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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)

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

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Proč nová doporučení?

- Vývoj zobrazovacích metod - zejména CT, PET/CT - nová velká kriteria!
- Nová data - první randomizovaná studie konvenční vs. chirurgické léčby IE
- Mezioborová spolupráce
- Diagnostický algoritmus
- Časná indikace operace v prevenci komplikací
- Endocarditis Team

Prevence

- 2009 ESC Guidelines omezují ATB profylaxi jen na pacienty v nejvyšším riziku
- NICE žádná profylaxe (2008)
- Analýza preskripce v UK
- Vnímaná horší prognóza IE u pacientů s nejvyšším rizikem tj. s chlopenními protézami
- 2015 Guidelines zachovaly ATB profylaxi u (malého počtu) vysoce rizikových pacientů, u výkonů s nejvyšším rizikem
- Dobrá dentální hygiena a pravidelné stomatologické prohlídky význam obecně

Table 3 Cardiac conditions at highest risk of infective endocarditis for which prophylaxis should be considered when a high-risk procedure is performed

Recommendations	Class[a]	Level[b]
Antibiotic prophylaxis should be considered for patients at highest risk for IE: (1) Patients with any prosthetic valve, including a transcatheter valve, or those in whom any prosthetic material was used for cardiac valve repair. (2) Patients with a previous episode of IE. (3) Patients with CHD: (a) Any type of cyanotic CHD. (b) Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains.	IIa	C

Recommendations	Class[a]	Level[b]
A. Dental procedures		
• Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa	IIa	C

Logistika

- Pacienti s komplikovanou IE mají být léčeni v referenčním centru

Recommendations	Class	Level
Patients with complicated IE should be evaluated and managed at an early stage in a reference centre, with immediate surgical facilities and the presence of a multidisciplinary “Endocarditis Team”, including an ID specialist, a microbiologist, a cardiologist, imaging specialists, a cardiac surgeon, and if needed a specialist in CHD.	IIa	B
For patients with non-complicated IE managed in a non-reference centre, early and regular communication with the reference centre and, when needed, with visit to the reference centre, should be made.	IIa	B

Endocarditis team + referenční centra

- Referenční centra
  - Endocarditis Team - infekcionista, mikrobiolog, kardiolog, kardiochirurg, radiolog, neurolog, neuroradiolog,,…
  - Okamžitá dostupnost diagnostických metod - mikrobiologie, zobrazovací metody TTE, TEE, CT, MR, nukleární metody
  - Okamžitá dostupnost kardiochirurgie, neurologie, intervenční neuroradiologie

Diagnóza IE

- Klinické podezření - horečka (90%) + embolické fenomeny (25% v době dg.)
- Mikrobiologie - hemokultury alespoň 3 x po 10 ml, aerobní i anaerobní inkubace, z periferní žíly, bakteremie je konstantní, před nasazením ATB
- Zobrazovací metody - echokardiografie, CT, nukleární metody

Modifikovaná Duke kritéria

Definite IE
Pathological criteria • Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or • Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis **Clinical criteria** • 2 major criteria; or • 1 major criterion and 3 minor criteria; or • 5 minor criteria
Possible IE
• 1 major criterion and 1 minor criterion; or • 3 minor criteria
Rejected IE
• Firm alternate diagnosis; or • Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or • No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or • Does not meet criteria for possible IE, as above

Definice kritérií

Major criteria

1. Blood cultures positive for IE

a. Typical microorganisms consistent with IE from 2 separate blood cultures:
   - *Viridans streptococci, Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus;* or
   - Community-acquired enterococci, in the absence of a primary focus; or

b. Microorganisms consistent with IE from persistently positive blood cultures:
   - ≥2 positive blood cultures of blood samples drawn >12 h apart; or
   - All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or

c. Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre >1:800

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.

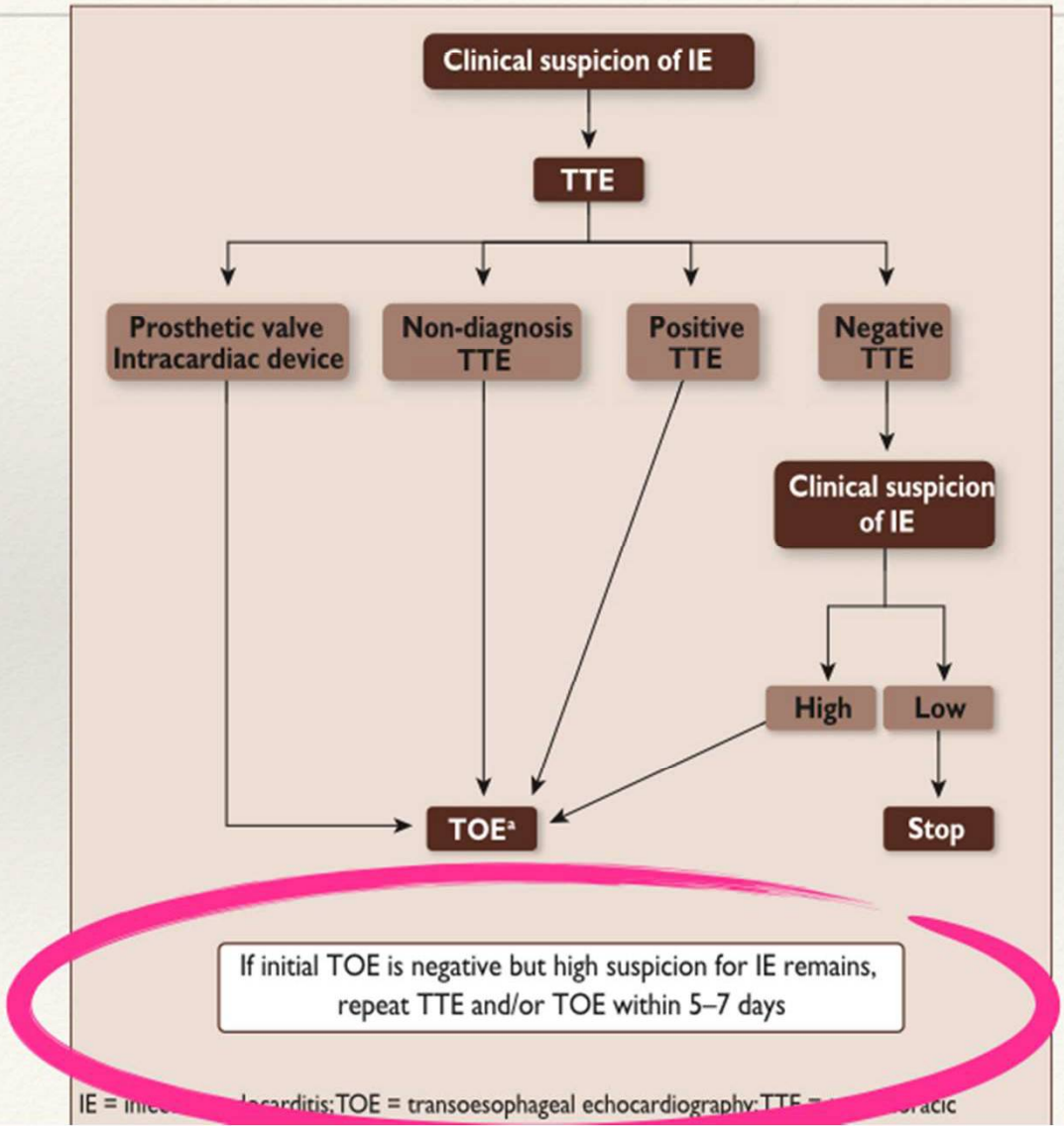
c. Detection paravalvular lesions by cardiac CT.

