IE:**

- Patients with previous IE and patients with surgically implanted prosthetic valves
- Patients with congenital heart diseases, surgery with prosthetic material, or a ventricular assist device

- The Guidelines recommend giving them prophylactic antibiotics before oral or dental procedures.

2023 ESC Guidelines for the management of endocarditis

The guidelines specify a prophylactic antibiotic regimen for high-risk dental procedures, for children and for adults with or without allergy to penicillin or ampicillin, given as a single dose 30 to 60 minutes before a procedure

A **new recommendation** is that systemic antibiotic prophylaxis may be considered for high-risk patients undergoing invasive procedures of the respiratory, gastrointestinal, or genitourinary tract, skin or musculoskeletal system.

Situation	Antibiotic	Single-dose 30–60 min before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin	2 g orally	50 mg/kg orally
	Ampicillin	2 g i.m. or i.v.	50 mg/kg i.v. or i.m.
	Cefazolin or ceftriaxone	1 g i.m. or i.v.	50 mg/kg i.v. or i.m.
Allergy to penicillin or ampicillin	Azithromycin or clarithromycin	500 mg orally	15 mg/kg orally
	Doxycycline	100 mg orally	<45 kg, 2.2 mg/kg orally >45 kg, 100 mg orally

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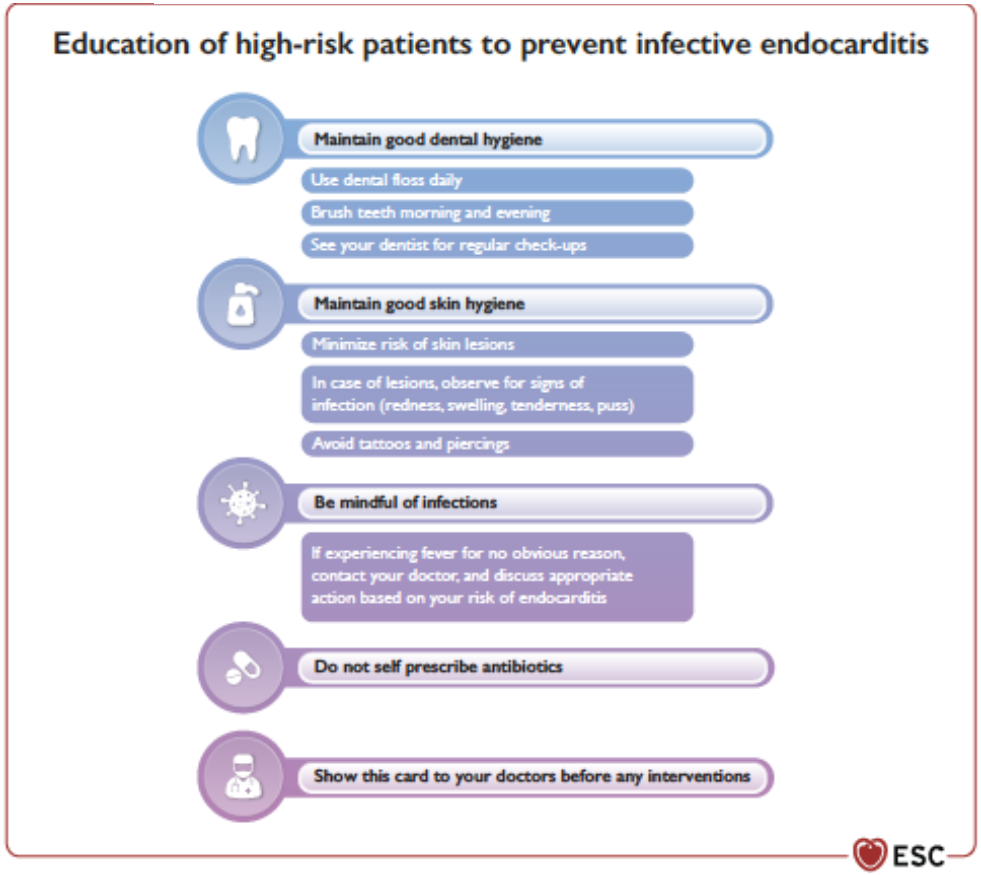

Education

The new guideline depicts what patients should do such as maintain good dental hygiene, avoid tattoos and piercings, be mindful of infections

The main targets for antibiotic prophylaxis are oral streptococci, but the emerging and increasing resistance of these bacteria are reasons why patients should not self-prescribe antibiotics

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Definition of EI

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.

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Major Criteria EI

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.
• [18F]-FDG-PET/CT(A).
• WBC SPECT/CT.

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Minor Criteria EI

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.

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2023 ESC Guidelines for the management of endocarditis

Recommendation TTE/TOE

Recommendation Table 5 — Recommendations for the role of echocardiography in infective endocarditis

Recommendations	Class[a]	Level[b]
A. Diagnosis		
TTE is recommended as the first-line imaging modality in suspected IE.[166,179]	I	B
TOE is recommended in all patients with clinical suspicion of IE and a negative or non-diagnostic TTE.[166,178,179]	I	B
TOE is recommended in patients with clinical suspicion of IE, when a prosthetic heart valve or an intracardiac device is present.[166,178,179]	I	B
Repeating TTE and/or TOE within 5–7 days is recommended in cases of initially negative or inconclusive examination when clinical suspicion of IE remains high.[178]	I	C
TOE is recommended in patients with suspected IE, even in cases with positive TTE, except in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.[165,166,179]	I	C
Performing an echocardiography should be considered in *S. aureus*, *E. faecalis*, and some *Streptococcus* spp. bacteraemia.[19,149,174]	IIa	B
B. Follow-up under medical therapy		
Repeating TTE and/or TOE is recommended as soon as a new complication of IE is suspected (new murmur, embolism, persisting fever and bacteraemia, HF, abscess, AVB).[165,166,179]	I	B
TOE is recommended when patient is stable before switching from intravenous to oral antibiotic therapy.[43,180]	I	B
During follow-up of uncomplicated IE, repeat TTE and/or TOE should be considered to detect new silent complications. The timing of repeat TTE and/or TOE depends on the initial findings, type of microorganism, and initial response to therapy.[165,166,179]	IIa	B
C. Intra-operative echocardiography		
Intra-operative echocardiography is recommended in all cases of IE requiring surgery.[181]	I	C
D. Following completion of therapy		
TTE and/or TOE are recommended at completion of antibiotic therapy for evaluation of cardiac and valve morphology and function in patients with IE who did not undergo heart valve surgery.[182–184]	I	C

2023 ESC Guidelines for the management of endocarditis

Diagnosis of IE and cardiac complications

Cardiac CT is more accurate than TOE for diagnosing perivalvular and periprosthetic complications of IE (abscesses, pseudoaneurysms, and fistulae) and is recommended if TOE is not conclusive

Diagnosis of IE and cardiac complications

18-FDG-PET/CT and white blood cell (WBC) single photon emission computed tomography (SPECT)/CT are recommended in suspected Prosthetic valve endocarditis and in cases of inconclusive echocardiography.

Recommendation Table 6 — Recommendations for the role of computed tomography, nuclear imaging, and magnetic resonance in infective endocarditis

Recommendations	Class[a]	Level[b]
Cardiac CTA is recommended in patients with possible NVE to detect valvular lesions and confirm the diagnosis of IE.[33,168,169]	I	B
[18F]FDG-PET/CT(A) and cardiac CTA are recommended in possible PVE to detect valvular lesions and confirm the diagnosis of IE.[22,129,209,210,237–239]	I	B
Cardiac CTA is recommended in NVE and PVE to diagnose paravalvular or periprosthetic complications if echocardiography is inconclusive.[20,168,169,185,186]	I	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and/or MRI) are recommended in symptomatic[c] patients with NVE and PVE to detect peripheral lesions or add minor diagnostic criteria.[22,197–200,210,213,240,241]	I	B
WBC SPECT/CT should be considered in patients with high clinical suspicion of PVE when echocardiography is negative or inconclusive and when PET/CT is unavailable.[213–216]	IIa	C
[18F]FDG-PET/CT(A) may be considered in possible CIED-related IE to confirm the diagnosis of IE.[22,129,209,210,237,238]	IIb	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and MRI) in NVE and PVE may be considered for screening of peripheral lesions in asymptomatic patients.[188,197–201]	IIb	B

