Cardiopathies acquises

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Plan du cours

- Maladie de Kawasaki
- Endocardite infectieuse
- Myocardite

Maladie de Kawasaki

Kawasaki – Les points clés

- **Vascularite systémique** qui touche essentiellement **les artères de moyen calibre** avec un tropisme électif pour **les artères coronaires** (gravité de la maladie)

- Les complications coronaires surviennent dans **15 à 25 %** des cas chez les enfants non traités

- L'administration précoce d'immunoglobulines humaines par voie intraveineuse a transformé le pronostic **en diminuant par 5** le risque d'anévrisme coronaire

- **Effet souvent spectaculaire sur la fièvre et l'altération de l'état général.**

Epidémiologie

- **Première cause de cardiopathie acquise de l'enfant dans les pays développés**
- **Tous les âges pédiatriques (80 % des cas avant 5 ans)**
- Tranche d'âge la plus touchée est entre 6 mois et 5 ans
- Les patients de **moins de 1 an** ou **de plus de 8 ans** sont rares mais ont un risque plus élevé d'anévrisme coronaire
- Incidence de la maladie augmente globalement dans le monde
- **Elle atteint chaque année:**
  - 265/100.00 enfants < 5 ans au Japon
  - 19/100.000 enfants < 5 ans aux USA.
  - extrapolation française: 600 nouveaux cas par an en France

Newburger JACC 2016

Etiologie inconnue…

Bactéries?

- Streptocoque pyogène, staphylocoque doré, mycoplasme, chlamydiae
- **Super antigène évoqué?**
- **Antigène classique?**

Virus?

Adénovirus, EBV, parvovirus, HSV, para-influenzae, VIH, rougeole, varicelle, Bocavirus

Prédisposition génétique?

Hypothèse: interaction prédisposition génétique-exposition à un agent environnemental

Burgner D . Int J Infect Dis 2005
Leung DY et al., J pediatr 2002.
Rowley AH. Curr Opin Pediatr 2007.

Caractéristiques cliniques: critères majeurs

La fièvre de plus de 5 jours et au moins 4 critères suivants

- La **conjonctivite** bulbaire non purulente

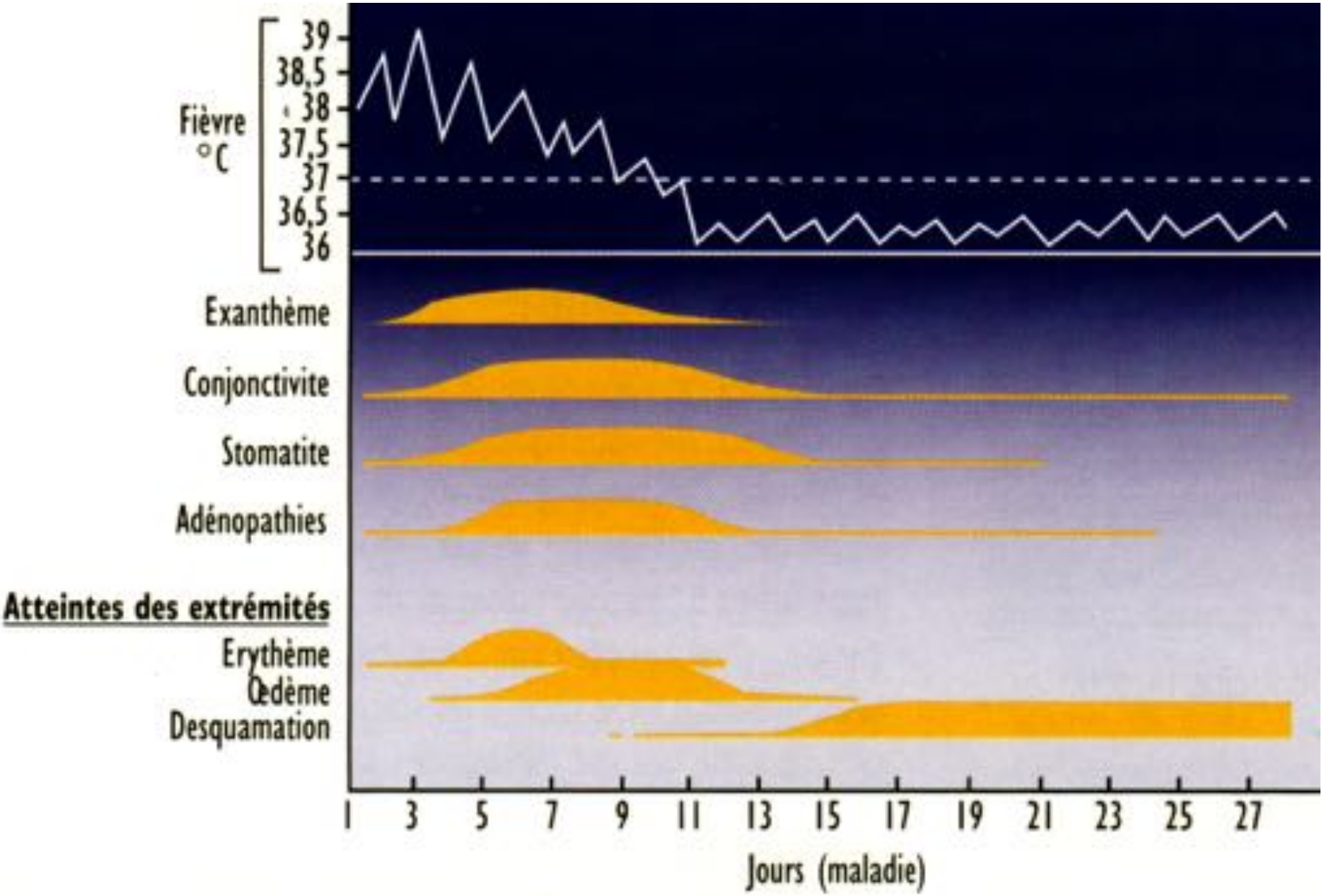
- **L'atteinte muqueuse** : la pharyngite, la chéilite, la langue framboisée, la stomatite

- **L'exanthème polymorphe du tronc**

- **L'atteinte des extrémités** : un érythème des paumes des mains et/ou des plantes des pieds, l'œdème palmo-plantaire, la desquamation palmo-plantaire secondaire

- **L'atteinte unilatérale des ganglions cervicaux**, de plus de 1.5 cm de diamètre

Critères majeurs définis par l'American Heart Association Committee On Rheumatic Fever, Endocarditis, and Kawasaki Disease


Fièvre °C
39
38,5
38
37,5
37
36,5
36
Exanthème
Conjonctivite
Stomatite
Adénopathies
Atteintes des extrémités
Erythème
Œdème
Desquamation
1
3
5
7
9
11
13
15
17
19
21
23
25
27
Jours (maladie)

Faciès typique d'un enfant avec une maladie de Kawasaki

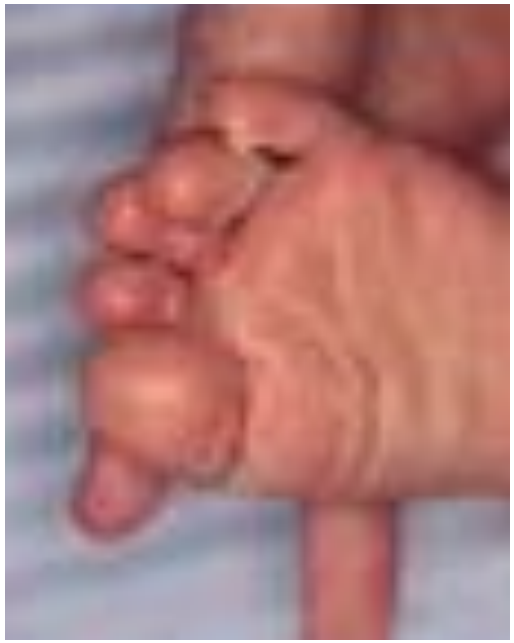
Conjonctivite bilatérale non purulente

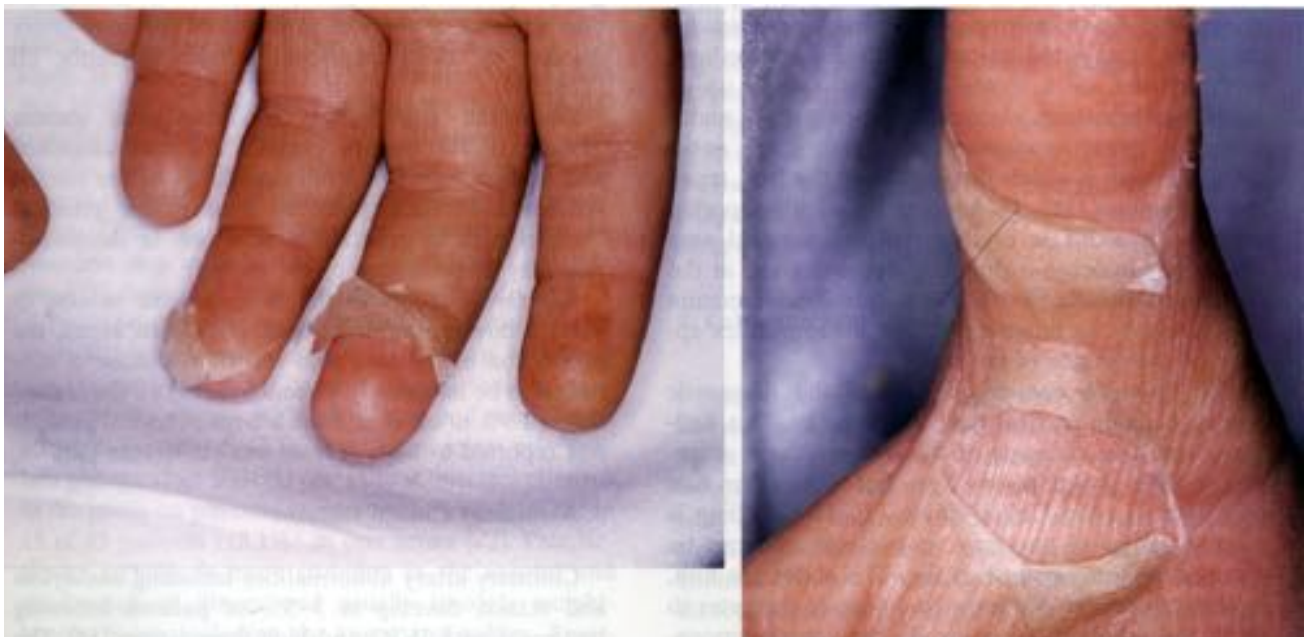
Atteinte muqueuse

Atteinte muqueuse

Atteinte des extrémités

Desquamation palmo-plantaire typique





Forme psoriasiforme

Inflammation sur cicatrice de BCG

Caractéristiques biologiques

- **Elévation de la CRP et du fibrinogène**
- Elévation de la vitesse de sédimentation (VS)

- **Hyperleucocytose** (PNN et formes immatures)
- Anémie, **thrombocytose**

- Hypo-albuminémie, hyponatrémie, augmentation des transaminase et δGT

- **Pyurie aseptique**, protéinurie, hématurie

- Hyperleucocytose du liquide synovial

- **Méningite lymphocytaire aseptique**

Diagnostic différentiel

Origine virale : Adénovirus, entérovirus, EBV, rougeole

Autres :

- -Scarlatine
- -Syndrome d'épidermolyse staphylococcique
- -Syndrome du choc toxique
- -Adénopathie bactérienne
- -Hypersensibilité aux médicaments
- -Syndrome de Steven-Johnson
- -Polyarthrite juvénile
- -Leptospirose

Bilan initial si suspicion de Kawasaki

1°) **Sanguin**
NFS, VS, fibrinogène
ionogramme avec albuminémie, transaminases, GGT, bilirubine
CRP

2°) **Bandelette urinaire +/- ECBU**

3°) **ECG**

4°) **Echographie cardiaque**

5°) **+/- Echographie abdominale**

6°) **+/-Echodoppler des vaisseaux** du cou et des artères mésentériques

7°) **Strepto-test**, sérologies virales pour éliminer
un diagnostic différentiel

Formes atypiques

Tableau clinique dominé par un symptôme inhabituel:

convulsions, œdème pulmonaire, diarrhée sanglante, ascite, obstruction des voies aériennes supérieures, épiglottite, adénopathies cervicales compressives ou hémolyse et défaillance multi-viscérale, syndrome néphrotique, hyponatrémie….

Formes de l'adulte

- première fois décrite en 1977
- symptômes majeurs décrits identiques
- Troubles digestifs, atteinte hépatique, signes articulaires et encéphalites sont plus fréquent

Les formes incomplètes

Ce concept a émergé au cours des dernières années:

Chez les patients ayant eu une fièvre depuis **au moins 5 jours** et au **moins deux critères cliniques de Kawasaki**, sans cause évidente, et des critères biologiques en faveur d'une inflammation systémique

Différent de la « forme atypique »

Manque **un** ou **plusieurs des cinq critères** diagnostiques majeurs

Plus fréquentes chez les enfants les plus jeunes, à risque d'anomalies coronaires

➡ Diagramme décisionnel proposé par l'American Academy of Paediatrics pour aider à la prescription d'IgG dans les formes incomplètes

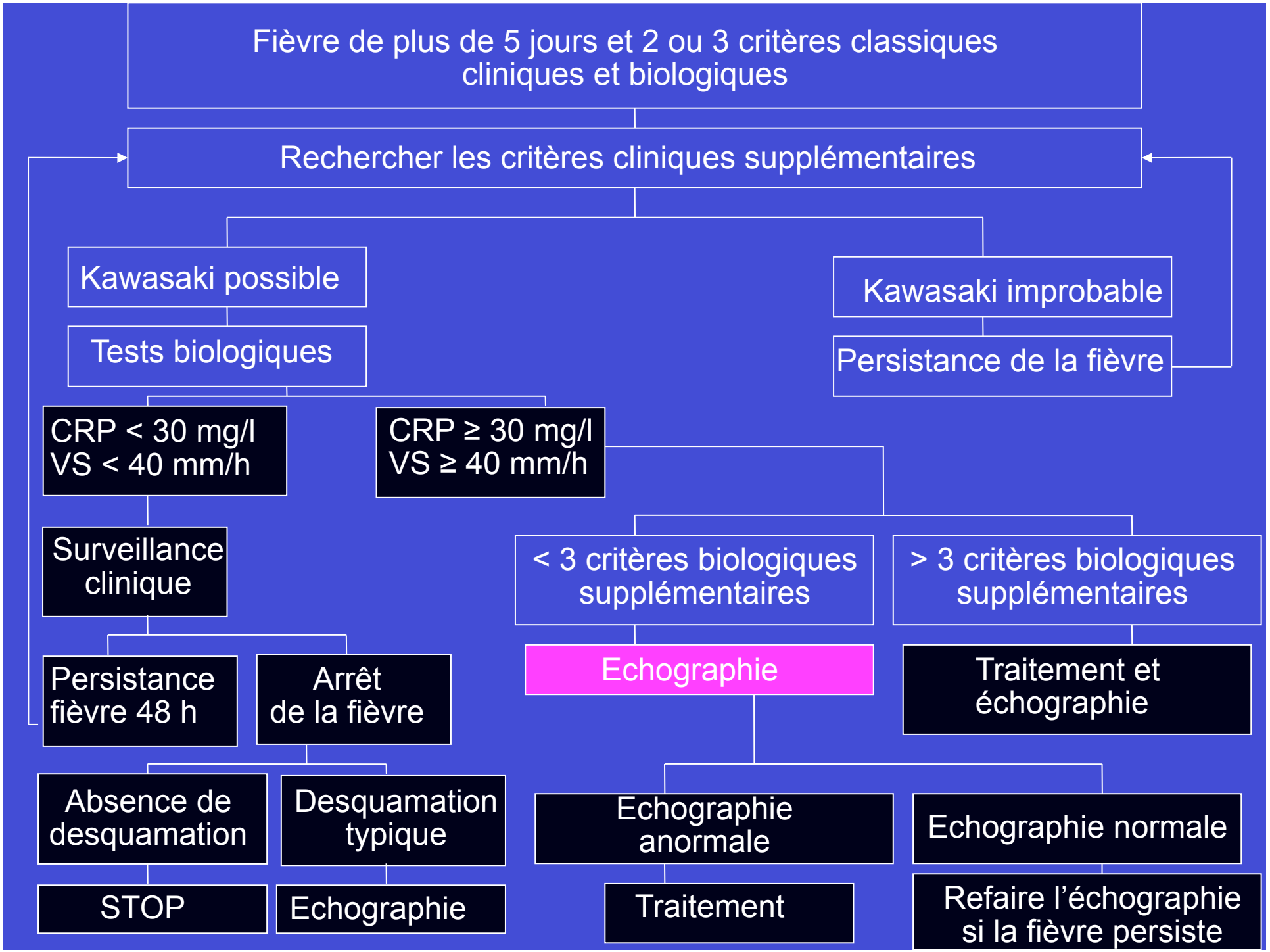
Newburger JW et al., Circulation. 2004

Critères cliniques et biologiques supplémentaires

Cardiovasculaires : dilatation des artères coronaires, anévrismes coronaires, infarctus, myocardite avec possible insuffisance cardiaque congestive, péricardite, épanchement péricardique, fuites valvulaires, troubles conductifs et troubles du rythme, anévrismes des vaisseaux du cou, des artères rénales, spléniques, hépatiques, pancréatiques, génitales, gangrènes distales et pseudo-Raynaud
Digestifs : diarrhées, vomissements, douleurs abdominales, hydrocholécyste, dysfonction hépatique
Respiratoires : toux et rhinorrhée
Neuro-méningés : troubles de la conscience avec irritabilité, apathie, état grognon, hypoacousie
Articulaires : arthrite, arthralgies
Autres : uvéite, érythème au niveau de la cicatrice de BCG, desquamation de l'aine

Albumine < ou égal 3g/dl
Anémie pour l'âge
Plaquettes ≥ à 450 000/ mm^3 à J7
Globules blancs ≥ à 15 000 / mm^3
ECBU ≥ à 10 globules blancs/ champ

D'après Newburger JW et al., Circulation. 2004


Fièvre de plus de 5 jours et 2 ou 3 critères classiques cliniques et biologiques
Rechercher les critères cliniques supplémentaires
Kawasaki possible
Tests biologiques
Kawasaki improbable
Persistance de la fièvre
CRP < 30 mg/l
VS < 40 mm/h
CRP ≥ 30 mg/l
VS ≥ 40 mm/h
Surveillance clinique
< 3 critères biologiques supplémentaires
> 3 critères biologiques supplémentaires
Persistance fièvre 48 h
Arrêt de la fièvre
Echographie
Traitement et échographie
Absence de desquamation
Desquamation typique
Echographie anormale
Echographie normale
STOP
Echographie
Traitement
Refaire l'échographie si la fièvre persiste

Echographie cardiaque

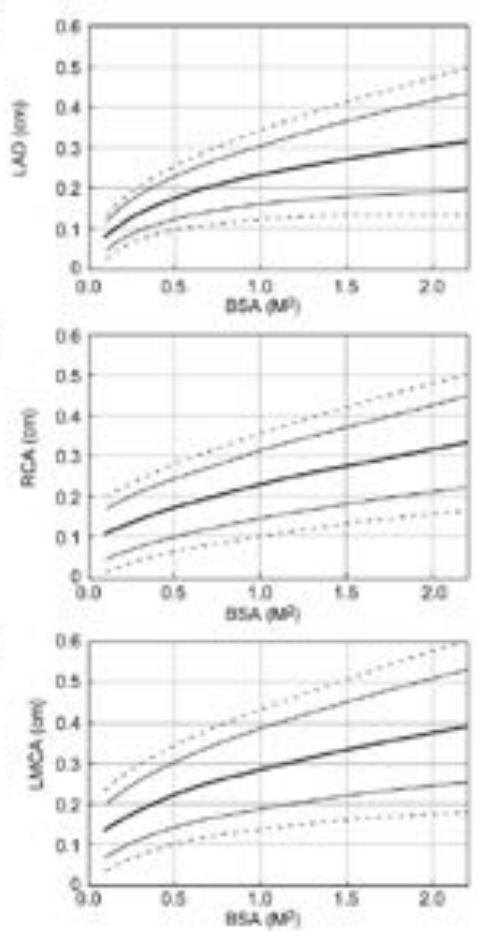
Echographie anormale

Z score de l'IVA ou CD ≥ à 2.5
et/ou anévrysmes coronaires

et/ou ≥ à 3 critères:
hyperéchogénicité coronaire
dysfonction ventriculaire gauche
insuffisance mitrale
péricardite ou
Z score de l'IVA ou de la CD à 2-2.5.

