Quoi de neuf sur les cardiomyopathies en 2021

Amicale des Cardiologues de la Côte d'Azur
18 Septembre 2021

Aix*Marseille université
FACULTÉ DE MÉDECINE DE MARSEILLE

TRAITÉ
DE
LA STRUCTURE
DU CŒUR,
DE SON ACTION,
ET
DE SES MALADIES.

Par M. SENAC, Médecin Consultant du Roy.

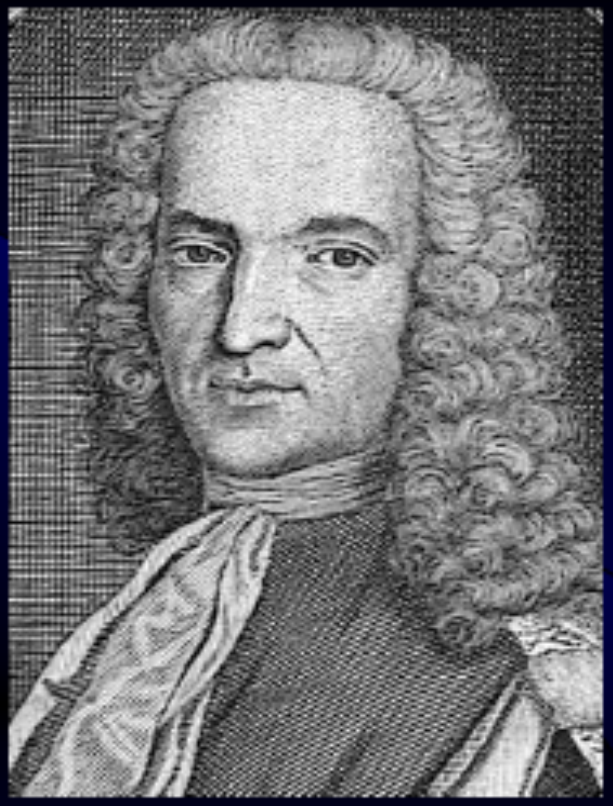
TOME PREMIER.

A PARIS,

Chez BRIASSON, rue Saint Jacques à la Science, & à l'Ange Gardien.

M. DCC. XLIX.

AVEC APPROBATION ET PRIVILEGE DU ROY.



Inflammation and abscesses of the heart muscle ARE VAGUE, because they are DIFFICULT TO RECOGNIZE. And if we have recognized it, can we treat it more effectively?

Jean-Baptiste Senac

Traite de la structure du coeur, de son action et des ses maladies, 1772

TABLE 1 Recapitulation of the Classification Systems for Cardiomyopathies in the Last 50 Years

Year	Definitions/Classifications	References
1956	Myocardial diseases classified as myocarditis *(inflammatory heart muscle disease)*, and myocardiosis *(other heart muscle diseases)*.	Blankerhorn and Gall (71)
1957	The term cardiomyopathy proposed for *uncommon, noncoronary heart muscle diseases*.	Bridgen (72)
1972	Cardiomyopathy described as *myocardial diseases of unknown origin*, and first classification proposed as *dilated, hypertrophic, and restrictive (or obliterative) cardiomyopathy*.	Goodwin and Oakley (73)
1980	WHO-ISFC adopts Goodwin and Oakley classification, and defines cardiomyopathies as *myocardial diseases of unknown etiology*. WHO-ISFC adds specific heart muscle diseases *(cause of myocardial affliction known)* to the classification.	Report of the WHO/ISFC Task Force on the Definition and Classification of Cardiomyopathies (74)
1996	WHO-ISFC updates its classification of cardiomyopathies (*diseases of myocardium associated with myocardial dysfunction)*. The update includes *arrhythmogenic right ventricular cardiomyopathy* and *unclassified cardiomyopathy*, but excludes specific heart muscle disease.	Richardson et al. (75)
1998	ISFC becomes WHF	
2006	AHA defines cardiomyopathies as *diseases of myocardium associated with mechanical and/or electrical dysfunction, which usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilation, due to a variety of causes that frequently are genetic*, classified as primary or secondary. Presents first visionary attempt to classify primary cardiomyopathy by genetic origin (genetic, acquired, or mixed)	Maron et al. (1)
2008	ESC defines cardiomyopathies as *myocardial disorder in which the heart muscle was structurally and functionally abnormal*. Classified dilated, hypertrophic, restrictive, arrhythmogenic right ventricular, or unclassified cardiomyopathy subtypes as familial/genetic and nonfamilial/nongenetic. Maintained the importance of phenotype preceding genetic classification for clinical practice.	Elliott et al. (2)
2013	WHF-MOGE(S) nosology proposes a descriptive genotype-phenotype nosology system.	Arbustini et al. (54,55)

TABLE 1 Recapitulation of the Classification Systems for Cardiomyopathies in the Last 50 Years

Cardiomyopathy: Definition

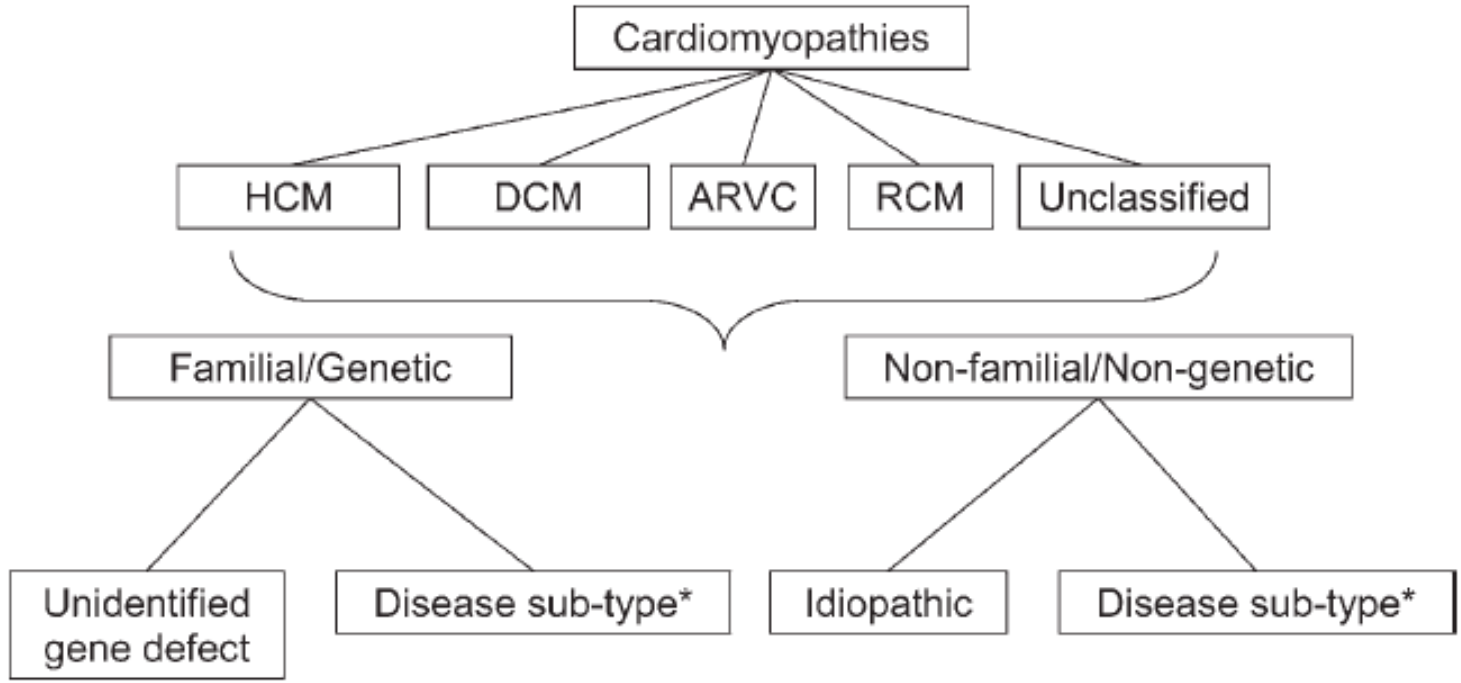
"A myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease sufficient to cause the observed myocardial abnormality."

ESC Working Group on Myocardial Pericardial Diseases (Elliott P et al. EHJ 2007)

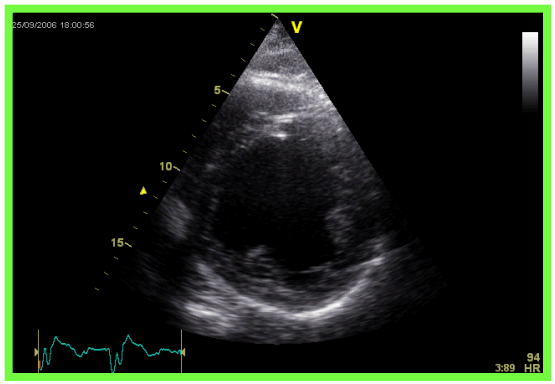
European Heart Journal (2008) **29**, 270–276
doi:10.1093/eurheartj/ehm342

ESC REPORT

Classification of the cardiomyopathies: a position statement from the european society of cardiology working group on myocardial and pericardial diseases

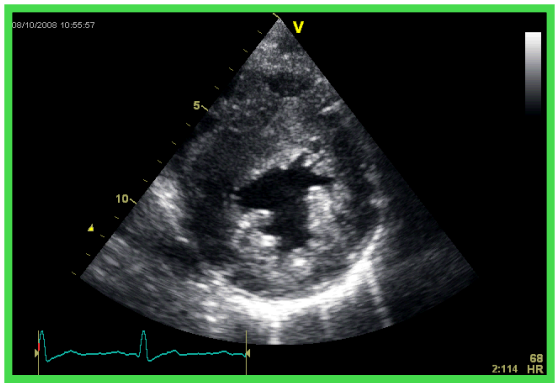


Types de cardiomyopathies



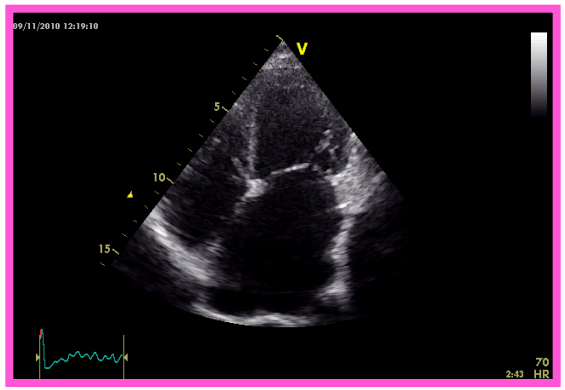
CMD

Cardiomyopathie dilatée
Cardiomyopathie hypocinétique

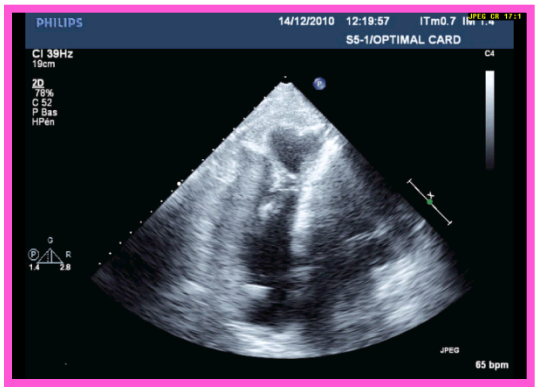


CMH

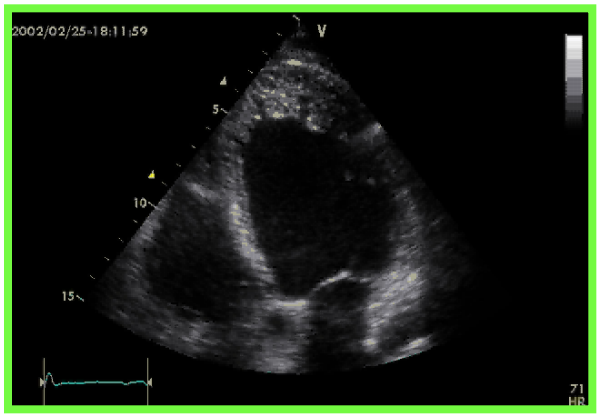
Cardiomyopathie hypertrophique



CMR



DVDA



Autres ???

