Endocardites infectieuses: prise en charge thérapeutique

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Conflits d’intérêts

- MSD
- Aerogen
- AdvanzPharma
- Pfizer
- Shionogi

5 questions

- Quand suspecter une endocardite ?
- Comment diagnostiquer ?
- Quel bilan effectuer ?
- Quel traitement antibiotique ?
- Quand (et qui) opérer ?

5 questions

- Quand suspecter une endocardite ?
- Comment diagnostiquer ?
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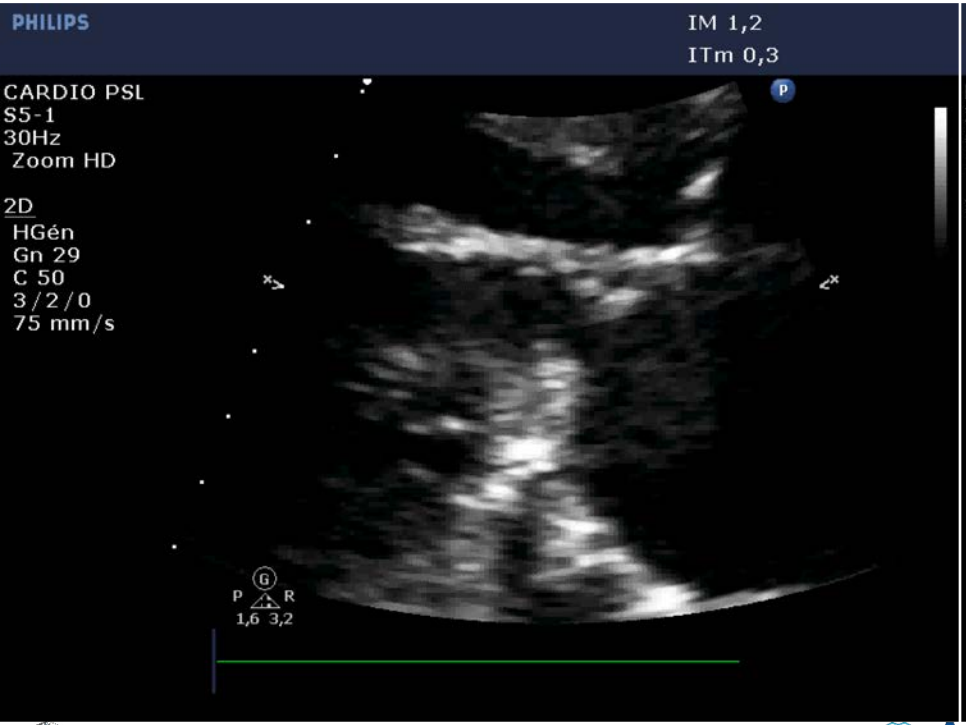
- Quel traitement antibiotique ?
- Quand (et qui) opérer ?

QUEL BILAN EFFECTUER?

But

- Identifier les malades qui relèveraient d'une chirurgie rapide (en urgence)
- Donc pour préciser
  - Taille des végétations
  - Extension locale des lésions
  - Retentissement systémique
    - Embolies
    - Anévrismes mycotiques

ETT ou ETO?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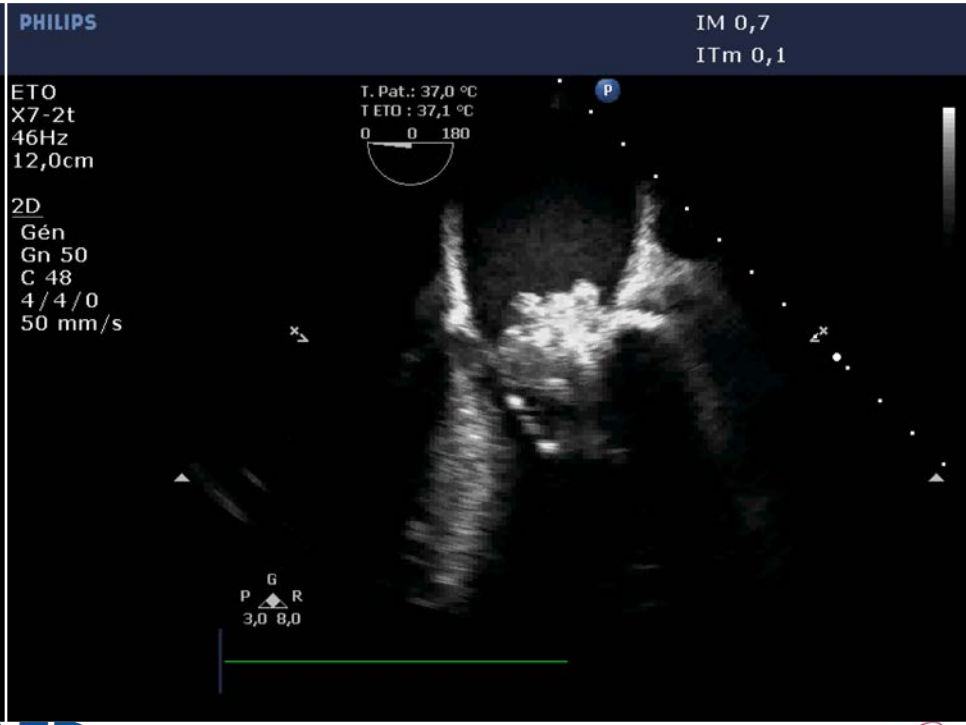
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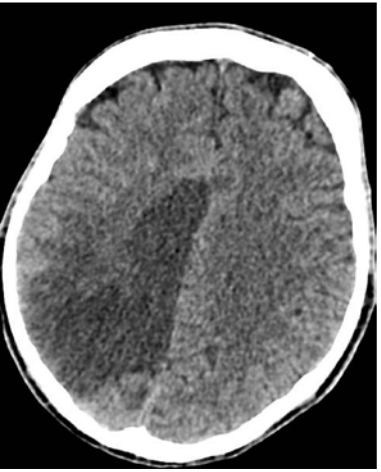
TDM cérébral