Minor criteria

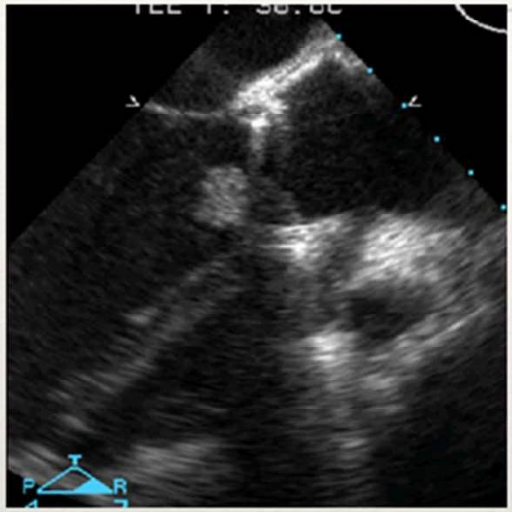
1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

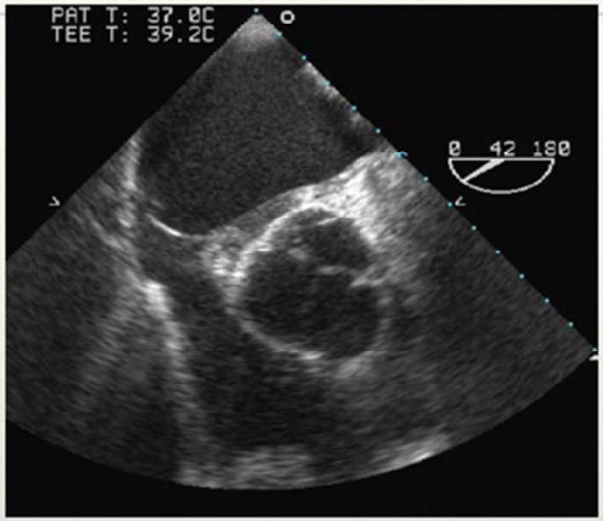
Indikace k echokardiografii

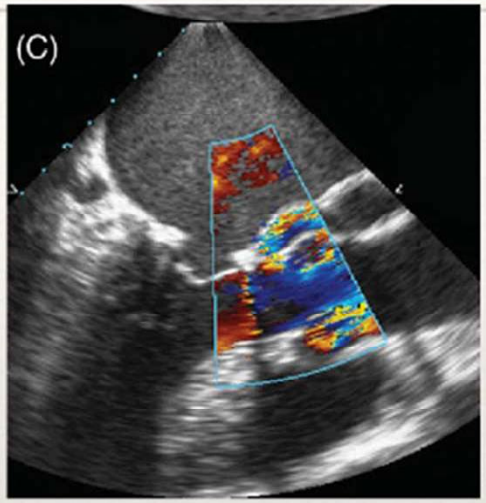
- **Senzitivita k dg. vegetací**
  - Nativní chlopně
    - TTE 70%
    - TEE 96%
  - Protézy
    - TTE 50%
    - TEE 92%
- **Specificita 90%**