D'après Newburger JW et al., Circulation. 2004

Taille normale des artères coronaires et valeurs de 2 et 3 DS



LAD = CG= coronaire gauche
RCA = CD= coronaire droite
LMCA = IVA = interventriculaire antérieure
BSA =surface corporelle en mètre carré

Complications cardiovasculaires

- **ECG et échographie hebdomadaire**
  - Dilatation des artères coronaires
  - Anévrismes coronaires
  - Infarctus
  - Myocardite avec possible insuffisance ventriculaire gauche sévère
  - Péricardite, épanchement péricardique
  - Fuites valvulaires par inflammation des valves cardiaques et particulièrement la valve mitrale (1 %)
  - Troubles conductifs et troubles du rythme par inflammation du tissu de conduction

Les anévrismes coronaires

- **Entre le 10ème et le 25ème jour d'évolution**
- 5 % lorsque le traitement est fait précocement = < 10 jours du début des symptomes
- Souvent multiples et siègent habituellement dans la partie proximale des artères coronaires

- Pronostic cardiaque dépend essentiellement de leur taille.

Selon les guideslines américains

Petite dilatation coronaire	Z score > 2,5 <5
Dilatation coronaire moyenne	Z score 5-10
Large dilatation coronaire	Z score > 10 ou > 8 mm

Newburger JACC 2016

Selon le ministère de la santé Japonaise

Anévrysmes de petite taille **< 4 mm**

Anévrysmes de taille moyenne entre **4 à 8 mm**

Anévrysme géant **> 8 mm**

Facteurs prédictifs de développement des anévrysmes

- Age inférieur à **1 an** et supérieur à **8 ans**
- **Sexe masculin**
- Fièvre et une éruption prolongées
- Persistance de la fièvre après les immunoglobulines nécessitant une **deuxième dose**
- Intensité et persistance du syndrome inflammatoire, de la thrombocytose, de l'anémie, de l'hyperleucocytose et de l'élévation de la CRP
- Persistance d'une albuminémie basse

Facteurs prédictifs de régression des anévrysmes

- Petite taille
- Âge < à un an
- Morphologie fusiforme plutôt que saculaire
- Localisation distale

Evolution naturelle

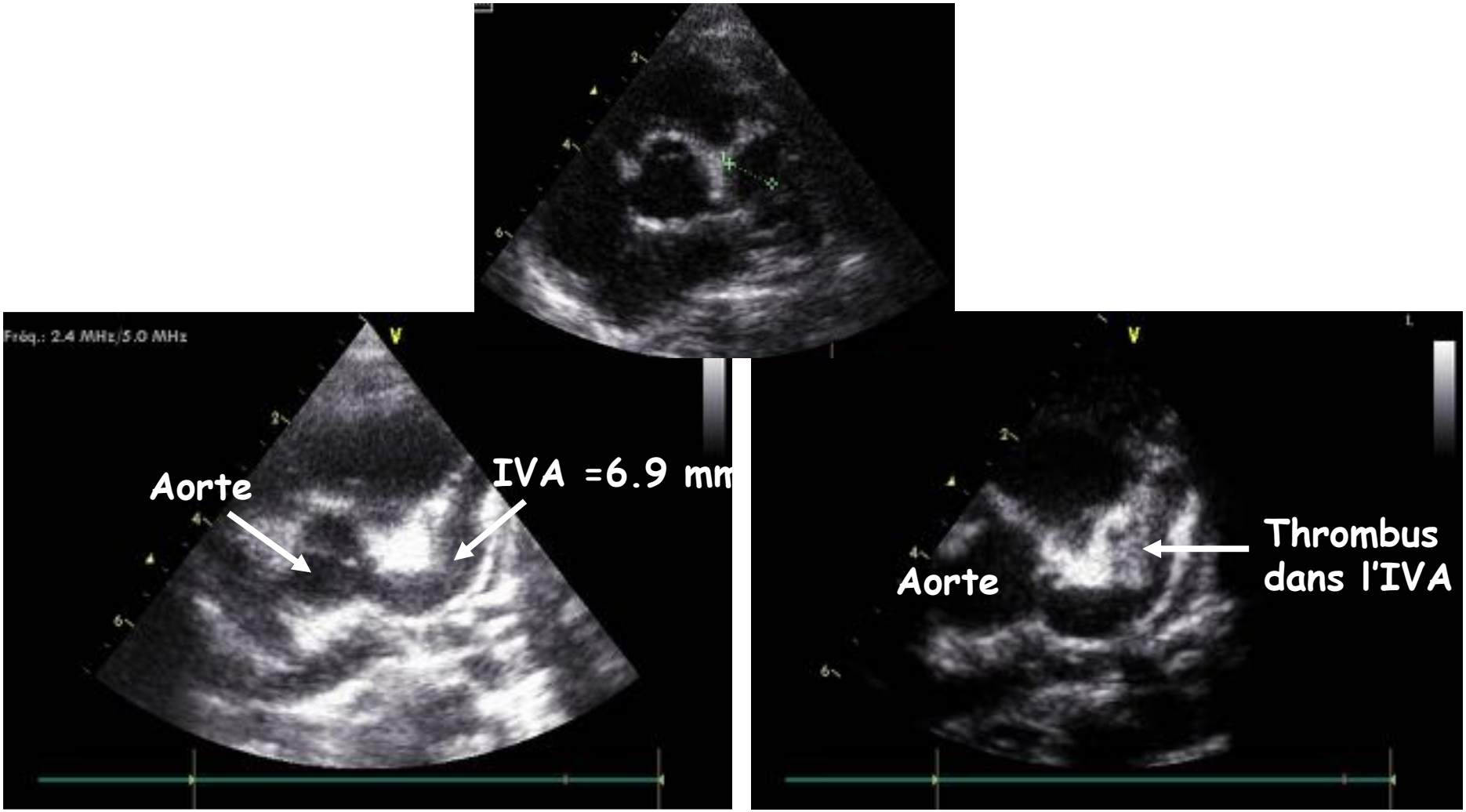
1°) La phase aiguë (J0-J10) : **atteinte cardiaque rare**

2°) La phase subaiguë (J10-J20) : **diagnostic de complication coronaire**

3°) La phase de convalescence (J20-J70) : **constatation d'anévrysmes et de sténoses cicatricielles** en cas de complication coronaire à la deuxième phase

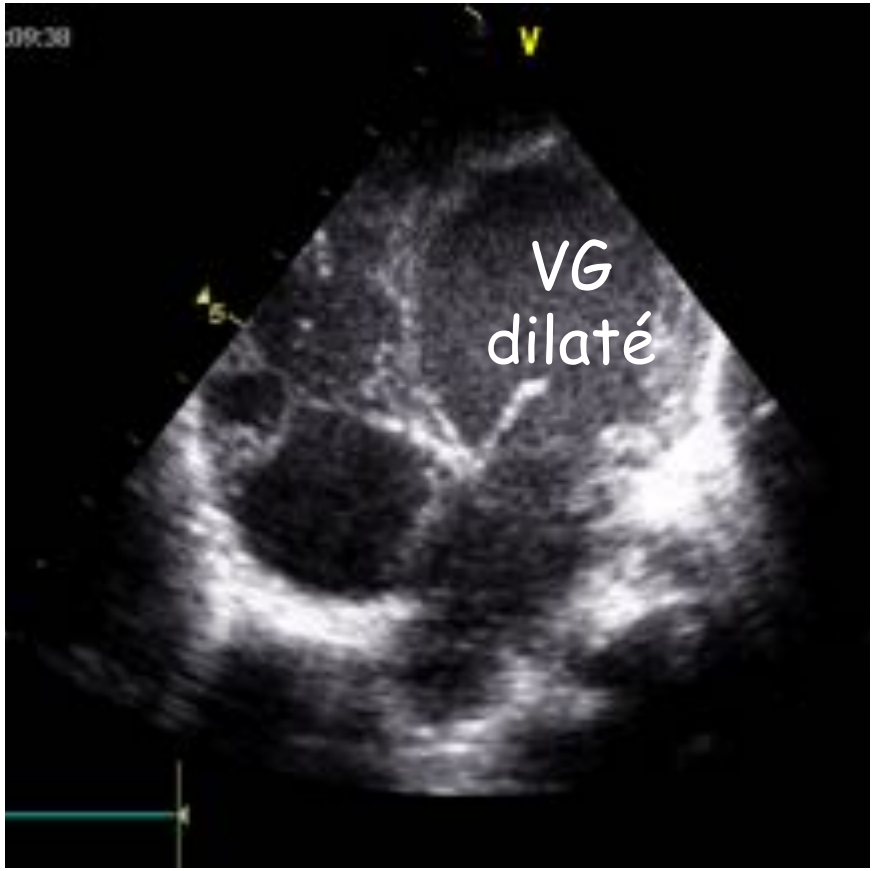
Exemples d'atteinte coronaires

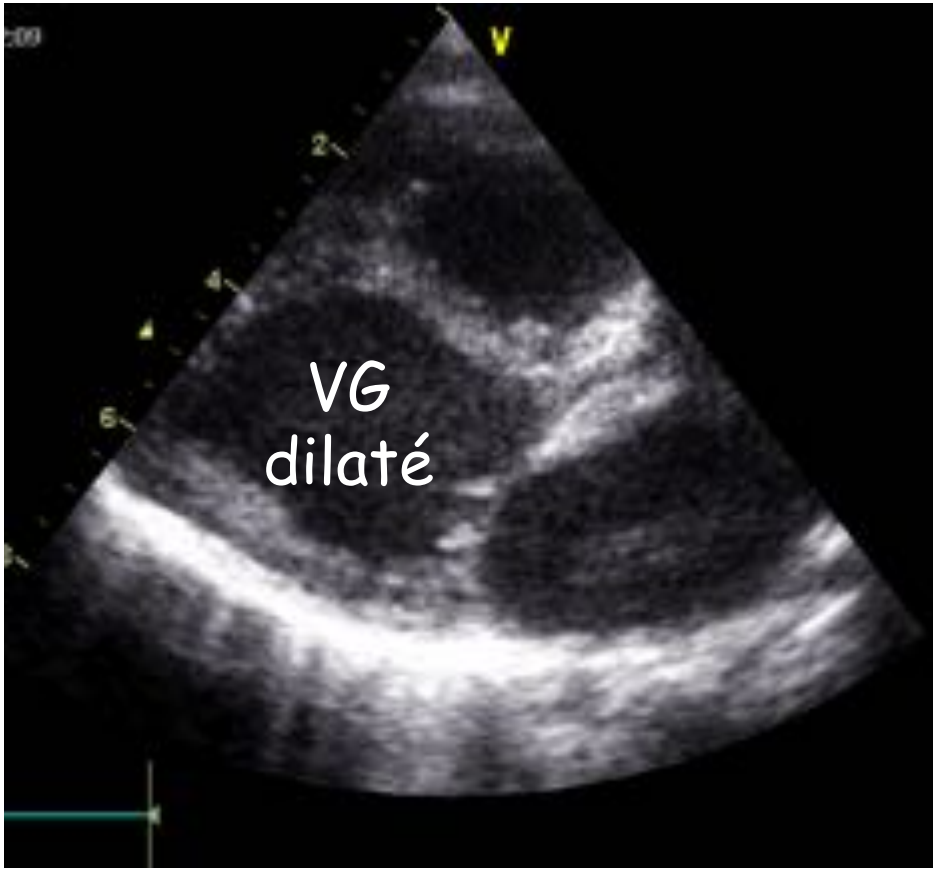
Dilatation anévrysmale des artères coronaires



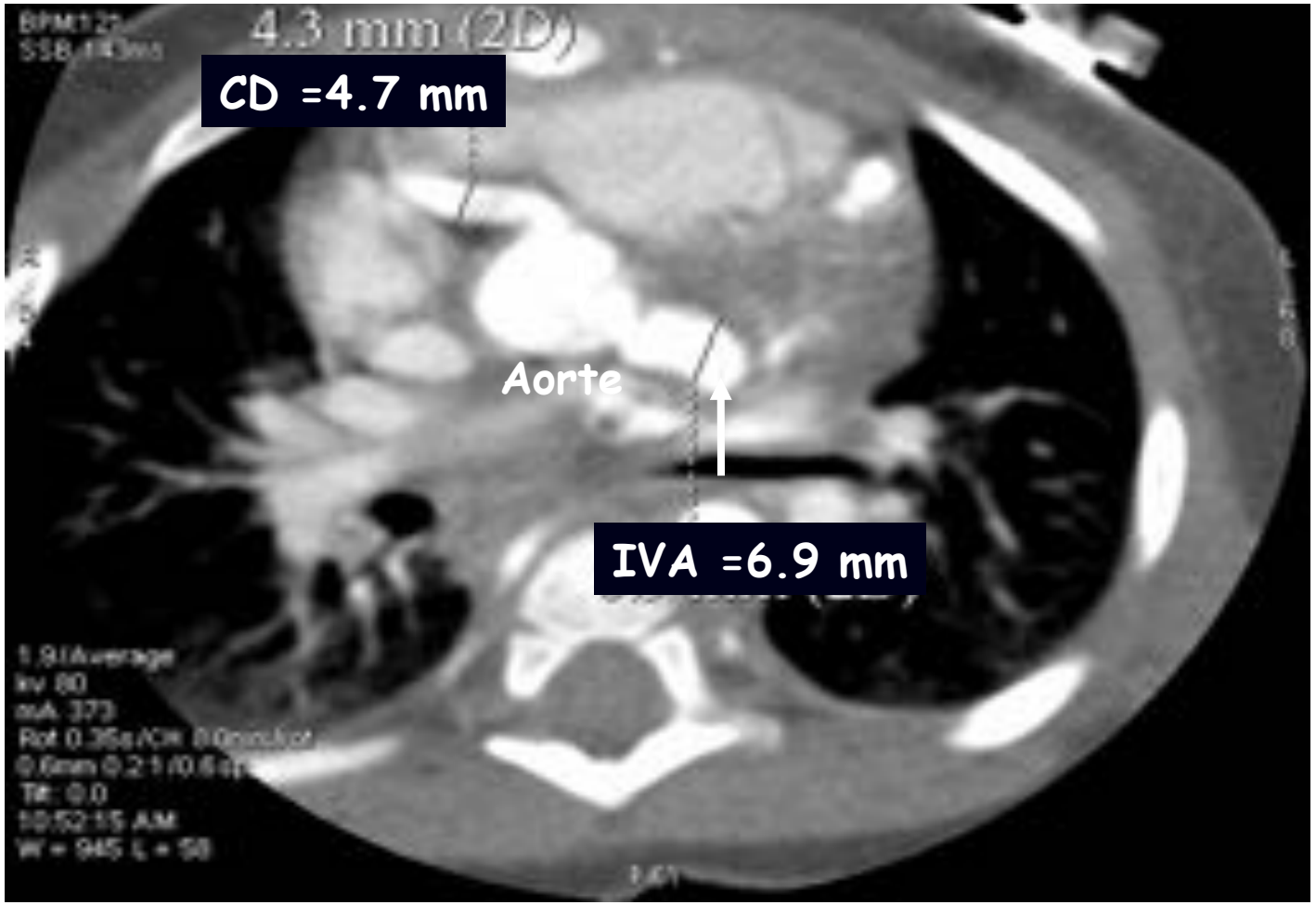
(A) IVA=interventriculaire antérieure
(B) thrombus dans l'IVA