ESC Position Statement

Table I Examples of different diseases that cause cardiomyopathies

	HCM	DCM	ARVC	RCM	Unclassified
Familial	Familial, unknown gene Sarcomeric protein mutations ß myosin heavy chain Cardiac myosin binding protein C Cardiac troponin I Troponin-T α-tropomyosin Essential myosin light chain Regulatory myosin light chain Cardiac actin α-myosin heavy chain Titin Troponin C	Familial, unknown gene Sarcomeric protein mutations (see HCM) Z-band Muscle LIM protein TCAP Cytoskeletal genes Dystrophin Desmin Metavinculin Sarcoglycan complex CRYAB Epicardin	Familial, unknown gene Intercalated disc protein mutations Plakoglobin Desmoplakin Plakophilin 2 Desmoglein 2 Desmocollin 2 Cardiac ryanodine receptor (RyR2) Transforming growth factor-β3 (TGFβ3)	Familial, unknown gene Sarcomeric protein mutations Troponin I (RCM +/− HCM) Essential light chain of myosin Familial amyloidosis Transthyretin (RCM + neuropathy) Apolipoprotein (RCM + nephropathy) Desminopathy Pseuxanthoma elasticum Haemochromatosis Anderson–Fabry disease Glycogen storage disease	Left ventricular non-compaction Barth syndrome Lamin A/C ZASP α-dystrobrevin
Non-familial	Obesity Infants of diabetic mothers Athletic training Amyloid (AL/prealbumin)	Myocarditis (infective/toxic/immune) Kawasaki disease Eosinophilic (Churg Strauss syndrome) Viral persistence Drugs Pregnancy Endocrine Nutritional — thiamine, carnitine, selenium, hypophosphataemia, hypocalcaemia Alcohol Tachycardiomyopathy	Inflammation?	Amyloid (AL/prealbumin) Scleroderma Endomyocardial fibrosis Hypereosinophilic syndrome Idiopathic Chromosomal cause Drugs (serotonin, methysergide, ergotamine, mercurial agents, busulfan) Carcinoid heart disease Metastatic cancers Radiation Drugs (anthracyclines)	Tako Tsubo cardiomyopathy

ARVC, arrhythmogenic right ventricular cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; RCM, restrictive cardiomyopathy.

ESC Position Statement: HCM

- Familial, unknown gene
- Sarcomeric protein mutations
  - β-myosin heavy chain
  - Cardiac myosin binding protein C
  - Cardiac troponin I
  - Troponin-T
  - α-tropomyosin
  - Essential myosin light chain
  - Regulatory myosin light chain
  - Cardiac actin
  - α-myosin heavy chain
  - Titin
  - Troponin C
  - Muscle LIM protein
- Glycogen storage disease (e.g. Pompe; PRKAG2, Forbes', Danon)
- Lysosomal storage diseases (e.g. Anderson–Fabry, Hurler's)
- Disorders of fatty acid metabolism
- Carnitine deficiency
- Phosphorylase B kinase deficiency
- Mitochondrial cytopathies
- Syndromic HCM
  - Noonan's syndrome
  - LEOPARD syndrome
  - Friedreich's ataxia
  - Beckwith–Wiedermann syndrome
  - Swyer's syndrome
- Other
  - Phospholamban promoter
  - Familial amyloid

ESC Position Statement: HCM

- Familial, unknown gene
- Sarcomeric protein mutations
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  - Cardiac myosin binding protein C
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Quoi de neuf sur les cardiomyopathies ?

1. **Les centres de Cardiomyopathies**

2. **Cardiomyopathies hypertrophiques**

3. **Amylose**

4. **Non compaction ventriculaire gauche**

Quoi de neuf sur les cardiomyopathies ?

1. *Les centres de Cardiomyopathies*
2. **Cardiomyopathies hypertrophiques**
3. **Amylose**
4. **Non compaction ventriculaire gauche**

C.H.U. TIMONE
POLE CARDIOVASCULAIRE ET THORACIQUE
UNITE / VALVULOPATHIES ET INSUFFISANCE CARDIAQUE

CENTRE DE COMPETENCE des CARDIOMYOPATHIES

(CCC)

10 ans d'activité

Hôpitaux Universitaires de Marseille | ap hm

Aix*Marseille université

FACULTÉ DE MÉDECINE DE MARSEILLE

Intérêt des centres de Cardiomyopathies

CENTRE DE COMPETENCE DES CARDIOMYOPATHIES

L' équipe pluridisciplinaire

Service de **Cardiologie:**

- **Pr Gilbert HABIB**
- **Dr Nicolas MICHEL,** Cardiologie, Echocardiographie
- **Dr Hélène MARTEL,** Cardiologie, Echocardiographie
- **Dr Flora LAVAGNA,** Cardiologie, Echocardiographie
- **Dr Jason VEYRIER,** Cardiologie, Echocardiographie
- **Dr Ludivine SABY,** Cardiologue, Echocardiographie
- **Dr Anne-Claire CASALTA,** Cardiologie, Echocardiographie
- **Dr Blandine SIMONNET,** Cardiologie, Echocardiographie
- **Josiane ELLOH,** IDE du CCC
- **Ludivine THIERRY,** IDE du CCC
- **Marina AGEN,** Ingénieur de Recherche du CCC
- **Marine Mony MOK, Axel RANCUREL,** Secrétariat du CCC

Service de **Génétique médicale :**

- **Pr Karine NGUYEN,** Service de Génétique clinique
- **Pr Martin KRAHN,** laboratoire de Génétique moléculaire
- **Pr Nicolas LEVY,** chef de service
- **Emilie CONSOLINO,** Conseillère en Génétique
- **Brigitte JARRET,** Psychologue
- **Roberto VITIELLO,** IDE
- **Florence PALLAVICCINI,** Secrétariat