Echokardiografická velká kritéria





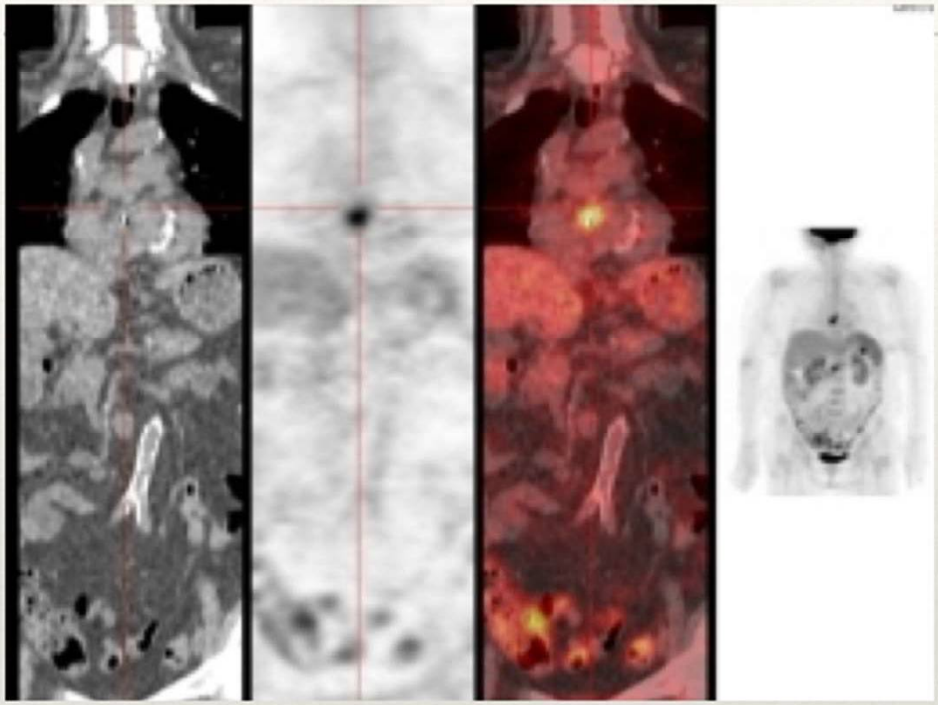


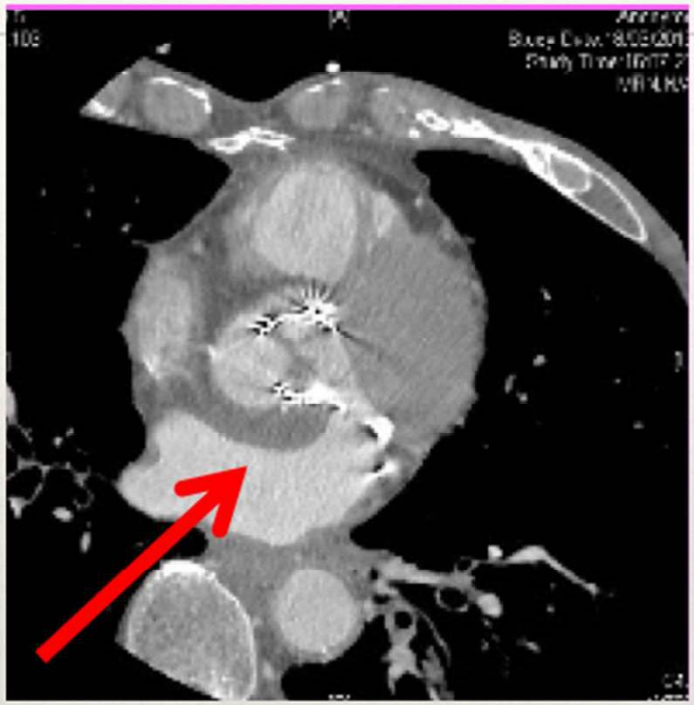
2. Imaging positive for IE

a. Echocardiogram positive for IE:

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

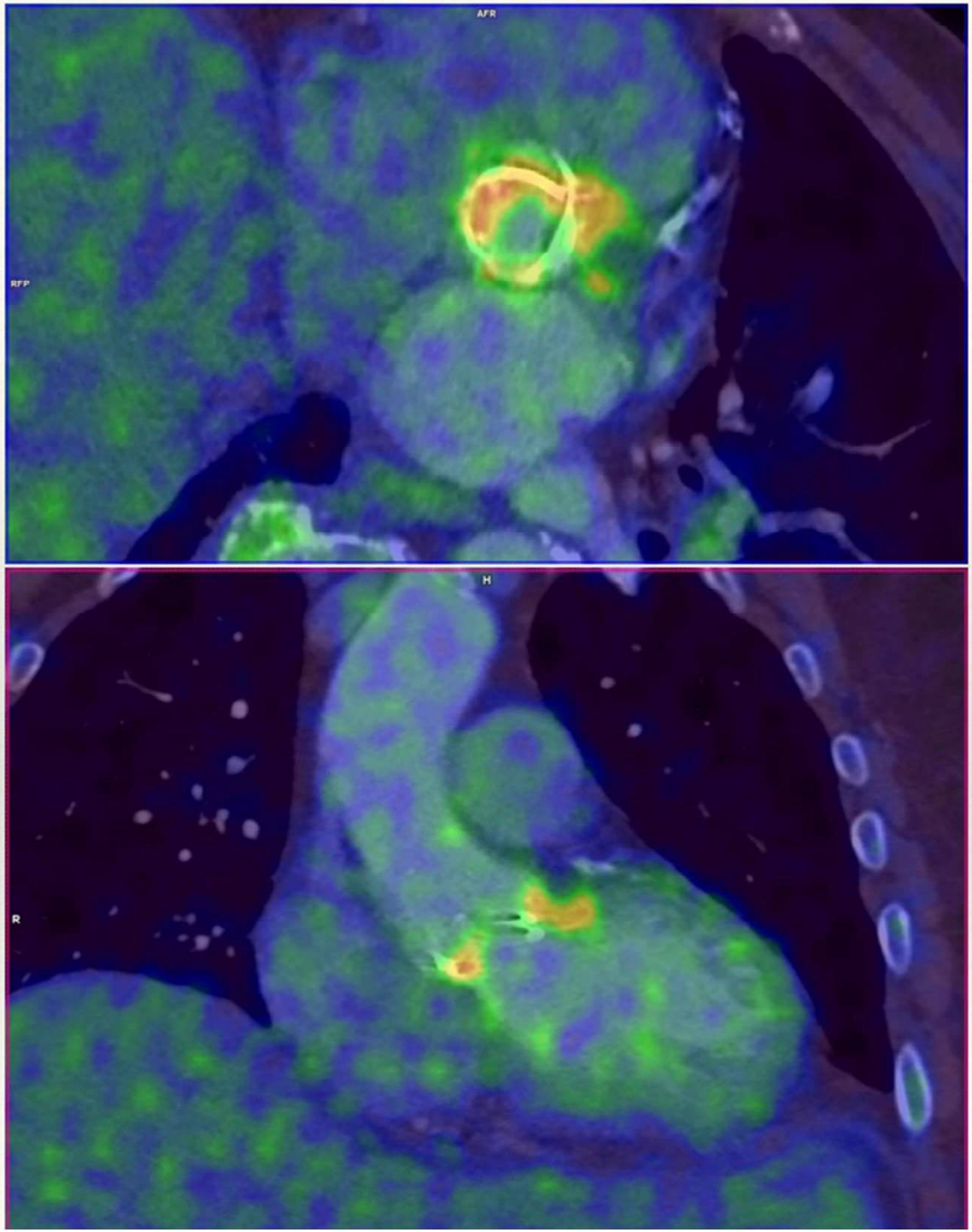
Nová velká kritéria !





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.