Dysfonction ventriculaire gauche sévère en échographie

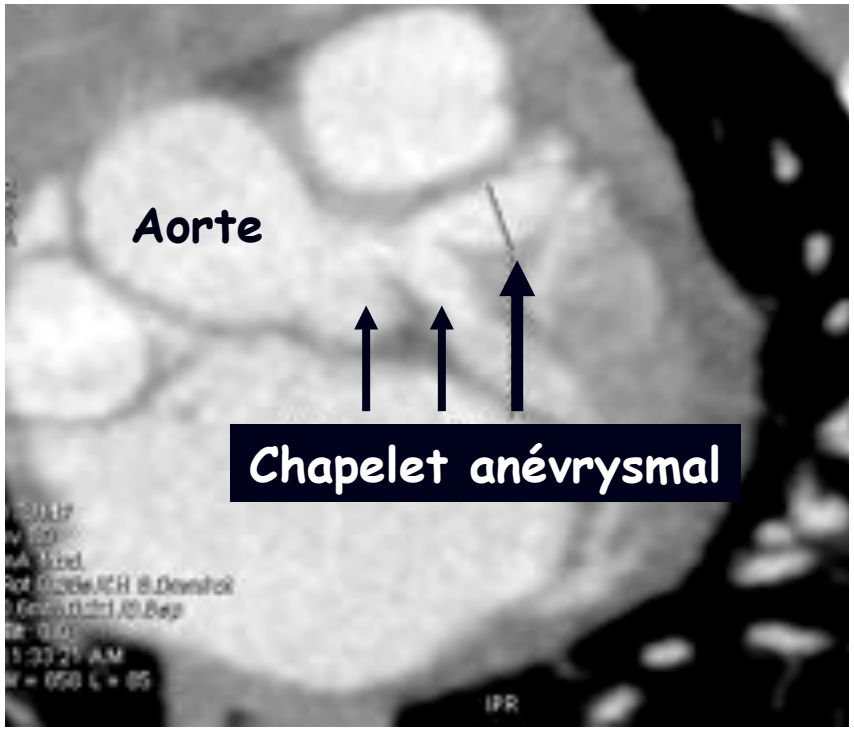


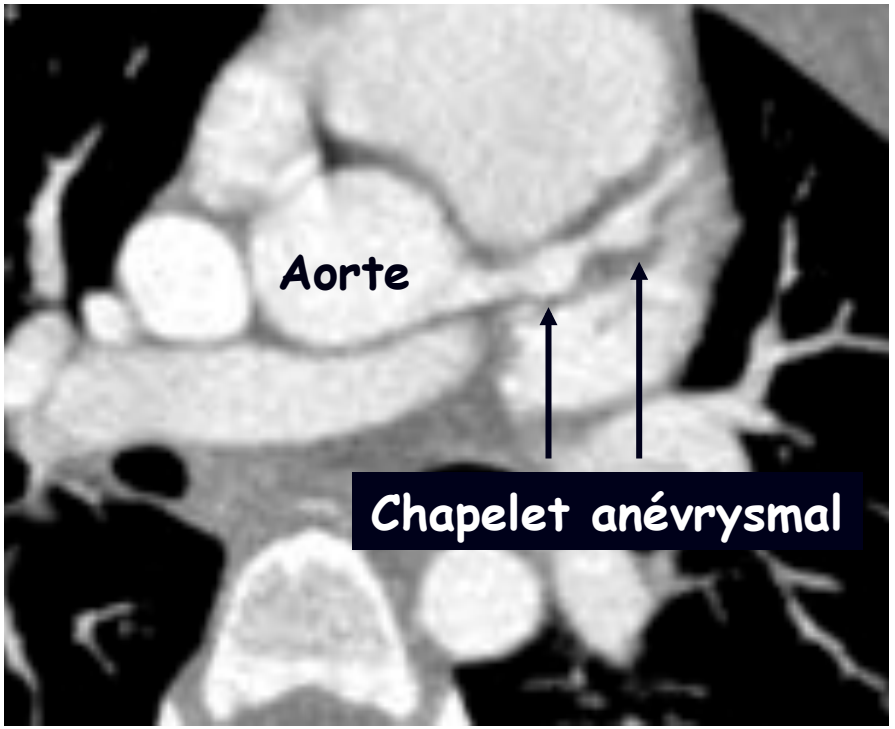


Dilatation anévrysmale des artères coronaires au scanner

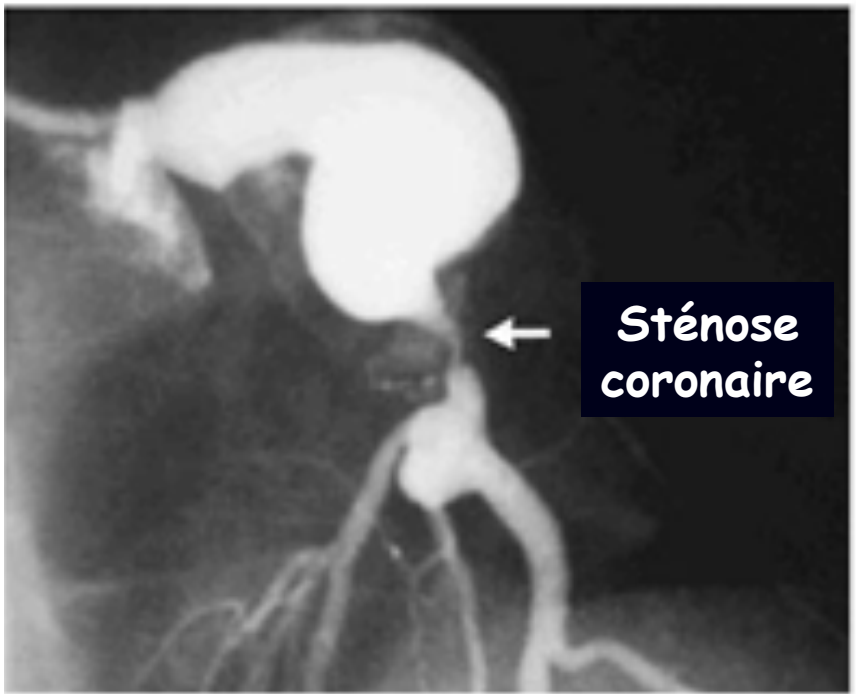


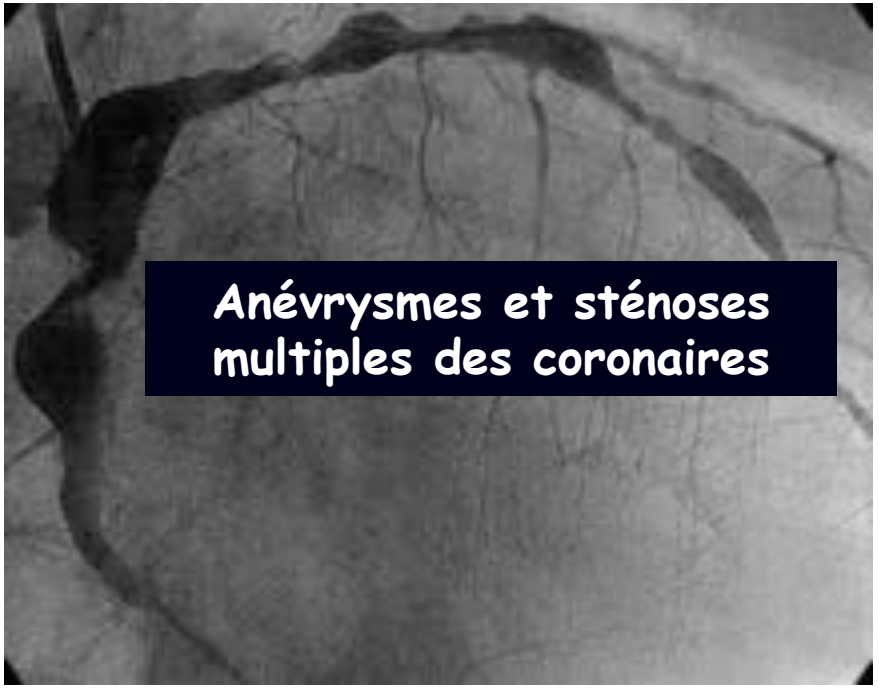
Dilatation anévrysmale de l'IVA en chapelet au scanner



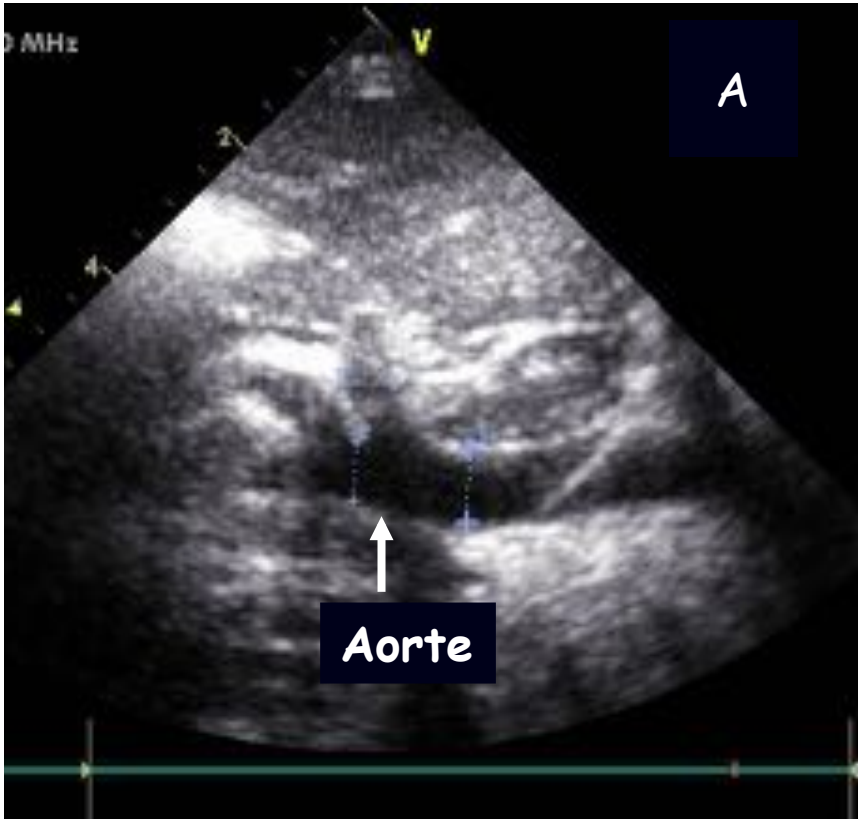


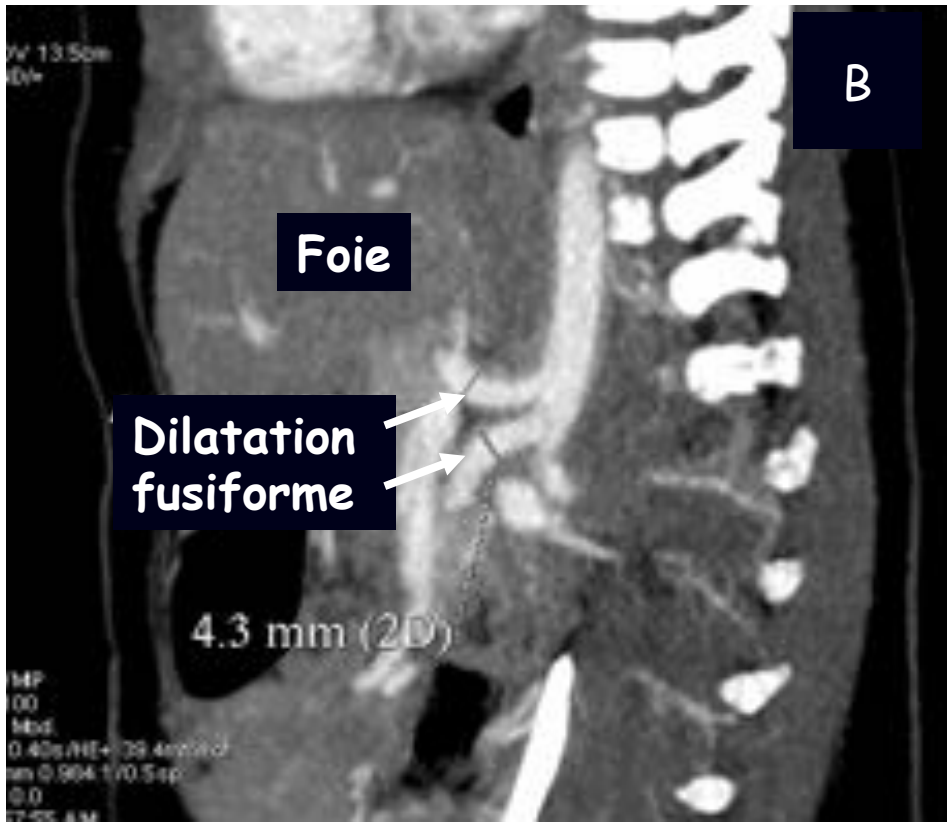
Anévrysme coronaire avec sténose coronaire au cathétérisme cardiaque





Atteinte diffuse des axes vasculaires





(A) épaississement pariétal hyperéchogène de l'aorte, de l'artère mésentérique supérieure et du tronc coeliaque en échographie

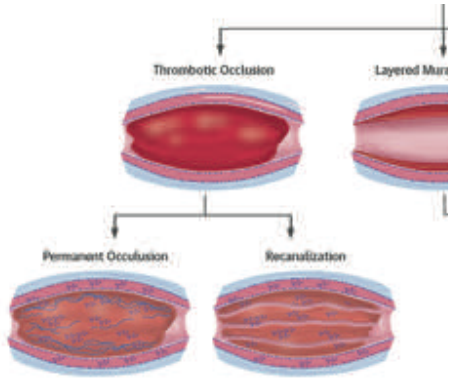
(B) dilatation fusiforme de l'artère mésentérique supérieure, du tronc caeliaque au scanner

Quelle est l'histoire naturelle des complications coronaires de la MK?

- Disparition complète dans plus de 50% des cas même en cas d'anévrisme dans les 2 ans
- Occlusion coronaire; sténoses localisées ou multiples parfois très tardives…
- Gravité des lésions tardives car multiples et chirurgie difficile

Anévrisme géants

- Mortalité et morbidité +++
- Survie à 30 ans: 88-90%



- Cardiac event free à 30 ans : 30%
- 26% infarctus myocardique
- Risque accru dans les 2 ans après le diagnostic
- 50% de bypass coronaire à 30 ans

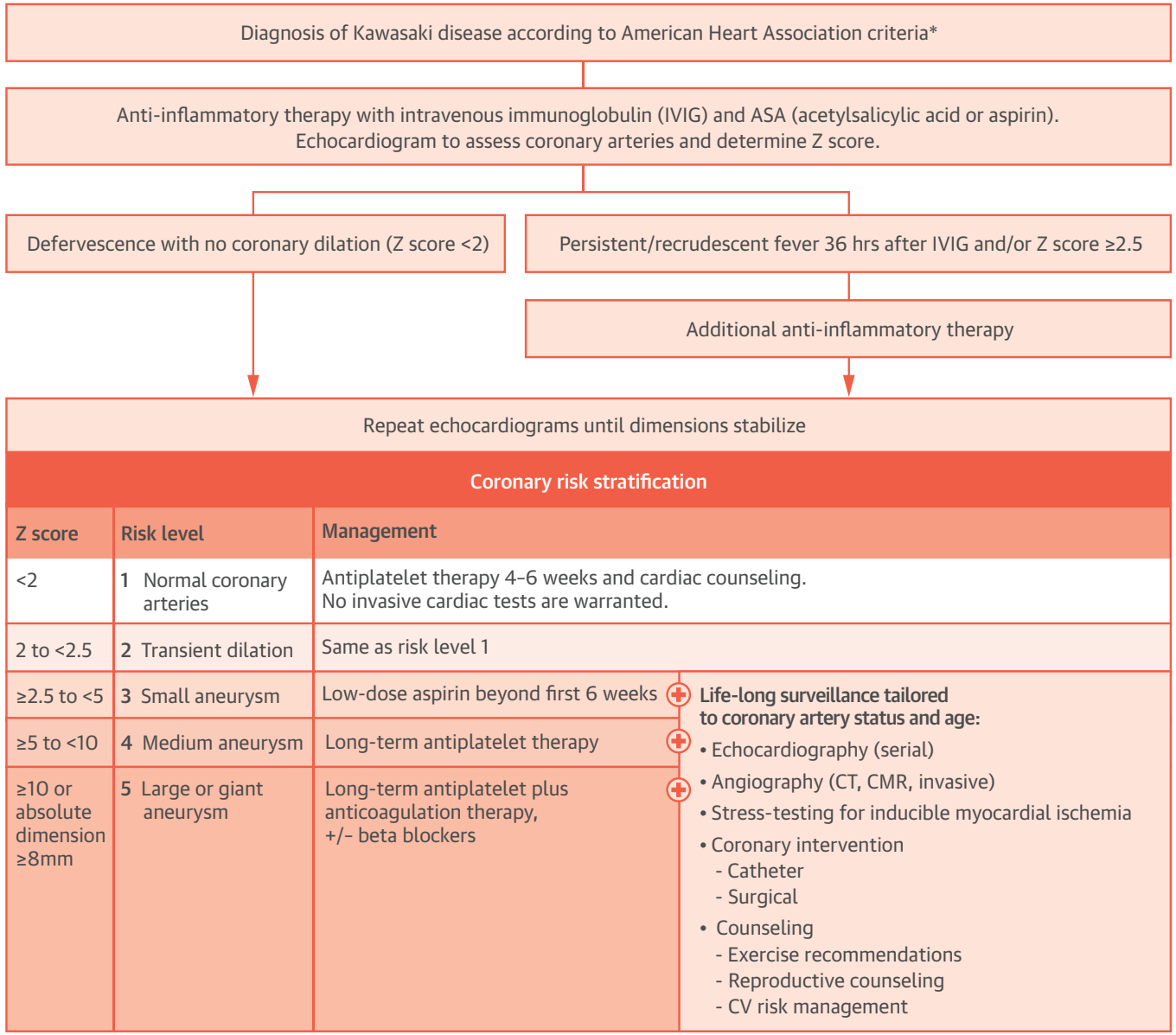
Le traitement

Repose sur :

- L'administration précoce de fortes doses d '**IgIV*** qui vise à réduire les symptômes et complications résultants du processus inflammatoire aigu associé à la maladie **(2g/kg en 8 à 12 heures, à posologie progressive)**

- **En association** à de **l'acide acétylsalicylique (AAS)**
- à fortes doses pour ses effets anti-inflammatoires et anti-thrombotiques **(30-80 mg/kg/j en 4 fois)** à la phase aiguë
- puis à **dose anti-agrégante plaquettaire** rapidement (50 mg avant 1 an, 100 mg après 1 an)

CENTRAL ILLUSTRATION Management of Kawasaki Disease



Newburger, J.W. et al. J Am Coll Cardiol. 2016;67(14):1738–49.

Recommandations américaines

TABLE 1 Principles in Acute Management of KD

1. The goal of therapy is to reduce systemic and tissue-level inflammation as rapidly as possible. For this reason, patients should be treated as soon as diagnosis can be confidently established.
2. All patients within the first 10 days of fever onset should be treated with IVIG. Patients diagnosed after 10 days should receive IVIG treatment if they are still febrile, have markedly elevated inflammatory parameters, or have coronary artery dilation.
3. Recrudescent fever at least 36 h after the end of IVIG infusion without other explanation is a marker for persistent inflammation and should prompt immediate and aggressive anti-inflammatory therapy
   a. Antibody-mediated hemolysis has become common in KD patients who have received IVIG retreatment and have type A or B blood; rescue therapies other than IVIG (e.g., infliximab, corticosteroids) should be considered.
4. Patients with coronary artery dilation (*z*-score >2.0) should be followed with a repeat echocardiogram at least twice a week until dimensions stabilize; additional anti-inflammatory therapy should be considered.
5. Patients with giant aneurysms should have frequent echocardiograms in the first 3 months of illness for thrombus surveillance, even after dimensions stabilize.
6. Infants under 6 months of age are at extremely high risk of aneurysm formation, even with timely therapy. They require echocardiograms every few days until dimensions have stabilized.
7. Patients with giant CAA (*z*-score ≥10) are at highest risk for thrombosis during the first 3 months after fever onset
   a. Systemic anticoagulation together with an antiplatelet agent should be administered until coronary dimensions improve.
   b. Low-molecular-weight heparin is easier to regulate than warfarin in infants, as well as in patients of any age, during the acute phase of illness or until hsCRP normalizes.

CAA = coronary artery aneurysm; hsCRP = high-sensitivity C-reactive protein; IVIG = intravenous immunoglobulin; KD = Kawasaki disease.

Newburger JACC 2016

Pronostic et évolution

Pronostic lié à la précocité du traitement

Le diagnostic doit être porté avant le 10ème jour afin de débuter précocement le traitement par les IgIV à fortes doses, seul traitement actuellement capable de diminuer la constitution d'anévrysmes

Amélioration clinique rapide

disparition de la fièvre et amélioration de l'état général dans les heures suivant les perfusions d'IgIV

Que faire en cas de persistance de la fièvre après une première cure d'IgIV?

- **Résistants:** 15 à 20 % des cas
- Associée à un risque plus élevé d'atteinte coronaire

- **CAT:** Recommencer mais avec quel traitement?

- **Score Egami**: Prediction of resistance to intravenous immunoglobulin treatment in patients with Kawasaki disease

- Critères prédictifs de résistance : PN hyperfragmentés, albumine basse, anomalies échographiques initiales

Newburger JW et al., Circulation. 2004

Egami K et al., J Pediatr 2006

Intérêt des bolus de corticoïdes associés à la deuxième dose d'IgIV dans les formes réfractaires ou résistantes?

Shohai Ogata et al., Pediatrics 2011

Rechercher les résistants?

Score prédictif d'Egami

A calculer avec les données du jour de la perfusion d'IgIV

1 point pour

- infants less than 6 months old,
- before 4 days of illness,
- platelet count <or= 300 x 10(9)/L,
- CRP >or= 80 mg/L,

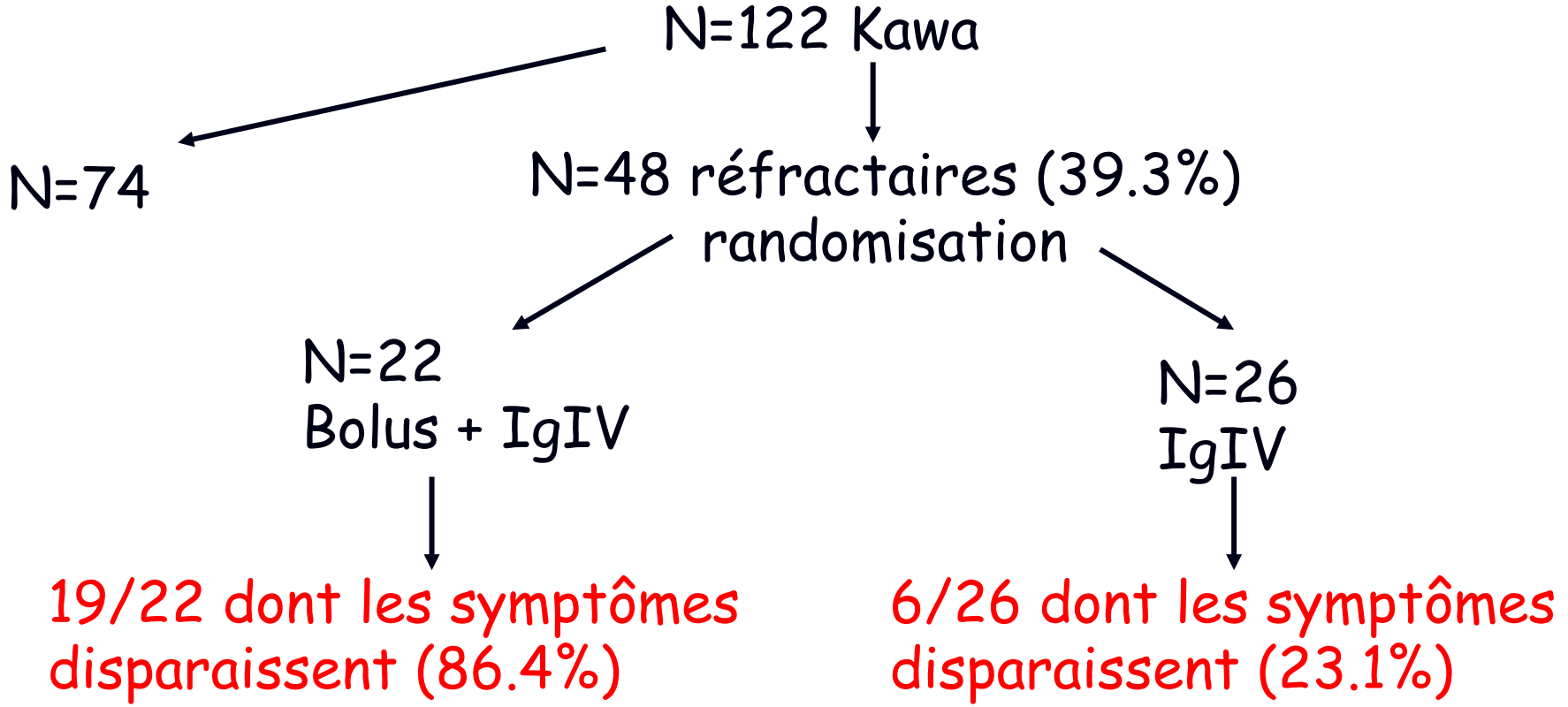
2 points pour

ALAT >or= 80 IU/L

Avec un cut off > ou égal à 3: identification des résistants avec Se 78% et Sp 76%

Egami K et al., J Pediatr 2006

Réfractaires: IgIV versus Bolus-IgIV



- Au final, nombre de patients dont z score > ou égal à 2.5 à M1 est supérieur dans groupe IgIV que bolus-IgIV (10/26 vs 2/22)
- Pas d'effet secondaire

Shohai Ogata et al., Pediatrics 2011

Devenir à long terme

TABLE 2 Principles in the Long-Term Management of Patients With KD

1. On the basis of available data, patients with no demonstrated coronary artery dilation by echocardiogram with excellent visualization of all arterial segments during the first weeks of illness appear to have normal cardiovascular status in early adulthood.
2. Remodeling (so-called regression) of aneurysms, especially if moderate or large, to normal internal lumen diameter is often accompanied by luminal myofibroblastic proliferation and abnormal vascular reactivity.
3. Patients with persistent CAA are at lifelong risk of progressive coronary artery stenosis or occlusion and worsening ischemia.
4. Patients with CAA documented at any stage require lifelong cardiovascular surveillance tailored to disease severity and age.
5. Testing should minimize exposure to ionizing radiation whenever possible.
6. Sedentary life-style should be avoided.
7. Women with coronary aneurysms can carry pregnancy successfully, but should have reproductive counseling.
8. Monitoring and counseling regarding traditional CV risk factors is appropriate to reduce the likelihood of later atherosclerosis.