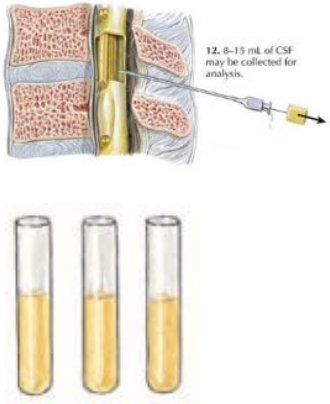
Complications neurologiques: 25% des endocardites

33% à 50% des endocardites en réanimation

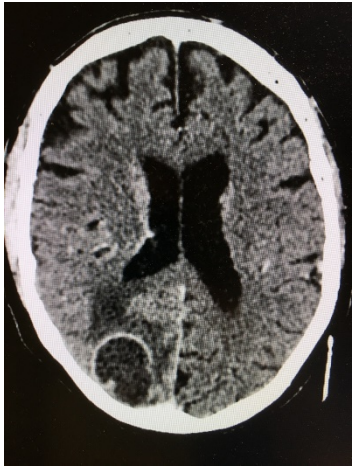


AVC ischémique 75%

Hgie intracranienne 25-50%



Meningite 33%

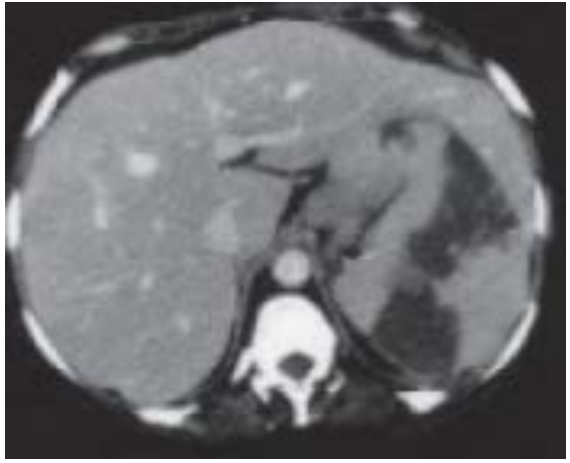


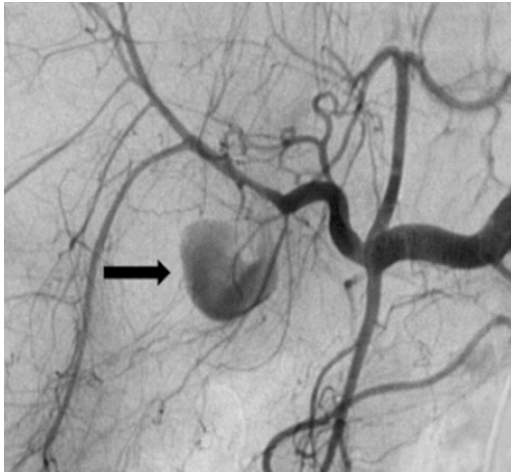
Abcès 10-15%

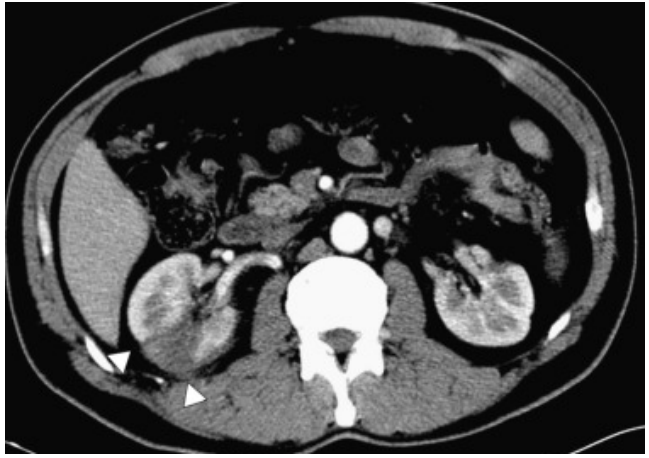
Anévrisme mycotique 10%

Sonneville, Neurologic Critical Care 2011

TDM corps entier







QUELLE ANTIBIOTHÉRAPIE?

Epidémiologie de l'endocardite en réanimation

	Staphylococcus aureus	*Streptococcus*	*Enterococcus*
Mourvillier, ICM 2004	50%	23%	6%
Sonneville, Crit Care Med 2011	46%	27%	8%
Leroy, AIC 2015	38%	35%	10%
Rambaud, AIC 2022	54%	22%	10%

Recommendations for antibiotic regimens for initial empirical treatment of infective endocarditis (before pathogen identification) (1)

Recommendations		Class	Level
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:			
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	IIa	C
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose		
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:			
Adult antibiotic dosage and route			
Vancomycin	30 mg/kg/day i.v. in 2 doses		
Daptomycin	10 mg/kg/day i.v. in 1 dose		
Gentamicin	3 mg/kg/day i.v. or i.m. in 1 dose	IIb	C
Rifampin	900–1200 mg i.v. or orally in 2 or 3 doses		

Traitement antibiotique des endocardites

- Monothérapie dans la plupart des cas
  - *S. aureus MS*: oxacilline 12 g/j 6 semaines (ou cefazoline)
    - Vanco ou dapto si meti R
  - *Streptococcus spp*: amoxicilline 100-200 mg/kg 4 semaines
- *Enteroccocus spp.*: bithérapie
  - Amoxicilline 200 mg/kg 6 semaines + gentamycine 3 mg/kg 2 semaines
  - Amoxicilline 200 mg/kg + ceftriaxone 4 g/ j 6 semaines

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)

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3948–4042
https://doi.org/10.1093/eurheartj/ehad193

Early Use of Daptomycin Versus Vancomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia With Vancomycin Minimum Inhibitory Concentration >1 mg/L: A Matched Cohort Study