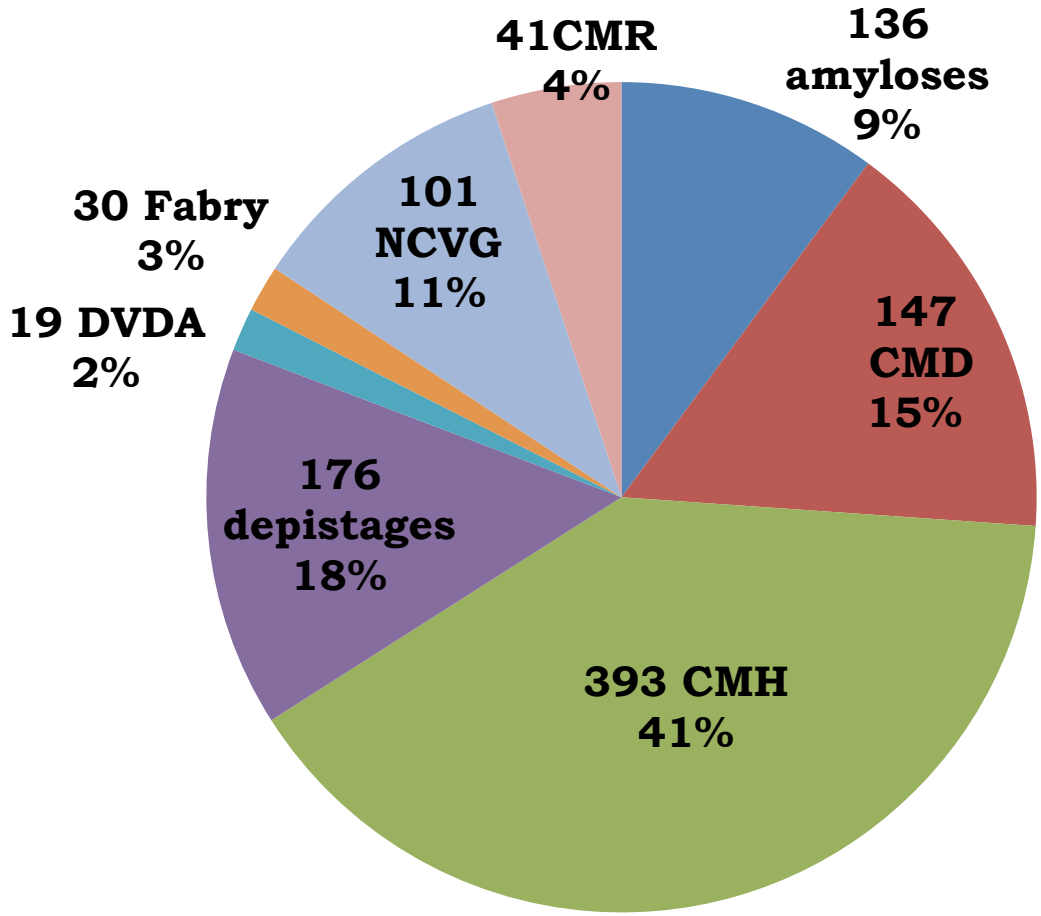
Pôle **Imagerie:**

- **Pr Alexis JACQUIER,** Radiologie
- **Dr Pierre-Antoine BARRAL,** Radiologie

Centre des Cardiomyopathies de Marseille

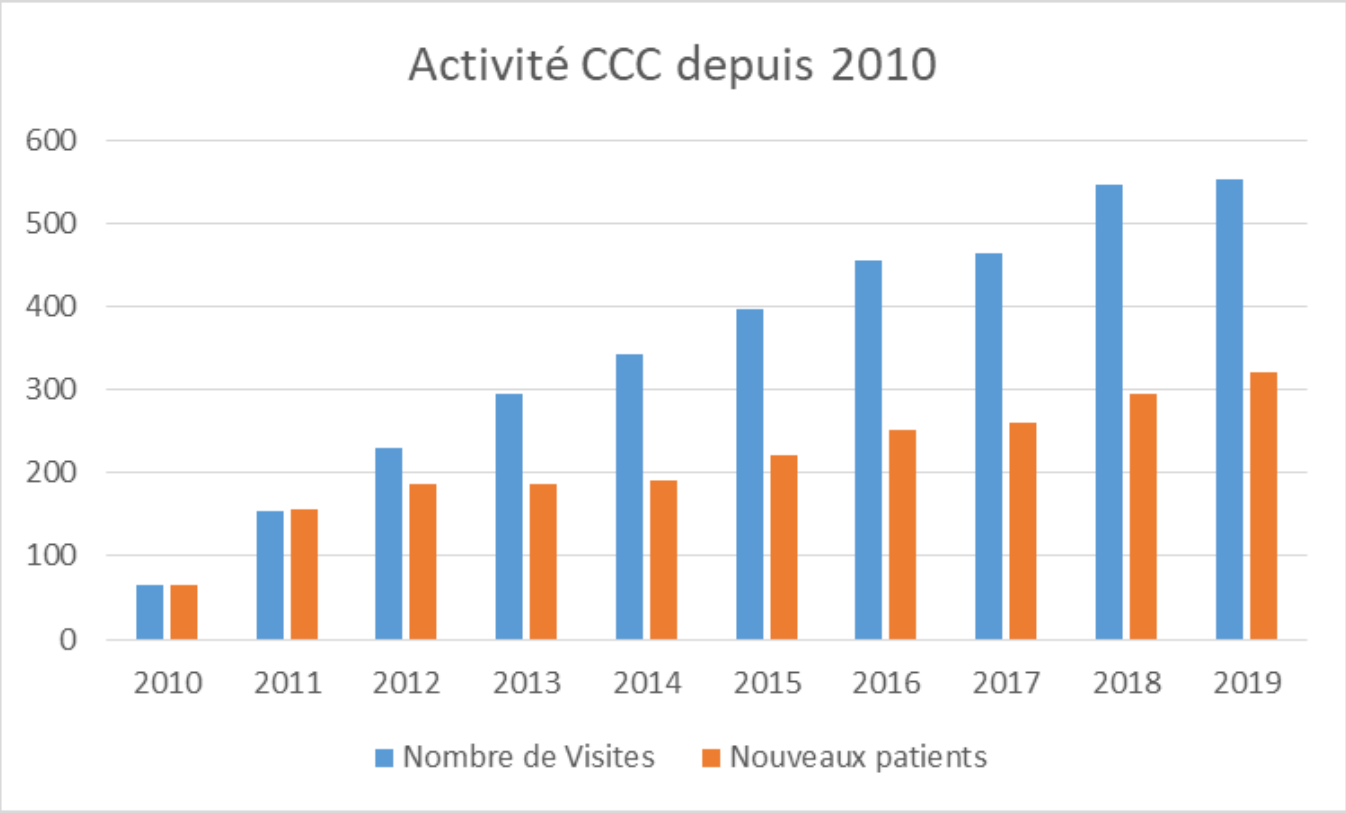
Répartition:
(Depuis Avril 2010)

Total: 1519 patients



CENTRE DE COMPETENCE DES CARDIOMYOPATHIES
Activité

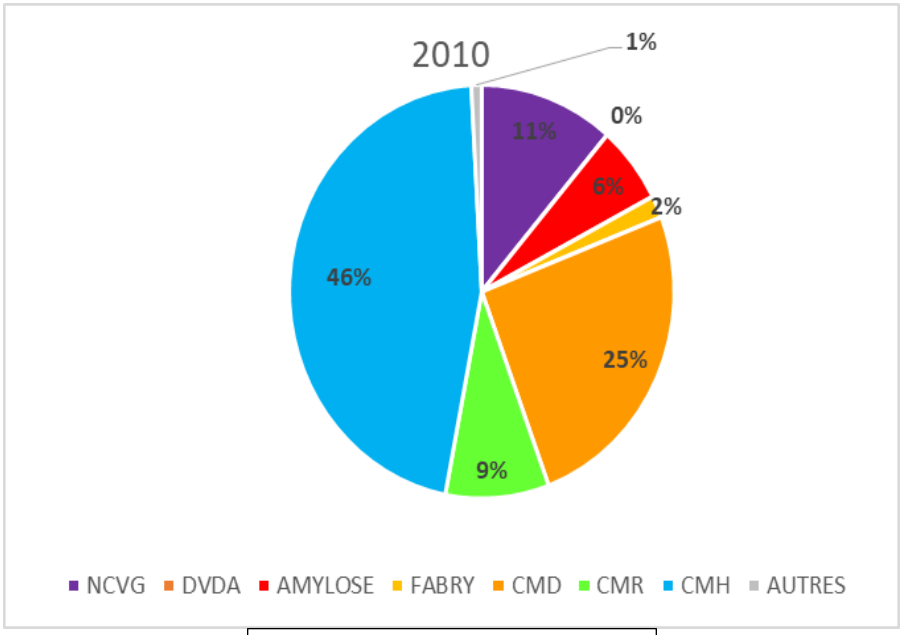
Depuis Avril 2010, l'activité du centre a considérablement augmenté
3501 Visites dont **2134** nouveaux patients



CENTRE DE COMPETENCE DES CARDIOMYOPATHIES

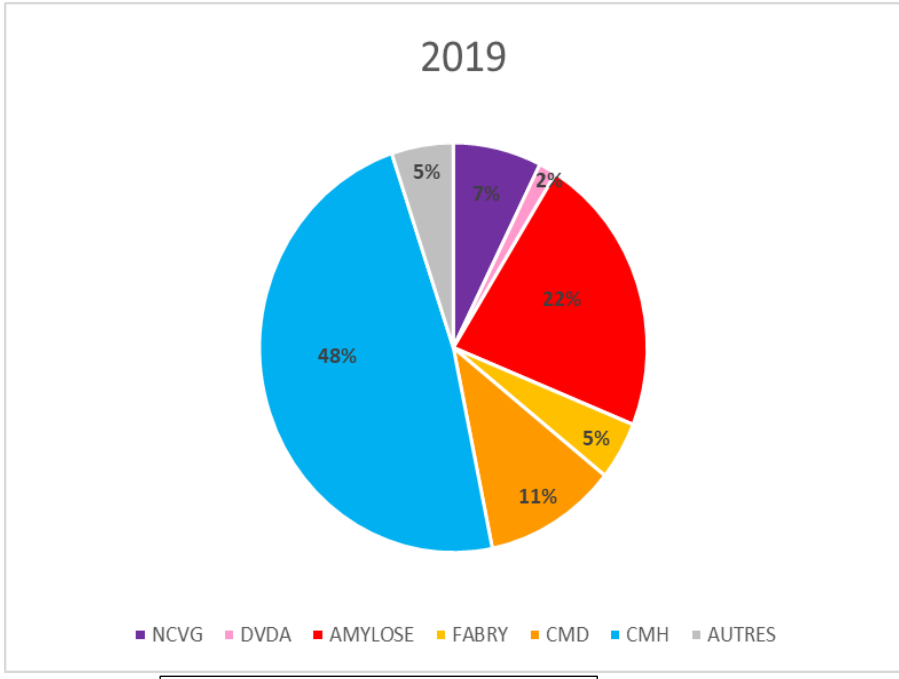
Activité

Répartition des motifs de consultations dans le CCC depuis 2010:



46% CMH
25% CMD
11% NCVG
6% Amylose
2% Maladie de Fabry

CMH 1er motif de Cs
Causes rares de CM: amylose et Fabry en augmentation



48% CMH
11% CMD
7% NCVG
22% Amylose
5% Maladie de Fabry

CENTRE DE COMPETENCE DES CARDIOMYOPATHIES
Recherche et Publications

European Journal of Heart Failure Advance Access published December 29, 2010

European Journal of Heart Failure
doi:10.1093/eurjhf/hfq225

Isolated left ventricular non-compaction in adults: clinical and echocardiographic features in 105 patients. Results from a French Registry

Gilbert Habib[1]*, Philippe Charron[2], Jean-Christophe Eicher[3], Roch Giorgi[4,5], Erwan Donal[6], Thierry Laperche[7], Dominique Boulmier[6], Cécile Pascal[8], Damien Logeart[9], Guillaume Jondeau[10], and Alain Cohen-Solal[9] On behalf of the Working Groups 'Heart Failure and Cardiomyopathies' and 'Echocardiography' of the French Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2017) 0, 1–32
doi:10.1093/ehjci/jex034

Multimodality imaging in restrictive cardiomyopathies: an EACVI expert consensus document

In collaboration with the 'Working Group on myocardial and pericardial diseases' of the European Society of Cardiology

Endorsed by the Indian Academy of Echocardiography

Gilbert Habib[1,2]*, Chiara Bucciarelli-Ducci[3], Alida L.P. Caforio[4], Nuno Cardim[5], Philippe Charron[6,7], Bernard Cosyns[8], Aurélie Dehaene[9], Genevieve Derumeaux[10], Erwan Donal[11], Marc R. Dweck[12], Thor Edvardsen[13,14], Paola Anna Erba[15],

CLINICAL GENETICS An International Journal of Genetics, Molecular and Personalized Medicine

Targeted panel sequencing and allelic spectrum in 95 unrelated adults with left ventricular non-compaction

Circulation: Genomic and Precision Medicine

RESEARCH LETTER

Whole Exome Sequencing Reveals a Large Genetic Heterogeneity and Revisits the Causes of Hypertrophic Cardiomyopathy

Experience of a Multicentric Study of 200 French Patients

Karine Nguyen, MD, PhD et al

Hypertrophic cardiomyopathy (HCM), the most common hereditary heart disease, is autosomal dominant with incomplete penetrance and variability.

Quoi de neuf sur les cardiomyopathies ?

1. **Les centres de Cardiomyopathies**

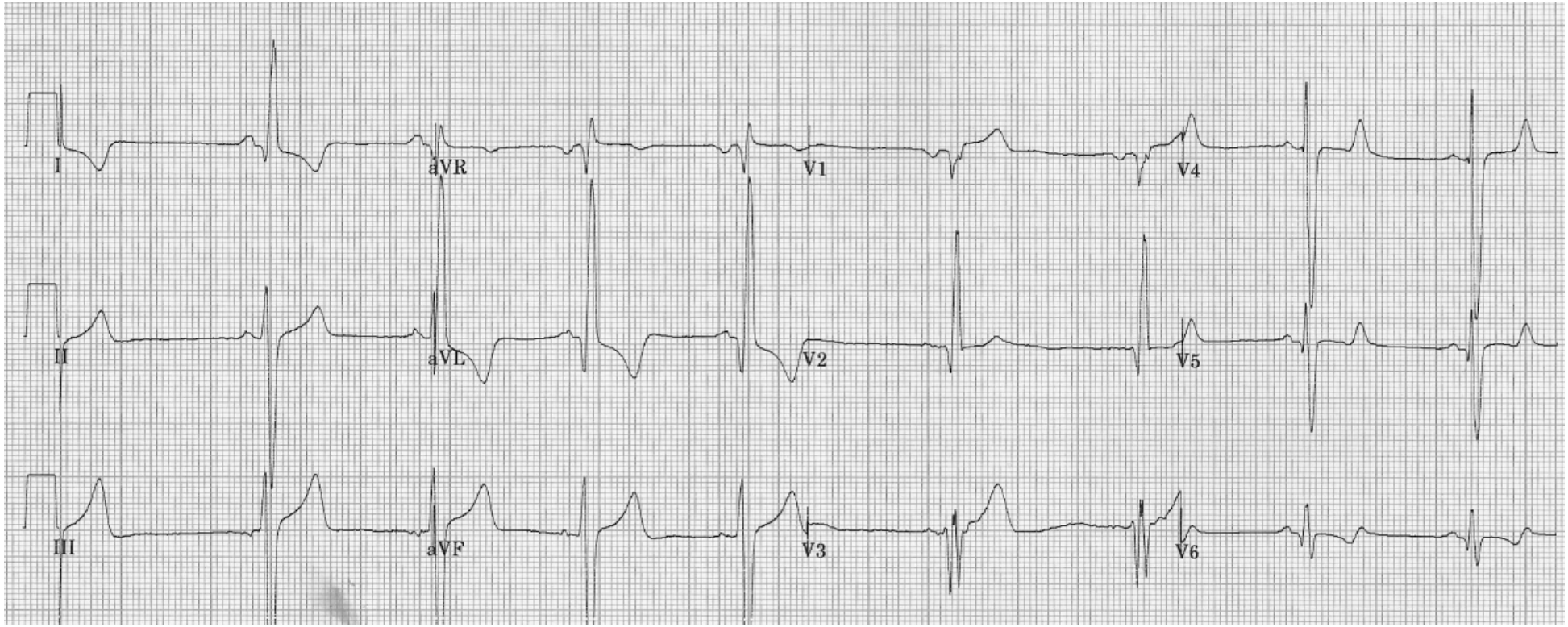
2. ***Cardiomyopathies hypertrophiques***