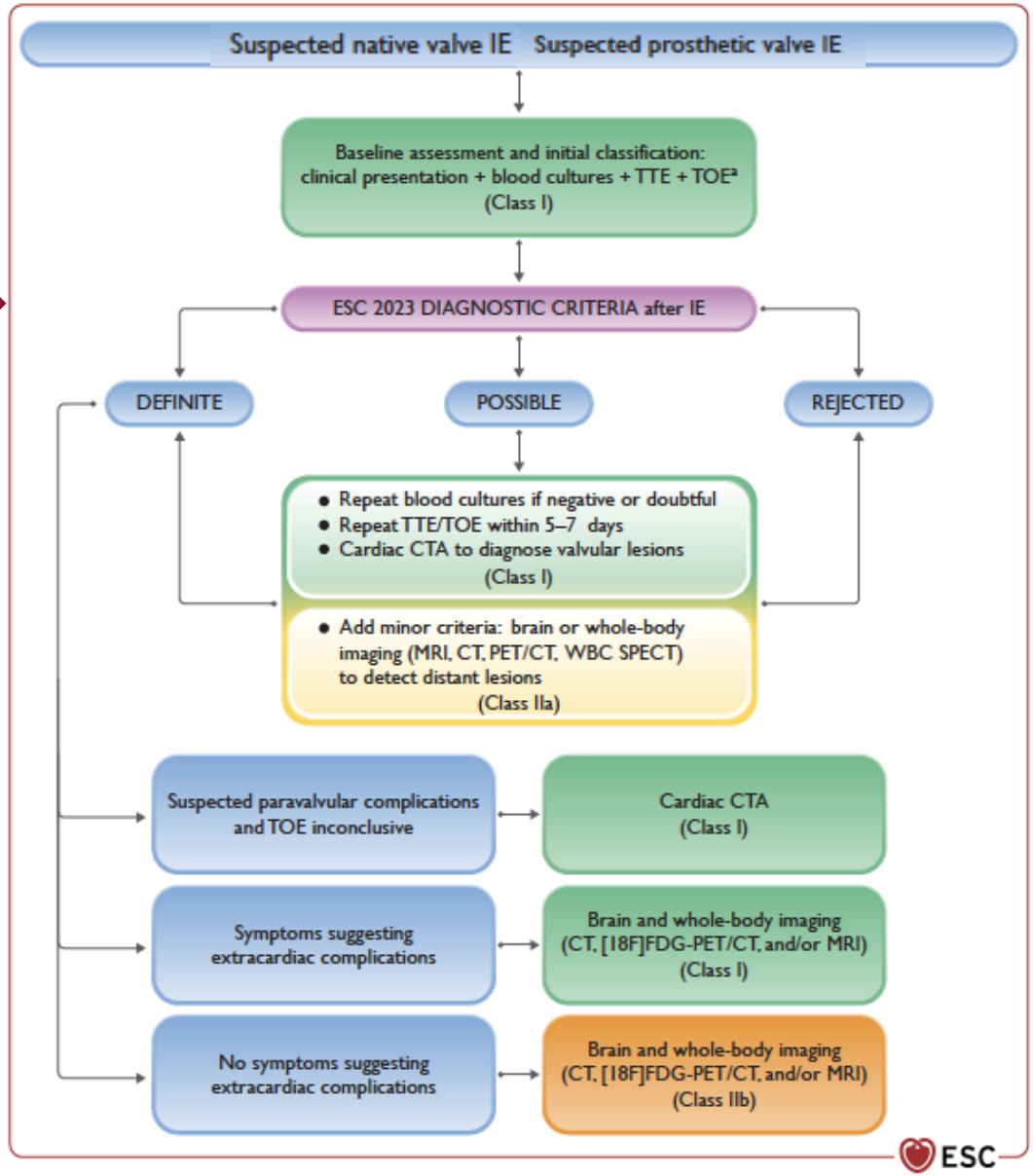
Flowchart

Criteria IE:

Definite

Possible

Rejected



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New Recommendation

Endocarditis following transcatheter aortic valve implantation (TAVI)

The risk of IE is higher within the first year following the procedure, and particularly within the initial 3 months

The clinical presentation is frequently atypical, with fever lacking in 13–20% of patients

No vegetations are detected in 38–60% of cases

The addition of 18-FDG-PET/CT and/or CTA to the diagnostic work-up of IE in TAVI changed the final clinical diagnosis in 33% of patients

PLOS ONE | PLOS ONE | https://doi.org/10.1371/journal.pone.0225077 January 17, 2020

RESEARCH ARTICLE

Infective endocarditis post-transcatheter aortic valve implantation (TAVI), microbiological profile and clinical outcomes: A systematic review

Adnan Khan[1]*, Aqsa Aslam[1], Khawar Naeem Satti[2], Sana Ashiq[1]

Enterococci were the most common causative organism isolated from 25.9% of cases followed by *Staphylococcus aureus* (16.1%) and coagulase-negative *Staphylococcus* species (14.7%).

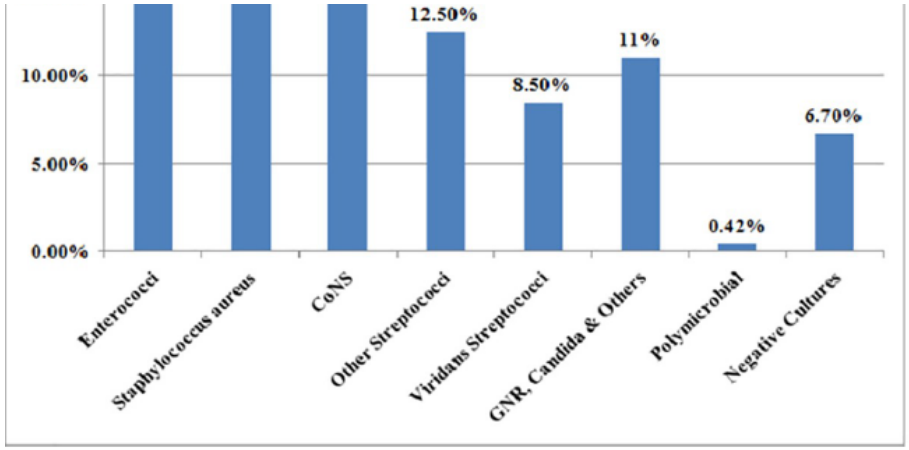
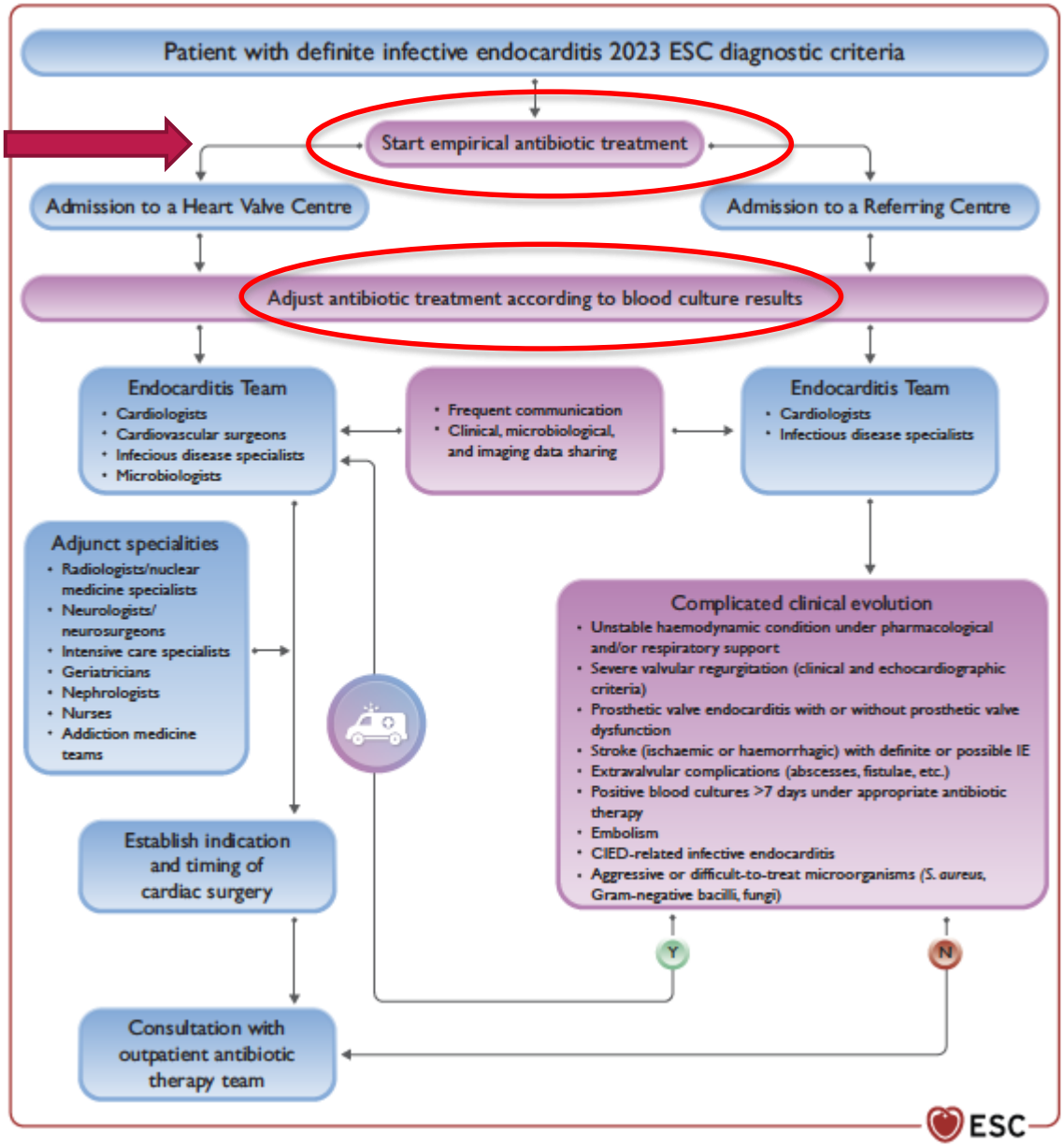


Fig 5. Causative organisms of post-TAVI infective endocarditis. The in-hospital mortality

Empirical
Antibiotic
Treatment



Targeted
Antibiotic
Treatment

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2023 ESC Guidelines for the management of endocarditis

Antibiotic Regimens

Recommendation Table 10 — Recommendations for antibiotic regimens for initial empirical treatment of infective endocarditis (before pathogen identification)[a]

Recommendations		Class[b]	Level[c]
In patients with community-acquired NVE or late PVE (≥12 months post-surgery), ampicillin in combination with ceftriaxone or with (flu)cloxacillin and gentamicin should be considered using the following doses:[255]		IIa	C
Adult antibiotic dosage and route			
Ampicillin	12 g/day i.v. in 4–6 doses		
Ceftriaxone	4 g/day i.v. or i.m. in 2 doses		
(Flu)cloxacillin	12 g/day i.v. in 4–6 doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose		
Paediatric antibiotic dosage and route			
Ampicillin	300 mg/kg/day i.v. in 4–6 equally divided doses		
Ceftriaxone	100 mg/kg i.v. or i.m. in 1 dose		
(Flu)cloxacillin	200–300 mg/kg/day i.v. in 4–6 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 3 equally divided doses		
In patients with early PVE (<12 months post-surgery) or nosocomial and non-nosocomial healthcare-associated IE, vancomycin or daptomycin combined with gentamicin and rifampin may be considered using the following doses:[395]		IIb	C
Adult antibiotic dosage and route			
Vancomycin[e]	30 mg/kg/day i.v. in 2 doses		
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose		
Rifampin	900–1200 mg i.v. or orally in 2 or 3 doses		
Paediatric antibiotic dosage and route			
Vancomycin[e]	40 mg/kg/day i.v. in 2–3 equally divided doses		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 3 equally divided doses		
Rifampin	20 mg/kg/day i.v. or orally in 3 equally divided doses		
Allergy to beta-lactams			
In patients with community-acquired NVE or late PVE (≥12 months post-surgery) who are allergic to penicillin, cefazolin, or vancomycin in combination with gentamicin may be considered using the following doses:		IIb	C