Murray, CID 2013

	DAP (n = 85)	VAN (n = 85)	*P* Value
Clinical failure[a]	17 (20.0%)	41 (48.2%)	<.001
Mortality at 30 d	3 (3.5%)	11 (12.9%)	.047
Persistent bacteremia	16 (18.8%)	36 (42.4%)	.001
Duration of bacteremia, d[b]	3 (2–5)	5 (3–8)	.003
Length of stay, d[b]	11 (8–18)	12 (8–17)	.532
Duration of treatment, d[b]	10 (8–17)	9 (6–16)	.324
Recurrence of MRSA bacteremia within 30 d[c]	0 (0.0%)	3 (4.1%)	.104
Readmission within 30 d[c]	16 (19.5%)	19 (25.3%)	.381
Total hospital charges, 2011 US dollars	$95 244 ($60 637–$156 020)	$86 504 ($48 030–$183 008)	0.643
Total medication charges, 2011 US dollars	$26 841 ($16 820–$39 659)	$15 848 ($7988–$29 240)	<0.001
Total laboratory charges, 2011 US dollars	$9235 ($6332–$14 456)	$10 276 ($5827–$17 206)	0.857

Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating *Enterococcus faecalis* Infective Endocarditis

Fernandez-Hidalgo, CID 2013

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Demographics			
Age, y, median (IQR)	70.4 (62.9–77.4)	69.8 (57.9–74.6)	.187
Male sex	114 (72%)	62 (71%)	.94
Definite IE (modified Duke criteria)	146 (92%)	84 (97%)	.151
Underlying condition			
CCI, median (IQR)	2 (2–4)	2 (1–4)	.053
Diabetes mellitus	53 (33%)	31 (36%)	.72
Chronic renal failure	53 (33%)	14 (16%)	.004
Neoplasm	29 (18%)	6 (7%)	.015
HIV infection	2 (1%)	6 (7%)	.017
Liver cirrhosis	13 (8%)	4 (5%)	.29
Hemodialysis	12 (8%)	3 (3%)	.199
Transplantation	10 (6%)	…	.040
Healthcare-associated infection	93 (59%)	35 (40%)	.006
Type of IE			.51
Native valve IE	98 (62%)	57 (66%)	
Prosthetic valve IE	59 (37%)	30 (34%)	
Pacemaker IE	2 (1%)	…	
Heart valve affected			.73
Aortic alone	73 (46%)	37 (43%)	
Mitral alone	46 (29%)	32 (37%)	
Aortic and mitral	30 (19%)	14 (16%)	
Tricuspid	5 (3%)	2 (2%)	
Aortic, mitral, and tricuspid	3 (2%)	…	
Mitral and tricuspid	1 (1%)	1 (1%)	
Unknown	1 (1%)	1 (1%)	
Vegetation size, mm, median (IQR)	10 (6–15)	10 (7–16)	.50

Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating *Enterococcus faecalis* Infective Endocarditis

Fernandez-Hidalgo, CID 2013

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Duration of antimicrobial treatment, d, median (IQR)			
Overall, in survivors	42 (39–46)	42 (35–44)	.122
Days until surgery	11 (6–22)	9 (3–22)	.34
Adverse events			
Overall	14 (9%)	38 (44%)	<.001
Overall obliging to withdraw treatment	2 (1%)	22 (25%)	<.001
Drug stopped due to rash/fever	1 (0.6%)	0	.46
Drug stopped due to leukopenia	1 (0.6%)	0	.46
Drug stopped due to new renal failure	0	20 (23%)	<.001
Drug stopped due to vestibular toxicity	0	2 (2%)	.055
Failures			
Death during treatment	35 (22%)	18 (21%)	0.81
Death during 3-mo follow-up	13 (8%)	6 (7%)	0.72
Adverse effects requiring treatment withdrawal	2 (1%)	22 (25%)	<0.001
Treatment failure requiring change of antimicrobials	2 (1%)	2 (2%)	0.54
Relapse	3/124 (3%)	3/69[a] (4%)	0.67

ORIGINAL ARTICLE

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. Fosbøl, 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.

400 endocardites du cœur gauche (25% prothèse valvulaire)
Evolution favorable après > 10 j d'antibiothérapie IV et
>7 j après la chirurgie, pas d'abcès paravalvulaire

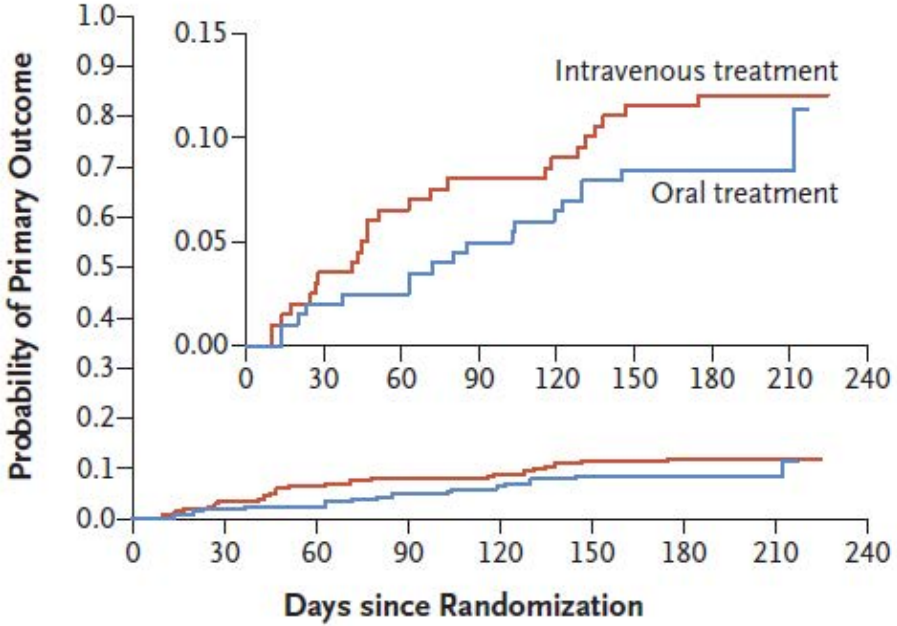
Randomisation traitement oral vs. traitement IV

N Engl J Med 2019;380:415-24.

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

N Engl J Med 2019;380:415-24.

Critère de jugement:
Mortalité
Chir cardiaque non prévue
Embolies
Rechute



No. at Risk

Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Temps médian avant passage voie orale = 17 j

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

N Engl J Med 2019;380:415-24.