Newburger JACC 2016

Endocardite

Endocardite infectieuse

Def: Infection/inflammation de l'endocarde = valves cardiaques

Dg: Echographie trans-thoracique voire ETO

- EI des VAV: sur le versant auriculaire
- EI des valves sigmoïdes: sur le versant ventriculaire

Hémocultures: au moins 3!!!!!!!!!!! (au mieux 6)

Pas d'ATB à l'aveugle

Scanner total body (cérébral, thoracique et abdominal)

Examen ophtalmologique, bandelette urinaire

Recherche porte d'entrée: examen dentaire, ORL, cutané, digestif, urinaire, KTC…

Table 11 Modified Duke criteria for the diagnosis of infective endocarditis (adapted from Li et al.[94])

MAJOR CRITERIA

Blood cultures positive for IE:

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

or

- Microorganisms consistent with IE from persistently positive blood cultures:
  At least two positive blood cultures of blood samples drawn > 12 h apart; or
  All of three or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

or

- Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titer > 1 : 800

Evidence of endocardial involvement

- Echocardiography positive for IE
  Vegetation - Abscess - New partial dehiscence of prosthetic valve
- New valvular regurgitation

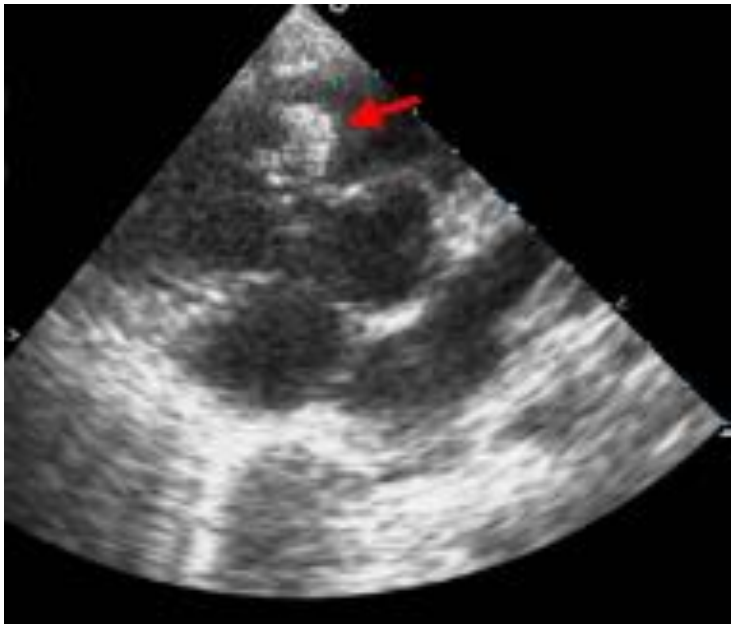
MINOR CRITERIA

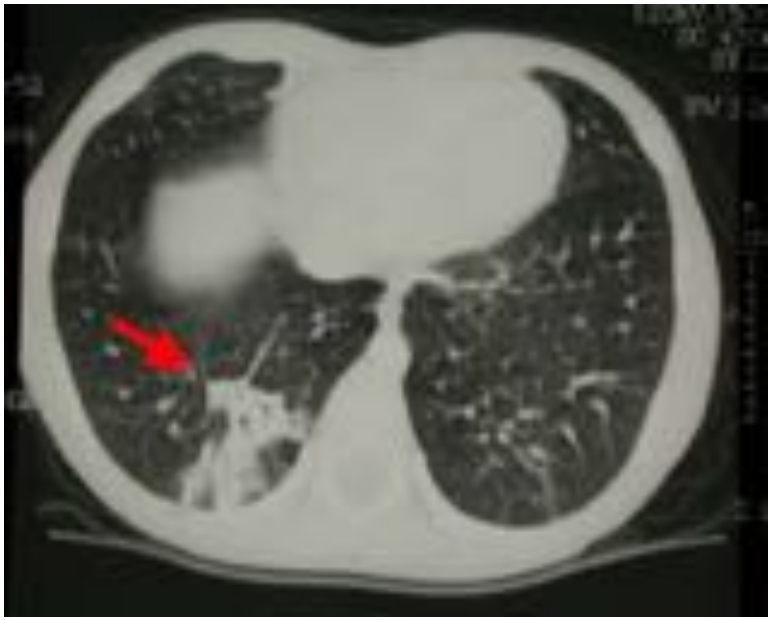
- Predisposition: predisposing heart condition, injection drug use
- Fever: temperature > 38 °C
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhages, conjunctival haemorrhages, Janeway lesions
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor
- Microbiological evidence: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE

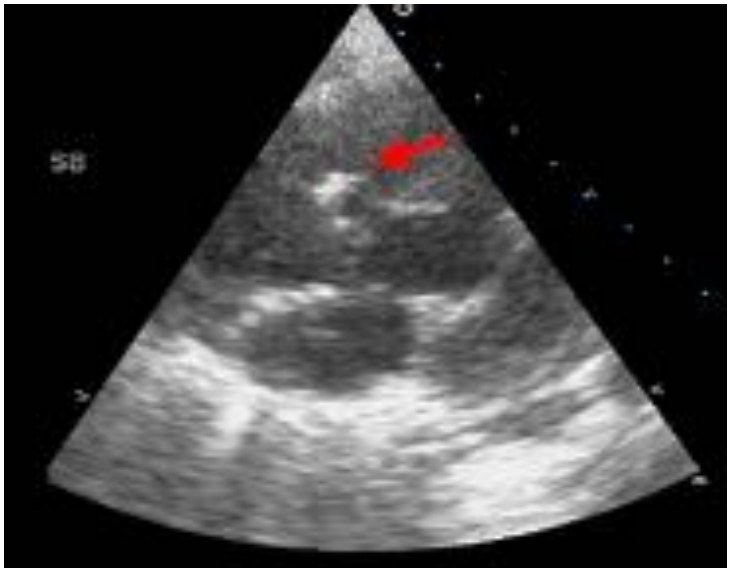
Diagnosis of IE is definite in the presence of	Diagnosis of IE is possible in the presence of
2 major criteria, or *1 major and 3 minor criteria, or* *5 minor criteria*	*1 major and 1 minor criteria, or* *3 minor criteria*

Adapted from Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Jr., Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;**30**:633–638.

Endocardite infectieuse







Endocardite: germes

- Streptocoques ++ 40%
- Staphylocoques 40%
- Autres : 10%
  - Escherichia Coli
  - BGN
  - HACEK
- Hémocultures négatives: 5 à 10%

Table 12 Predictors of poor outcome in patients with IE

Patient characteristics
- Older age
- Prosthetic valve IE
- Insulin-dependent diabetes mellitus
- Comorbidity (e.g frailty, previous cardiovascular, renal or pulmonary disease)

Presence of complications of IE
- Heart failure
- Renal failure
- Stroke
- Septic shock
- Periannular complications

Microorganism
- S. aureus
- Fungi
- Gram-negative bacilli

Echocardiographic findings
- Periannular complications
- Severe left-sided valve regurgitation
- Low left ventricular ejection fraction
- Pulmonary hypertension
- Large vegetations
- Severe prosthetic dysfunction
- Premature mitral valve closure and other signs of elevated diastolic pressures

Endocardite: ttt médical

- **Principes généraux**
  - Bi-thérapie ATB
  - Bactéricide
  - Intraveineux
  - Prolongé: 4 à 6 semaines
  - Adaptée (antibiogramme)
  - Taux sériques efficaces

Endocardite: ttt chirurgical

- **Indications**
  - Complications hémodynamiques
  - Sepsis non contrôlé
  - Embol gauche
  - Végétation > 10mm
  - Abcès
- **Types de chirurgie**
  - Eviter prothèse mécanique
  - Plastie, Ross, homogreffe

Endocardite: prévention

Table 4 Cardiac conditions at highest risk of infective endocarditis for which prophylaxis is recommended when a high risk procedure is performed

Recommendations: prophylaxis	Class[a]	Level[b]
Antibiotic prophylaxis should only be considered for patients at highest risk of IE 1. Patients with a prosthetic valve or a prosthetic material used for cardiac valve repair 2. Patients with previous IE 3. Patients with congenital heart disease a. cyanotic congenital heart disease, without surgical repair, or with residual defects, palliative shunts or conduits b. congenital heart disease with complete repair with prosthetic material whether placed by surgery or by percutaneous technique, up to 6 months after the procedure c. when a residual defect persists at the site of implantation of a prosthetic material or device by cardiac surgery or percutaneous technique	IIa	C
Antibiotic prophylaxis is no longer recommended in other forms of valvular or congenital heart disease	III	C

[a]Class of recommendation.
[b]Level of evidence.

Endocardite: prévention

Table 5 Recommendations for prophylaxis of infective endocarditis in highest risk patients according to the type of procedure at risk

Recommendations: prophylaxis	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
Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissue, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces. Prophylaxis is also not recommended following the shedding of deciduous teeth or trauma to the lips and oral mucosa	III	C
B - Respiratory tract procedures[c]: **Antibiotic prophylaxis is not recommended for respiratory tract procedures, including** bronchoscopy or laryngoscopy, transnasal or endotracheal intubation	III	C
C - Gastrointestinal or urogenital procedures[c]: **Antibiotic prophylaxis is not recommended for** gastroscopy, colonoscopy, cystoscopy or transoesophageal echocardiography	III	C
D - Skin and soft tissue[c]: **Antibiotic prophylaxis is not recommended for any procedure**	III	C

[a]Class of recommendation.
[b]Level of evidence.
[c]For management when infections are present, please refer to text.

Endocardite: prévention

Table 6 Recommended prophylaxis for dental procedures at risk

		Single dose 30–60 minutes before procedure	
Situation	**Antibiotic**	**Adults**	**Children**
No allergy to penicillin or ampicillin	Amoxicillin or ampicillin*	2 g p.o. or i.v.	50 mg/kg p.o. or i.v.
Allergy to penicillin or ampicillin	Clindamycin	600 mg p.o. or i.v.	20 mg/kg p.o. or i.v.

Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin and ampicillin.
*Alternatively cephalexin 2 g i.v. or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.

POPULATION CONGENITALE - ENFANTS

Infective Endocarditis in Children With Congenital Heart Disease

Cumulative Incidence and Predictors

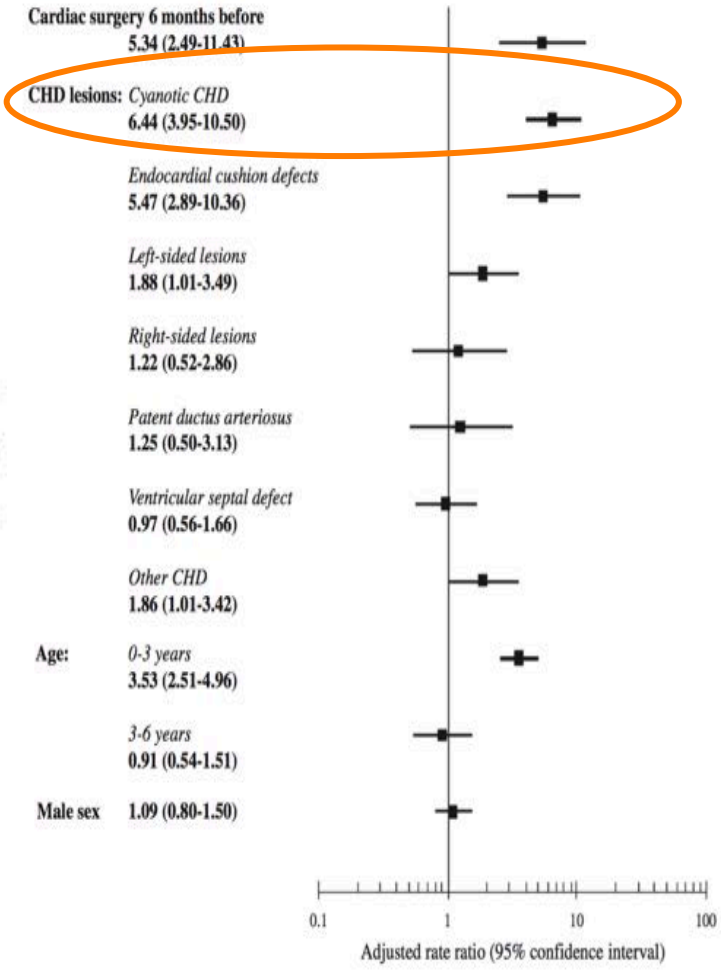
34 279 enfants avec CC suivis de 0 à 18 ans

Incidence annualisée = 4.1 / 10 000 pt-année

Table 2. Lesion Group–Specific Cumulative Incidence and Incidence Rate of IE in Children With CHD

CHD Lesions	Cumulative Incidence (95% CI) per 1000 Children			Incidence Rate (95% CI) per 10000 Person-Years
	0–6 y	0–12 y	0–18 y	
Cyanotic CHD	16.8 (11.9–23.8)	23.3 (17.0–31.8)	31.0 (22.5–42.7)	20.7 (15.4–27.7)
Endocardial cushion defects	5.5 (2.3–13.1)	8.7 (4.1–18.6)	11.1 (5.4–22.9)	7.7 (3.9–15.4)
Left-sided lesions	2.7 (1.3–5.7)	4.8 (2.6–8.7)	7.9 (4.4–14.0)	4.4 (2.6–7.4)
Right-sided lesions	2.3 (1.0–5.5)	2.3 (1.0–5.5)	4.2 (1.5–11.5)	2.9 (1.3–6.5)
Patent ductus arteriosus	3.2 (1.4–7.1)	3.2 (1.4–7.1)	3.2 (1.4–7.1)	3.5 (1.6–7.7)
Ventricular septal defect	2.0 (1.2–3.2)	2.4 (1.5–3.8)	3.2 (1.9–5.3)	2.4 (1.5–3.7)
Atrial septal defect	1.9 (1.3–2.9)	2.2 (1.5–3.4)	3.0 (1.9–4.8)	2.3 (1.6–3.4)
Other CHD	2.9 (1.4–5.8)	3.7 (1.8–7.3)	5.5 (2.9–10.6)	3.7 (2.0–6.7)
Overall	3.2 (2.6–3.9)	4.2 (3.5–5.1)	6.1 (5.0–7.5)	4.1 (3.5–4.9)

CHD indicates congenital heart disease; CI, confidence interval; and IE, infective endocarditis.



POPULATION CONGENITALE - ADULTES

Table 4 **Prediction model for developing IE, and score chart for the risk of developing IE up to 5 and 10 years**

Predictor	HR(95% CI)	Points
Baseline valve-containing prosthetics	3.57(2.38–5.36)	3
Main defect[a]		
Pulmonary atresia with ventricular septal defect	4.05(1.85–8.86)	3
Double-outlet right ventricle	3.01(0.91–9.94)	2
Tetralogy of Fallot	1.81(0.99–3.33)	1
Univentricular heart	1.69(0.51–5.54)	1
Left-sided lesions	1.55(0.99–2.44)	1
Other	1	0
Multiple defects	1.68(1.15–2.46)	1
History of IE	2.21(1.22–4.01)	2
Male	1.89(1.28–2.81)	1

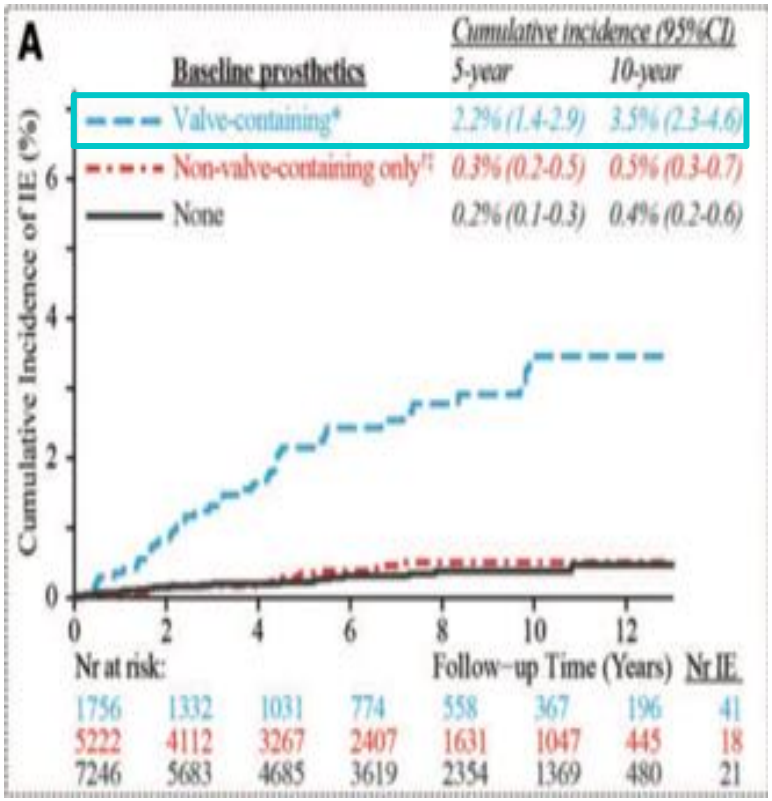
Score (sum points)

	Score									
	0	1	2	3	4	5	6	7	8	>8
Predicted 5 year risk (%)	<1	<1	1	1	1	2	3	4	7	9
Predicted 10 year risk (%)	<1	1	1	1	3	3	5	7	12	15

Registre CONCOR (14 224 patients>18 ans)