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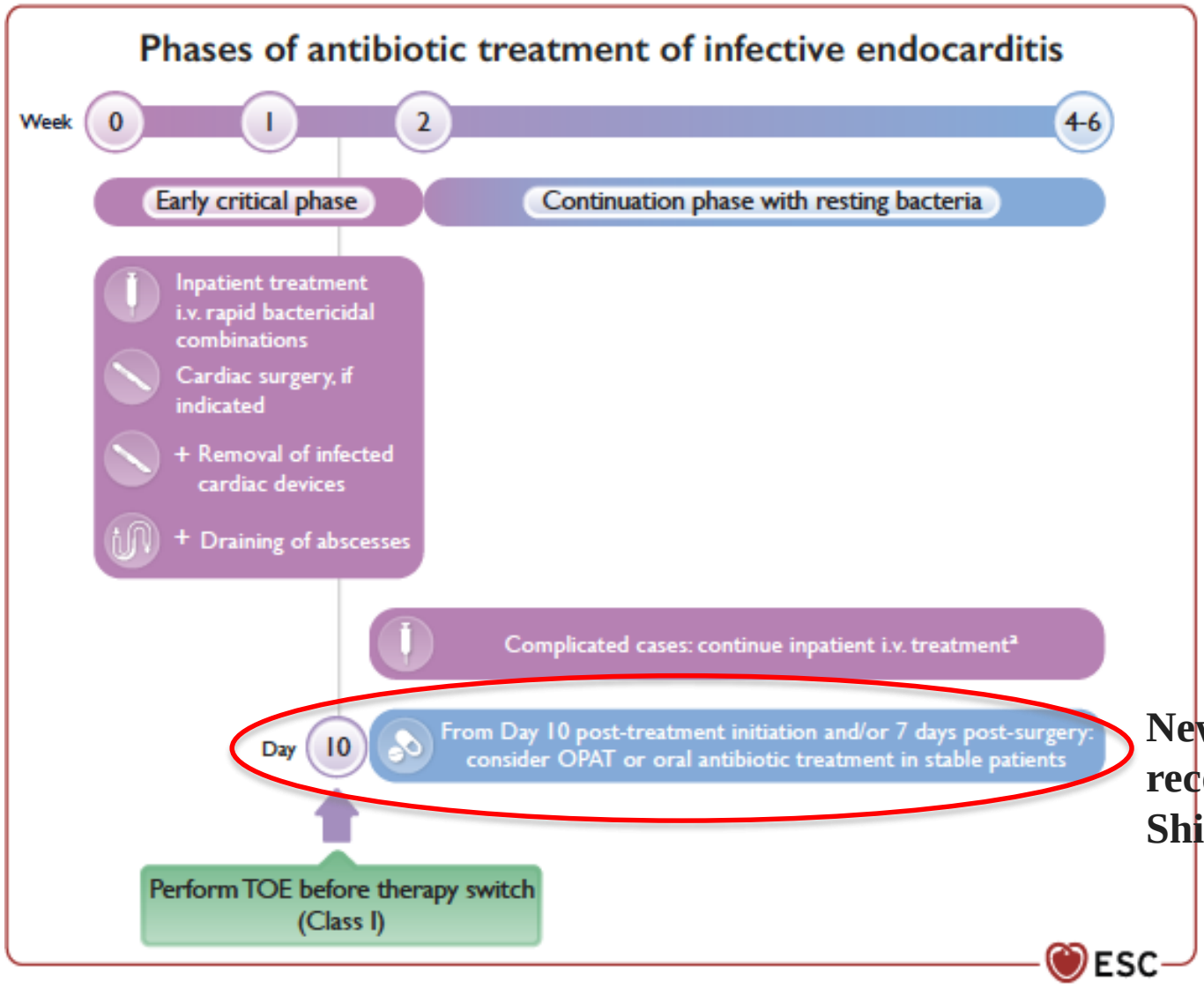
New recommendation

- Increased level of recommendation and a clearer definition of prevention and prophylaxis of endocarditis in higher-risk patients.

- An increasing role of nonechocardiographic, advanced cardiac imaging techniques in the diagnosis of endocarditis.

- **Earlier Shift to Oral Antibiotics at Home**

Another very important point is the increasing use of oral outpatient antibiotic therapy based on the Partial Oral Treatment of Endocarditis (POET) randomized trial



New recommendation Shift IV/OS

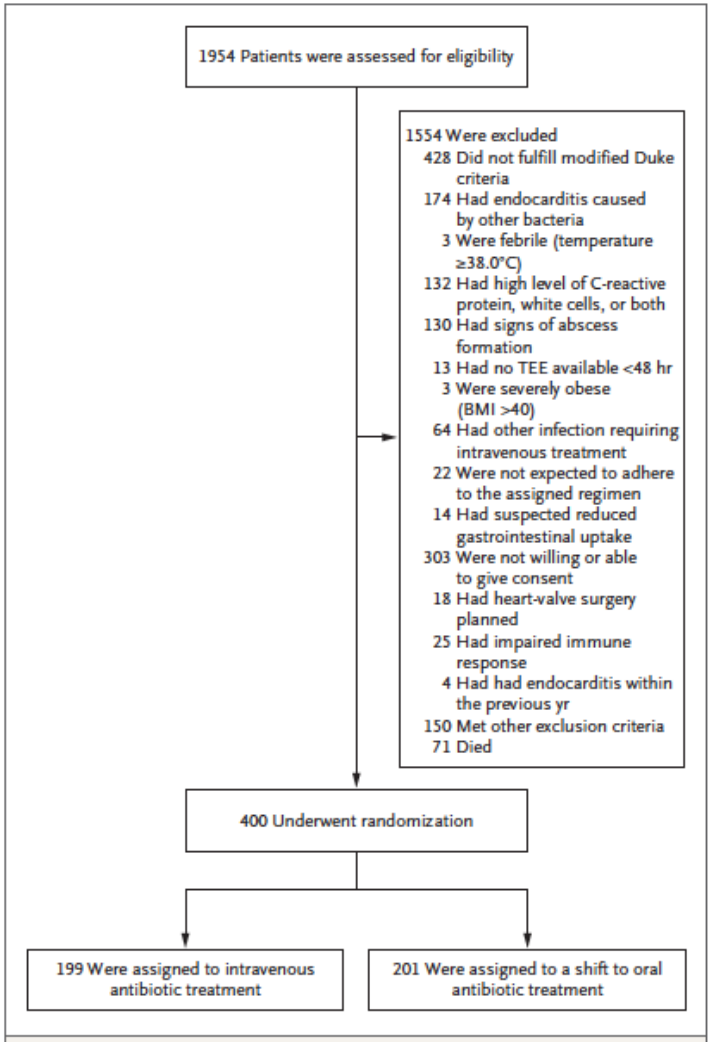
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

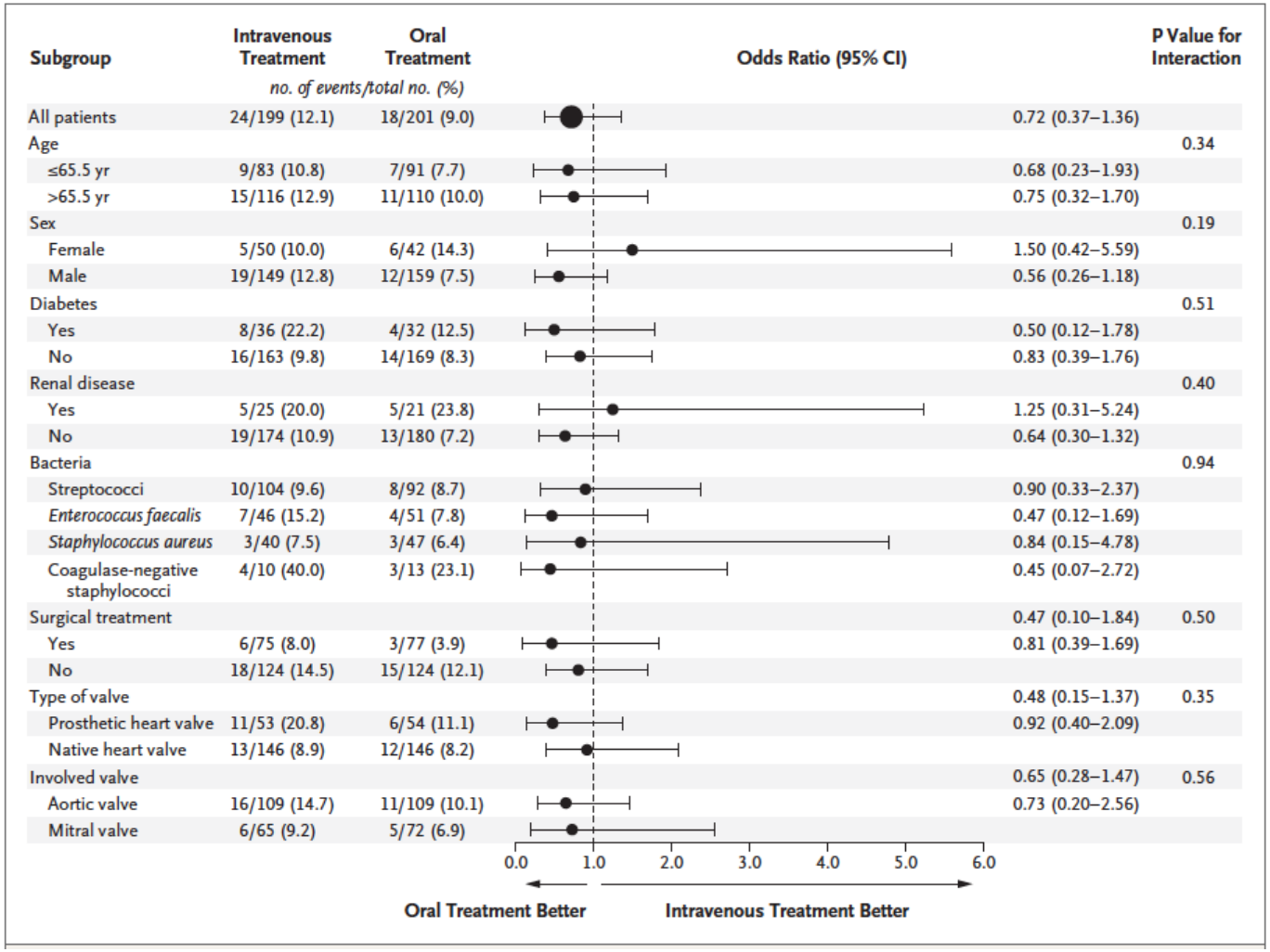


- A randomized study
- 400 patients
- Left Side Endocarditis
- 199 intravenous treatment
- 201 intravenous treatment
  + switch to oral antibiotic
- The patients shifted from iv to os on about day 10-17