Staphylococcus aureus Oral treatment, n= 47	Dicloxacillin + rifampicin (33%) Amoxicillin + rifampicin (29%) Moxifloxacin + rifampicin (7%) Linezolid + rifampicin (7%)
Coagulase negative *staphylococcus* Oral treatment, n= 13	Fusidic acid + Linezolid (38%) Rifampicin + Linezolid (31%) Amoxicillin + Linezolid (8%) Moxiflacin + Linezolid (8%)
Streptococcus Oral treatment, n= 92	Amoxicillin + Rifampicin (12%) Amoxicillin + Moxifloxacin (47%) Rifampicin + Linezolid (9%) Moxifloxacin + Linezolid (9%) Amoxicillin + Linezolid (8%)
Enterococcus Oral treatment, n= 51	Amoxicillin + Moxifloxacin (47%) Amoxicillin + Linezolid (25%) Amoxicillin + Rifampicin (12%) Moxifloxacin + Rifampicin (10%)

QUAND (ET QUI) OPÉRER?

ESC European Society of Cardiology
European Heart Journal (2019) 40, 3222–3233
doi:10.1093/eurheartj/ehz620
FASTTRACK CLINICAL RESEARCH
Valvular heart disease

Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study

European Heart Journal (2019) **40**, 3222–3233

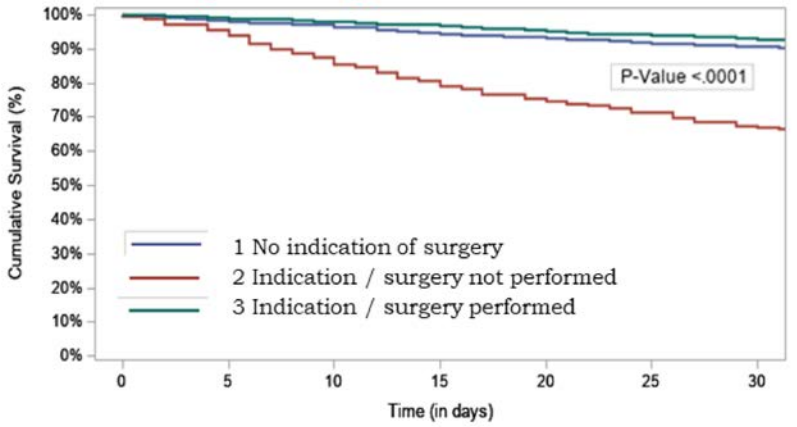
3116 endocardites

Table 4 Multivariable Cox regression analysis for all causes of death at discharge (1-month period)

	Hazard ratio	95% CI	*P*-value*
Charlson index	1.07	[1.04–1.11]	<0.0001
Creatinine >2 mg/dL	1.58	[1.19–2.11]	<0.0017
Congestive heart failure	2.09	[1.58–2.77]	<0.0001
Vegetation length > 10 mm	2.12	[1.64–2.73]	<0.0001
Cerebral complication	2.21	[1.61–3.04]	<0.0001
Abscess	1.50	[1.07–2.10]	0.0186
Indication—surgery not performed	2.84	[2.00–4.03]	<0.001
Indication—surgery performed	0.63	[0.43–0.92]	0.0169

In-hospital mortality in EURO-ENDO

adjusted Kaplan-Meier curves



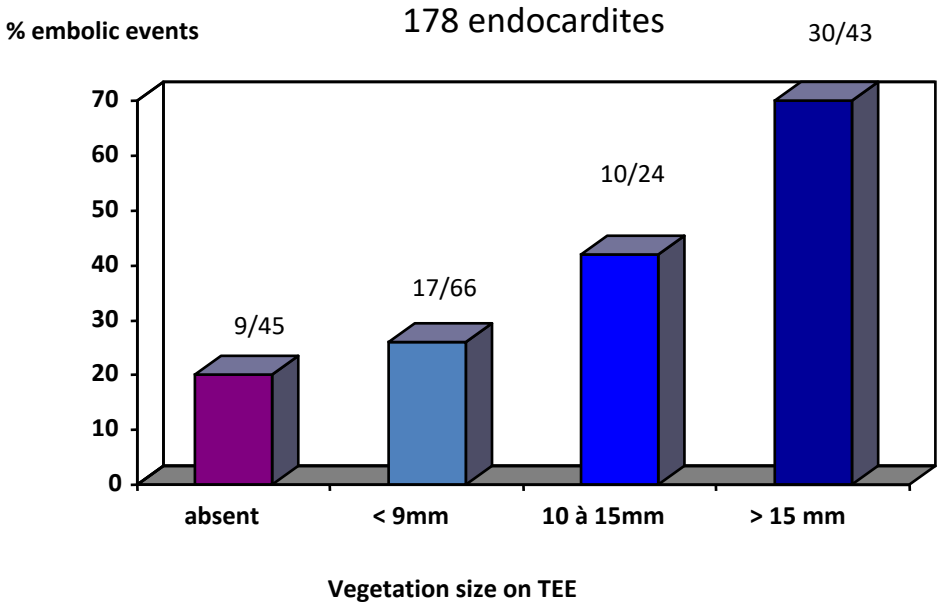
3 types d’indication chirurgicale

- Insuffisance cardiaque liée à une dysfonction valvulaire
- Prévention des embolies
- Infection non contrôlée
  - Extension para-valvulaire (abcès)
  - Echec de l’antibiothérapie ou risque élevé d’échec de l’antibiothérapie

Risque embolique

FDR embolie

- Embolie préalable
- Taille de la végétation
- *Staphylococcus aureus*
- Timing antibiothérapie