3. **Amylose**

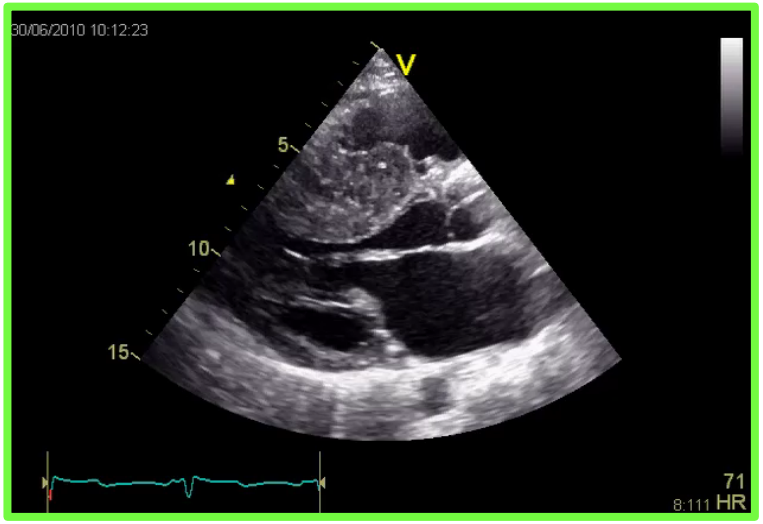
4. **Non compaction ventriculaire gauche**

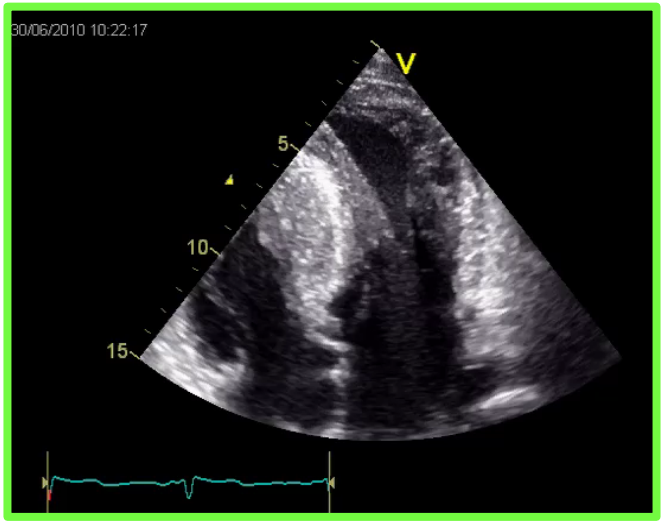
Cas clinique n°1

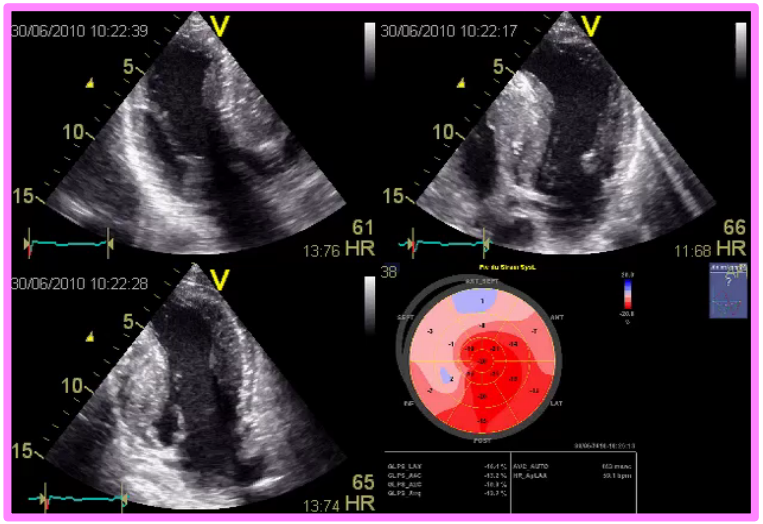
- **Homme de 19 ans**
- **cardiomyopathie hypertrophique de l'enfance**
- **dyspnée d'effort modérée**

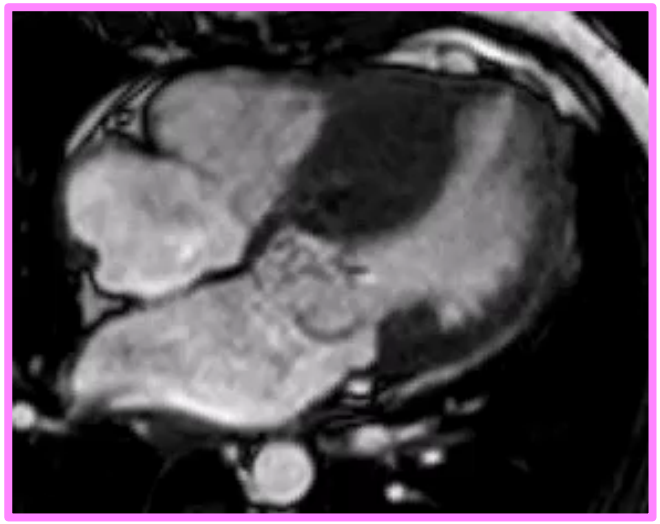

I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

CM hypertrophique: imagerie









ESC Position Statement 2008

	HCM	DCM	ARVC	RCM	Unclassified
Fa	Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Left ventricular non-compaction
	Sarcomeric protein mutations	Sarcomeric protein mutations (see HCM)	Intercalated disc protein mutations	Sarcomeric protein mutations	Barth syndrome
	ß myosin heavy chain	Z-band	Plakoglobin	Troponin I (RCM +/− HCM)	Lamin A/C
	Cardiac myosin binding protein C	Muscle LIM protein	Desmoplakin	Essential light chain of myosin	ZASP
	Cardiac troponin I	TCAP	Plakophilin 2	Familial amyloidosis	α-dystrobrevin
	Troponin-T	Cytoskeletal genes	Desmoglein 2	Transthyretin (RCM + neuropathy)	
	α-tropomyosin	Dystrophin	Desmocollin 2	Apolipoprotein (RCM + nephropathy)	
	Essential myosin light chain	Desmin	Cardiac ryanodine receptor (RyR2)	Desminopathy	
	Regulatory myosin light chain	Metavinculin	Transforming growth factor-β3 (TGFβ3)	Pseuxanthoma elasticum	
	Cardiac actin	Sarcoglycan complex		Haemochromatosis	
	α-myosin heavy chain	CRYAB		Anderson–Fabry disease	
	Titin	Epicardin		Glycogen storage disease	
	Troponin C	Nuclear membrane			
	Muscle LIM protein	Lamin A/C			
	Glycogen storage disease (e.g. Pompe; PRKAG2, Forbes', Danon)	Emerin			
	Lysosomal storage diseases (e.g. Anderson–Fabry, Hurler's)	Mildly dilated CM			
	Disorders of fatty acid metabolism	Intercalated disc protein mutations (see ARVC)			
	Carnitine deficiency	Mitochondrial cytopathy			
	Phosphorylase B kinase deficiency				
	Mitochondrial cytopathies				
	Syndromic HCM				
	Noonan's syndrome				
	LEOPARD syndrome				
	Friedreich's ataxia				
	Beckwith–Wiedermann syndrome				
	Swyer's syndrome				
	Other				
	Phospholamban promoter				
	Familial amyloid				

Etude HYPERGEN

Nouvelle stratégie diagnostique dans la prise en charge des cardiomyopathies hypertrophiques impliquant une approche génétique

Assistance Publique Hôpitaux de Marseille

Investigateur Coordinateur : Pr Gilbert HABIB / Dr Karine N'GUYEN
Promoteur : DRCI de l'Assistance Publique des Hôpitaux de Marseille
Ingénieur coordinateur: Cécile LAVOUTE

- 200 patients inclus (Juin 2015-Octobre 2016)
  - Marseille: 75
  - Rennes: 68
  - Dijon: 31
  - Bordeaux: 13
  - Pitie salpêtrière: 13