Za snímky děkuji
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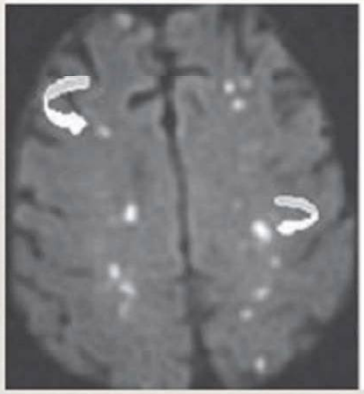
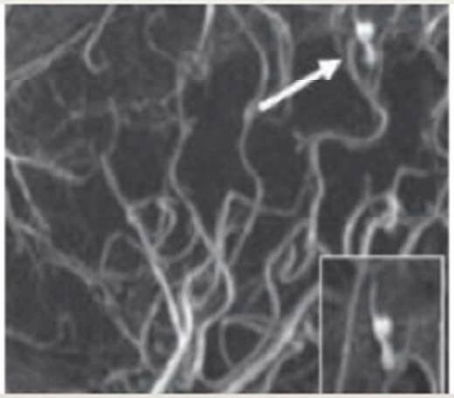
Neurologické komplikace IE

MRI

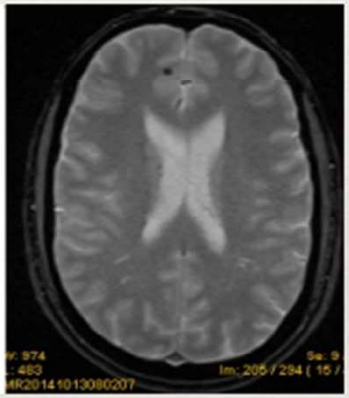


Embolizace



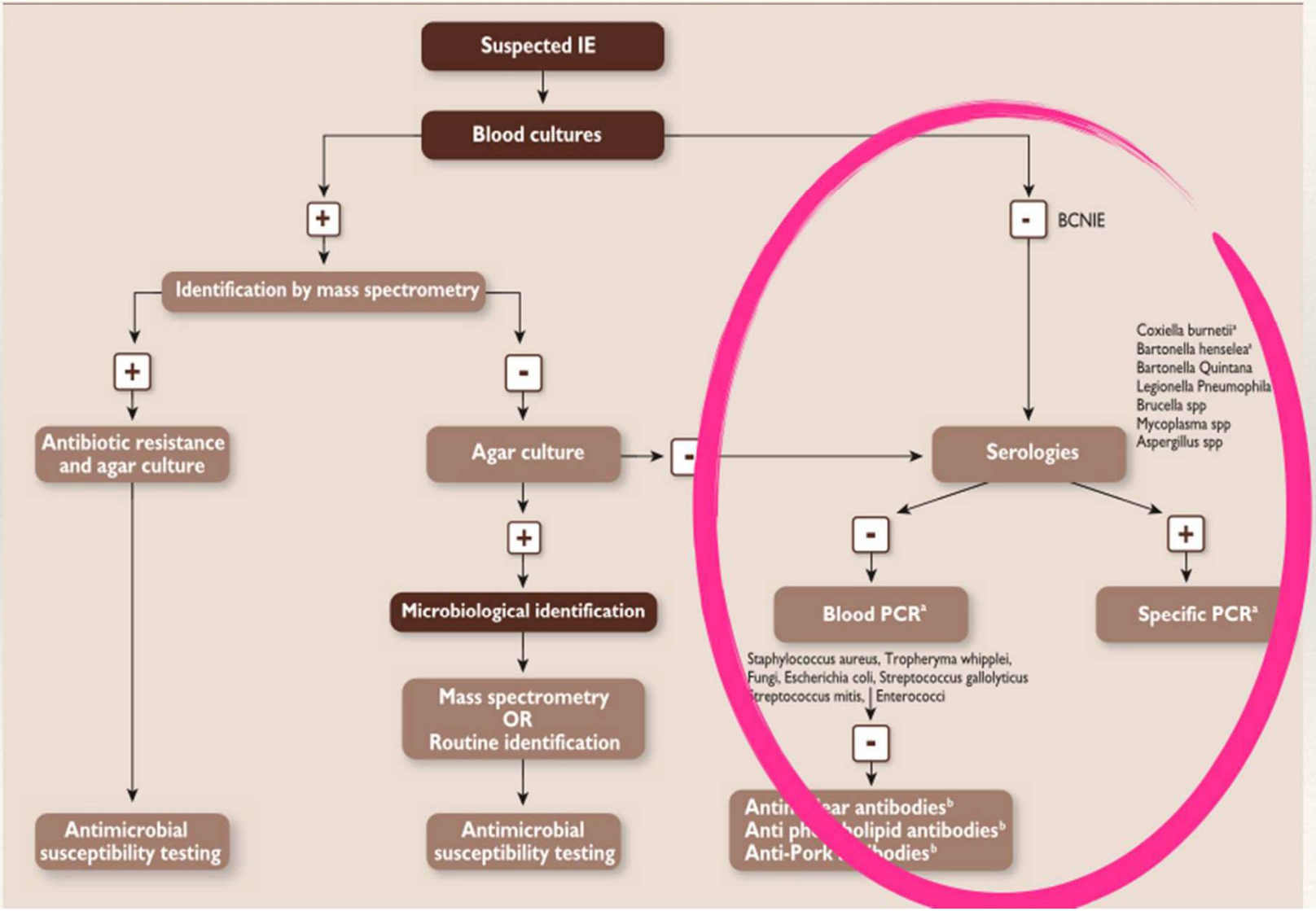
Infekční aneurysma

Malá kriteria

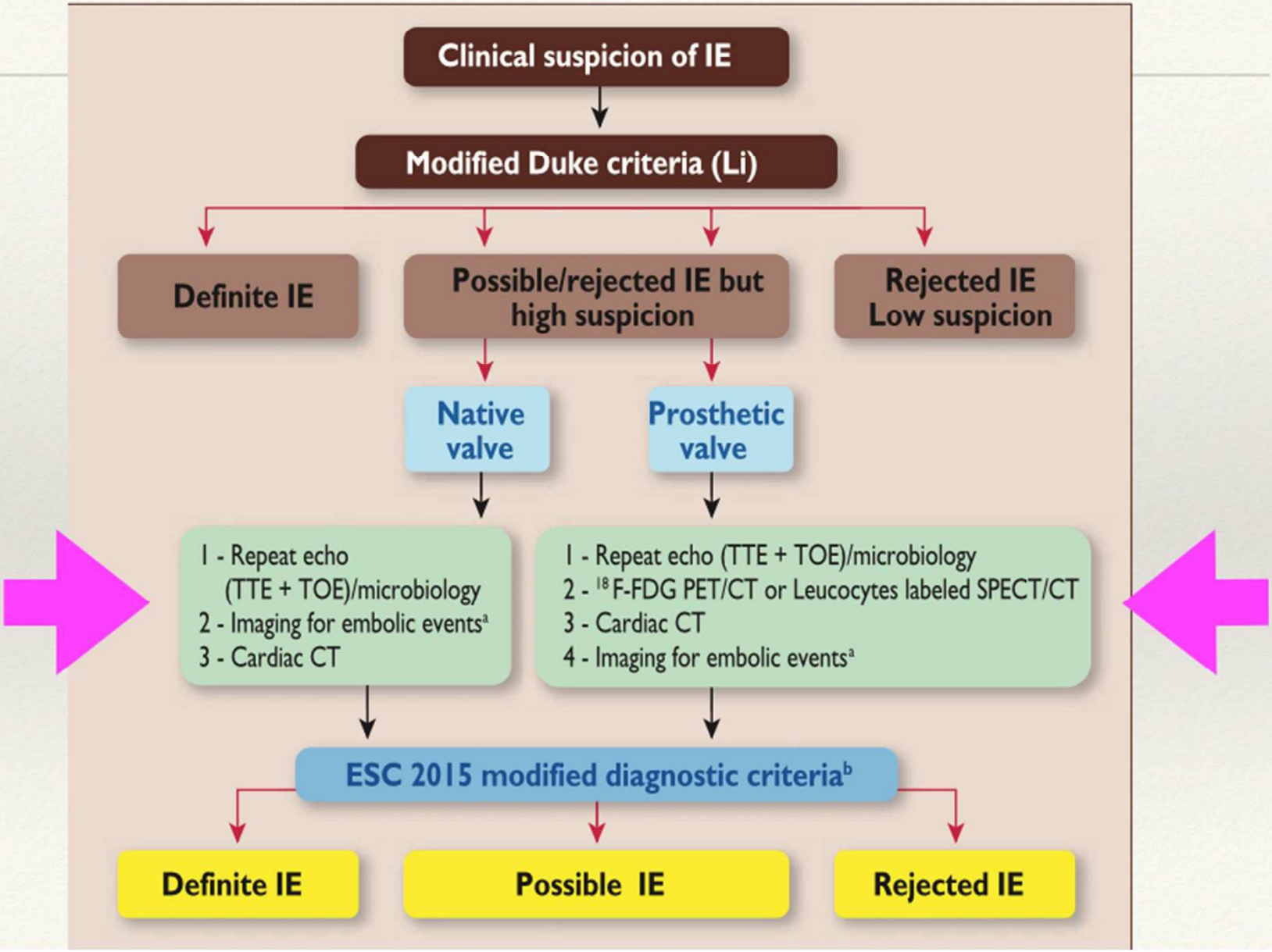


Mikrokrvácení v T2 obraze nepatří mezi malá kriteria

Diagnostický algoritmus mikrobiologické diagnostiky



Diagnostický algoritmus 2015



Terapie

- Úspěšná léčba IE závisí na eradikaci mikrobů antibiotiky
- Chirurgie přispívá odstraněním infikovaného materiálu/tkáně + korekce komplikací

Indikace k operaci

- Operována asi polovina pacientů s IE
- Časná konzultace kardiochirurga
- Endocarditis team
- Indikace k operaci - emergentní (do 24 hod), urgentní (<7 dní), elektivní
  - srdeční selhání
  - nekontrolovaná infekce
  - prevence embolických komplikací

Srdeční selhání