Di Salvo, JACC 2001

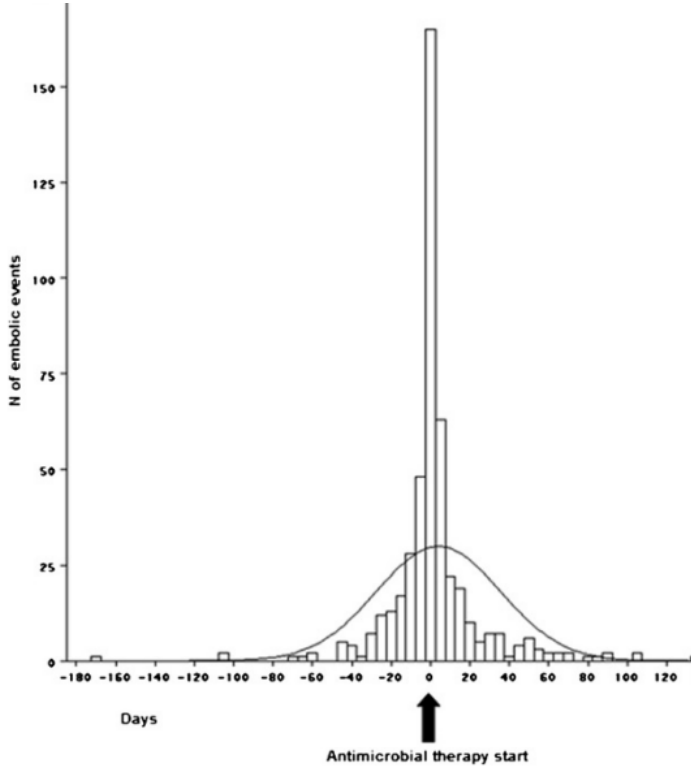
Risque embolique

- FDR embolie:
  - Embolie préalable
  - Taille de la végétation
  - *Staphylococcus aureus*
  - Timing antibiothérapie

Left-sided IE: multivariate analysis of factors associated with embolism

Variable	Odds ratio	95% CI	*p*
Age	1.0	1.0 – 1.0	NS
Mitral vs aortic valve	0.8	0.6 – 1.1	NS
Prosthetic vs native valve	1.5	1.0 – 2.2	NS
Size of vegetation ≥ 13 mm	**2.1**	**1.5 – 2.8**	**0.0001**
Staphylococcus aureus	**2.1**	**1.5 – 3.1**	**0.0001**
Enterococcus species	0.8	0.5 – 1.3	NS
Anticoagulant therapy	1.5	0.9 – 2.3	NS

N = 1306 episodes of left-sided IE.



Rizzi *et al. BMC Infectious Diseases* 2014, **14**:230

Timing de la chirurgie

Indication chirurgicale	Urgence vitale: Dans les 24 hrs	Indication urgente: Dans les 3–5 jours	Non urgent: pendant la même hospitalisation
Hémodynamique	Choc cardiogénique, fuite aortique massive, fistule	Insuffisance cardiaque	Fuite valvulaire sévère sans insuffisance cardiaque
Embolique		Prévention des embolies (végétation ≥10 mm et embolie préalable)	
Infectieuse		Abcès, faux anévrisme	

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

- Patients en Corée du sud avec endocardite du cœur gauche (âge médian 48 ans, *Streptococcus* 60% des cas)
  - Taille de végétation > 10 mm et fuite significative (sans insuffisance cardiaque)
- Randomisation chirurgie rapide (< 48 h) versus traitement conventionnel (avec chirurgie dans 77% des cas)
- Critère de jugement primaire: décès/ évènements emboliques / rechute de l'infection / hospitalisation pour insuffisance cardiaque

Kang, NEJM 2012

The NEW ENGLAND JOURNAL of MEDICINE

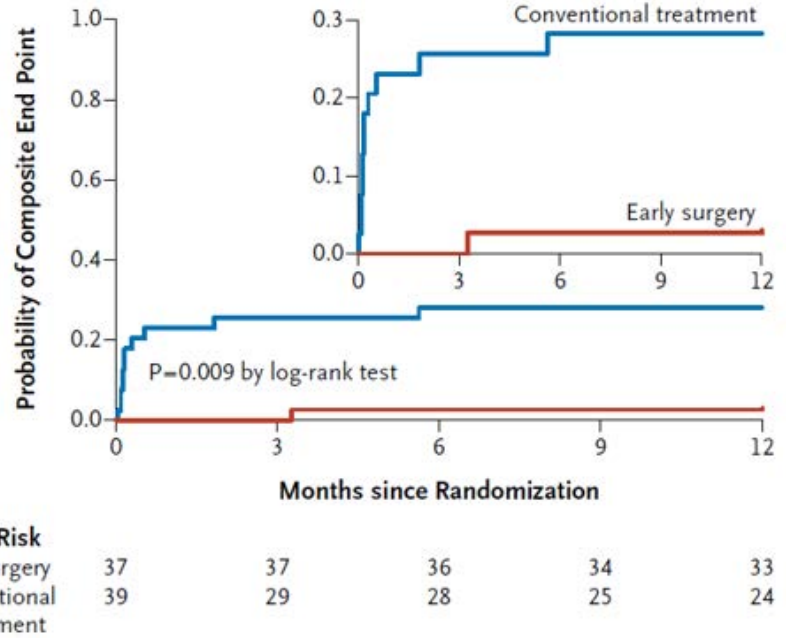
ORIGINAL ARTICLE

Early Surgery versus Conventional Treatment for Infective Endocarditis

Kang, NEJM 2012

Table 3. Clinical End Points.

Outcome	Conventional Treatment (N=39)	Early Surgery (N=37)	P Value
Primary end point — no. (%)			
In-hospital death or embolic event at 6 wk	9 (23)	1 (3)	0.01
In-hospital death	1 (3)	1 (3)	1.00
Embolic event at 6 wk			
Any	8 (21)	0	0.005
Cerebral	5 (13)	0	
Coronary	1 (3)	0	
Popliteal	1 (3)	0	
Splenic	1 (3)	0	

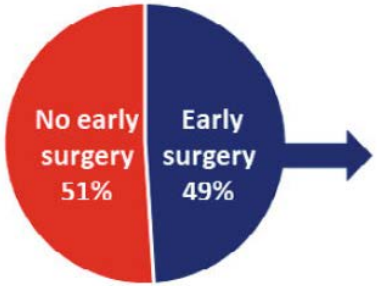


ESC
European Society of Cardiology

Characteristics, management, and outcomes of patients with left-sided infective endocarditis complicated by heart failure: a substudy of the ESC-EORP EURO-ENDO (European infective endocarditis) registry