CHU Dijon

CHU Rennes

CHU Bordeaux

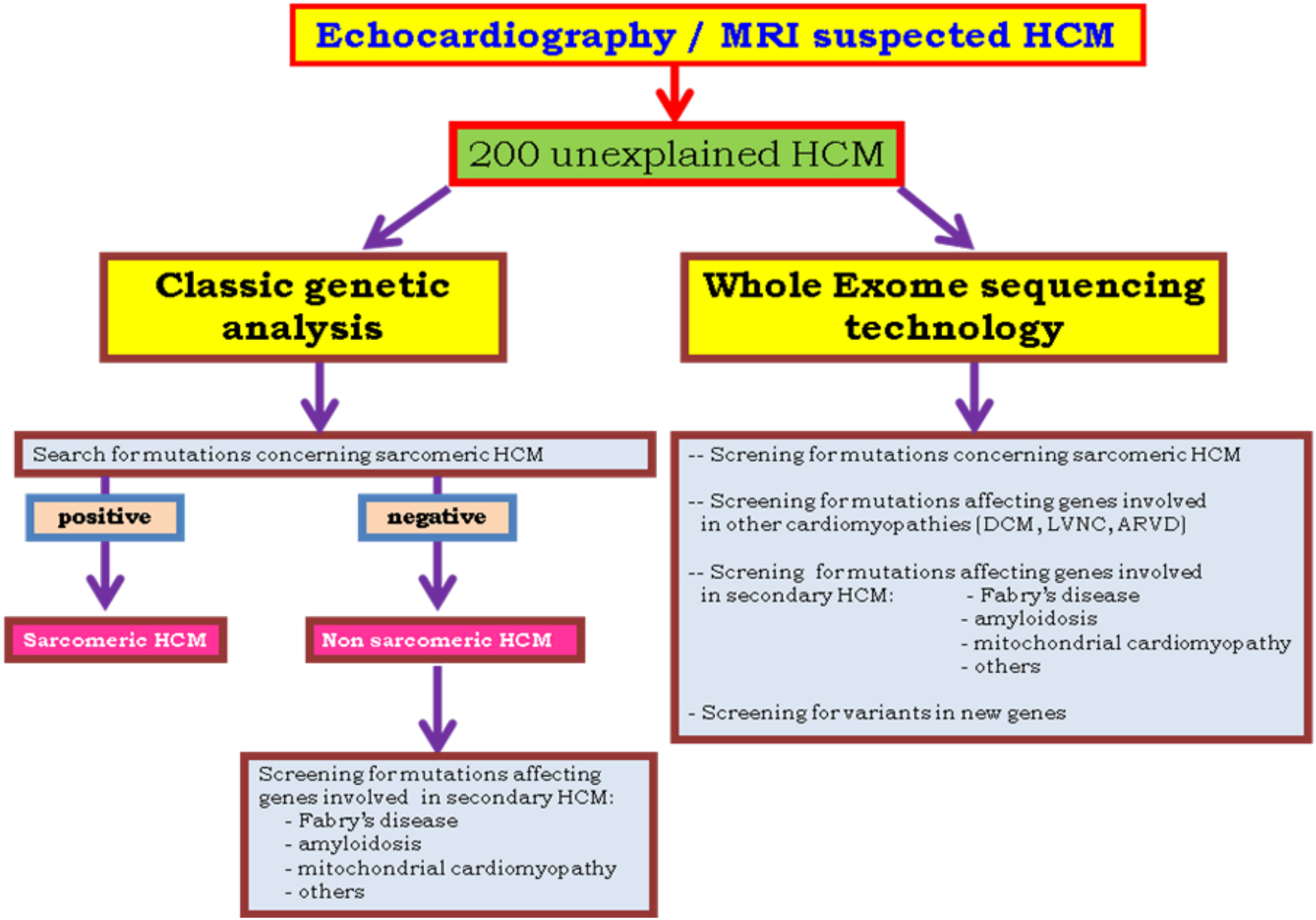
AP HP - Pitié Salpêtrière

NOUVELLE STRATEGIE DIAGNOSTIQUE DANS LA CMH INCLUANT UNE NOUVELLE APPROCHE GENETIQUE

Etude multicentrique prospective

Objectif de l'étude

Appliquer une nouvelle stratégie diagnostique chez les patients porteurs d'une CMH, incluant l'analyse de l'exome (WES)


Echocardiography / MRI suspected HCM
200 unexplained HCM
Classic genetic analysis
Whole Exome sequencing technology
Search for mutations concerning sarcomeric HCM
positive
negative
Sarcomeric HCM
Non sarcomeric HCM
Screening for mutations affecting genes involved in secondary HCM:
- Fabry's disease
- amyloidosis
- mitochondrial cardiomyopathy
- others
-- Screening for mutations concerning sarcomeric HCM
-- Screening for mutations affecting genes involved in other cardiomyopathies (DCM, LVNC, ARVD)
-- Screening for mutations affecting genes involved in secondary HCM:
- Fabry's disease
- amyloidosis
- mitochondrial cardiomyopathy
- others
- Screening for variants in new genes

Circulation: Genomic and Precision Medicine

RESEARCH LETTER

Whole Exome Sequencing Reveals a Large Genetic Heterogeneity and Revisits the Causes of Hypertrophic Cardiomyopathy

Experience of a Multicentric Study of 200 French Patients

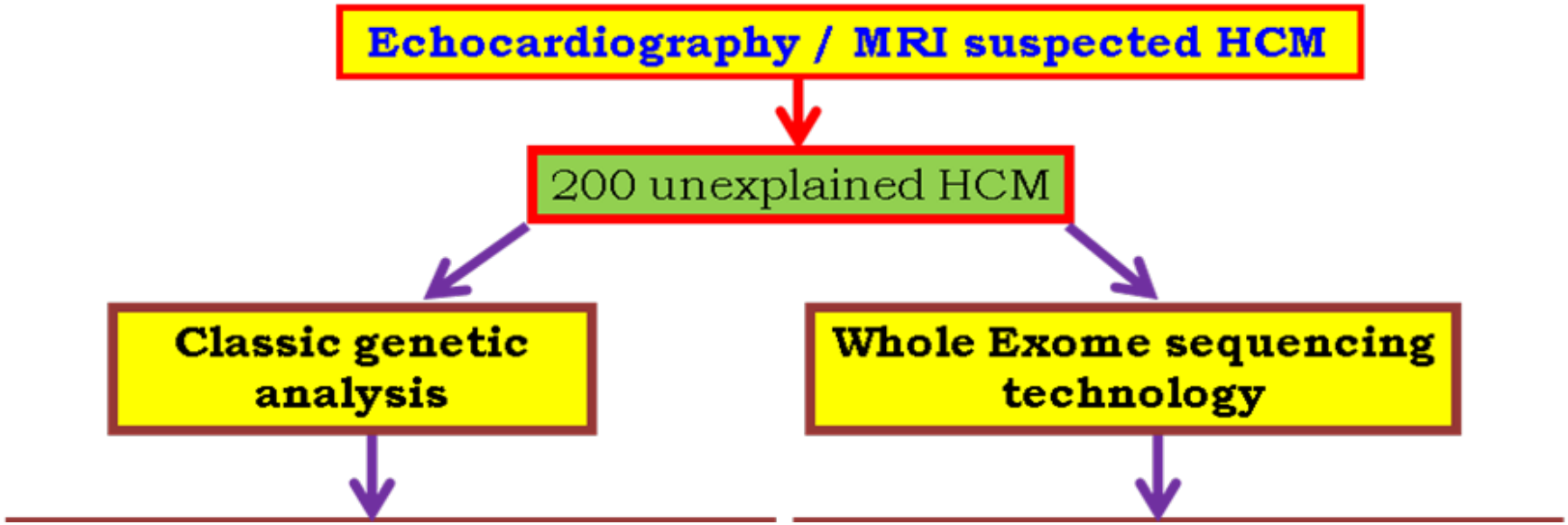
Karine Nguyen, MD, PhD
et al

Hypertrophic cardiomyopathy (HCM), the most common hereditary heart disease, is autosomal dominant with incomplete penetrance and variability. Heterozygous mutations in 5 sarcomeric genes (*MYBPC3*, *MYH7*, *TNNT2*

NOUVELLE STRATEGIE DIAGNOSTIQUE DANS LA CMH INCLUANT UNE NOUVELLE APPROCHE GENETIQUE

Etude multicentrique prospective

Premiers résultats



Sensibilité = 35%

Sensibilité = 87%

Circulation: Genomic and Precision Medicine

RESEARCH LETTER

Whole Exome Sequencing Reveals a Large Genetic Heterogeneity and Revisits the Causes of Hypertrophic Cardiomyopathy

Experience of a Multicentric Study of 200 French Patients

1. HYPERGEN study validated the yield of WES in HCM. WES detected additional mutations in patients with 1 mutation identified by targeted sequencing, suggesting larger genetic heterogeneity than previously thought, and perhaps oligogenism

2. WES confirmed the prominent involvement of MYBPC3 and MYH7 but also showed unexpected frequency of mutations in TTN and FLNC as well as in SCN5A, RYR2, and other ion channel genes, suggesting overlap between HCM and arrhythmia genes.

3. Familial segregation studies will refine the interpretation of variants' pathogenicity and will be the next step of the HYPERGEN project.

CENTRE DE COMPETENCE « CARDIOMYOPATHIES »

Activité

ABCC9	NM_020297
ACAD9	NM_014049
ACTC1	NM_005159
ACTN2	NM_001103
ALPK3	NM_020778
ANKRD1	NM_014391
BAG3	NM_004281
CAV3	NM_033337
CRYAB	NM_001885
CSRP3	NM_003476
CTNNA3	NM_013266
DES	NM_001927
DSC2	NM_024422
DSG2	NM_001943
DSP	NM_004415
DTNA	NM_001390
EMD	NM_000117
EYA4	NM_001301013
FBN1	NM_000138
FHL1	NM_001159702
FLNC	NM_001458
GAA	NM_00152
GATA4	NM_002052
GLA	NM_000169
HCN4	NM_005477
JPH2	NM_020433
KRAS	NM_0033360
LAMA4	NM_001105206
LAMP2	NM_002294
LDB3	NM_001171610 NM_007078
LMNA	NM_170707
MYBPC3	NM_000256
MYH6	NM_002471
MYH7	NM_000257
MYL2	NM_000432
MYL3	NM_000258
MYLK2	NM_033118
MYOM1	NM_003803
MYOZ2	NM_016599
MYPN	NM_032578
NEBL	NM_00393
NEXN	NM_144573
NKX2-5	NM_004387
PDLIM3	NM_014476
PKP2	NM_004572
PLN	NM_002667
PRDM16	NM_022114
PRKAG2	NM_016203
PTPN11	NM_002834
RAF1	NM_002880
RBM20	NM_001134363
RYR2	NM_001035
SCN5A	NM_198056
SOS1	NM_005633
TAZ	NM_000116
TCAP	NM_003673
TMEM43	NM_024334
TMPO	NM_003276
TNNC1	NM_003280
TNNI3	NM_000363
TNNT2	NM_001001430
TPM1	NM_001018005
TTN	NM_001267550
TTR	NM_000371
VCL	NM_014000

Listes de gènes CARDIOGEN v2018 Cardiomyopathies (65 gènes au total : niveau 1 = 5 gènes + niveau 2 = 60 gènes)

Stratégie du laboratoire à Marseille

1 seule analyse de 65 gènes d'emblée dont les gènes sarcomériques fréquents *MYBPC3, MYH7, MYL2, TNNT2, TNNI3*