End point: treatment success after the end of therapy

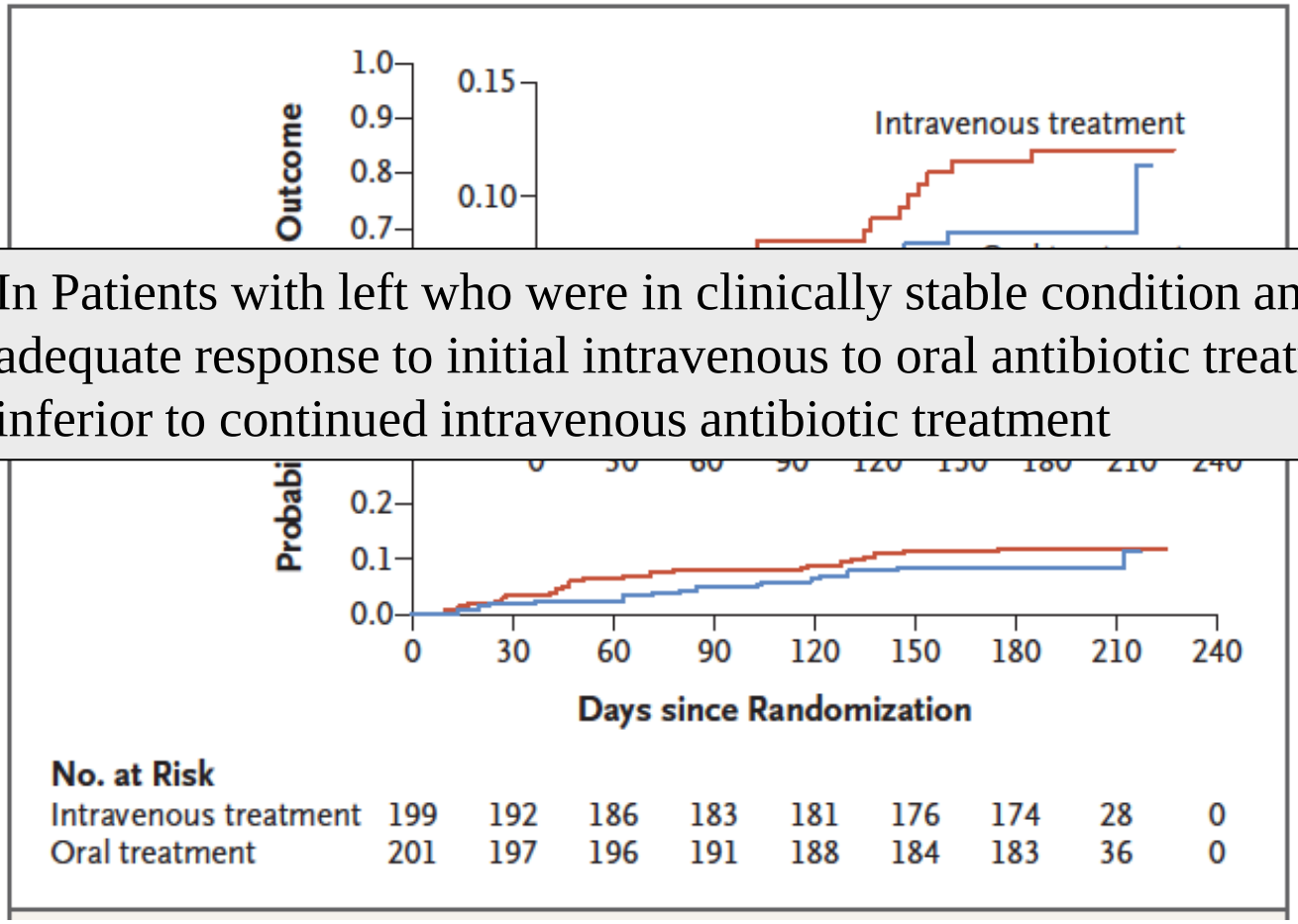
N ENGL J MED 380;5 NEJM.ORG JANUARY 31, 2019

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

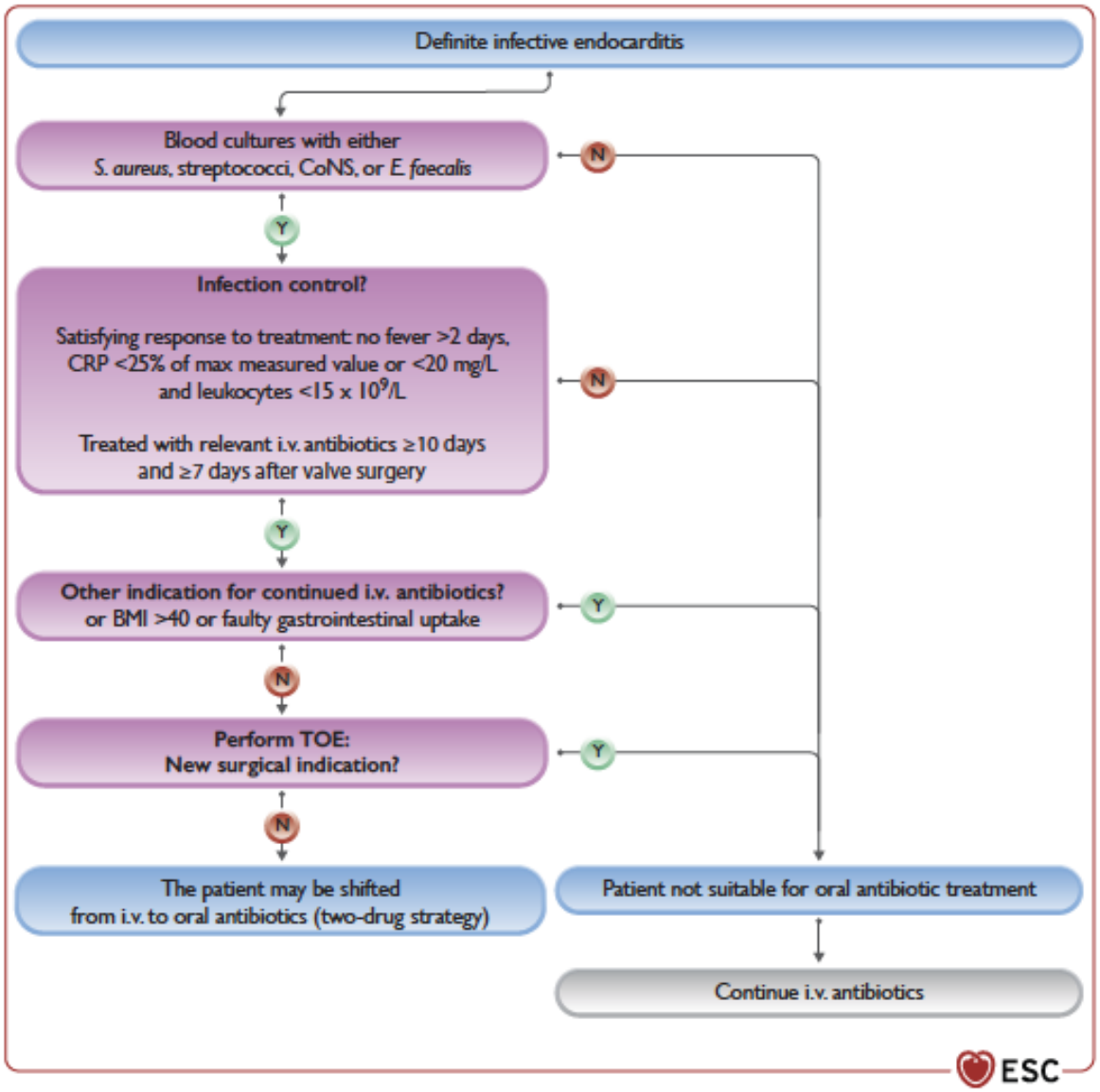


Subgroup	Intravenous Treatment	Oral Treatment	Odds Ratio (95% CI)	P Value for Interaction
	no. of events/total no. (%)			
All patients	24/199 (12.1)	18/201 (9.0)	0.72 (0.37–1.36)	
Age				0.34
≤65.5 yr	9/83 (10.8)	7/91 (7.7)	0.68 (0.23–1.93)	
>65.5 yr	15/116 (12.9)	11/110 (10.0)	0.75 (0.32–1.70)	
Sex				0.19
Female	5/50 (10.0)	6/42 (14.3)	1.50 (0.42–5.59)	
Male	19/149 (12.8)	12/159 (7.5)	0.56 (0.26–1.18)	
Diabetes				0.51
Yes	8/36 (22.2)	4/32 (12.5)	0.50 (0.12–1.78)	
No	16/163 (9.8)	14/169 (8.3)	0.83 (0.39–1.76)	
Renal disease				0.40
Yes	5/25 (20.0)	5/21 (23.8)	1.25 (0.31–5.24)	
No	19/174 (10.9)	13/180 (7.2)	0.64 (0.30–1.32)	
Bacteria				0.94
Streptococci	10/104 (9.6)	8/92 (8.7)	0.90 (0.33–2.37)	
Enterococcus faecalis	7/46 (15.2)	4/51 (7.8)	0.47 (0.12–1.69)	
Staphylococcus aureus	3/40 (7.5)	3/47 (6.4)	0.84 (0.15–4.78)	
Coagulase-negative staphylococci	4/10 (40.0)	3/13 (23.1)	0.45 (0.07–2.72)	
Surgical treatment			0.47 (0.10–1.84)	0.50
Yes	6/75 (8.0)	3/77 (3.9)	0.81 (0.39–1.69)	
No	18/124 (14.5)	15/124 (12.1)		
Type of valve			0.48 (0.15–1.37)	0.35
Prosthetic heart valve	11/53 (20.8)	6/54 (11.1)	0.92 (0.40–2.09)	
Native heart valve	13/146 (8.9)	12/146 (8.2)		
Involved valve			0.65 (0.28–1.47)	0.56
Aortic valve	16/109 (14.7)	11/109 (10.1)	0.73 (0.20–2.56)	
Mitral valve	6/65 (9.2)	5/72 (6.9)		