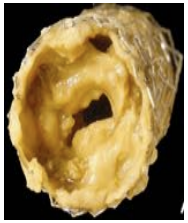
Incidence EI : **1.33/1000 pt-years**

Prothèse valvulaire: **HR=3.57(2.58–5.36)**



Kuijpers et al. Eur Heart Jour 2017

INCIDENCES COMPARATIVES

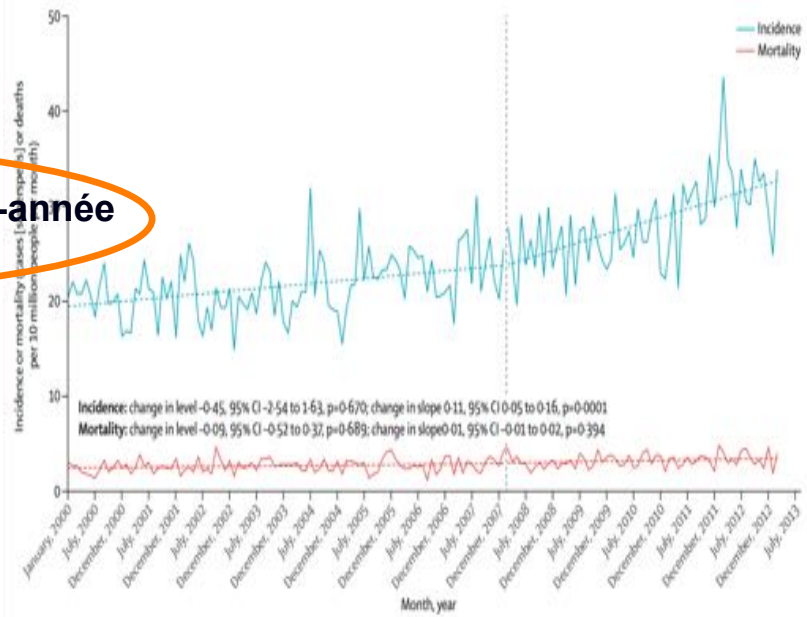


Valve Melody : **0.8 – 3% pt-année**

Valves/conduits pulmonaire chir : **0.5 - 3% pt-année**

TAVI: **0.67 – 2.1% pt-année**

Valves Ao/mitrale chir : **0.3 – 1.2% pt-année**



Dispositifs electroniques implantables : **1.9/1000 device-année**

Patients avec CC: **0.4 – 1.33 / 1000 pt-année**

Population générale : **30 -100/ million pt-année**

Miranda et al. Eur Heart Jour 2016
Wang et al. JAMA 2007
Rushani et al. Circulation 2013
Habib et al. Eur Heart Jour 2015
Dayer et al. Lancet 2015

COMPARER CE QUI EST COMPARABLE

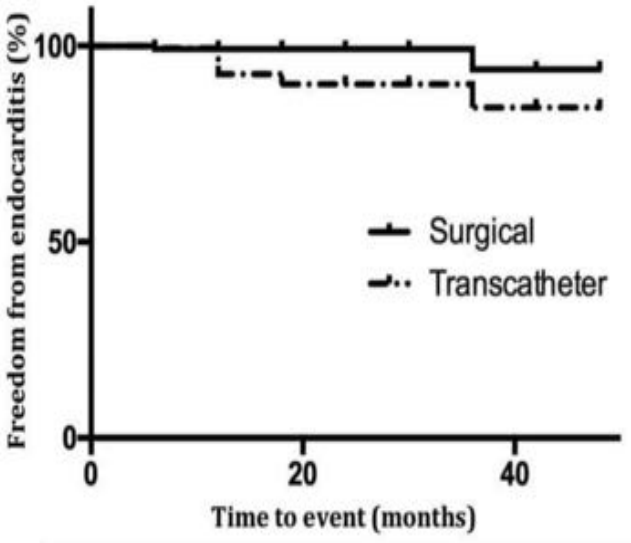
Table 2 Demographic characteristics.

	Overall (*n* = 86)	IE (*n* = 5)
Age (years)	23.9 ± 10.5	29.8 ± 16.
Men/women	51/35	4/1
Body surface (m^2)	1.6 ± 0.3	1.8 ± 0.3
Type of CHD		
TOF	22 (25)	1
PAVSD	20 (23)	1
Truncus arteriosus	11 (13)	0
Aortic valve disease	13 (15)	2
PS	2 (2)	0
TGA-VSD-PS	2 (2)	1
DORV	4 (5)	0
Other	12 (14)	0
Co-morbidities	18	3
22q11 deletion	8	1
Noonan syndrome	1	0
Other syndrome	5	0
Trisomy 21	1	0
Beta thalassaemia	1	1
HCV	2	1
Portal cavernoma	1	1

Table 1. Baseline Characteristics and Procedural Details

Characteristics	Total, n=509	No TAVI-PVE, n=491	TAVI-PVE, n=18
Age, y (SD)	80 (6.9)	80 (6.9)	78 (6.9)
Men, n (%)	296 (58)	279 (57)	17 (94)
BMI, kg/m² (SD)	26.8 (5.1)	26.8 (5.2)	26.9 (3.5)
Arterial hypertension, n (%)	294 (58)	283 (58)	11 (61)
Diabetes mellitus, n (%)	103 (20)	99 (20)	4 (22)
Coronary artery disease, n (%)	259 (51)	249 (51)	10 (56)
Peripheral artery disease, n (%)	52 (10)	48 (10)	4 (22)
Chronic kidney disease†, n (%)	196 (39)	189 (38)	7 (39)
COPD, n (%)	73 (14)	72 (15)	1 (6)
Previous CVA, n (%)	72 (14)	69 (14)	3 (17)
Permanent pacemaker, n (%)	40 (8)	39 (8)	1 (6)
NYHA≥3, n (%)	364 (72)	352 (72)	12 (67)
Angina pectoris, n (%)	196 (39)	189 (38)	7 (39)
Syncope, n (%)	71 (14)	66 (13)	5 (28)
Previous endocarditis, n (%)	0 (0)	0 (0)	0 (0)

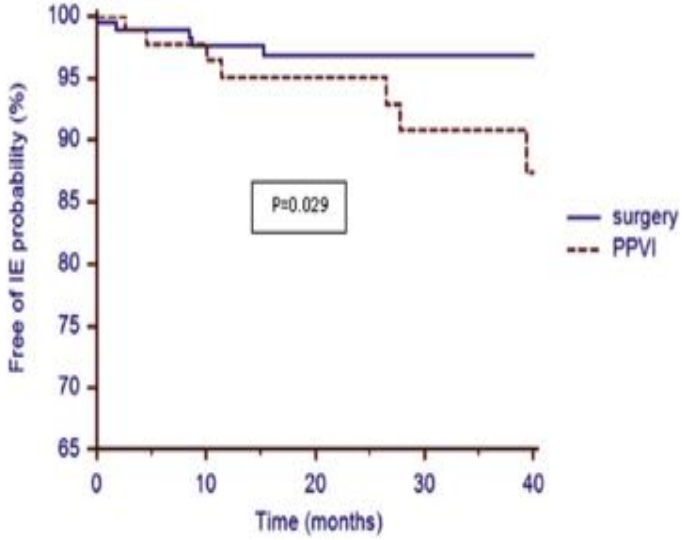
VALVES PERCUTANÉES VS CHIRURGICALES



134 chir et 208 percut (33 Sapien)

Incidence IE: 0.5 vs 1.5 %pt/années

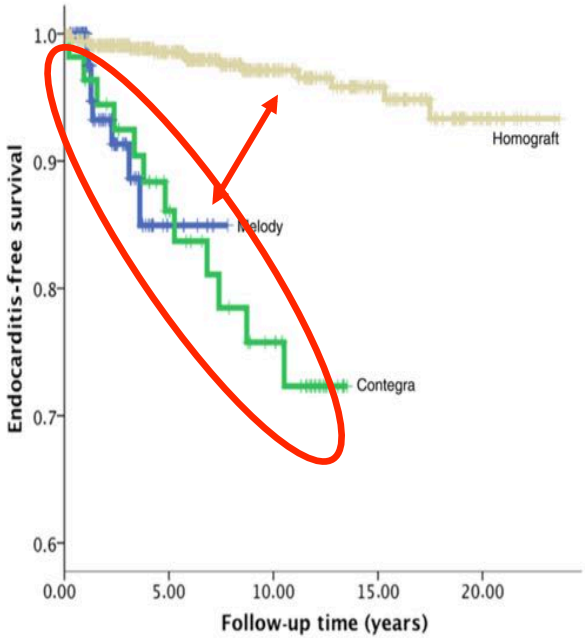
Lluri et al. CCI 2017



195 chir et 93 percut (0 Sapien)

Incidence IE: 1.2 vs 3.9 %pt/années

Malekzadeh-Milani et al. JTCS 2014



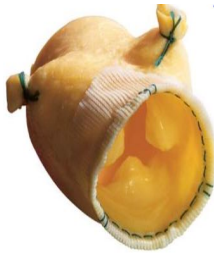
631 chir et 107 percut (0 Sapien)

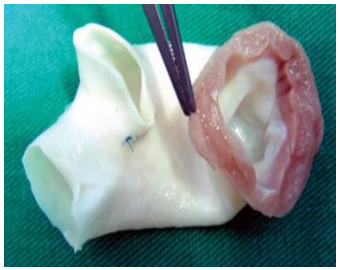
Incidence IE: 0.8 vs 2.7 vs 3% %pt/années

Van Dijck et al. Heart 2014

SUBSTRAT VALVULAIRE

Author	Year	n	Substrate	EI Cumulative incidence	EI Annualized Incidence (% pt-year)	Median Follow-up (years)
Albanesi	2014	12/106	Contegra	**11.3**		**7.6**
Malekzadeh	2014	5/190	Homografts Contegra	**2.6**	**1.2**	**2**
Ramanan	2015	6/115	Freestyle	**5.4**	**-**	**4.3**
Mery	2016	23/586	Homograft Contegra Porcine valve	**4**	**-**	**7**
Ugaki	2016	21/298	Contegra Homograft	**7**	**-**	**3.4**

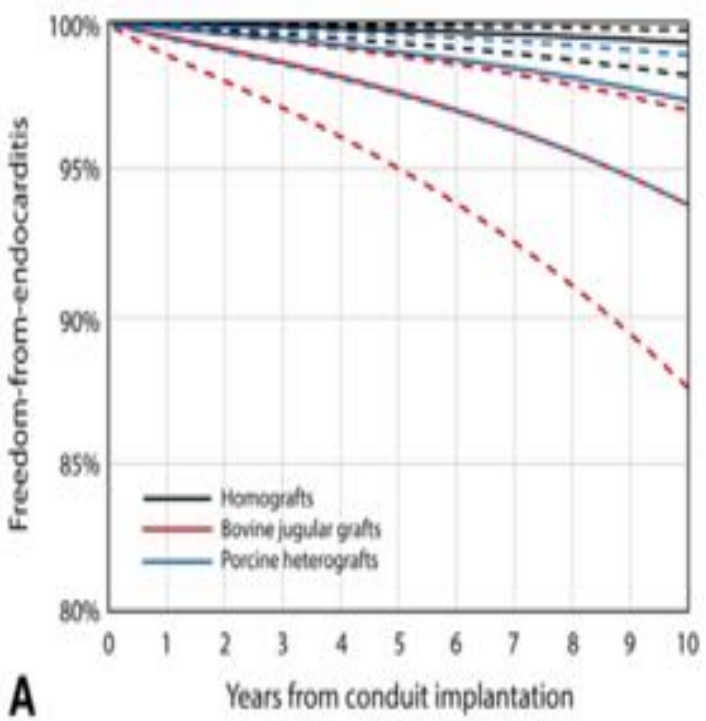


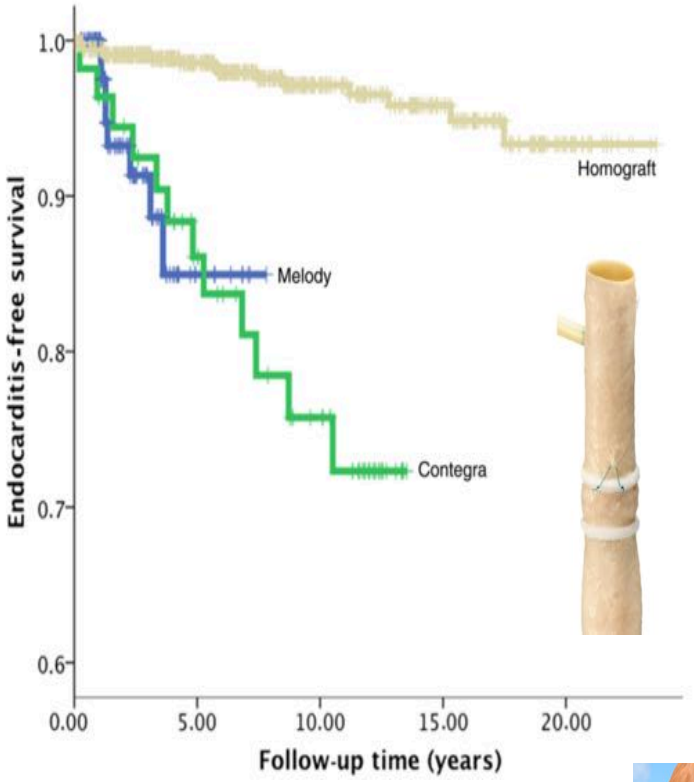


Tous les dispositifs valvulaires sont susceptibles d'être le siège d'une EI
Avec une incidence variable mais significative

Albanesi et al. EJCTS 2014
Ramanan et al. Ann Thorac Surg 2015
Ugaki et al. Ann Thorac Surg 2016
Mery et al. JTCS 2016

SUBSTRAT VALVULAIRE





- EI plus fréquente chez les patients avec **VJB**
- **Quelle que soit la techniqued'implantation** (i.e. Contegra et Melody)
- Comparés aux homogreffes **RR=8.7 and 9.7** pour Melody et Contegra

Malekzadeh-Milani et al. JTCS 2014
Van Dijck et al. Heart 2014

Mery et al. JTCS 2016
Ugaki et al. Ann Thorac Surg 2015

SUBSTRAT VALVULAIRE

A Systematic Review of Infective Endocarditis in Patients With Bovine Jugular Vein Valves Compared With Other Valve Types

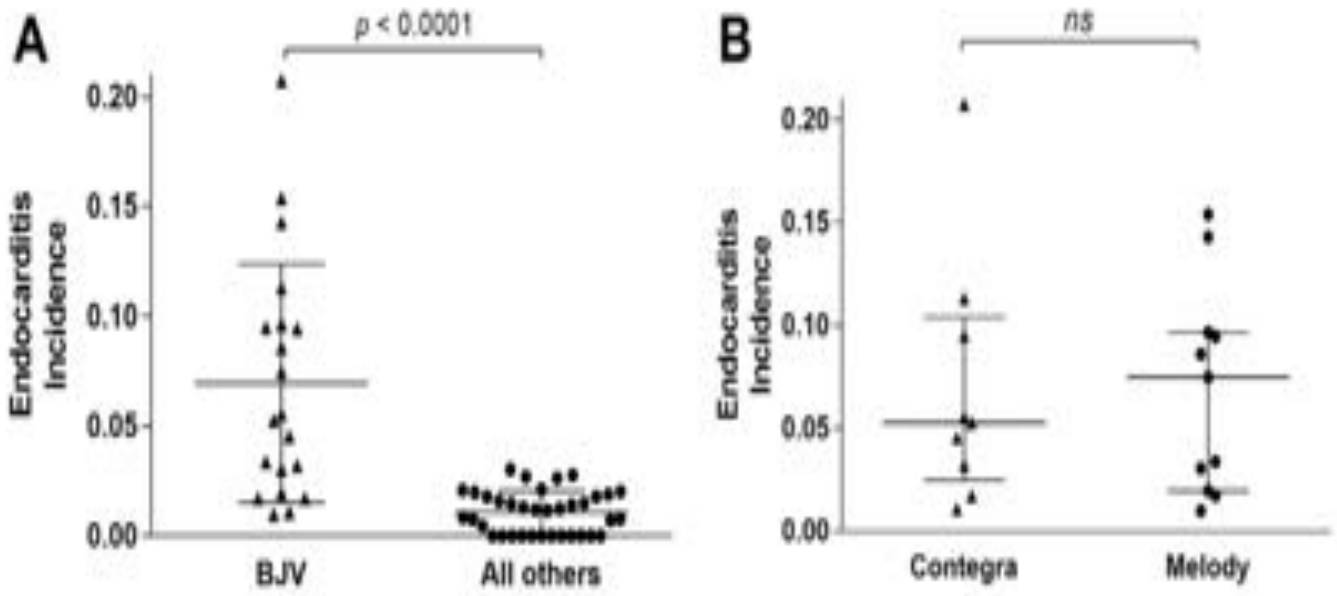
Méta-analyse sur IE chez les patients avec RVP chirurgical ou percutané

7063 patients

Incidence cumulative globale = 2.5%

VJB vs autres substituts : 5.4% vs 1.2%; p < 0.0001

FIGURE 2 Incidence of Infective Endocarditis in BJV Compared to Other Valves



Sharma et al. JACC Int. 2017

VALVE SAPIEN

Infective Endocarditis Risk After Percutaneous Pulmonary Valve Implantation With the Melody and Sapien Valves

TABLE 1 Patient Demographics, Procedural Data, and Post-Procedural Outcomes

	PPVI With Melody Valve (n = 32)	PPVI With Sapien Valve (n = 47)	Standardized Difference
Age (yrs)	19.9 (15.8-28.9)	26.3 (18.9-39.9)	0.58*
Weight (kg)	56.5 ± 13.5	65.8 ± 17.6	0.59*
Male (%)	53.1	66.0	0.26
Genetic syndrome (%)	18.8	10.6	-0.23
History of severe infectious disease (%)	9.4	8.5	-0.03
History of endocarditis (%)	6.3	2.1	-0.20
Pacemaker/defibrillator (%)	6.3	10.6	0.16
Congenital heart diseases (%)			
Conotruncal malformation	81.3	68.1	
Ross procedure	9.4	21.3	
TGA	3.1	0.0	
PA-IVS/PVS	3.1	4.3	
DORV	3.1	6.4	
RVOT (%)			
Native RVOT	3.1	25.5	
Bioprosthesis	9.4	23.4	
Homograft	25.0	31.9	
Conduits	62.5	19.2	
RVOT lesion (%)			
Stenosis	84.4	50.0	
Regurgitation	0.0	35.7	
Mixed	15.6	14.3	

TABLE 1 Continued

	PPVI With Melody Valve (n = 32)	PPVI With Sapien Valve (n = 47)	Standardized Difference
Infective endocarditis during follow-up (%)	25.0	0.0	-0.80*
Pulmonary valve replacement during follow-up (%)	25.0	4.3	-0.59*
Percutaneous	3.1	2.1	-0.06
Surgical	21.9	2.1	-0.63*
Death during follow-up (%)	3.1	2.1	-0.06

Values are median [interquartile range] or %. Standardized difference computed as the difference in means or proportions divided by the SE. *Significant imbalance.

DORV = double-outlet right ventricle; PA-IVS = pulmonary atresia with intact ventricular septum; PPVI = percutaneous pulmonary valve implantation; PVS = pulmonary valve stenosis; RVOT = right ventricle outflow tract; TGA = transposition of the great arteries.