+ FLNC

+ LMNA

+ GLA, TTR* et *HCN4

↓

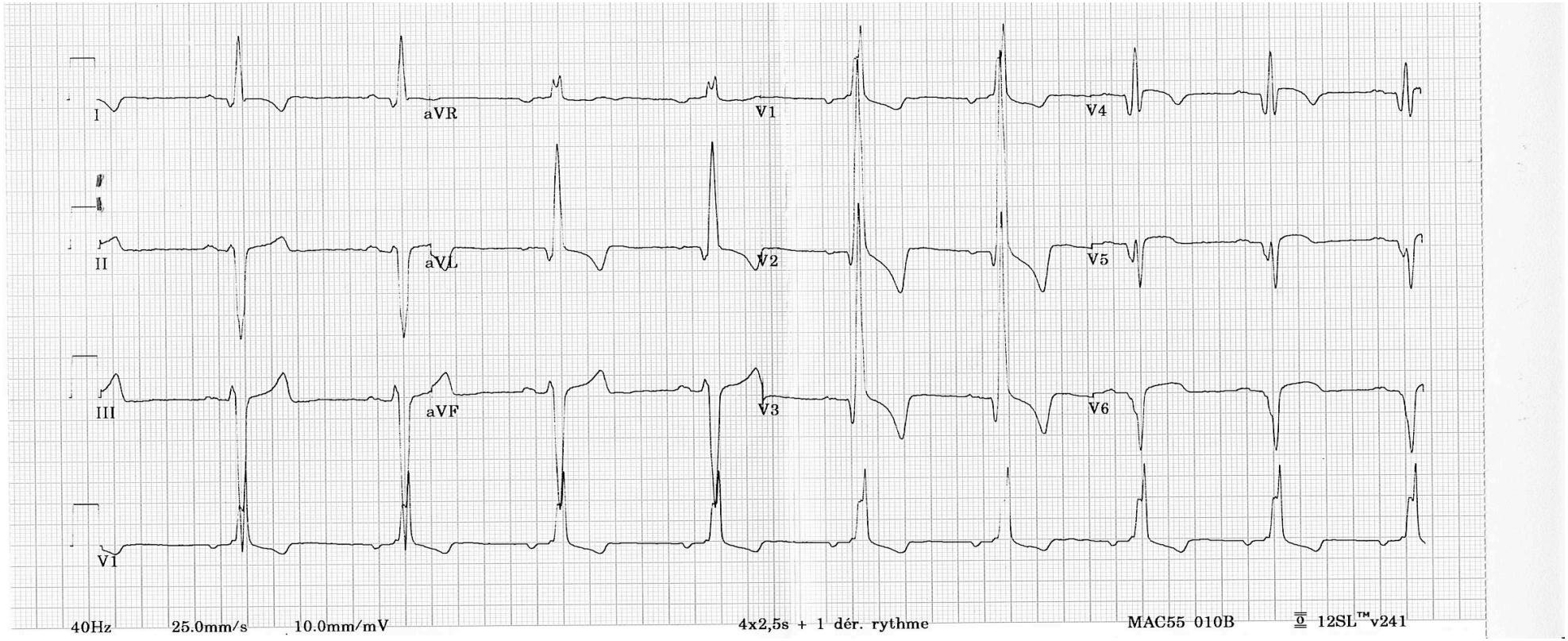
Maladie de Fabry et amylose héréditaire à TTR recherchées dés l'analyse de 1ère intention devant une CMH

RENDEMENT: 40-50% DE PATIENTS MUTÉS CMH/CMD

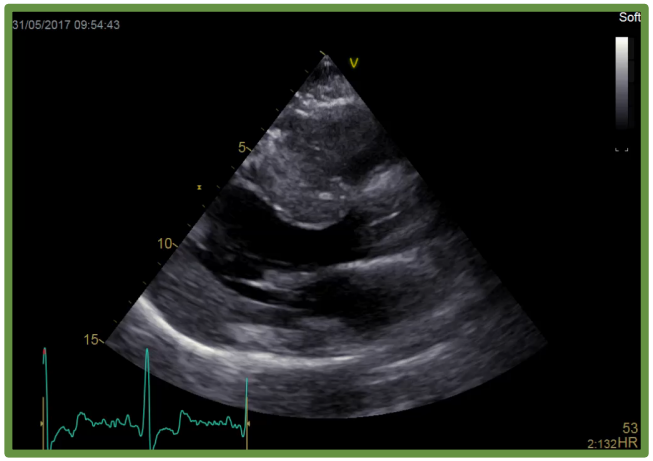
Cas Clinique n° 9: maladie de Fabry

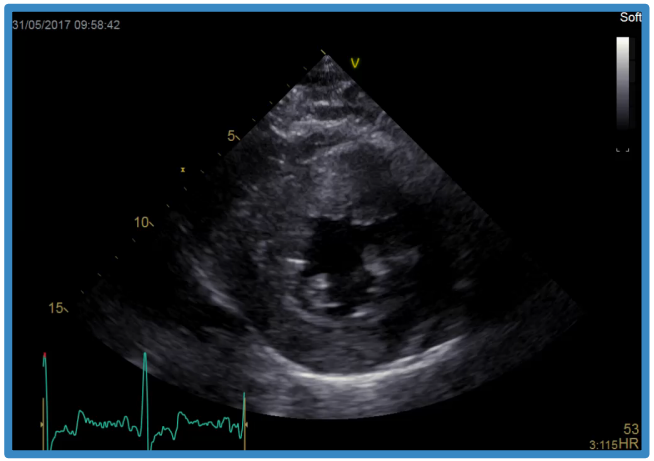
- Homme de 61 ans
- Bilan de paresthésies -> découverte HTA et HVG
- Atcd digestifs anciens, troubles visuels récents non explorés.
- Lipothymies, frère CMH?
- Mutation GLA hémizygote p.S238N (c.713G>A)
- Lyso GB3= 6 ng/ml (N<1,8 ng/ml) - alpha gal < 0,8 (N> 15,3)

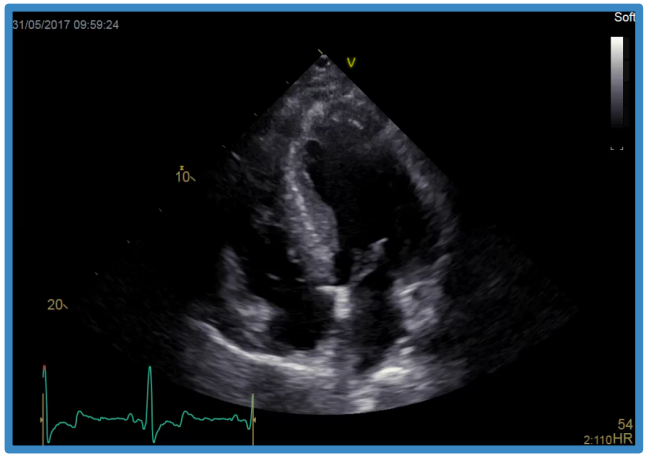
Cas Clinique n° 9: maladie de Fabry

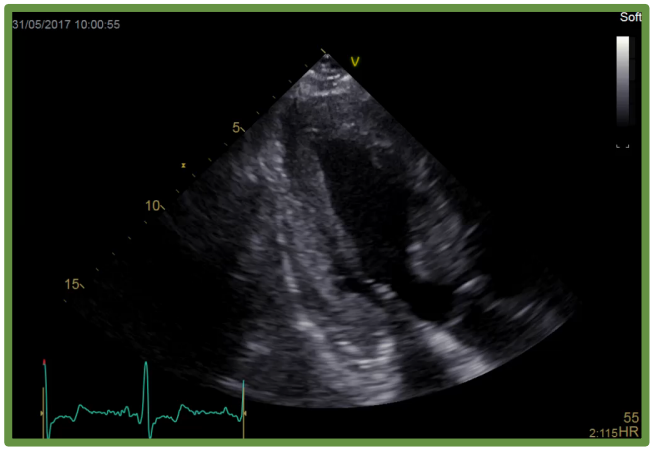


Cas Clinique n° 9: maladie de Fabry

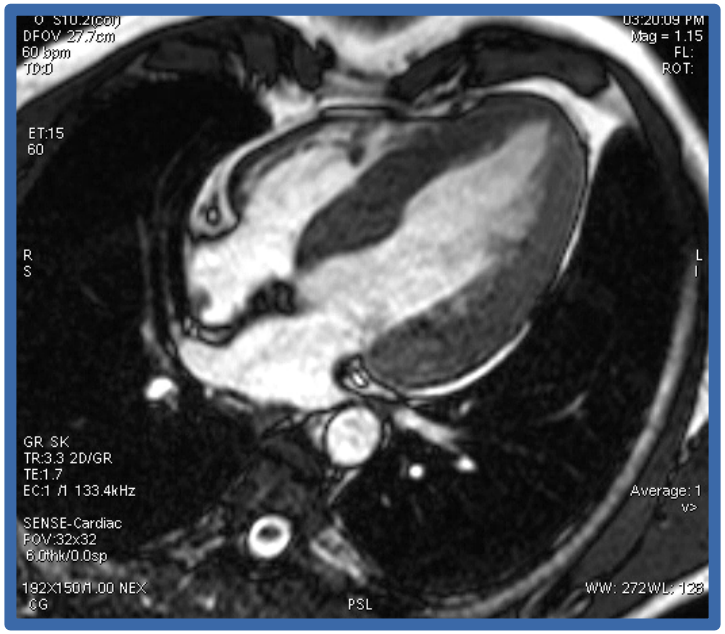


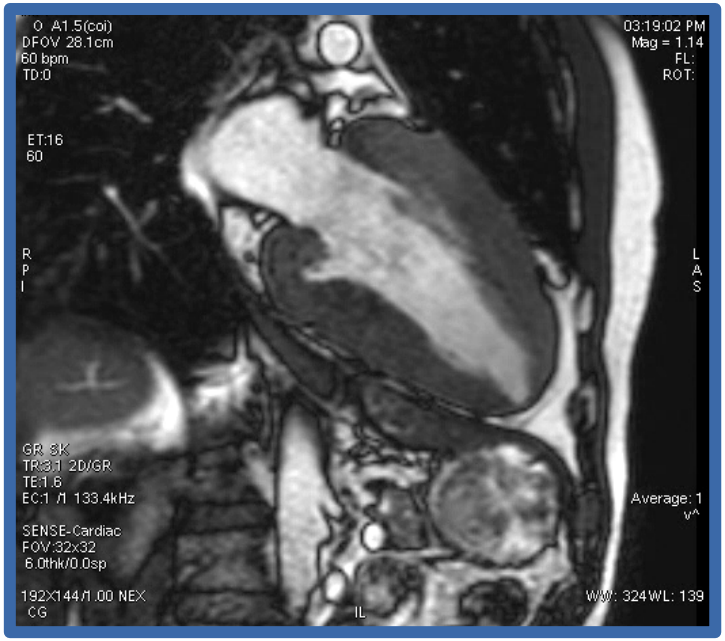






Cas Clinique n° 9: maladie de Fabry





Quoi de neuf sur les cardiomyopathies ?