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

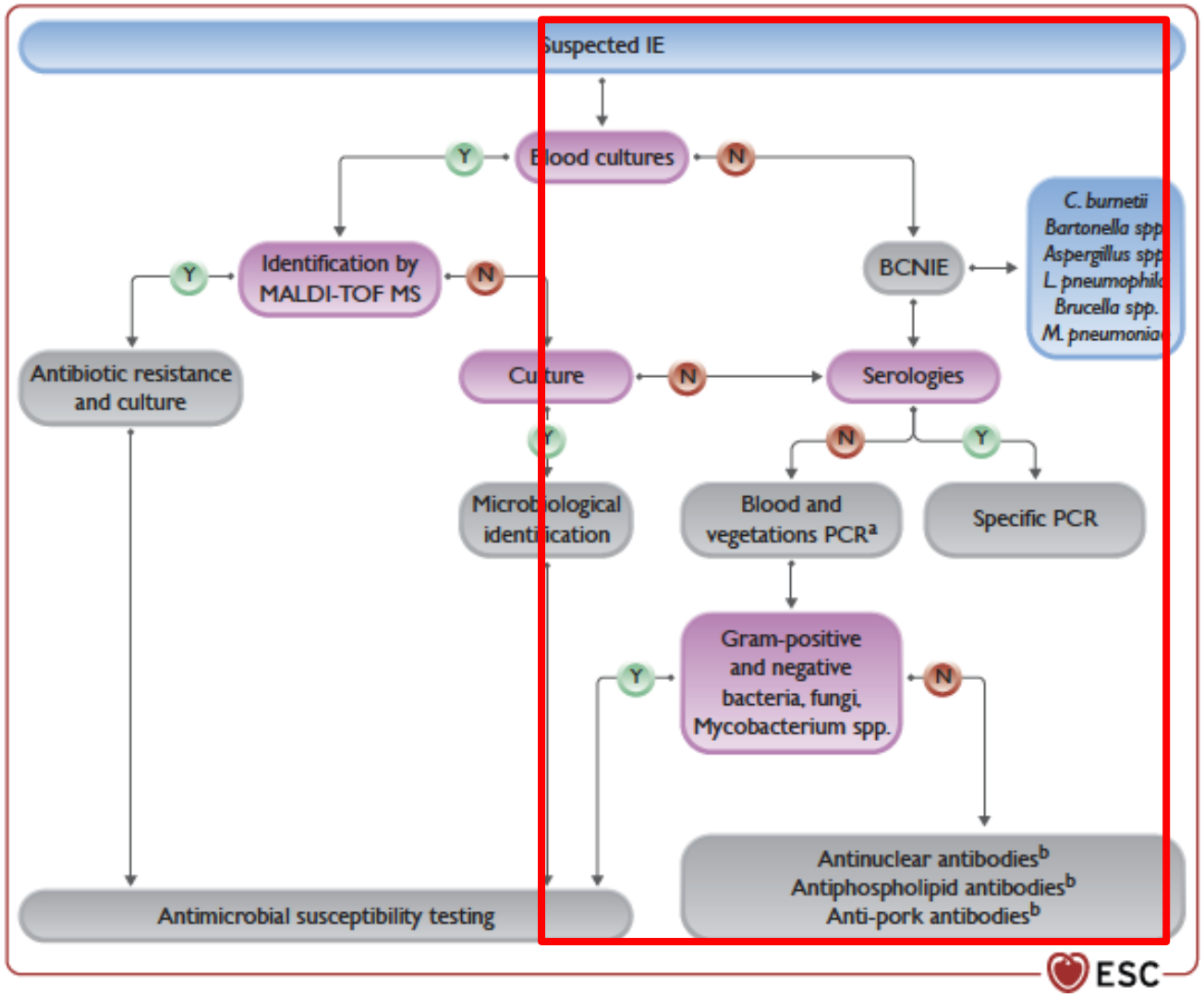


In Patients with left who were in clinically stable condition and who had an adequate response to initial intravenous to oral antibiotic treatment was non inferior to continued intravenous antibiotic treatment



The first phase can last up to 2 weeks of hospital i.v. treatment using combinations of rapidly bactericidal antibiotics

After this period, perform TOE and if clinically stable patients can end the antibiotic treatment at home with oral antibiotic regimens for up to 4-6 weeks



Blood Cultures Negative:

Start work up to investigate rare causes of infection

2023 ESC Guidelines for the management of endocarditis

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

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

Table 11 Antibiotic treatment of blood culture-negative infective endocarditis

Pathogens	Proposed therapy[a]	Treatment outcome
Brucella spp.	Doxycycline (200 mg/24 h) plus cotrimoxazole (960 mg/12 h) plus rifampin (300–600 mg/24 h) for ≥3–6 months[b] orally	Treatment success defined as an antibody titre <1:60. Some authors recommend adding gentamicin for the first 3 weeks
C. burnetii (Q fever agent)	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally (>18 months of treatment)	Treatment success defined as anti-phase I IgG titre <1:400, and IgA and IgM titres <1:50
Bartonella spp.[d]	Doxycycline 100 mg/12 h orally for 4 weeks plus gentamicin (3 mg/24 h) i.v. for 2 weeks	Treatment success expected in ≥90%
Legionella spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 weeks or clarithromycin (500 mg/12 h) i.v. for 2 weeks, then orally for 4 weeks plus rifampin (300–1200 mg/24 h)	Optimal treatment unknown
Mycoplasma spp.	Levofloxacin (500 mg/12 h) i.v. or orally for ≥6 months[e]	Optimal treatment unknown
T. whipplei (Whipple's disease agent)[f]	Doxycycline (200 mg/24 h) plus hydroxychloroquine (200–600 mg/24 h)[c] orally for ≥18 months	Long-term treatment, optimal duration unknown

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European Heart Journal (2023) 00, 1–95
https://doi.org/10.1093/eurheartj/ehad193

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)

New recommendation

Earlier Surgical Intervention

The new guidelines also recommend that "once there is an indication to do cardiac surgery, it should be promptly performed"

Surgery is indicated to remove infected material and drain abscesses, for patients with heart failure or uncontrolled infection and to prevent embolism.

2023 ESC Guidelines for the management of endocarditis

New recommendation

Guidelines have defined

- **Emergency indications** that should be done within 24 hours
- **Urgent indications** which should be done within 3 to 5 days
- **Non urgent indications** more than 5 days but within the same hospitalization

The Guidelins encourage surgeons and nonsurgeons that once there is an indication for surgery, there's not a lot of benefit to just waiting to improve survival.

The Guidelines recommend surgery for early prosthetic valve endocarditis, within 6 months of valve surgery, with new valve replacement and complete debridement.

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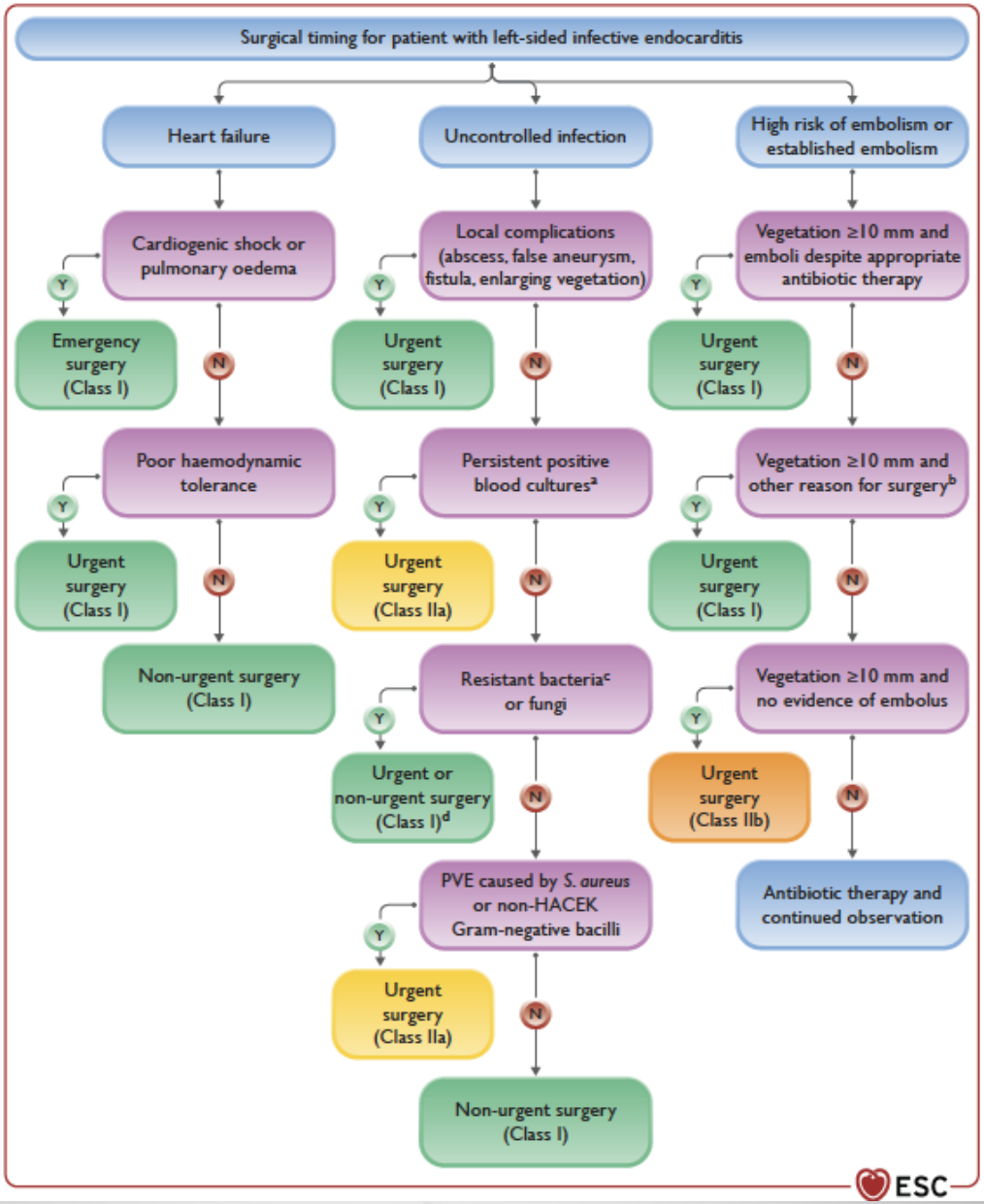
Recommendations for the main indications of surgery in infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)		
(i) Heart failure		
Emergency surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary oedema or cardiogenic shock.	I	B
Urgent surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.	I	B
(ii) Uncontrolled infection		
Urgent surgery is recommended in locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation, prosthetic dehiscence, new AVB).	I	B
Urgent or non-urgent surgery is recommended in IE caused by fungi or multiresistant organisms according to the haemodynamic condition of the patient.	I	C
(iii) Prevention of embolism		
Urgent surgery is recommended in aortic or mitral NVE or PVE with persistent vegetations ≥10 mm after one or more embolic episodes despite appropriate antibiotic therapy.	I	B
Urgent surgery is recommended in IE with vegetation ≥10 mm and other indications for surgery.	I	C