- Nejčastější komplikace IE, 42-60% NVE
- Nejčastější indikace k operaci
- Střední/těžké srdeční selhání je významný prediktor hospitalizační, 6 m, roční mortality

Indications for surgery	Timing[a]	Class[b]	Level[c]
1. Heart failure			
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B

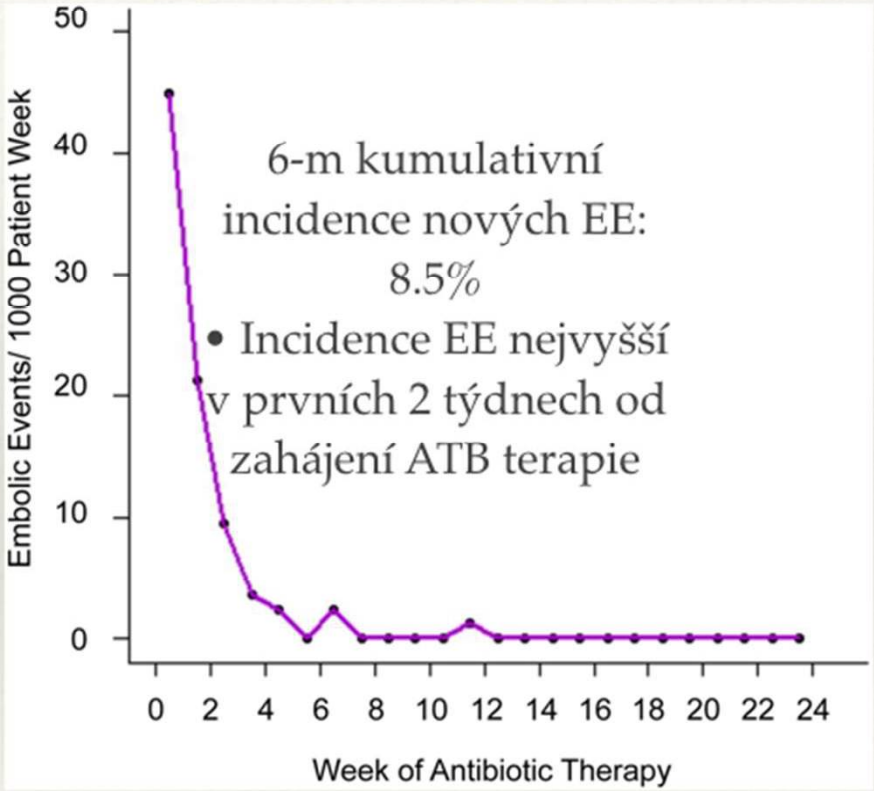
Nekontrolovaná infekce

- Perzistující infekce +lokálně nekontrolovaná infekce
- Druhá nejčastější indikace k operaci
- Nejobávanější komplikace IE

2. Uncontrolled infection			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B
Infection caused by fungi or multiresistant organisms	Urgent/ elective	I	C
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	IIa	B
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	IIa	C

Embolizace

- Výskyt 20-50%, klesá od zahájení ATB
- Nejčastější v prvních 2 týdnech
- Souvisí s velikostí a mobilitou vegetací
- Nejčastěji mozek, slezina
- Němá v 20–50%