Hascoet et al. JACC Int. 2017

VALVE SAPIEN

- Monocentrique
- 2 cohortes non contemporaines: courbe d'apprentissage, prévention
- Populations peu comparables
  - Melody: conduits ou homogreffes (87% vs 51% Sapien)
  - Sapien: voies droites larges, pas de post dilatation
- Suivi plus court pour valves Sapien (1 an vers 4.9 ans)
- Pas de données sur les gradients résiduels (facteur prédisposant)

VALVE SAPIEN

COMPASSION TRIAL

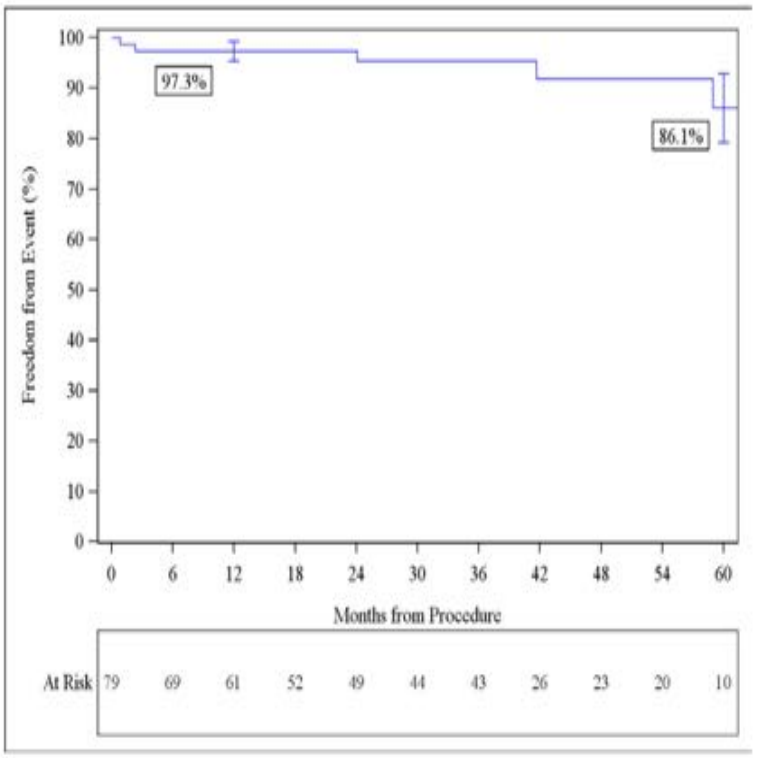
79 patients, Lésions mixtes

Suivi médian 3 ans

Table 9: Incidence of Site-Reported Serious Adverse Events by Study Visit (with CEC adjudication where available) in the Safety Population (N=79)

Adverse Event	≤ 30 Days		31 – 365 Days		All Events	
	Events	Patients with Event	Events	Patients with Event	Events	Patients with Event
Any Serious Adverse Event	29	3/ 79 (29.1%)	22	13/ 79 (16.5%)	132	38/ 79 (48.1%)
Other	2	2/ 79 (2.5%)	10	6/ 79 (7.6%)	37	13/ 79 (16.5%)
Infection (excluding endocarditis)	1	1/ 79 (1.3%)	3	3/ 79 (3.8%)	12	7/ 79 (8.9%)
CHF	1	1/ 79 (1.3%)	0	0/ 79 (0.0%)	11	4/ 79 (5.1%)
Electrolyte and/or CBC and platelet counts abnormal	1	1/ 79 (1.3%)	2	1/ 79 (1.3%)	11	2/ 79 (2.5%)
Valve stenosis	0	0/ 79 (0.0%)	1	1/ 79 (1.3%)	9	6/ 79 (7.6%)
Arrhythmia	2	2/ 79 (2.5%)	0	0/ 79 (0.0%)	8	6/ 79 (7.6%)
Endocarditis	1	1/ 79 (1.3%)	2	2/ 79 (2.5%)	5	4/ 79 (5.1%)

Clinical Figure 6: Freedom from Endocarditis at 5 Years (Safety Population, N=79)



Edwards SAPIEN XT Transcatheter Heart Valve with the NovaFlex1Delivery System. Vol. 2016. https://www.accessdata.fda. gov/cdrh_docs/pdf13/p130009s037d.pdf

PREVENTION - EDUCATION

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
Antibiotic prophylaxis is not recommended in other forms of valvular or CHD.	III	C

OST-IMPLANTATI

t, parents, médeci

ggrégants au long

tibioprophylaxie à

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
• Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces or following the shedding of deciduous teeth or trauma to the lips and oral mucosa	III	C
B. Respiratory tract procedures[c]		
• Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, or transnasal or endotracheal intubation	III	C
C. Gastrointestinal or urogenital procedures or TOE[c]		
• Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE	III	C
D. Skin and soft tissue procedures[c]		
• Antibiotic prophylaxis is not recommended for any procedure	III	C

FACTEURS AGGRAVANTS

Portes d'entrée évitables

Manque observance

Déficiences mentales

Education - Prophylaxie EI

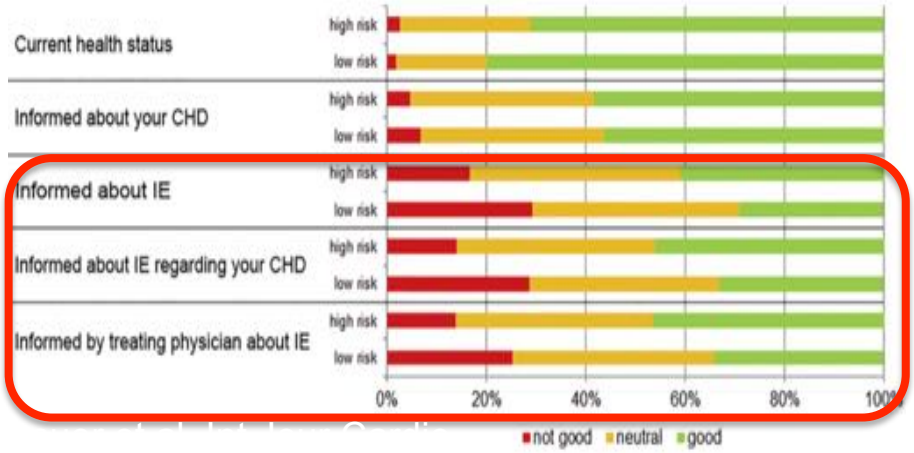


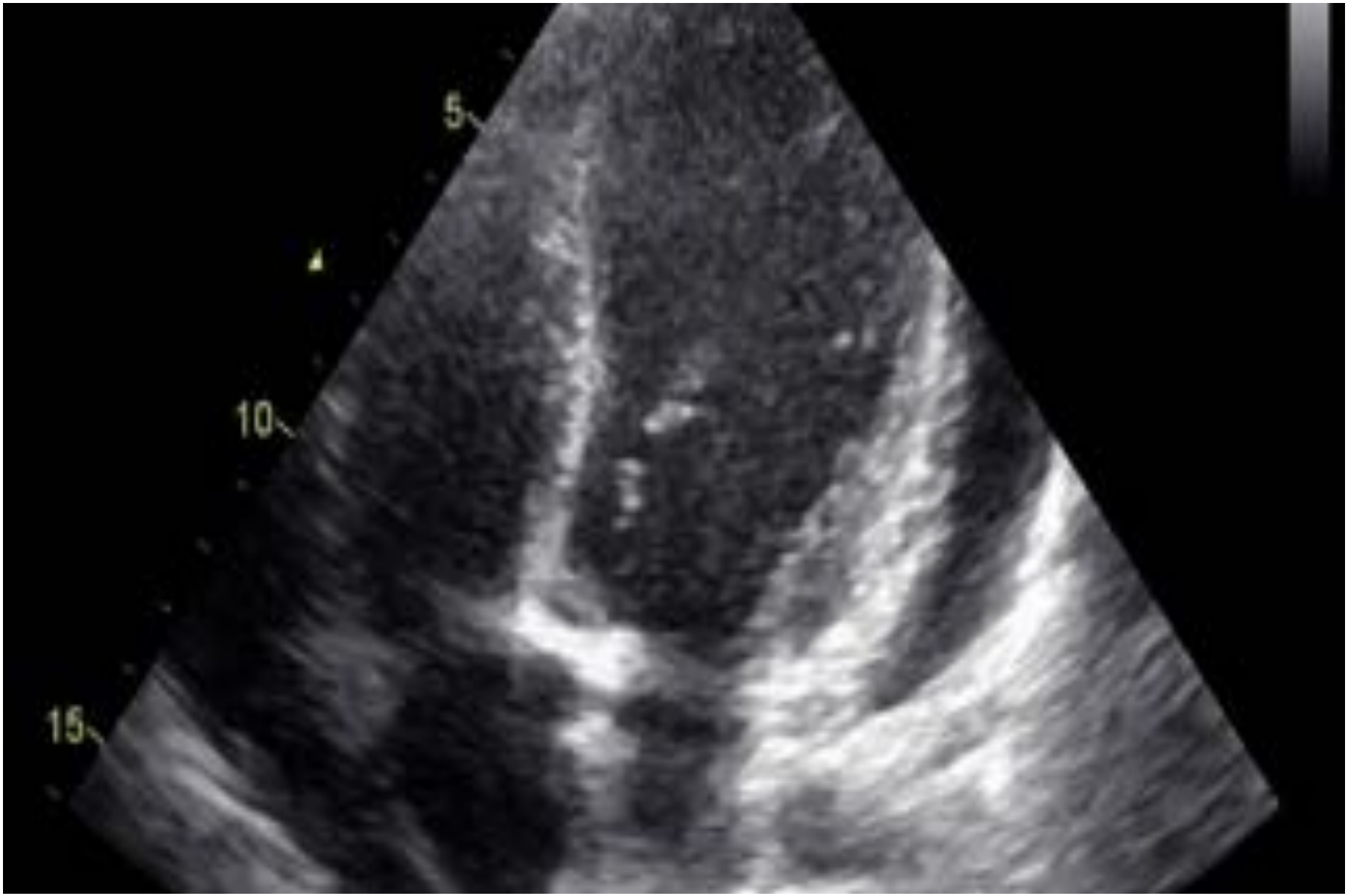
Table 1. Details of the 14 Index Bloodstream Bacterial Infection Cases

Case	Age, y	Sex	Time From Procedure to Systemic Infection (mo)	Underlying Cardiac Condition	Infecting Organism	Number of Positive Blood Cultures	Circumstances of Infection
1	4	Male	9	TOF/PA	*Streptococcus viridans*	3	Tooth extraction
2	28	Male	14	Congenital AS, S/P Ross procedure	*Streptococcus viridans*	4	None
3	41	Male	16	D-TGA	*Staphylococcus lugdunensis*	3	None
4	29	Male	56	D-TGA	*Streptococcus mitis*	3	Infection of oral ulcer
5	29	Male	53	TOF/PA	Coagulase negative *Staphylococcus*	2	Traumatic finger cut with subsequent cellulitis
6	25	Male	5	DORV	*Streptococcus anginosus* group	2	Pneumonia
7	42	Male	24	TOF/PA	Methicillin-resistant *Staphylococcus aureus*	2	Dental procedure
8	56	Male	10	TOF/PA	Methicillin-resistant *Staphylococcus aureus*	2	Sternal wound infection
9	14	Male	26	TOF/PA	*Streptococcus mitis*	3	Dental cleaning preceded
10	49	Male	20	TOF/PA	Methicillin-resistant *Staphylococcus aureus*	3	None
11	10	Male	18	TOF/PA	*Haemophilus parainfluenzae*	3	Bacterial gastroenteritis
12	21	Female	4	TOF	*Streptococcus viridans*	2	None
13	17	Male	30	Truncus Arteriosus	*Streptococcus mutans*	2	None
14	18	Male	1	TOF/PA	*Staphylococcus epidermidis*	2	Tracheostomy-associated infection

Buber et al. Circ Intrv 2013

Cas clinique: Pierre Hervé, né le 26/06/1995

- **Septembre 2011** : épisode fébrile d'allure grippale
- **Octobre 2011:** arthralgies et réapparition de la fièvre à 39°C en plateau avec des myalgies et éruption cutanée.
- **Décembre en Tunisie:** aggravation des symptômes avec fièvre asthénie, arthralgies des genoux, coudes, chevilles, poignets et doigts bilatérales et altération de l'état général avec une perte de 7 kg en un mois.
- **Janvier 2012 :** hospitalisation
  - Syndrome inflammatoire.
  - Myélogramme normal pour une suspicion de maladie de Still devant cette fièvre prolongée
  - transfert…


5
10
15

V
5
10
83
HR

L 1.10 cm
L 0.89 cm
V

Résultats

Clinique: Pouls amples, TA: 108/33,
souffle systolique et diastolique

ECG: BAV I

ECHO:

- végétation hyperéchogène mobile de 10 x 8 mm sur la grande valve mitrale.
- perforation de la grande valve avec une fuite.
- **bicuspidie aortique.**
- végétation de 5 mm sur la sigmoïde aortique postérieure. Il n'y a pas de perforation vue sur les sigmoïdes aortiques. Il n'y a pas d'abcès du trigone aortique vu.
- La fuite aortique avec pression diastolique basse et reflux diastolique au niveau de l'isthme aortique supérieur à 0.35 m/s. La fuite aortique est très excentrée.
- épanchement péricardique circonférentiel de 10 mm non compressif.
- VG dilaté

Attitude

- **Hémocultures:** positives à **Streptococcus mutans** sensible à la Ceftriaxone.
- Consultation stomato, ORL: RAS
- **Cutanée:** éruption cutanée maculo-papuleuse érythémateuse sur la jambe et les membres supérieurs et une lésion purpurique sur l'index droit.
- **Fond d'œil:** taches de Roth en périphérie et para-maculaires et un signe de Tyndall vitréen.
- **Scanner thoraco-abdomino-cérébral** a montré un abcès sur le pôle inférieur de chaque rein et également des images suspectes d'emboles cérébraux
- **IRM cérébrale** : plusieurs emboles de petite taille dans différents territoires droits et gauches notamment capsulo-lenticulaires droit et dans le pédoncule cérébral droit. Ces emboles sont d'âges différents. Il y a également une lacune du corps calleux de la substance blanche frontale interne évoquant une lacune anoxique plus ancienne.

- **Que faites-vous?**

Attitude

- Traitement initialement probabiliste par Claforan, Gentamycine et Fosfomycine.
- Puis arrêt Fosfomycine
- Indication opératoire rapide (J5 ATB):
  - Abcès du trigone, perforation mitrale et Ao
  - Plastie mitrale et Bentall avec homogreffe aortique
  - 6 semaines ATB

Byrne et al., Ann Thorac Surg 2011; 91:2012-9)

Byrne et al., Ann Thorac Surg 2011; 91:2012-9)

B) Timing of surgery in patients with neurologic complications

1. In patients who have had a major ischemic stroke or any intracranial hemorrhage, it is reasonable to delay valve replacement for at least 4 weeks from the stroke, if possible. (Class IIa, Level of evidence C)
2. If there is a decline in cardiac function, recurrent stroke or systemic embolism or uncontrolled infection despite adequate antibiotic therapy, a delay of less than 4 weeks may be reasonable, particularly in patients with small areas of brain infarction. (Class IIb, Level of evidence C)

II) Aortic Valve Endocarditis

A) Native aortic valve endocarditis

1. When surgery is indicated, a mechanical or stented tissue valve is reasonable in native aortic valve endocarditis if the infection is limited to the native aortic valve or to the aortic annulus. Valve choice should be based on age, life expectancy, comorbidities, and compliance with anticoagulation. (Class IIa, Level of evidence B)
2. A homograft may be considered in native aortic valve endocarditis when the infection is limited to the native aortic valve or to the aortic annulus. (Class IIb, Level of evidence B)

B) Native aortic valve endocarditis with periannular abscess

1. When periannular abscess is associated with IE, it is reasonable to use a mechanical or stented tissue valve if radical debridement is carried out and the valve can be anchored to healthy and strong tissue. (Class IIa, Level of evidence B)
2. It may be reasonable to use a homograft in native aortic valve endocarditis with periannular abscess and extensive annular or aortic wall destruction requiring aortic root replacement/reconstruction or extensive aortic-ventricular discontinuity. (Class IIb, Level of evidence B)

Léo – VDDI réparé à 1.5 ventricules

10/10/12: Consultation aux urgences NEM: syndrome fébrile ressemblant à un syndrome grippal.

« **DS:** Je l'ai surtout vu pour m'assurer qu'il n'y avait pas de végétations quelque part dans ce cœur : il n'y en a pas. Il a simplement un syndrome grippal. «

24 après: choc septique à staphylocoque doré

Porte d'entrée?

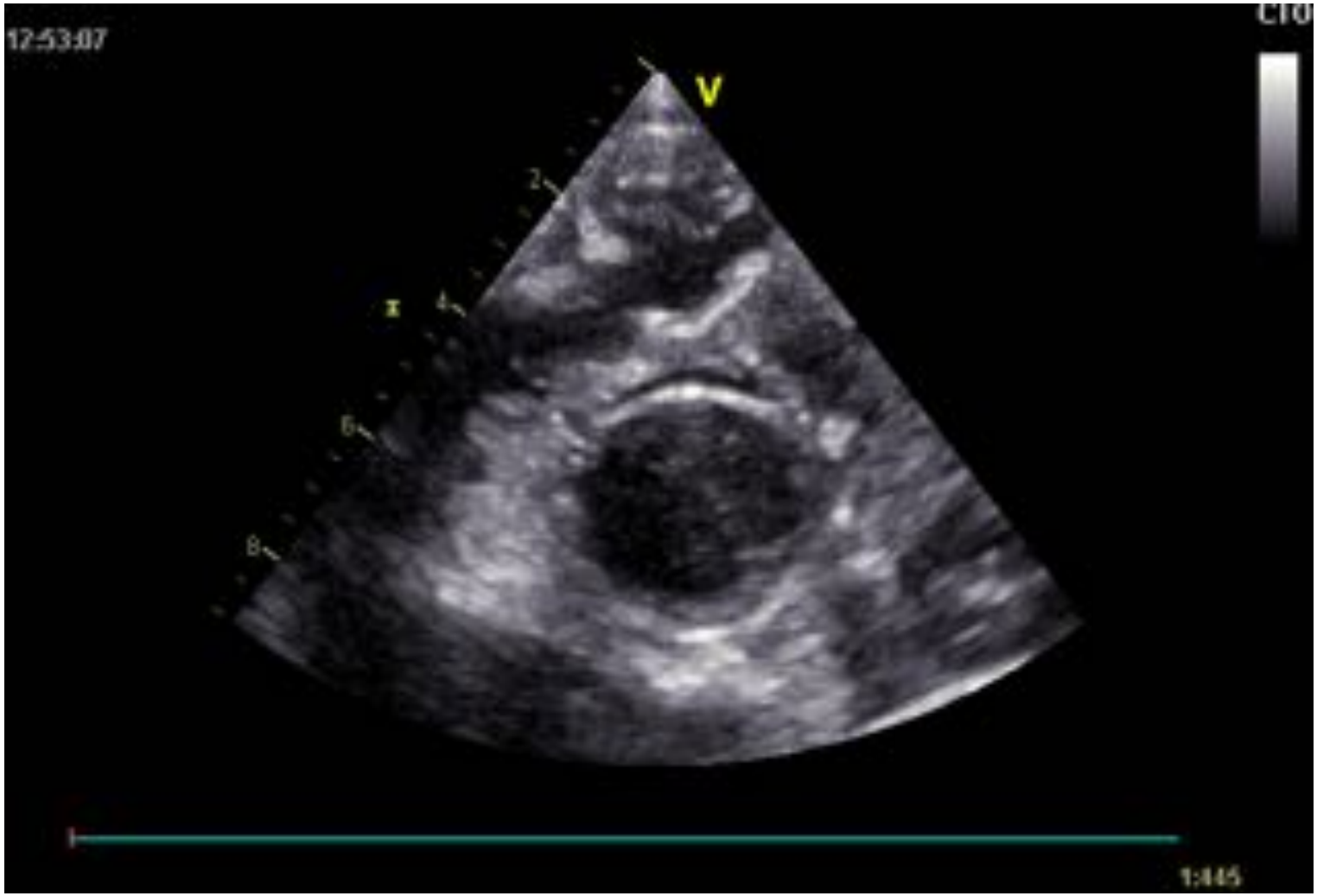
Léo

- 08/12/2012
- KONNO BENTALL.
- REMPLACEMENT DU TUBE VD/AP.
- DÉBRIDEMENT DES ABCÈS CARDIAQUES.