Bohbot, European Journal of Heart Failure 2022

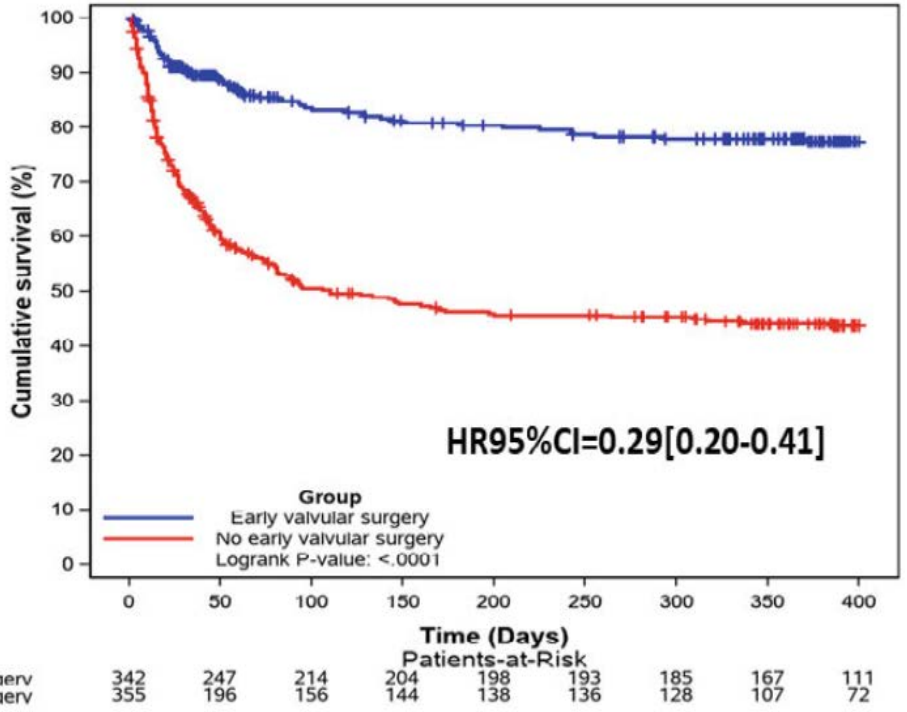
698 patients with left-sided IE and CHF



- Younger
- Less comorbidities
- More severe valvular damage:

↑ *Vegetation size*
↑ *Severe regurgitations*
↑ *Perivalvular complications*

- Less uncontrolled infection



En réanimation, on a souvent une indication et une contre-indication en même temps…

- Principales raisons d'admission en réanimation:
  - complications neurologiques
  - insuffisance cardiaque, choc cardiogénique
  - choc septique

Neurological Complications of Infective Endocarditis

Risk Factors, Outcome, and Impact of Cardiac Surgery: A Multicenter Observational Study

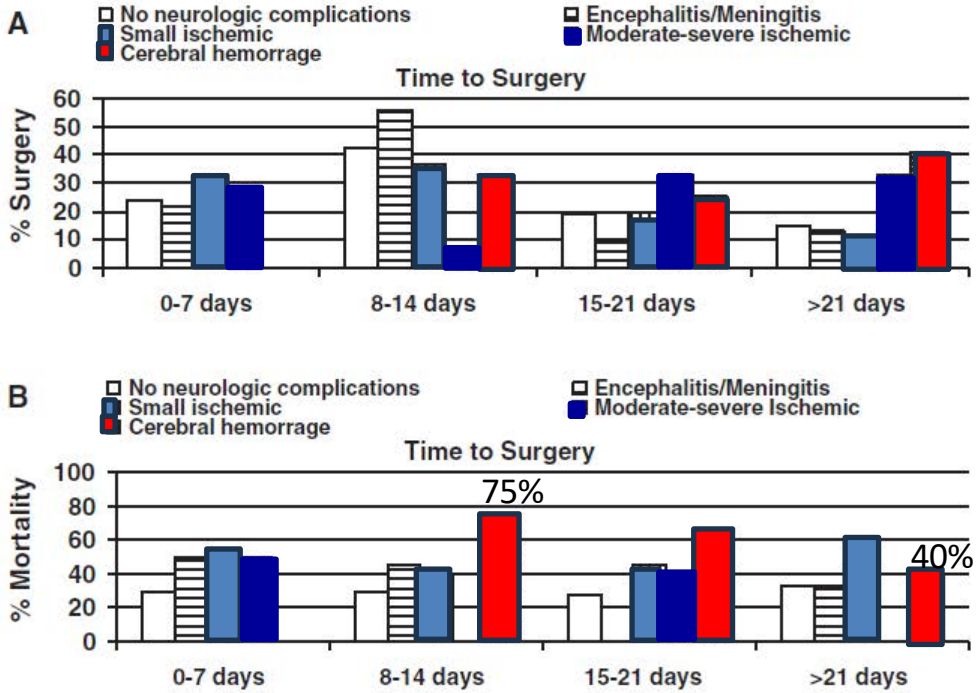


Figure 2. A, Percentage of patients undergoing cardiac surgery and timing of the procedure by type of neurological complication. **B**, Percentage of patients with each neurological complication who had a fatal outcome after cardiac surgery according to the time to surgery (only patients who had operations are included).

Small ischemic complication: transient ischemic attack or minor infarction (embolism affecting <30% of 1 brain lobe)

Moderate-severe ischemic complication: multiple cerebral embolisms or a single embolism affecting ≥30% of a brain lobe

Garcia-Cabrera, Circulation 2013

Neurological Complications of Infective Endocarditis

Risk Factors, Outcome, and Impact of Cardiac Surgery: A Multicenter Observational Study

Mortalité en cas de complication neurologique: 45% vs 24%

Bien que la chirurgie puisse aggraver les lésions neurologiques, le risque de saignement intracrânien après chirurgie apparait faible en cas de :

- AVC ischémiques de petite taille lorsque la chirurgie a lieu immédiatement
- AVC ischémique modérés à sévères lorsque la chirurgie est effectuée après 2 semaines

Chez les patients ayant une hémorragie intracrânienne, il est préférable d'attendre ≥4 semaines