Flowchart

Surgical Timing for Patient with Left sided IE



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European Heart Journal (2023) **00**, 1–95
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2023 ESC Guidelines for the management of endocarditis

New recommendation for EI and Stroke

Patients who present with stroke and require surgery are not uncommon

Ischemic stroke should not be a reason to delay surgery, and patients with hemorrhagic stoke, with favorable features, can undergo surgery.

Table 1. Clinical Signs and Complications of Infective Endocarditis

Sign	Patients, %
Fever	86-96
New murmur	48
Worsening of old murmur	20
Hematuria	26
Vascular embolic event	17
Splenomegaly	11
Splinter hemorrhages	8
Osler nodes	3
Janeway lesions	5
Roth spots	2
Complication	
Stroke	17-20
Nonstroke embolization	23-33
Heart failure	14-33
Intracardiac abscess	14-20
New conduction abnormality	8

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2023 ESC Guidelines for the management of endocarditis

Recommendation Table 13 — Recommendations for the treatment of neurological complications of infective endocarditis

Recommendations	Class[a]	Level[b]
Brain CT or MRA is recommended in patients with IE and suspected infective cerebral aneurysms.[490]	I	B
Neurosurgery or endovascular therapy is recommended for large aneurysms, those with continuous growth despite optimal antibiotic therapy, and ruptured intracranial infective cerebral aneurysms.[485]	I	C
If non-invasive techniques are negative and the suspicion of infective aneurysm remains, invasive angiography should be considered.[488]	IIa	B
In embolic stroke, mechanical thrombectomy may be considered if the expertise is available in a timely manner.[484]	IIb	C
Thrombolytic therapy is not recommended in embolic stroke due to IE.[481,491]	III	C

Recommendation Table 17 — Indications and timing of cardiac surgery after neurological complications in active infective endocarditis

Recommendations	Class[a]	Level[b]
After a transient ischaemic attack, cardiac surgery, if indicated, is recommended without delay.[454,468]	I	B
After a stroke, surgery is recommended without any delay in the presence of HF, uncontrolled infection, abscess, or persistent high embolic risk, as long as coma is absent and the presence of cerebral haemorrhage has been excluded by cranial CT or MRI.[451,468,473,567,568,570–578]	I	B
Following intracranial haemorrhage, delaying cardiac surgery >1 month, if possible, with frequent re-assessment of the patient's clinical condition and imaging should be considered.[571]	IIa	C
In patients with intracranial haemorrhage and unstable clinical status due to HF, uncontrolled infection or persistent high embolic risk, urgent or emergency surgery should be considered weighing the likelihood of a meaningful neurological outcome.[199,581–584]	IIa	C

Infection (2020) 48:323–332
https://doi.org/10.1007/s15010-020-01415-6

REVIEW

Infections causing stroke or stroke-like syndromes

Pasquale Pagliano[1] · Anna M. Spera[1] · Tiziana Ascione[2] · Silvano Esposito[1]

Received: 14 January 2020 / Accepted: 20 March 2020 / Published online: 1 April 2020

- Stoke-like presentation can be reported in 25% of endocarditis
- Diagnosis impact in terms of antibiotic treatment choices and outcome
- Probability of survival of patients with infective endocarditis according to the presence or absence of neurologic complication

Stroke-like presentation of endocarditis

The incidence of neurologic complications in patients suffering an infective endocarditis was investigated in a large Spanish study collecting retrospective data of more than 1200 cases from 8 reference centres [30]. The study highlighted that 340 (25%) patients with infective endocarditis experienced neurologic complications and that ischaemic events accounted for 56% of these cases. Small embolism with transient neurologic symptoms was reported in the majority of ischaemic cases, but those with more severe presentation frequently had multiple embolisms and involvement of both brain hemispheres. Moreover, haemorrhagic events were reported in 60 cases (18%), with a high percentage of cases with primary haemorrhage. On the basis of the multivariate analysis of the factors associated with brain embolism during endocarditis, *Staphylococcus aureus* and a vegetation size > 30 mm were associated with both ischaemic or haemorrhagic events and those with an age > 70 years reported more frequently haemorrhagic events. The results of this study demonstrated that stroke-like presentations can be reported in many cases with endocarditis, suggesting particular attention for patients presenting with an oligosymptomatic stroke and fever.

Scheggi *et al. BMC Infectious Diseases* (2022) 22:554
https://doi.org/10.1186/s12879-022-07533-w

BMC Infectious Diseases

RESEARCH Open Access

Impact of septic cerebral embolism on prognosis and therapeutic strategies of infective endocarditis: a retrospective study in a surgical centre

Valentina Scheggi[1,5*], Silvia Menale[2,5], Barbara Tonietti[6], Costanza Bigiarini[1,5], Jacopo Giovacchini[2,5], Stefano Del Pace[2,5], Nicola Zoppetti[4], Bruno Alterini[1,5], Pier Luigi Stefàno[3,5] and Niccolò Marchionni[2,5]

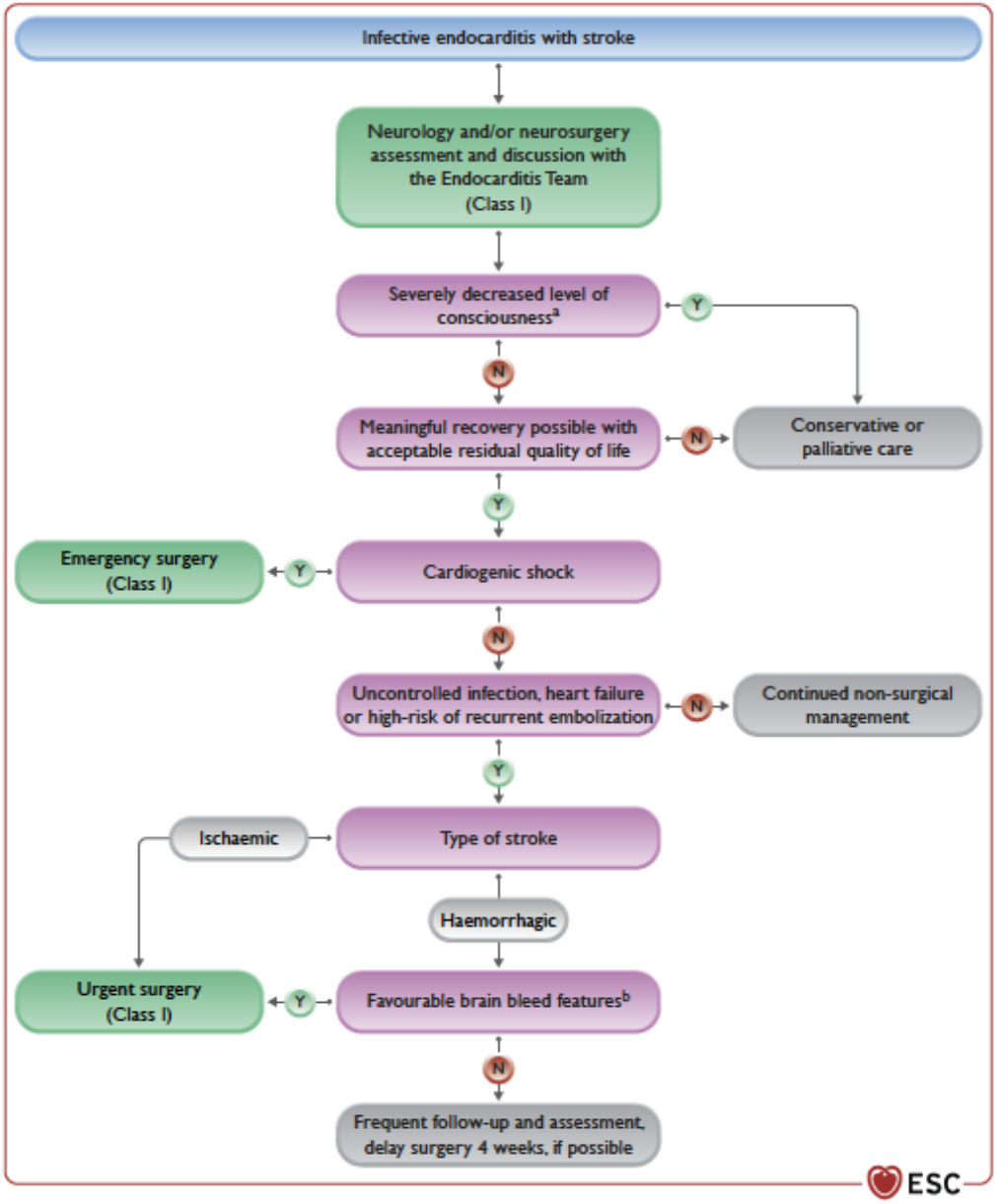
Impact of septic cerebral embolism on prognosis and therapeutic strategies of infective endocarditis: a retrospective study in a surgical centre