1. **Les centres de Cardiomyopathies**

2. **Cardiomyopathies hypertrophiques**

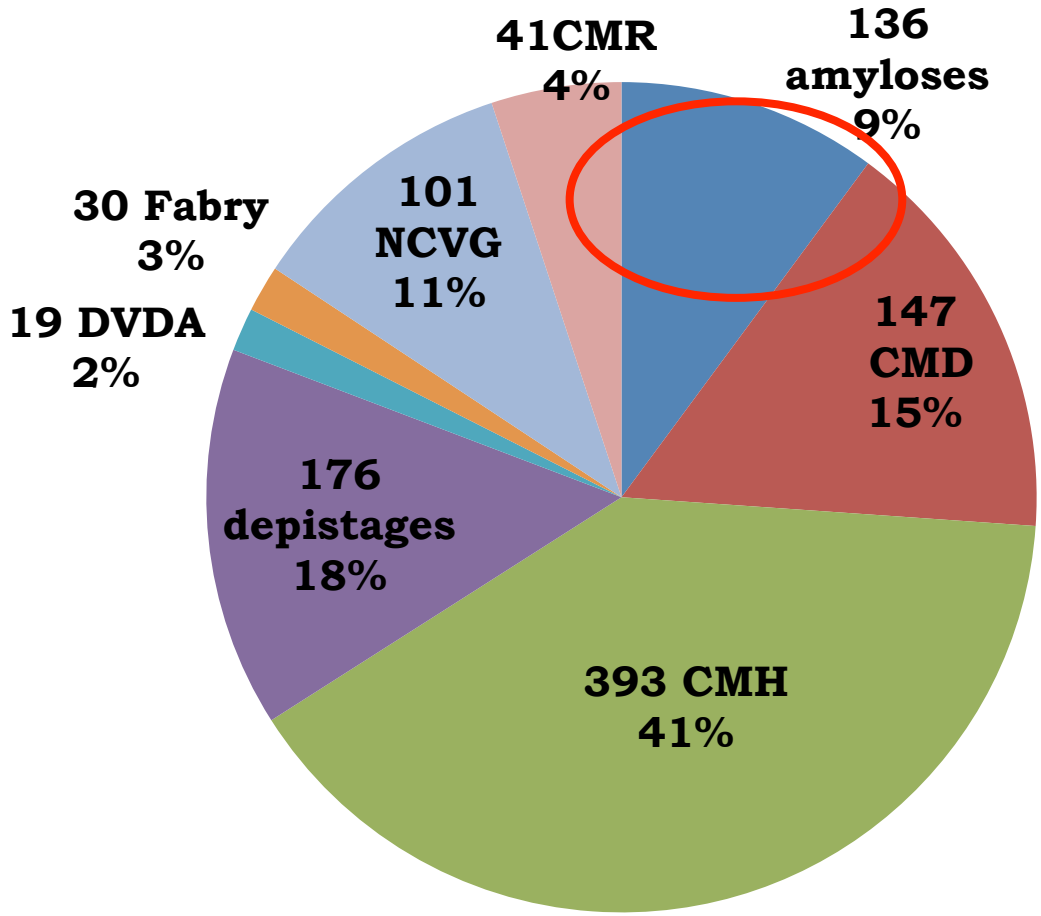
3. ***Amylose***

4. **Non compaction ventriculaire gauche**

Centre des Cardiomyopathies de Marseille

Répartition:
(Depuis Avril 2010)

Total: 1519 patients



Centre des Cardiomyopathies de Marseille

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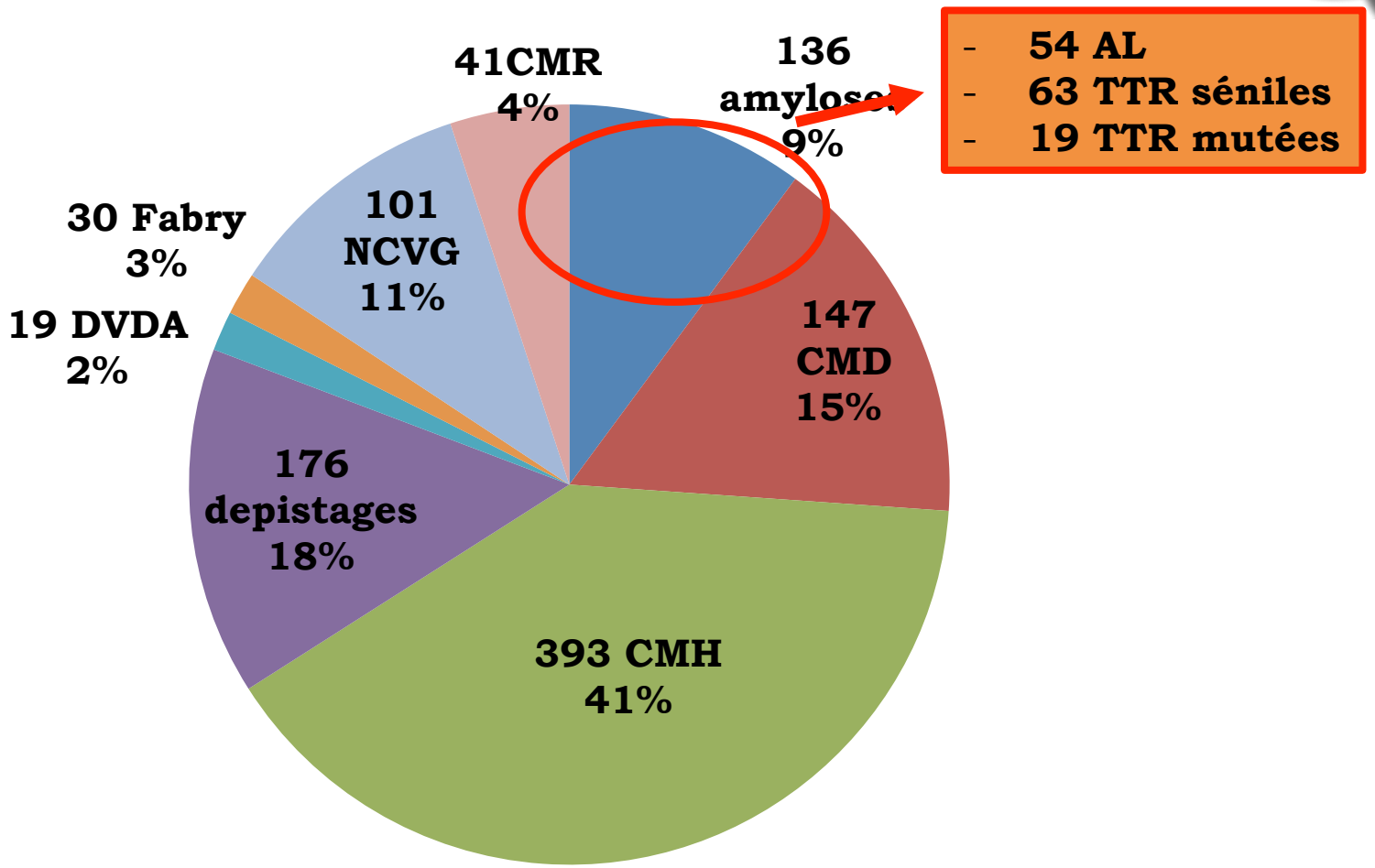

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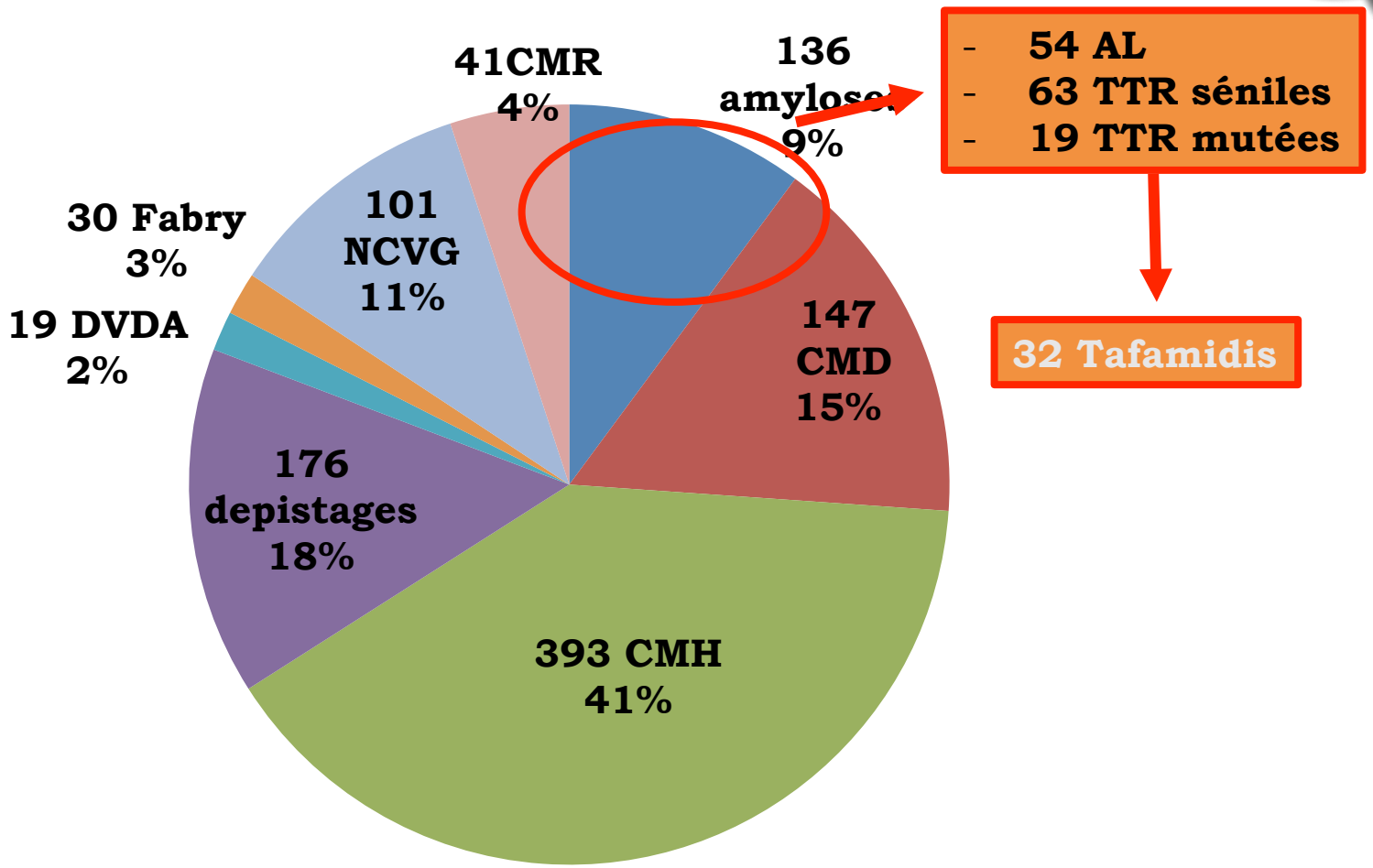