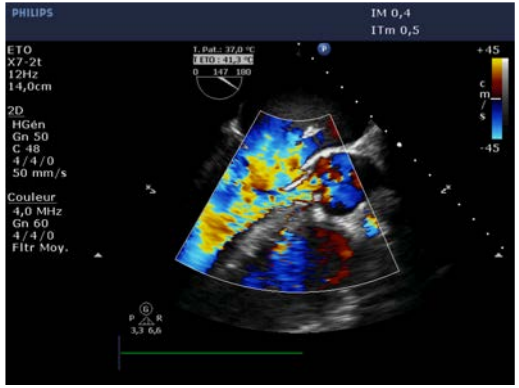
Garcia-Cabrera, Circulation 2013

Timing de la chirurgie et risque opératoire

Indication chirurgicale	Urgence vitale: Dans les 24 hrs	Indication d'urgence: Dans les 3–5 jours	Non urgent: pendant la même hospitalisation
Hémodynamique	Choc cardiogénique, fuite aortique massive, fistule	Insuffisance cardiaque	Fuite valvulaire sévère sans insuffisance cardiaque
Embolique		Prévention des embolies	
Infectieuse		Abcès, faux anévrisme	

Risque chirurgical	Contre-indication absolue	Contre-indication relative	Pas de contre-indication
Complications neurologiques	Hémorragie intra crânienne	AVC ischémique large (>30% d'un lobe)	AVC ischémique non sévère sans trouble de la vigilance
Comorbidités, âge	Altération sévère de l'état général	Chirurgie tridux	
Sévérité	Défaillance multi-viscérale Choc septique		

Chirurgie de l’endocardite



Urgence vitale

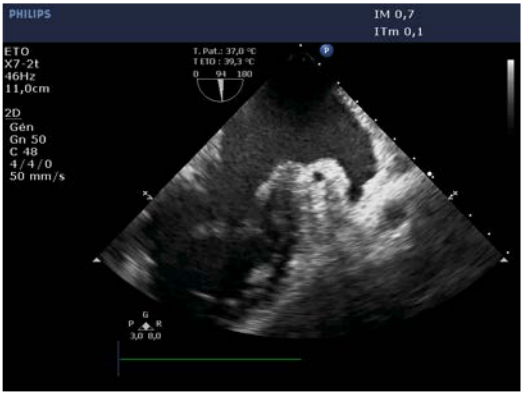
Choc cardiogénique
Fuite aortique massive

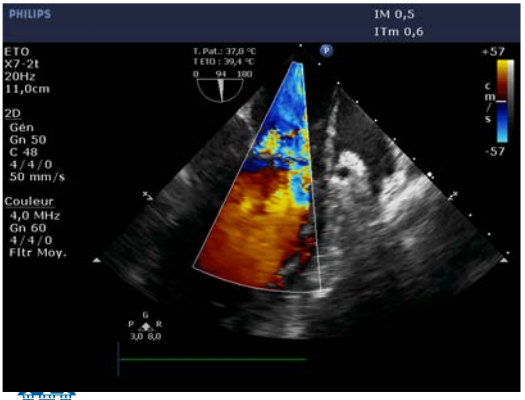
Contre-indication absolue

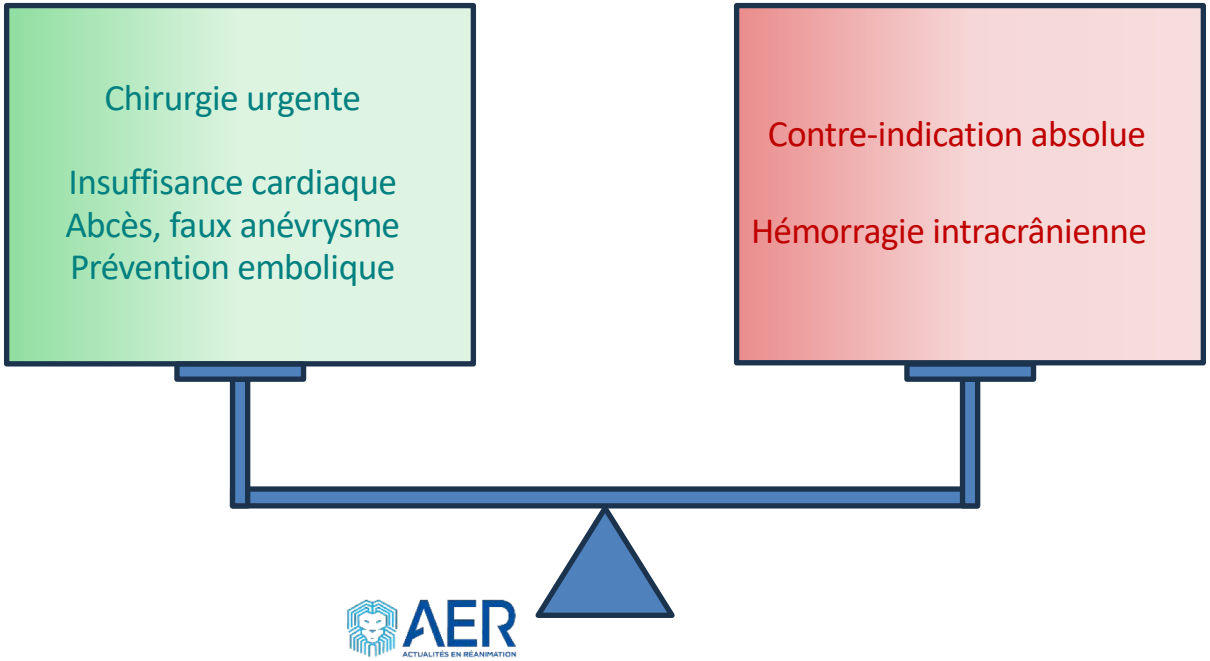
Hémorragie intra-cranienne

AER
ACTUALITÉS EN RÉANIMATION

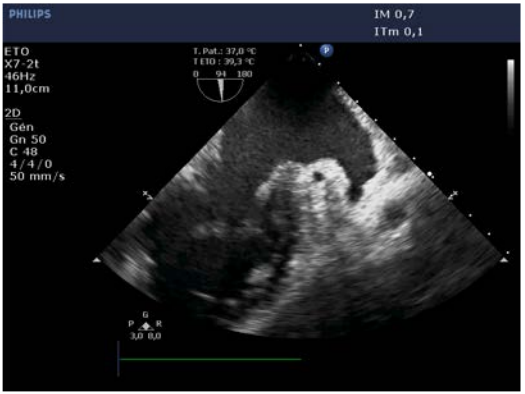
Attente et ré-évaluation régulière du rapport bénéfice-risque