- Of 551 patients with IE in the registry, 126 (23%) had a neurologic complication
- Cerebral embolism was significantly more frequent in patients with large vegetations, mitral valve infection and *Staphylococcus aureus* infection
- Patients with neurologic complications were often excluded from surgery despite an indication
- Similar survival rates for each treatment group

Table 2 Therapeutic strategies and mortality of patients with infective endocarditis, by presence of cerebral embolism

	Cerebral embolism		p value
	No (N = 425)	Yes (N = 126)	
Treatment (N, %)			
Excluded from surgery despite indication	40 (9.5%)	20 (15.8%)	0.002
Surgery	329 (77.4%)	102 (81.0%)	
No indication for surgery	56 (13.1%)	4 (3.2%)	
Thirty-day mortality (N, %)	36 (8.5%)	13 (10.3%)	NS
Three-year mortality (N, %)	135 (31.8%)	48 (38.1%)	NS

Scheggi *et al. BMC Infectious Diseases* (2022) 22:554
https://doi.org/10.1186/s12879-022-07533-w



Flowchart

IE with Stroke presentation

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https://doi.org/10.1093/eurheartj/ehad193

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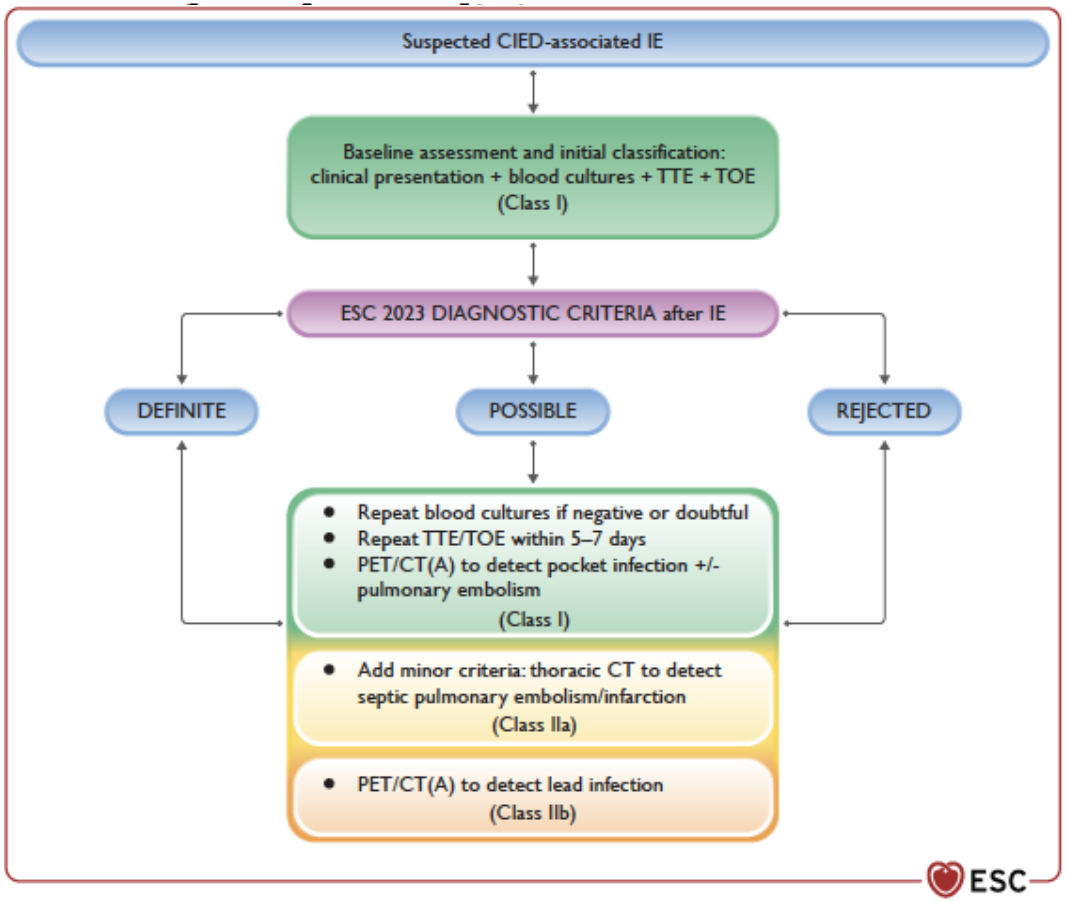


New recommendation

The guidelines provide a figure for the management of CIED-related infective endocarditis.

ESC European Society of Cardiology
European Heart Journal (2023) 00, 1–95
https://doi.org/10.1093/eurheartj/ehad193

ESC GUIDELINES

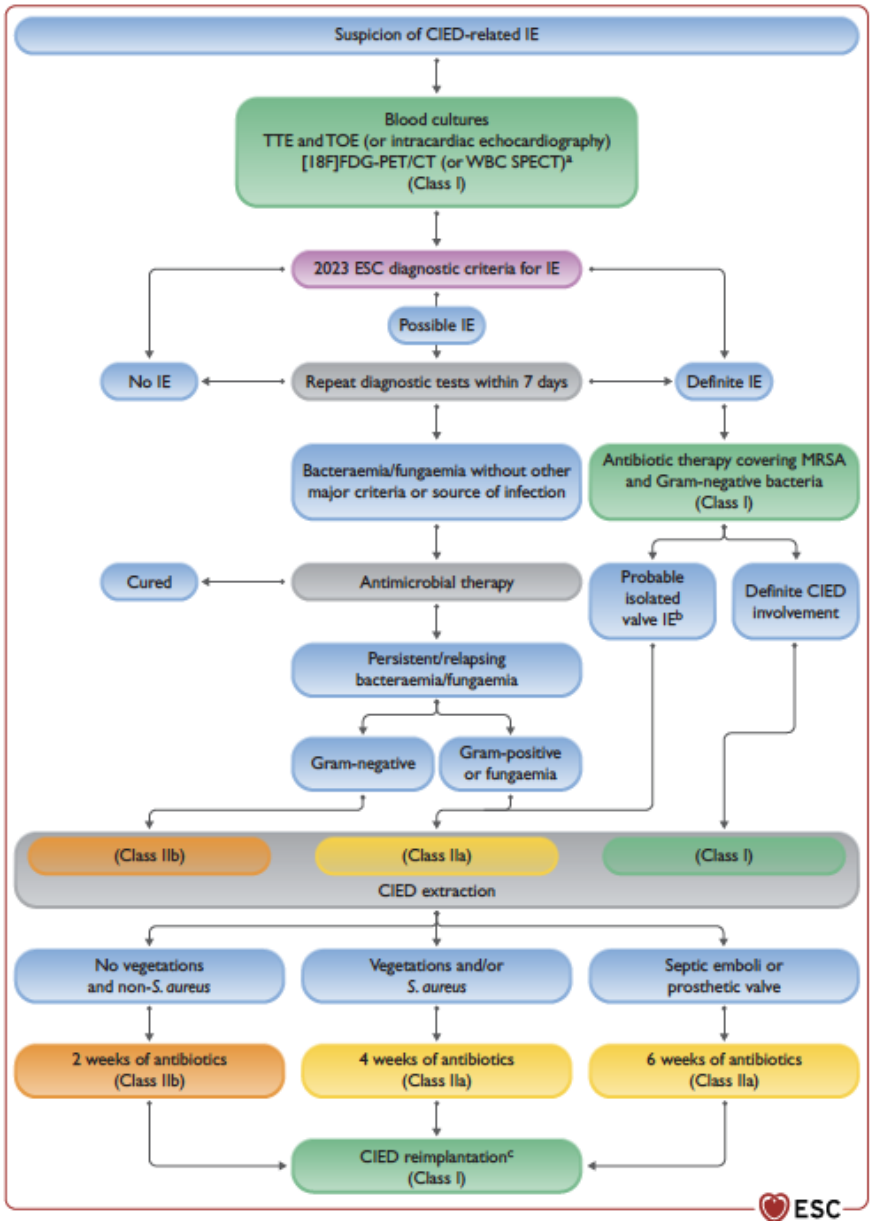
2023 ESC Guidelines for the management of endocarditis

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

Cardiovascular implanted electronic device-related IE is defined as evidence of CIED infection with clinical signs of pocket infection

Local infection usually results from bacterial flora from the patient's skin that is introduced into the pocket at the time of incision despite surgical preparation. Seeding via bacteraemia from a distant focus is less frequent

Complete CIED removal is recommended for all patients with confirmed infection of the lead(s), as conservative treatment is associated with increased mortality.