Hubert S- J Am Coll Cardiol 2013;62:1384–92

Rozměr vegetace vs. riziko embolizace

Variable	Univariate Analysis p Value	Multivariate Analysis: Hazard Ratio (95% Confidence Interval)	Multivariate Analysis: p Value
Age	0.15	1.01 (0.99–1.03)	0.18
Diabetes	0.05	1.30 (0.61–2.80)	0.50
Previous embolism	0.04	1.40 (0.74–2.65)	0.30
Atrial fibrillation	0.07	1.66 (0.81–3.41)	0.17
Vegetation length (mm) (stratified)*	0.001		
>0 to ≤10		1.26 (0.24–6.69)	0.79
>10		4.46 (1.06–18.88)	0.04
Staphylococcus aureus	0.07	1.78 (0.85–3.76)	0.13

Hubert S- J Am Coll Cardiol 2013;62:1384–92

Embolizace

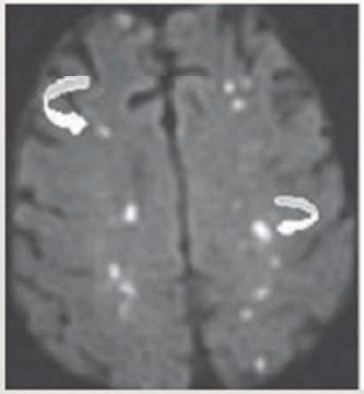
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episode despite appropriate antibiotic therapy	Urgent	I	B
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C

Table 26 **Indications for surgical treatment of right-sided infective endocarditis**

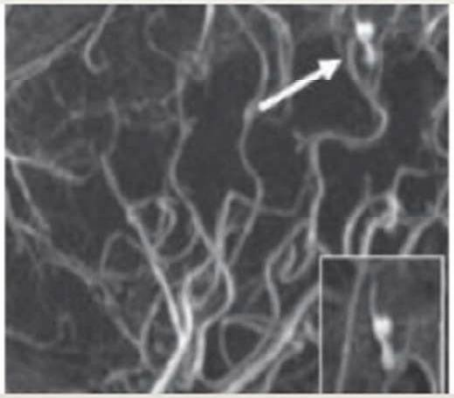
Recommendation	Class[a]	Level[b]
Surgical treatment should be considered in the following scenarios: • Microorganisms difficult to eradicate (e.g. persistent fungi) or bacteraemia for > 7 days (e.g. *S. aureus*, *P. aeruginosa*) despite adequate antimicrobial therapy or • Persistent tricuspid valve vegetations > 20 mm after recurrent pulmonary emboli with or without concomitant right heart failure or • Right HF secondary to severe tricuspid regurgitation with poor response to diuretic therapy	IIa	C

Neurologické komplikace IE

MRI

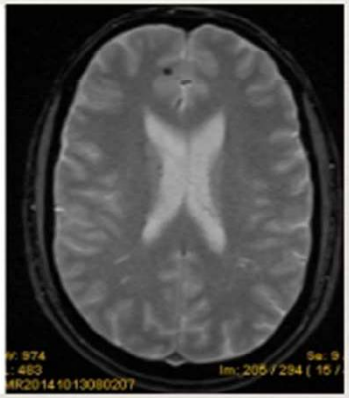


Embolizace



Infekční aneurysma

Malá kriteria



Mikrokrvácení v T2 obraze nepatří mezi malá kriteria

Indikace k operaci při neurologické komplikaci

Recommendations	Class	Level
After a **silent embolism** or **transient ischaemic attack**, cardiac surgery, if indicated, is recommended without delay.	I	B
Neurosurgery or endovascular therapy is indicated for very large, enlarging or ruptured intracrani**al infectious aneurysms**.	I	C
Following intracranial haemorrhage, surgery should generally **be postponed** for ≥1 month.	IIa	B
After **a stroke**, surgery indicated for HF, uncontrolled infection, abscess, or persistent high embolic risk should be considered without any delay as long as **coma** is absent and the presence of **cerebral haemorrhage** has been excluded by cranial CT or MRI.	IIa	B
Intracranial infectious aneurysms should be looked for in patients with IE and **neurological symptoms**. **CT or MR angiography** should be considered for diagnosis. If non-invasive techniques are negative and the suspicion of intracranial aneurysm remains, **conventional angiography** should be considered.	IIa	B

Doporučení IE ESC 2015

- Profylaxe jen pro vysoce rizikové, prevence pro všechny
- Multidisciplinární "endocarditis team"
- Hemokultury a echokardiografie základem diagnostiky
- Nová CT a PET, SPECT/CT diagnostická kriteria a algoritmus k zpřesnění dagnostiky
- Časná indikace k operaci ke zlepšení prognózy

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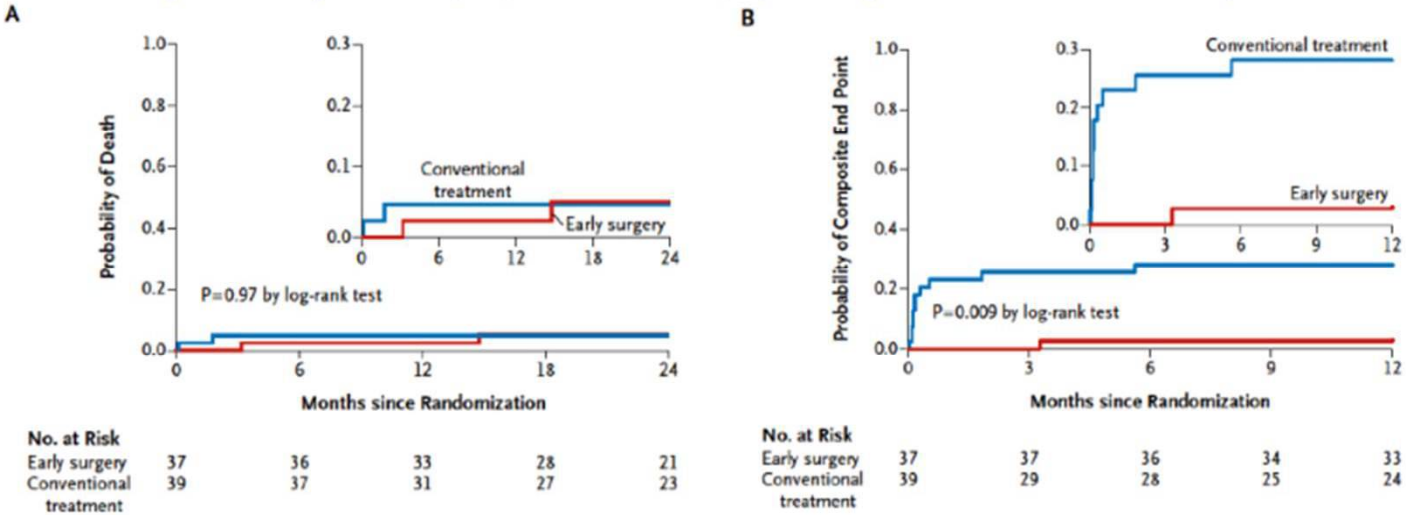
Časná operace vs. konvenční léčba