- Durée de CEC : 335 mn (quasi 6 h!!!!)
- Durée de clampage aortique : 146 mn + 23 mn

J10 post op

J10 post op



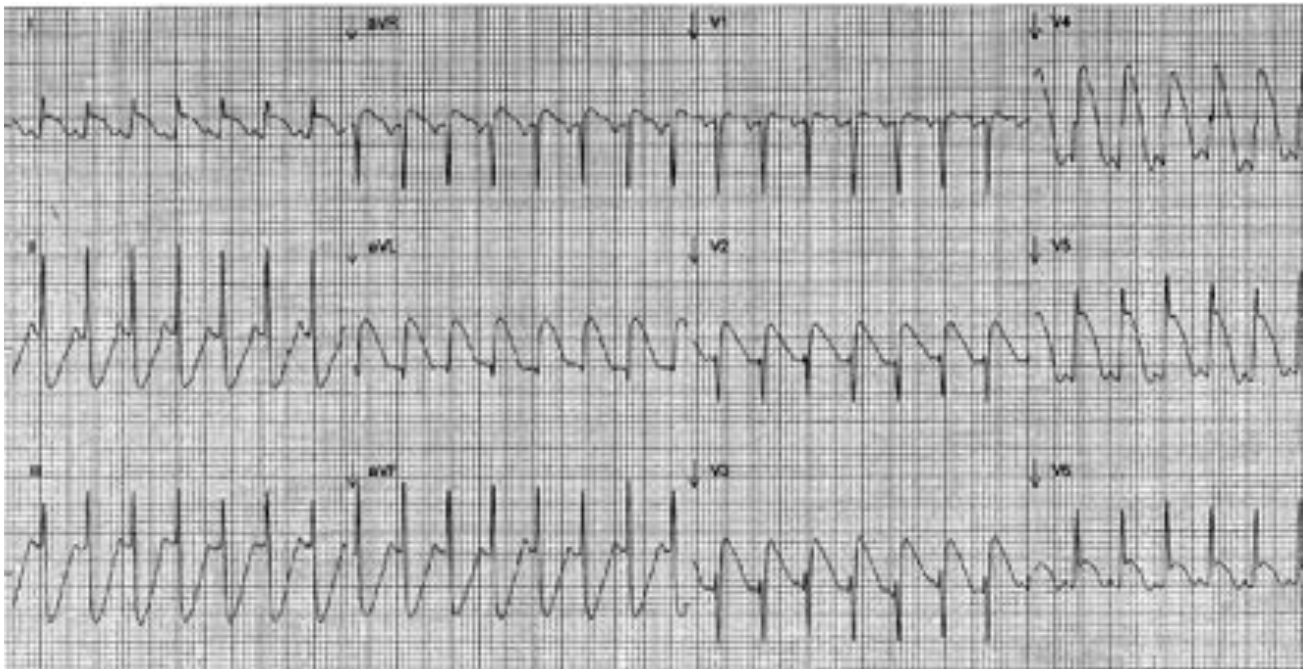
Léo

- réapparition des végétations pulmonaires à J10
- collection autour du tube de Ven Pro.

- Le scanner réalisé le 20/12/2012 montre des collections rétro-sternales probablement abcédées.

- **Inscription sur liste le 23.12.2012**
- **Transplantation cardiaque le 30/12/12**

Myocardites aiguës



Généralités

- Série autopsique: identification d'une myocardite dans 8,6% à 12% en cas de mort subite
- Evolution vers la CMD possible et non exceptionnelle

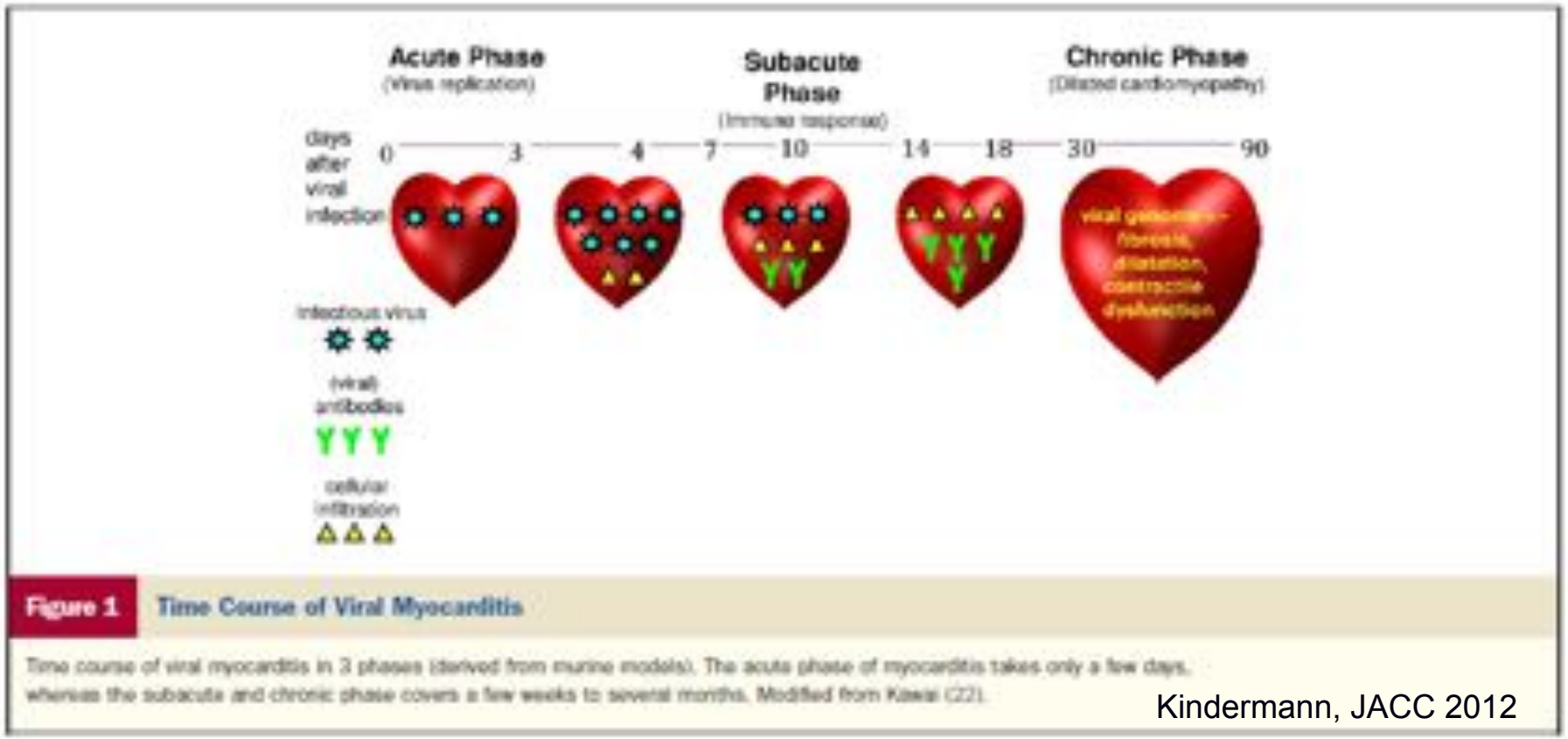


Figure 1 Time Course of Viral Myocarditis

Time course of viral myocarditis in 3 phases (derived from murine models). The acute phase of myocarditis takes only a few days, whereas the subacute and chronic phase covers a few weeks to several months. Modified from Kawai (22).

Kindermann, JACC 2012

Symptômes cliniques

- Syndrome pseudo-grippal
- Douleur thoracique
- **Dyspnée, détresse respiratoire (68%)**
- **Tachycardie (58%)**
- AEG, léthargie (39%)
- Hépatomégalie (36%)
- Fièvre (30%)
- **Choc cardiogénique** (Forme fulminante, 5 à 10 cas par millions d'habitants et par an)
- **Mort subite** (TDR ou TDC)
- Insuffisance cardiaque chronique

Mc Carthy , NEJM 2000
Freedman et al. Pediatrics 2007
Durani Y et al. AJEM 2009

Etiologies des myocardites

Table 1 Etiology of Myocarditis

Etiology	Subgroups Examples
Infectious	Bacterial: *Chlamydia, Corynebacterium diphtheria, Legionella, Mycobacterium tuberculosis, Mycoplasma, Staphylococcus, Streptococcus A, Streptococcus pneumoniae*
	Fungal: *Actinomyces, Aspergillus, Candida, Cryptococcus*
	Helminthic: *Echinococcus granulosus, Trichinella spiralis*
	Protozoal: *Toxoplasma gondii, Trypanosoma cruzi*
	Viral: Adenovirus, Echovirus, Enterovirus (e.g., Coxsackievirus), Herpes Viruses (Human Cytomegalovirus, Epstein-Barr virus, Human Herpesvirus 6), Human Immunodeficiency virus (HIV), Influenza A virus, Parvovirus B19
	Rickettsial: *Coxiella burnetti, Rickettsia typhi*
	Spirochetal: *Borrelia burgdorferi, Leptospira, Treponema pallidum*
Autoimmune diseases	Celiac disease, Churg-Strauss syndrome, Crohn's disease, dermatomyositis, giant cell myocarditis, hypereosinophilic syndrome, Kawasaki disease, lupus erythematosus, lymphofollicular myocarditis, rheumatoid arthritis, sarcoidosis, scleroderma, ulcerative colitis
Hypersensitivity reactions to drugs	Penicillin, ampicillin, cephalosporins, tetracyclines, sulfonamids, antiphlogistics, benzodiazepines, clozapine, loop and thiazide diuretics, methyldopa, smallpox vaccine, tetanus toxoid, tricyclic antidepressants
Toxic reactions to drugs	Amphetamines, anthracyclines, catecholamines, cocaine, cyclophosphamide, 5-fluorouracil, phenytoin, trastuzumab
Toxic	Ethanol
Others	Arsenic, copper, iron, radiotherapy, thyreotoxicosis

Kindermann et al. JACC 2012

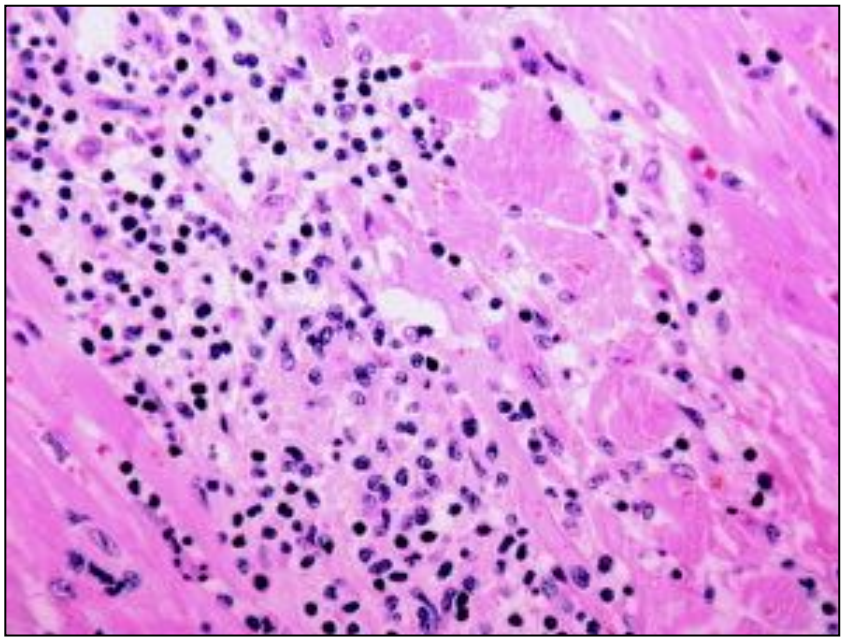
Clinique et traitement

- **Myocardite segmentaire focale:** Repos
- **Myocardite aiguë diffuse chez l'enfant**
  - Surveillance +/- assistance circulatoire (HNF)
  - Traitement d'attaque:
    - Immunomodulateurs, immunosuppresseurs, Anti-inflammatoire, immunoadsorption
    - Plutôt non chez l'adulte mais…
    - Quid de l'enfant?
- **Myocardite chronique active**
  - Discuter immunosupresseurs

Diagnostic difficile: Critères de Dallas

BEM Indication de classe I dans 2 situations:

- Tableau de myocardite fulminante
- Défaillance cardiaque d'étiologie inexpliquée évoluant depuis 2 semaines à 3 mois, VG dilaté, TV, BAV haut degré, ne répondant pas au traitement standard



Infiltration lymphocytaire
Signe de nécrose non ischémique

Cooper LT et al. Circulation 2007
Magnani JW et al. Circulation 2006

Problèmes des critères de Dallas

1986

- Myocardite avec atteinte hétérogène du myocarde -> Biopsies multiples > 5
- **Geste invasif**: mortalité 0,5%, complications 5%: perforation cardiaque, hémopéricarde, tamponnade
- Geste plus risqué chez le nourrisson
- Variabilité d'interprétation même entre experts
- « Goldstandard » mais discutée ++

Lake Louise Criteria: IRM

Trois séquences IRM contributives:

- 1. Œdème en T2
- 2. rehaussement précoce du myocarde
- 3. rehaussement tardif du myocarde

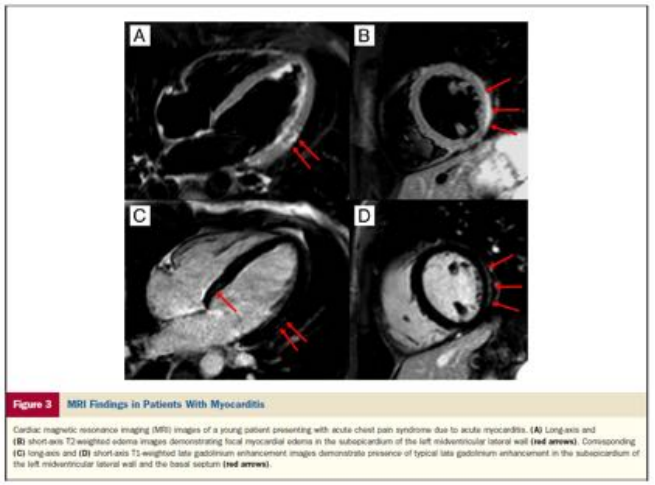


Figure 3 MRI Findings in Patients With Myocarditis

Cardiac magnetic resonance imaging (MRI) images of a young patient presenting with acute chest pain syndrome due to acute myocarditis. **(A)** Long-axis and **(B)** short-axis T2-weighted edema images demonstrating focal myocardial edema in the subepicardium of the left midventricular lateral wall **(red arrows)**. Corresponding **(C)** long-axis and **(D)** short-axis T1-weighted late gadolinium enhancement images demonstrate presence of typical late gadolinium enhancement in the subepicardium of the left midventricular lateral wall and the basal septum **(red arrows)**.

- Diagnostic positif si > 2 critères :
  - Hypersignal T2
  - Ratio Signal myocarde / muscle périph a
    injection de Gadolinium
  - Hypersignal en rehaussement tardif

- Refaire IRM à 1-2 semaines si:
  - 0 critère mais symptômes trop récents, forte suspicion clinique
  - 1 seul critère présent

Friedrich MG et al. JACC 2009

Traitement
ce qui est admis …

Traitement

- **Selon les guidelines**
- **Selon la classe fonctionnelle NYHA**
  - IEC
  - Diurétiques
  - B-bloquant
  - ARA II
- **Formes sévères: Réanimation**
  - **Traitement « agressif »**
  - **Assistance circulatoire** (> 60 à 80 % survivants et récupération ad integrum possible)
  - **Drogues Inotropes positives et héparine!**

Kindermann, et al., JACC 2012
Amabile et al. Heart 2006

Traitement
ce qui est discuté …

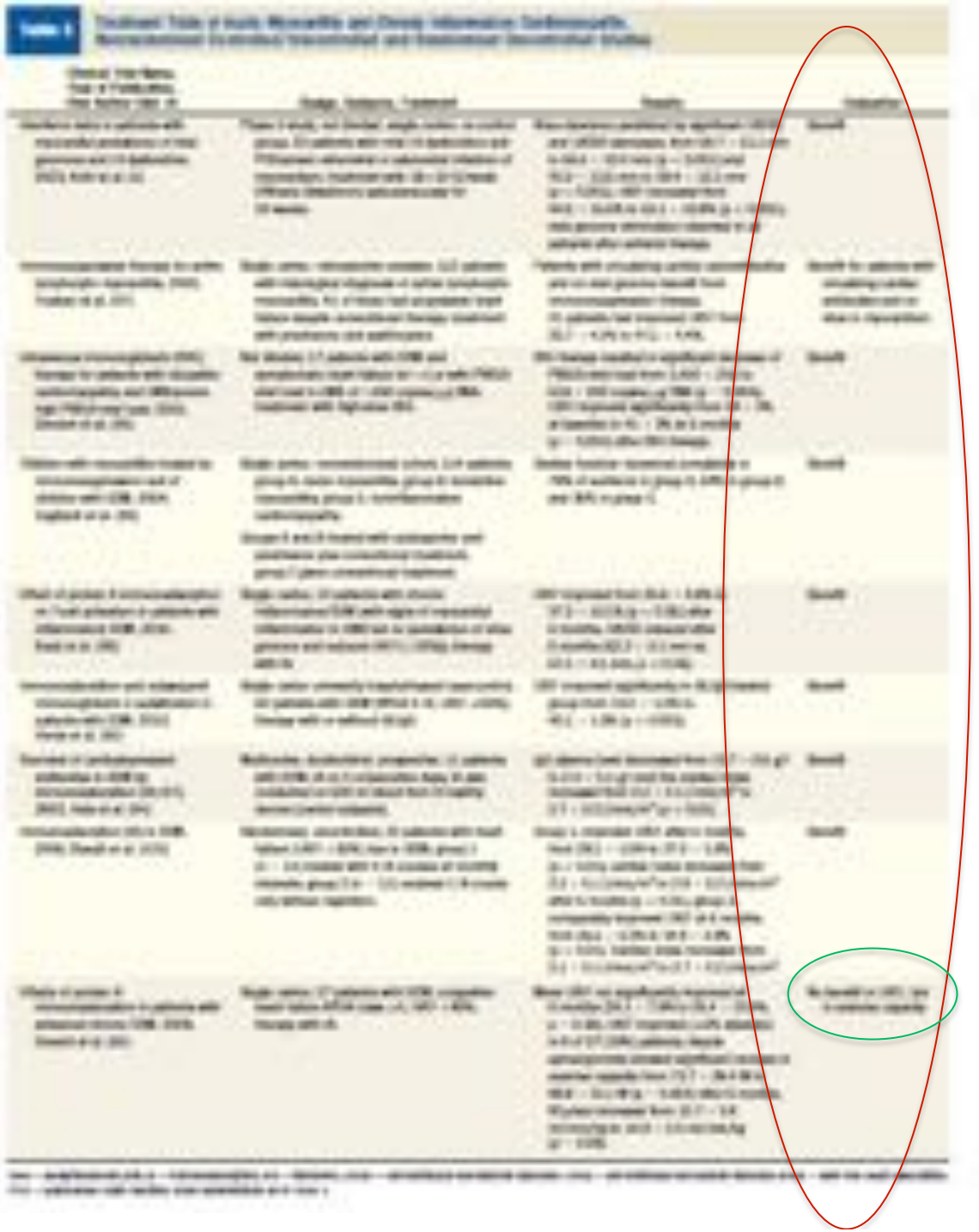
Immunoglobulines
Anti inflammatoires
Antiviraux
Immunosuppresseurs

Essais randomisés et contrôlés

Table 2 Treatment Trials of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy, Randomized Controlled Studies