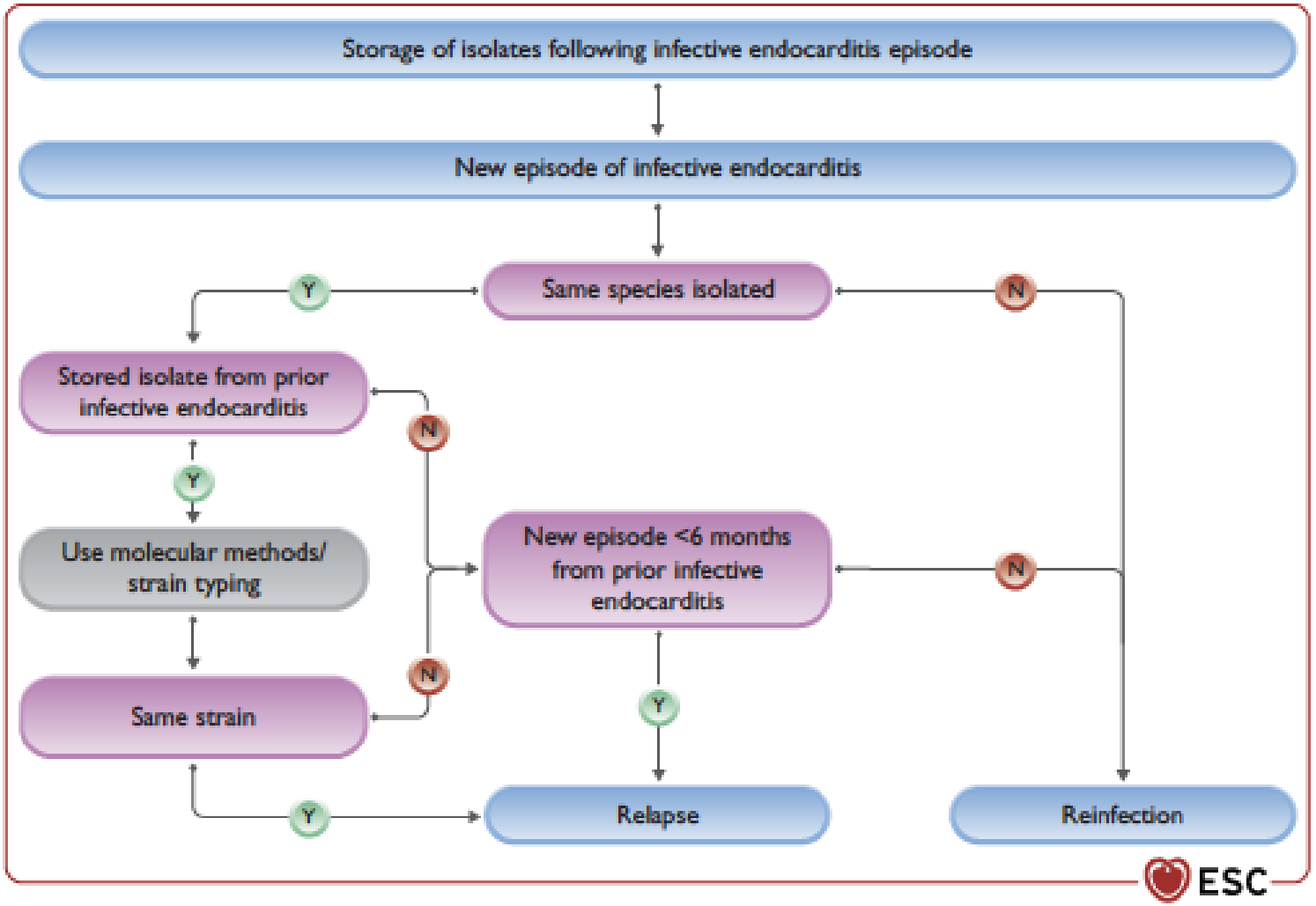
Reimplantation should be performed at a site distant from that of the previous generator, and delayed until signs and symptoms of local and systemic infection have resolved and blood cultures are negative

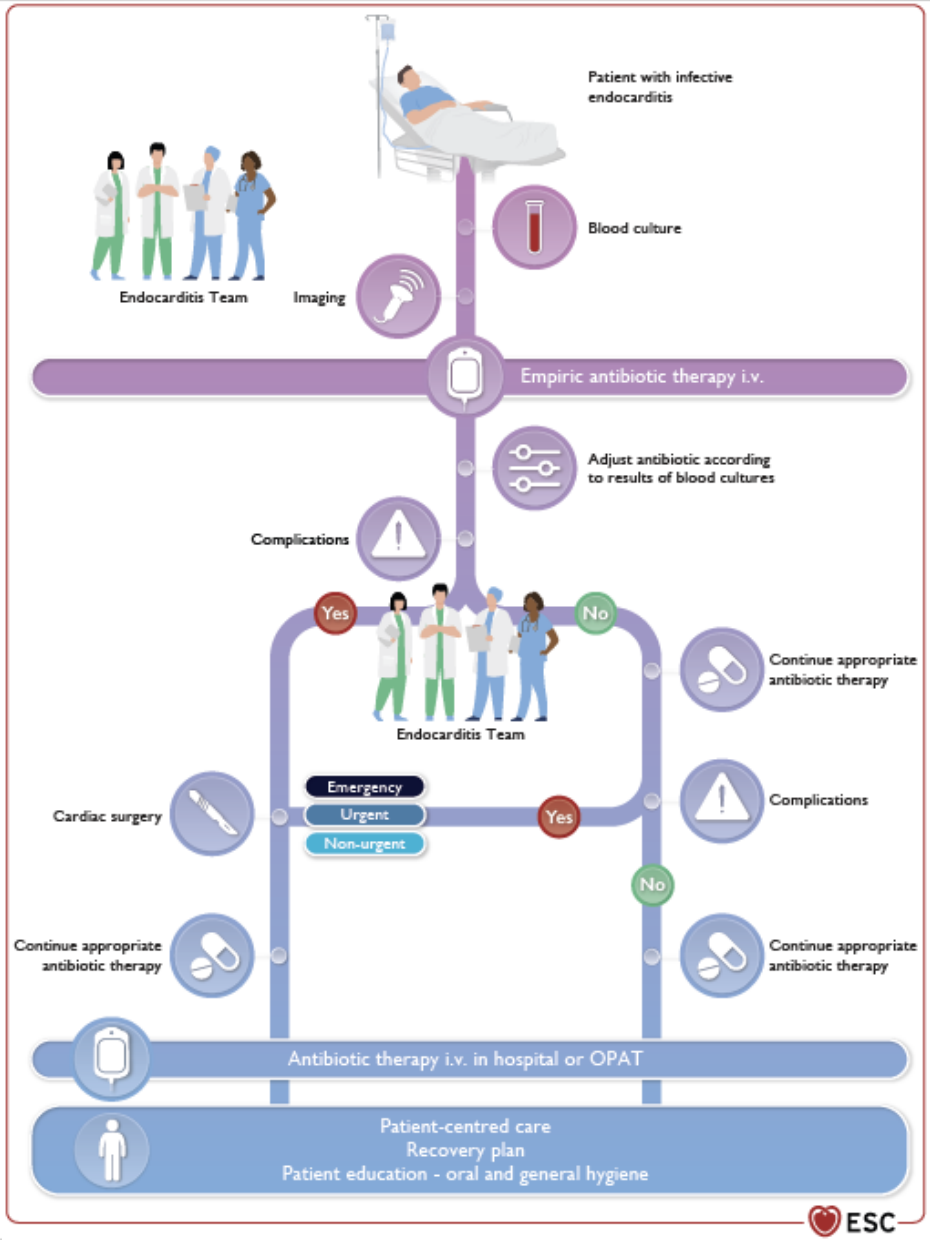
ESC Pocket Guidelines App
Convenient resources available directly on your mobile device

2023 titles with new functionalities and interactive tools have been added:

- **ACS**
- **CVD and diabetes**
- **Cardiomyopathies**
- **Endocarditis**
- **Focused Update on Heart Failure**

The ESC Pocket Guidelines App is free from the app stores below or on your desktop by clicking here: https://guidelines.escardio.org/


Storage of isolates following infective endocarditis episode
New episode of infective endocarditis
Same species isolated
Y
N
Stored isolate from prior infective endocarditis
N
Y
Use molecular methods/ strain typing
New episode <6 months from prior infective endocarditis
N
N
Same strain
Y
Y
Relapse
Reinfection
ESC


Patient with infective endocarditis
Blood culture
Endocarditis Team
Imaging
Empiric antibiotic therapy i.v.
Adjust antibiotic according to results of blood cultures
Complications
Yes
No
Endocarditis Team
Continue appropriate antibiotic therapy
Emergency
Urgent
Non-urgent
Cardiac surgery
Yes
Complications
No
Continue appropriate antibiotic therapy
Continue appropriate antibiotic therapy
Antibiotic therapy i.v. in hospital or OPAT
Patient-centred care
Recovery plan
Patient education - oral and general hygiene
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European Heart Journal (2023) **00**, 1–95
https://doi.org/10.1093/eurheartj/ehad193

2023 ESC Guidelines for the management of endocarditis

New recommendation

POET Trial: Earlier Shift to Oral Antibiotics at Home
Another very important point is the increasing use of oral outpatient antibiotic therapy based on the Partial Oral Treatment of Endocarditis (POET) randomized trial

In **POET Trial** patients in stable condition who had endocarditis on the left side of the heart caused by Streptococci*, Enterococcus faecalis, Staphylococcus aureus*, or CoN Staphylococci were randomly assigned to continue treatment with intravenous (IV) antibiotics (199 patients) or to shift to step-down treatment with oral antibiotics (201 patients) after at least 10 days of initial treatment with IV antibiotics.

European Heart Journal (2015) **36**, 3075–3123
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

AHA Scientific Statement

Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications

A Scientific Statement for Healthcare Professionals From the American Heart Association

Endorsed by the Infectious Diseases Society of America

2023 ESC Guidelines for the management of endocarditis

Recommendation Table 12 — Recommendations for the main indications of surgery in infective endocarditis (native valve endocarditis and prosthetic valve endocarditis)[a]

Recommendations	Class[b]	Level[c]
(I) Heart failure		
Emergency[d] surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary oedema or cardiogenic shock.[420,423,424,429,476,477]	I	B
Urgent[d] surgery is recommended in aortic or mitral NVE or PVE with severe acute regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance.[5,420–422,429]	I	B
(II) Uncontrolled infection		
Urgent[d] surgery is recommended in locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation, prosthetic dehiscence, new AVB).[5,420,421,429,445]	I	B
Urgent[d] or non-urgent surgery is recommended in IE caused by fungi or multiresistant organisms according to the haemodynamic condition of the patient.[420]	I	C
Urgent[d] surgery should be considered in IE with persistently positive blood cultures >1 week or persistent sepsis despite appropriate antibiotic therapy and adequate control of metastatic foci.[436,437]	IIa	B
Urgent[d] surgery should be considered in PVE caused by *S. aureus* or non-HACEK Gram-negative bacteria[5,385,449]	IIa	C
(III) Prevention of embolism		
Urgent[d] surgery is recommended in aortic or mitral NVE or PVE with persistent vegetations ≥10 mm after one or more embolic episodes despite appropriate antibiotic therapy.[451,455,457,471,478]	I	B
Urgent[d] surgery is recommended in IE with vegetation ≥10 mm and other indications for surgery.[5,460,465,466,471,478]	I	C
Urgent[d] surgery may be considered in aortic or mitral IE with vegetation ≥10 mm and without severe valve dysfunction or without clinical evidence of embolism and low surgical risk.[460,463,465,473,478]	IIb	B