Early Surgery versus Conventional Treatment for Infective Endocarditis

Randomization of pts. with severe valve disease, and large vegetations to early surgery (37 patients) or conventional treatment (39)

Primary EP: in hospital death, EE, recurrence of IE, repeat hospitalization due to the development of CHF



Kang DH – N Eng J Med 2012: 366:2466-73

Endocarditis team

2. Patients with non-complicated IE can be initially managed in a non-reference centre, but with regular communication with the reference centre, consultations with the multidisciplinary 'Endocarditis Team', and, when needed, with external visit to the reference centre.

Characteristics of the reference centre

1. Immediate access to diagnostic procedures should be possible, including TTE, TOE, multislice CT, MRI, and nuclear imaging.
2. Immediate access to cardiac surgery should be possible during the early stage of the disease, particularly in case of complicated IE (HF, abscess, large vegetation, neurological, and embolic complications).
3. Several specialists should be present on site (the 'Endocarditis Team'), including at least cardiac surgeons, cardiologists, anaesthesiologists, ID specialists, microbiologists and, when available, specialists in valve diseases, CHD, pacemaker extraction, echocardiography and other cardiac imaging techniques, neurologists, and facilities for neurosurgery and interventional neuroradiology .

Role of the 'Endocarditis Team'

1. The 'Endocarditis Team' should have meetings on a regular basis in order to discuss cases, take surgical decisions, and define the type of follow-up.
2. The 'Endocarditis Team' chooses the type, duration, and mode of follow up of antibiotic therapy, according to a standardized protocol, following the current guidelines.
3. The 'Endocarditis Team' should participate in national or international registries, publicly report the mortality and morbidity of their centre, and be involved in a quality improvement programme, as well as in a

Léčba neurologických komplikací

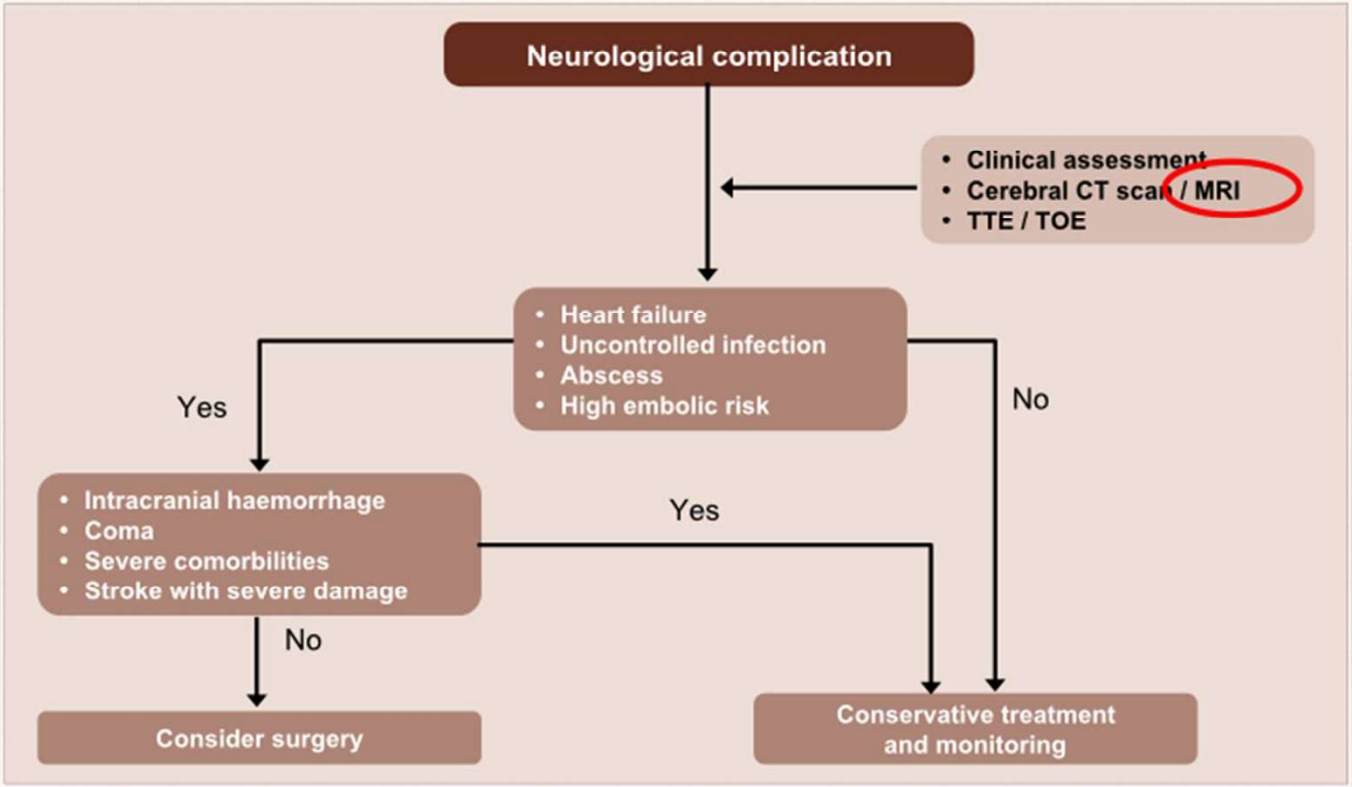


Table 16 Antibiotic treatment of infective endocarditis due to oral streptococci and *Streptococcus* bovis group[a]