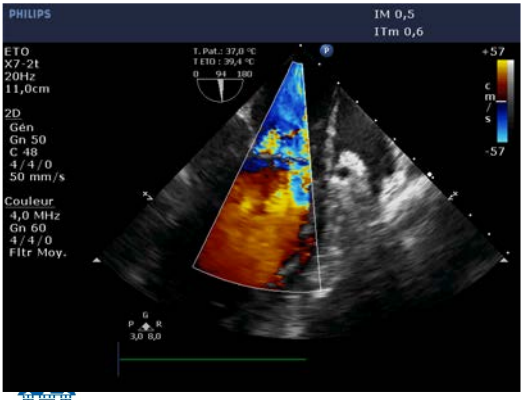


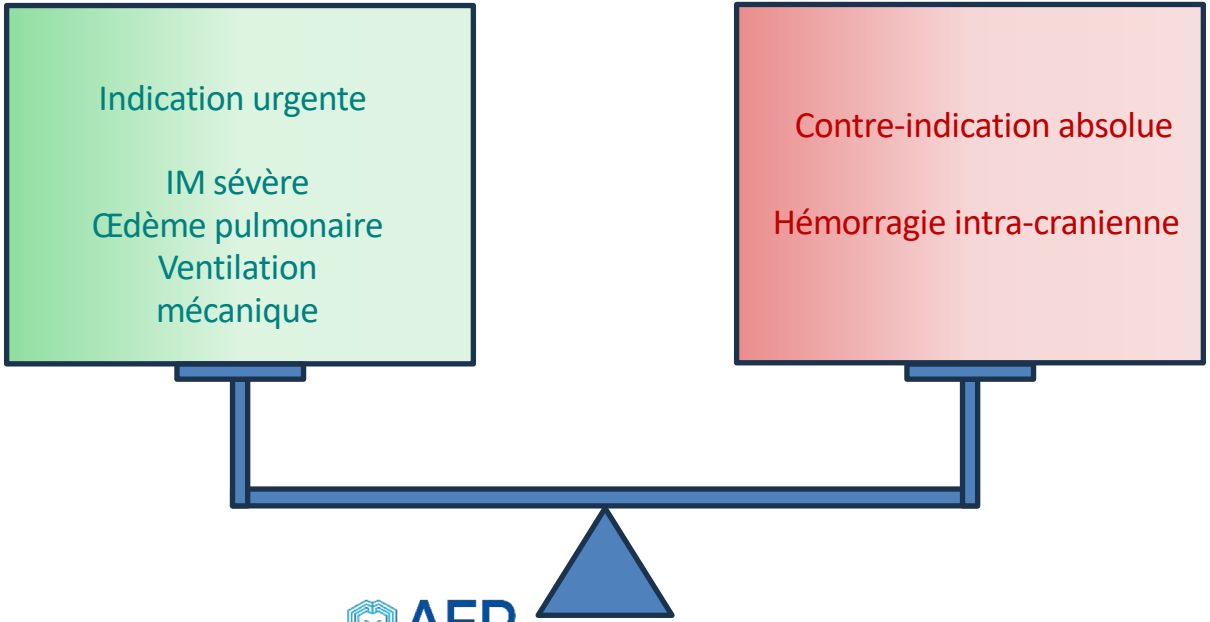




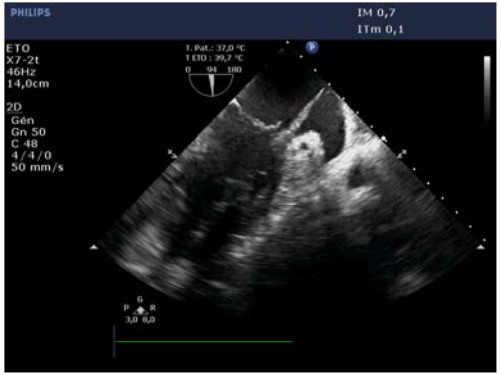
Attente et ré-évaluation régulière du rapport bénéfice-risque







Chirurgie de l’endocardite

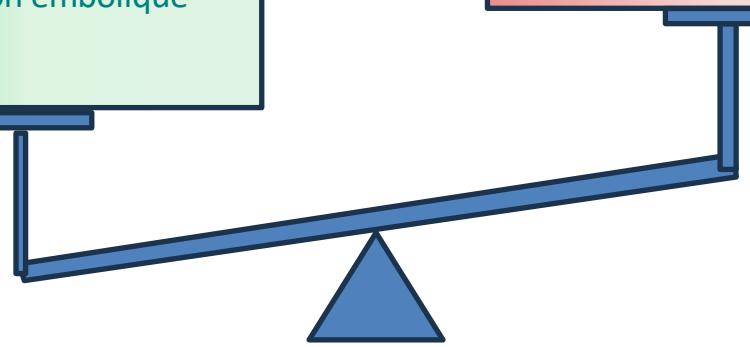


Chirurgie urgente

Insuffisance cardiaque
Abcès, faux anévrysme
Prévention embolique

Contre-indication relative

AVC ischémique large



AER
ACTUALITÉS EN RÉANIMATION

Conclusion: endocardite en réanimation

- Pas si rare que ça, de plus en plus d'endocardites liées aux soins
- Bactériémie à Staphylocoque, Streptocoque ou Entérocoque: penser à l'endocardite
- Principales raisons d'admission en réanimation:
  - complications neurologiques
  - insuffisance cardiaque, choc cardiogénique
  - choc septique
- Le traitement antibiotique est bien codifié. Relais oral pour quelques patients
- Chirurgie rapide si pas de contre-indication
- L'indication chirurgicale et son timing sont parfois difficiles, nécessitant une discussion multidisciplinaire

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