Clinical Trial Name, Year of Publication, First Author (Ref. #)	Design, Subjects, Treatment	Results	Evaluation
Prednisone in idiopathic DCM, 1986, Fuentes et al. (90)	Single-center, prospective, randomized, placebo-controlled; 102 patients with idiopathic DCM with inflammatory features; treatment with prednisone or placebo.	Mean EF increased by 4.3 ± 1.6% in the prednisone group, compared to 0.1 ± 0.8% in the control group ($p < 0.004$).	Benefit
European study of epidemiology and treatment of inflammatory heart disease (ESETHID), 1999, Mahrholdt et al. (91)	Multicenter, double-blind, randomized, placebo-controlled, pooled-subgroup analysis; 162 patients with biopsy-proven acute or chronic myocarditis and LVEF <45%. Cytomegalovirus-induced myocarditis treated with hyperimmunoglobulin; Enterovirus-positive myocarditis treated with interferon alpha; Adenovirus-positive myocarditis treated with IgG and IgM immunoglobulin. Virus-negative myocarditis, considered autoimmune, treated with immunosuppressor therapy (prednisolone and azathioprine). All groups compared to placebo.	Inflammation was eliminated in 63% of patients in treatment group and 40% in placebo group.	No benefit
Interferon and thyroid hormones in the therapy of human myocarditis and idiopathic DCM, 1994, Wolf et al. (92).	Single-center, randomized, open-label, not blinded; pooled treatment group analysis; 38 patients with EMB-proven myocarditis or DCM; 12 patients treated conventionally, 13 treated with interferon-alpha and conventional treatment, and 13 with thyroxinmodulin and conventional treatment.	LVEF improved in 21 (81%) of 26 patients after interferon-alpha or thyroxinmodulin and in 8 (66%) of 12 conventionally treated patients ($p = 0.06$) at 2-year follow-up.	Benefit
Myocarditis treatment trial, 1998, Mason et al. (71)	Multicenter, randomized, controlled trial; 111 patients with myocarditis and LVEF <45%; conventional therapy alone (group 1); or combined immunosuppressive therapy with prednisone plus cyclosporine or azathioprine (group 2); pooled treatment group analysis.	No difference in survival between 2 groups ($p = 0.34$); mean change in LVEF at 28 weeks did not differ significantly between the 2 groups.	No benefit or harm
Immunomodulation therapy with IVIG in patients with chronic heart failure, 2001, Gullestad et al. (96)	Randomized, placebo-controlled, double-blind trial; 40 patients with chronic DCM or ICM. Therapy with IVIG vs. placebo. Primary endpoint LVEF change at 6 months.	IVIG, but not placebo, reduced markedly how to plasma levels of anti-inflammatory mediators IL-10, IL-1 receptor antagonist, and soluble TNF receptors. IVIG, but not placebo, induced significant increase in LVEF from 26 ± 8% to 31 ± 9% ($p < 0.01$).	Benefit at 6 months, not sustained at 12 months
Intravenous immune globulin in recent-onset dilated cardiomyopathy or myocarditis, 2001, McNamara et al. (82)	Multicenter, double-blinded, randomized, controlled study; 62 patients with recent-onset (6 months) heart failure and unexplained DCM. therapy with intravenous immune globulin vs. placebo.	Overall LVEF improved, 0.20 ± 0.08 to 0.41 ± 0.17 at 6 months ($p = 0.001$) and 0.43 ± 0.14 ($p < 0.001$ vs. baseline) at 12 months. Increase identical in patients given IVIG and patients given placebo.	No benefit
Immunosuppressive treatment of inflammatory dilated cardiomyopathy, 2003, Wojnicz R et al. (93)	Randomized, placebo-controlled, not blinded; 84 patients with DCM, symptoms >6 months, and increased HLA expression in myocardium; immunosuppressive therapy with prednisolone and azathioprine vs. placebo.	No significant differences in primary endpoint (composite of death, heart transplantation, and hospital readmission) between the 2 study groups (22.8% for immunosuppression, 20.0% for placebo). LVEF increased and LV systolic diameter decreased.	Equivocal benefit
Immunosuppressive therapy in patients with virus negative inflammatory cardiomyopathy (TIMIC study), 2003, Frustaci A et al. (94)	Randomized, double-blind, placebo-controlled; 85 patients with biopsy-proven virus negative inflammatory cardiomyopathy; prednisone and azathioprine for 6 months (group 1) or placebo (group 2).	Group 1, significantly improved LVEF and decreased LV dimensions. Group 2, more slowed improved LVEF.	Benefit

Essais non randomisés et/ou non contrôlés



Traitement

- Immunoglobulines chez l'adulte ?
  « NON »
  - idem que placebo

N= 62

Controlled Trial of Intravenous Immune Globulin in Recent-Onset Dilated Cardiomyopathy

Dennis M. McNamara, MD; Richard Holubkov, PhD; Randall C. Starling, MD; G. William Dec, MD; Evan Loh, MD; Guillermo Torre-Amione, MD; Alan Gass, MD; Karen Janosko, RN, MSN; Tammy Tokarczyk, RN, BSN; Paul Kessler, MD; Douglas L. Mann, MD; Arthur M. Feldman, MD, PhD; for the Intervention in Myocarditis and Acute Cardiomyopathy (IMAC) Investigators

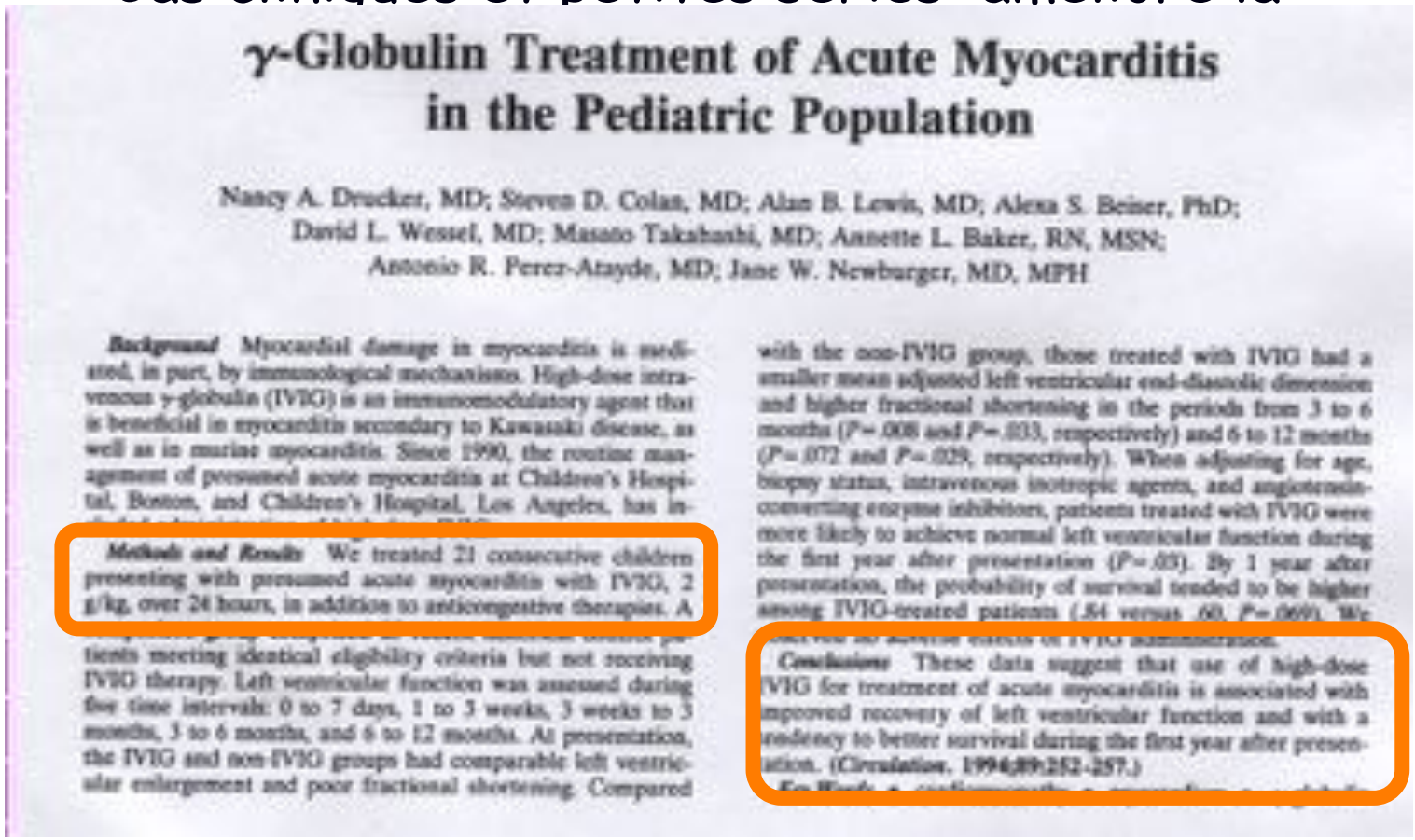
Background—This prospective placebo-controlled trial was designed to determine whether intravenous immune globulin (IVIG) improves left ventricular ejection fraction (LVEF) in adults with recent onset of idiopathic dilated cardiomyopathy or myocarditis.

Methods and Results—Sixty-two patients (37 men, 25 women; mean age ±SD 43.0±12.3 years) with recent onset (≤6 months of symptoms) of dilated cardiomyopathy and LVEF ≤0.40 were randomized to 2 g/kg IVIG or placebo. All underwent an endomyocardial biopsy before randomization, which revealed cellular inflammation in 16%. The primary outcome was change in LVEF at 6 and 12 months after randomization. Overall, LVEF improved from 0.25±0.08 to 0.41±0.17 at 6 months ($P<0.001$) and 0.42±0.14 ($P<0.001$ versus baseline) at 12 months. The increase was virtually identical in patients receiving IVIG and those given placebo (6 months: IVIG 0.14±0.12, placebo 0.14±0.14; 12 months: IVIG 0.16±0.12, placebo 0.15±0.16). Overall, 31 (56%) of 55 patients at 1 year had an increase in LVEF ≥0.10 from study entry, and 20 (36%) of 56 normalized their ejection fraction (≥0.50). The transplant-free survival rate was 92% at 1 year and 88% at 2 years.

Conclusions—These results suggest that for patients with recent-onset dilated cardiomyopathy, IVIG does not augment the improvement in LVEF. However, in this overall cohort, LVEF improved significantly during follow-up, and the short-term prognosis remains favorable. **(*Circulation*. 2001;103:2254-2259.)**

Traitement

- Immunoglobulines chez l'enfant? « NON mais.. »
  - pas d'étude randomisée
  - Cas cliniques et petites séries: améliore la



γ-Globulin Treatment of Acute Myocarditis in the Pediatric Population

Nancy A. Drucker, MD; Steven D. Colan, MD; Alan B. Lewis, MD; Alexa S. Beiser, PhD; David L. Wessel, MD; Masato Takahashi, MD; Annette L. Baker, RN, MSN; Antonio R. Perez-Atayde, MD; Jane W. Newburger, MD, MPH

Background Myocardial damage in myocarditis is mediated, in part, by immunological mechanisms. High-dose intravenous γ-globulin (IVIG) is an immunomodulatory agent that is beneficial in myocarditis secondary to Kawasaki disease, as well as in murine myocarditis. Since 1990, the routine management of presumed acute myocarditis at Children's Hospital, Boston, and Children's Hospital, Los Angeles, has in-

Methods and Results We treated 21 consecutive children presenting with presumed acute myocarditis with IVIG, 2 g/kg, over 24 hours, in addition to anticongestive therapies. A

tients meeting identical eligibility criteria but not receiving IVIG therapy. Left ventricular function was assessed during five time intervals: 0 to 7 days, 1 to 3 weeks, 3 weeks to 3 months, 3 to 6 months, and 6 to 12 months. At presentation, the IVIG and non-IVIG groups had comparable left ventricular enlargement and poor fractional shortening. Compared

with the non-IVIG group, those treated with IVIG had a smaller mean adjusted left ventricular end-diastolic dimension and higher fractional shortening in the periods from 3 to 6 months ($P=.008$ and $P=.033$, respectively) and 6 to 12 months ($P=.072$ and $P=.029$, respectively). When adjusting for age, biopsy status, intravenous inotropic agents, and angiotensin-converting enzyme inhibitors, patients treated with IVIG were more likely to achieve normal left ventricular function during the first year after presentation ($P=.03$). By 1 year after presentation, the probability of survival tended to be higher among IVIG-treated patients (.84 versus .60, $P=.069$). We

Conclusions These data suggest that use of high-dose IVIG for treatment of acute myocarditis is associated with improved recovery of left ventricular function and with a tendency to better survival during the first year after presentation. (*Circulation*. 1994;89:252-257.)

Traitement

- Immunoglobulines pour myocardite et encephalite: « OUI? »

Bhatt 2012

Methods	Quasi-randomised (based on day of the week patients were hospitalised); unblinded; no placebo; all survivors appeared to complete the study
Participants	83 children (range 2 months to 12 years of age) with acute viral infection, fever for < 2 weeks, cerebrospinal fluid pleocytosis, clinical evidence of encephalitis, onset of heart failure after viral illness started, LVEF < 40%
Interventions	IVIG 400 mg/kg daily for 5 consecutive days
Outcomes	Survival; LVEF at discharge
Notes	Funding: none recorded Language of publication: English

Cochrane Review 2015

Traitement

- AINS et colchicine chez l'adulte ?
  « NON » (Oui pour péricardite…)

- Antiviraux?
- « ? »

Interferon-β Treatment Eliminates Cardiotropic Viruses and Improves Left Ventricular Function in Patients With Myocardial Persistence of Viral Genomes and Left Ventricular Dysfunction

Uwe Kühl, PhD; Matthias Pauschinger, MD; Peter Lothar Schwimmbeck, MD; Bettina Seeberg; Conny Lober, MD; Michel Noutsias, MD; Wolfgang Poller, MD; Heinz-Peter Schultheiss, MD

Background—Viral infections are important causes of myocarditis and may induce cardiac dysfunction and finally lead to dilated cardiomyopathy. We investigated whether interferon (IFN)-β therapy is safe and may achieve virus clearance and prevent deterioration of left ventricular (LV) function in patients with myocardial virus persistence.

Methods and Results—In this phase II study, 22 consecutive patients with persistence of LV dysfunction (history of symptoms, 44±27 months) and polymerase chain reaction–proven enteroviral or adenoviral genomes were treated with 18×10^6 IU/week IFN-β (Beneferon) subcutaneously for 24 weeks. Histological and immunohistological analysis of endomyocardial biopsies was used to characterize myocardial inflammation. LV diameters and ejection fraction were assessed by echocardiography and angiography, respectively. During the treatment period, IFN-β was well tolerated by all patients. No patient deteriorated. Clearance of viral genomes was observed in 22 of 22 of patients after antiviral therapy. Virus clearance was paralleled by a significant decrease of LV end diastolic and end systolic diameters, decreasing from 59.7±11.1 to 56.5±10.0 mm ($P<0.001$) and 43.2±13.6 to 39.4±12.1 mm ($P<0.001$), respectively. LV ejection fraction increased from 44.6±15.5% to 53.1±16.8% ($P<0.001$).

Conclusions—At 6 months, IFN-β treatment was safe in patients with myocardial enteroviral or adenoviral persistence and LV dysfunction and resulted in elimination of viral genomes (22 of 22 patients) and improved LV function (15 of 22 patients). (***Circulation.* 2003;107:2793-2798.**)

Traitement

- Immunosuppresseurs chez l'adulte?

« peut être »

  - Prednisone, ciclosporine, azathioprine
  - Effets non significatifs pour certains, bénéfiques pour d'autres sur fonction VG et NYHA

A CLINICAL TRIAL OF IMMUNOSUPPRESSIVE THERAPY FOR MYOCARDITIS

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Abstract *Background. Myocarditis is a serious disorder, and treatment options are limited. This trial was designed to determine whether immunosuppressive therapy improves left ventricular function in patients with myocarditis.*

Methods. We randomly assigned 111 patients with a histopathological diagnosis of myocarditis and a left ventricular ejection fraction of less than 0.45 to receive conventional therapy alone or combined with a 24-week regimen of immunosuppressive therapy. Immunosuppressive therapy consisted of prednisone with either cyclosporine or azathioprine. The primary outcome measure was a change in the left ventricular ejection fraction at 28 weeks.

Results. In the group as a whole, the mean (±SE) left ventricular ejection fraction improved from 0.25±0.01 at base line to 0.34±0.02 at 28 weeks ($P<0.001$). The mean change in the left ventricular ejection fraction at 28 weeks did not differ significantly between the group of patients who received immunosuppressive therapy (a gain of 0.10; 95 percent confidence interval, 0.07 to 0.12) and the control group (a gain of 0.07; 95 percent confidence interval, 0.03 to 0.12). A higher left ventricular ejection fraction at base line, less intensive conventional drug therapy at base line, and a shorter duration of disease, but not the treatment assignment, were positive independent predictors of the left ventricular ejection fraction at week 28. There was no significant difference in survival between the two groups ($P=0.96$). The mortality rate for the entire group was 20 percent at 1 year and 56 percent at 4.3 years. Features suggesting an effective inflammatory response were associated with less severe initial disease.

Conclusions. Our results do not support routine treatment of myocarditis with immunosuppressive drugs. Ventricular function improved regardless of whether patients received immunosuppressive therapy, but long-term mortality was high. (N Engl J Med 1995;333:269-75.)

Traitement

- Immunosuppresseurs chez l'enfant?
  « OUI? »
  - Améliore fonction VG, diminue troubles du rythme

    Chan KY et al. JACC 1991

    Balaji S et al. Br Heart J 1994

    Camargo PR et al. Pediatr Cardiol 1995

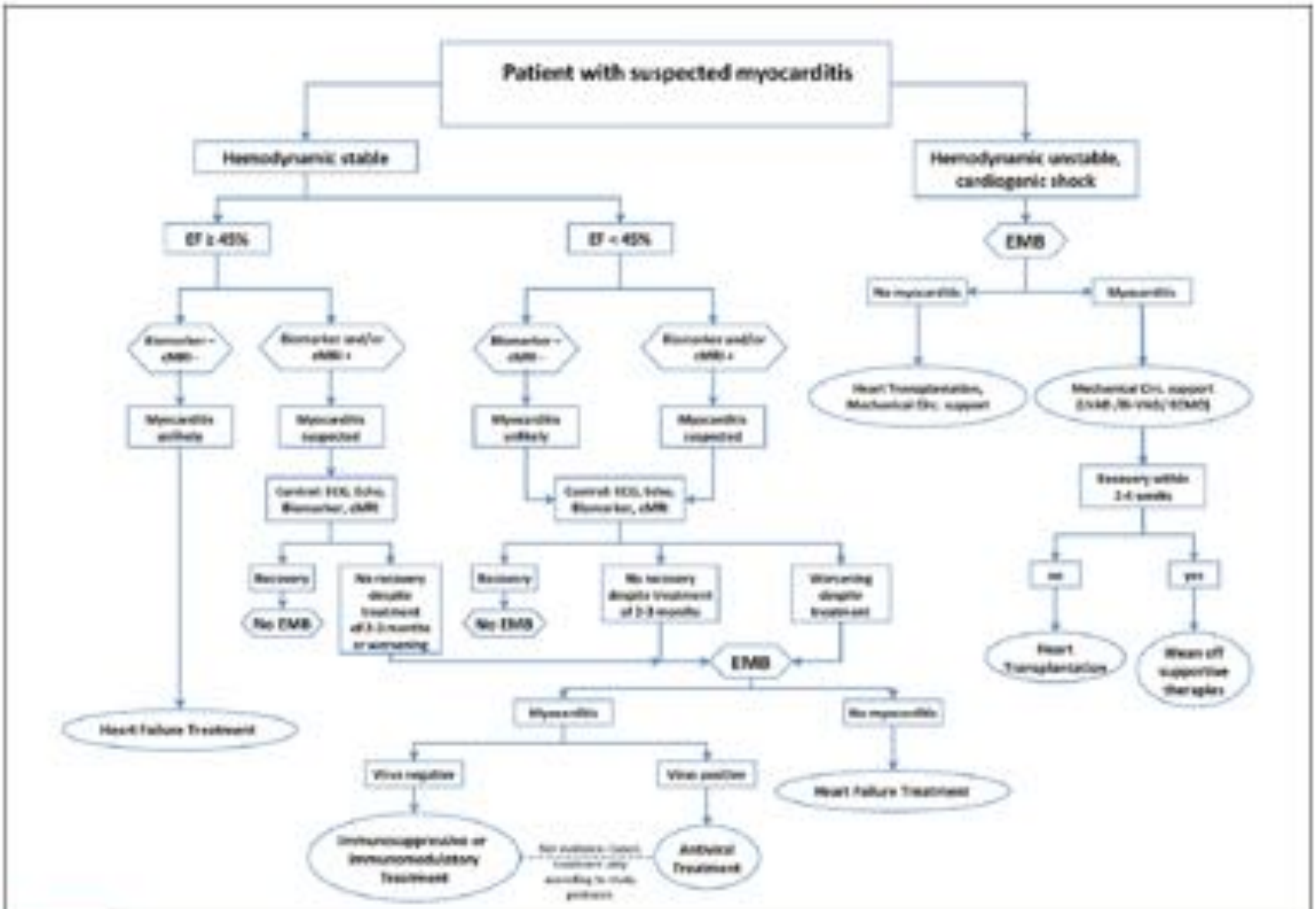

Figure 5 Proposed Diagnostic and Therapeutic Algorithm for Suspected Myocarditis

Proposed diagnostic and therapeutic algorithm for patients with suspected acute myocarditis considering biomarkers, cardiac magnetic resonance imaging (CMRI), and endomyocardial biopsy (EMB). BiVAD = biventricular assist device; Circ. = circulatory; ECMO = extracorporeal membrane oxygenation; LV = left ventricular; LVAD = left ventricular assist device.

Kindermann et al. JACC 2012

Pronostic

- Bon pronostic
  - Myocardite active
  - Fonction VG préservée
- Myocardite fulminate
  - Très bon pronostic à long terme
  - Complète récupération possible
- Mauvais pronostic
  - Dysfonction VD, PAP élevée, syncope, PA basse, Fc élevée, QRs > 120 msec…