Antibiotic	Dosage and route	Duration (weeks)	Class[b]	Level[c]	Ref.[d]	Comments
Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci						
Standard treatment: 4-week dur						
Penicillin G or Amoxicillin[e] or Ceftriaxone[f]	12–18 million U 100–200 mg/kg 2 g/day i.v. or i.r **Paediatric dos** Penicillin G 200 Amoxicillin 300 Ceftriaxone 100					
Standard treatment: 2-week dur						
Penicillin G or Amoxicillin[e] or Ceftriaxone[f] combined with Gentamicin[h] or Netilmicin	12–18 million U 100–200 mg/kg 2 g/day i.v. or i.r 3 mg/kg/day i.v. 4–5 mg/kg/day **Paediatric dos** Penicillin G, am Gentamicin 3 m doses					
In beta-lactam allergic patients[j]						
Vancomycin[l]	30 mg/kg/day i.v **Paediatric dos** Vancomycin 40					
Strains relatively resistant to p						
Standard treatment						
Penicillin G or Amoxicillin[e] or Ceftriaxone[f] combined with Gentamicin[h]	24 million U/day 200 mg/kg/day i. 2 g/day i.v. or i.r 3 mg/kg/day i.v.					
In beta-lactam allergic patients[j]						
Vancomycin[l] with Gentamicin[k]	30 mg/kg/day i.v 3 mg/kg/day i.v. or i.m. in 1 dose **Paediatric doses:**[£] As above	2	I	C		

Table 17 Antibiotic treatment of infective endocarditis due to *Staphylococcus* spp.

Antibiotic	Dosage and route	Duration (weeks)	Class[i]	Level[j]	Ref.[k]	Comments
Native valves						
Methicillin-susceptible staphylococci						
(Flu)cloxacillin or oxacillin	12 g/day i.v. in 4–6 doses **Paediatric doses:**[r] 200–300 mg/kg/day i.v. in 4–6 equally di doses	4–6	I	B	6,8, 128, 135,	Gentamicin addition is not recommended because clinical benefit has not been demonstrated and there is increased renal toxicity
Alternative therapy[p] Cotrimoxazole[s] with Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 d 1800mg/day i.v. in 3 doses **Paediatric doses:**[t] Sulfamethoxazole 60 mg/kg/day and Trimethoprim 12 mg/kg/day (i.v. in 2 do Clindamycin 40 mg/kg/day (i.v. in 3 dose					
Penicillin-allergic patients[h] or methicillin-resistant staphylococ						
Vancomycin[u, v]	30–60 mg/kg/day i.v. in 2–3 doses **Paediatric doses:**[t] 40 mg/kg/day i.v. in 2–3 equally divided				6,8, 135, 136,	**Cephalosporins** (cefazolin 6 g/day or cefotaxime 6 g/da (i.v./d in 3 doses) are recommended for penicillin-allergic patients with non-anaphylactic reactions with methicillin-susceptible endocarditis
Alternative therapy[v, x] Daptomycin[t, d]	10 mg/kg/day i.v. once daily **Paediatric doses:**[t] 10 mg/kg/day i.v. once daily	4–6	IIa	C		**Daptomycin** is selected to recommended for MSSA and MRSA bacteraemia with vancomycin MIC > 1 mg/L
Alternative therapy[p] Cotrimoxazole[s] with Clindamycin	Sulfamethoxazole 4800 mg/day and Trimethoprim 960 mg/day (i.v. in 4–6 d 1800mg/day IV in 3 doses					
Prosthetic valves						
Methicillin-susceptible staphylococci						
(Flu)cloxacillin or oxacillin with Rifampin[e] and Gentamicin[f]	12 g/day i.v. in 4–6 doses 900–1200 mg i.v. or orally in 2 or 3 di doses 3 mg/kg/day i.v. or i.m. in 1 or 2 doses **Paediatric doses:**[r] Oxacillin and (Flu)cloxacillin as above Rifampin 20 mg/kg/day i.v. or orally in 3 equally divided doses	≥ 6	I	B	6,8, 136,	**Cephalosporins** (cefazolin 6 g/day or cefotaxime 6 g/day (i.v./d in 3 doses) are recommended for penicillin-allergic patients with non-anaphylactic reactions with methicillin-susceptible endocarditis Starting rifampin 3–5 days later than vancomycin and gentamicin has been suggested by some experts. Gentamicin can be given in a single daily dose in order to
Penicillin-allergic patients[h] and methicillin-resistant staphyloco						
Vancomycin[h] with Rifampin[e] and Gentamicin[f]	30–60 mg/kg/day i.v. in 2–3 doses 900–1200 mg i.v. or orally in 2 or 3 di doses 3 mg/kg/day i.v. or i.m. in 1 or 2 doses **Paediatric dosing:**[r] As above	≥ 6	I	B		
		2	I	B		

Table 18 Antibiotic treatment of infective endocarditis due to *Enterococcus* spp.

Antibiotic	Dosage and route	Duration, weeks	Class[g]	Level[h]	Ref.[i]	Comments
Beta-lactam and gentamicin-susceptible strains (for resistant isolates see [a,b,c])						
Amoxicillin*	200 mg/kg/day i.v. in 4–6 doses	4–6	I	B	6,8, 129, 135, 136, 186	6-week therapy recommended for patients with > months symptoms or PVE
with						
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose	2–6**	I	B		
	Paediatric doses:[e] Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Gentamicin 3 mg/kg/day i.v. or i.m. in 3 equally divided doses					
Ampicillin with Ceftriaxone	200 mg/kg/day i.v. in 4–6 doses	6	I	B	183–185	This combination is active against *Enterococcus faeca* strains with and without HLAR, being the combination of choice in patients with HLAR *E. faecalis* endocarditis. This combination is not active against *E. faecium*
	4 g/day i.v. or i.m. in 2 doses	6	I	B		
	Paediatric doses:[e] Amoxicillin as above Ceftriaxone 100 mg/kg/12 h i.v. or i.m.					
Vancomycin[f]	30 mg/kg/day i.v. in 2 doses	6	I	C		Gentamicin can be given in a single daily dose in order to
with Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose	6	I	C		
	Paediatric doses:[e] Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses Gentamicin as above					

Indications for surgery	Timing[a]	Class[b]	Level[c]
1. Heart failure			
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	Emergency	I	B
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	Urgent	I	B
2. Uncontrolled infection			
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	Urgent	I	B
Infection caused by fungi or multiresistant organisms	Urgent/ elective	I	C
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	Urgent	IIa	B
PVE caused by staphylococci or non-HACEK gram-negative bacteria	Urgent/ elective	IIa	C
3. Prevention of embolism			
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episode despite appropriate antibiotic therapy	Urgent	I	B
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent	IIa	B
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and no other indication for surgery[e]	Urgent	IIb	C