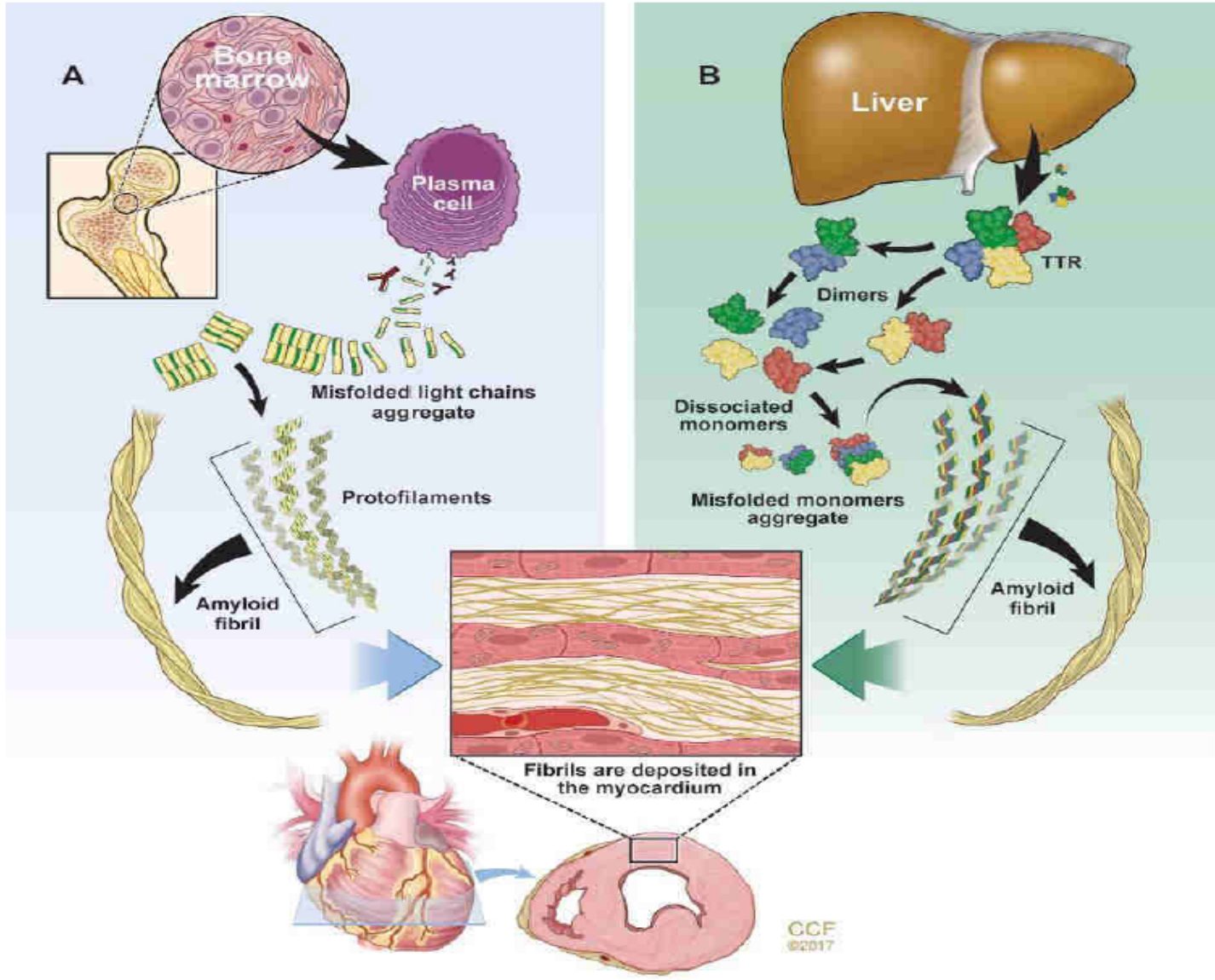


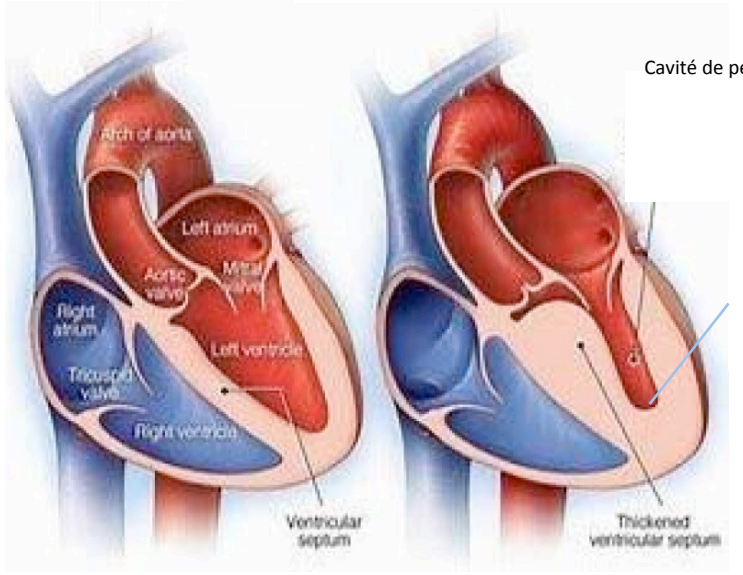
Figure 1. The 2 main types of amyloidosis that affect the heart. (A) Immunoglobulin light chain amyloidosis (AL) results from aberrant plasma cell production of monoclonal light chains that misfold. (B) Transthyretin amyloidosis (ATTR) results from transthyretin (TTR) produced by the liver that dissociates into monomers and misfolds. The misfolded proteins aggregate to form oligomers, protofilaments, and mature amyloid fibrils that deposit extracellulary in the interstitial space of the myocardium.

Physiopathologie

L'infiltration amyloïde : un épaississement et d'une rigidité de la paroi ventriculaire

Normal

Cardiomyopathie hypertrophique



Cavité de petit volume

Épaississement du ventricule gauche(VG)

Altération de la fonction diastolique (relaxation)

- Le volume télédiastolique du ventricule gauche (VTDVG)

↓

Altération de la fonction systolique (contraction)

- Mesurée par la déformation longitudinale est une mesure sensible de la/ Strain altéré

↓

Insuffisance cardiaque congestive, arythmie

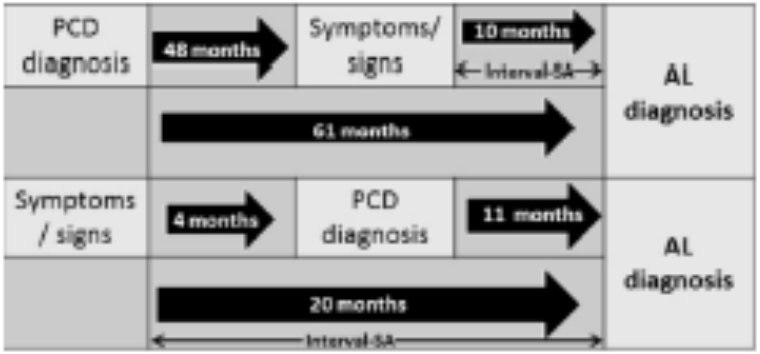
- Le NT-proBNP; marqueur du stress myocardique

↓

Difficultés à la marche et à effectuer des activités de la vie quotidienne
Hospitalisations et décès cardiovasculaires

Amylose AL: il faut « faire vite »

- Insuffisance cardiaque: survie médiane sans traitement = **6 mois**
- Un diagnostic trop tardif: délai médian = **20 mois après les symptômes/signes**



Interval-SA; intervalle entre les symptômes, les valeurs anormales de laboratoire et l'amylose; PCD : dyscrasie plasmocytaire; s/s : symptômes/ signes.

\+

- **30%** de morts subites dans les 90 jours suivants le diagnostic

(dissociation éléctro-mécanique+++)

➢ **Avoir un index de suspicion élevé**
➢ **Urgence thérapeutique**

Epidemiologie

Frequency and distribution of senile cardiovascular amyloid

A clinicopathologic correlation

Gibbons MD et al. 1983

85 autopsies de patients >80ans

25% des patients ont une amylose dite sénile

Prevalence of Cardiac Amyloidosis in Patients Referred for Transcatheter Aortic Valve Replacement

Scully P et al. JACC 2017

101 patients référés au TAVI
Réalisation de scintigraphie DPD

14% des patients ont une amylose TTR

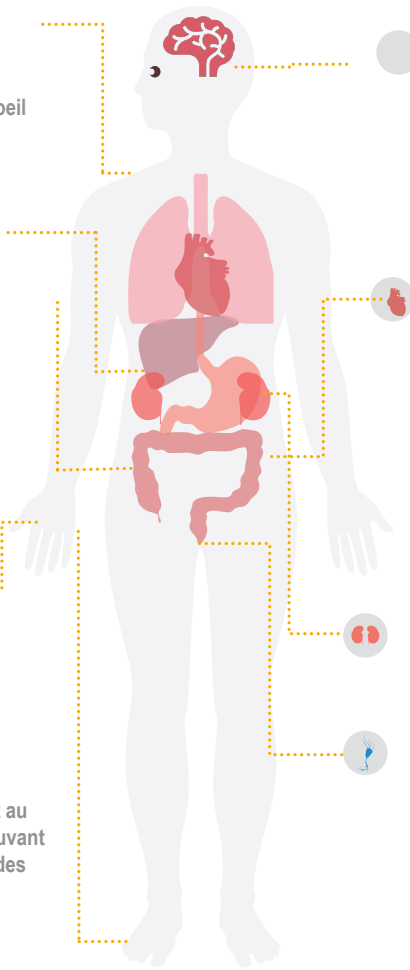
Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction

Esther González-López[1], Maria Gallego-Delgado[1], Gonzalo Guzzo-Merello[1], F. Javier de Haro-del Moral[2], Marta Cobo-Marcos[1], Carolina Robles[1], Belén Bornstein[3,4,5], Clara Salas[6], Enrique Lara-Pezzi[7], Luis Alonso-Pulpon[1], and Pablo Garcia-Pavia[1,7*]

120 patients avec HFpEF + SIV >12mm
Réalisation de scintigraphie DPD

13% des patients ont une amylose TTR

Manifestations cliniques de l'amylose



MANIFESTATIONS OCULAIRES[1]
- Myodésopsie ("corps flottants")
- Glaucome
- Vaisseaux sanguins anormaux dans l'oeil
- Anomalie au niveau de la pupille

STENOSE LOMBAIRE RARE[2]

MANIFESTATIONS GI[1]
- Nausées et vomissement
- Satiété précoce
- Diarrhée chronique
- Constipation sévère
- Alternance diarrhée/constipation
- Perte de poids involontaire

SYNDROME DU CANAL CARPIEN BILATERAL[1-3]

NEUROPATHIE PERIPHERIQUE SENSORI-MOTRICE[1]
- Atteinte nerveuse débutant souvent au niveau des pieds, ascendante et pouvant progresser aux mains et au niveau des parties centrales du corps

MANIFESTATIONS SNC[1]
- Démence progressive
- Mal de tête
- Ataxie
- Crise convulsive
- Parésie spastique
- Episode ressemblant à un AVC

MANIFESTATIONS CARDIO-VASCULAIRES[1,4-6]
- Rythme cardiaque irrégulier
- Blocs de conduction
- Insuffisance cardiaque (incluant: dyspnée, asthénie, oedème périphérique)
- Epaississement de la paroi ventriculaire avec fraction d'ejection préservée et absence de dilatation ventriculaire gauche

NEPHROPATHIE[1]
- Protéinurie
- Insuffisance rénale

NEUROPATHIE AUTONOMIQUE[1]
- Hypotension orthostatique
- Infections urinaires récidivantes (causes par une retention urinaire)
- Dysfonction sexuelle
- Troubles de la sudation

1. Conceição I, et al. J Peripher Nerv Syst. 2016;21(1):5-9; 2. Donnelly JP, Hanna M. Cleve Clin J Med. 2017;84(12 suppl 3):12-26; 3. Ikram A, et al. J Card Fail. 2017;23(8):S11-S12 (P021); 4. Coelho T, et al. A physician's guide to transthyretin amyloidosis. Research Gate Amyloidosis Foundation, 2006. https://www.researchgate.net/publication/265490881_A_Physician's_Guide_to_Transthyretin_Amyloidosis_Authored_by. Accessed January 3, 2018; 5. Gertz MA, et al. Am J Cardiol. 2016;118(7 suppl):S107-S112; 6. Galat A, et al. Eur Heart J. 2016;37(47):3525-31; 7.Ando Y, et al. Orphanet J Rare Dis. 2013 Feb 20;8:31;

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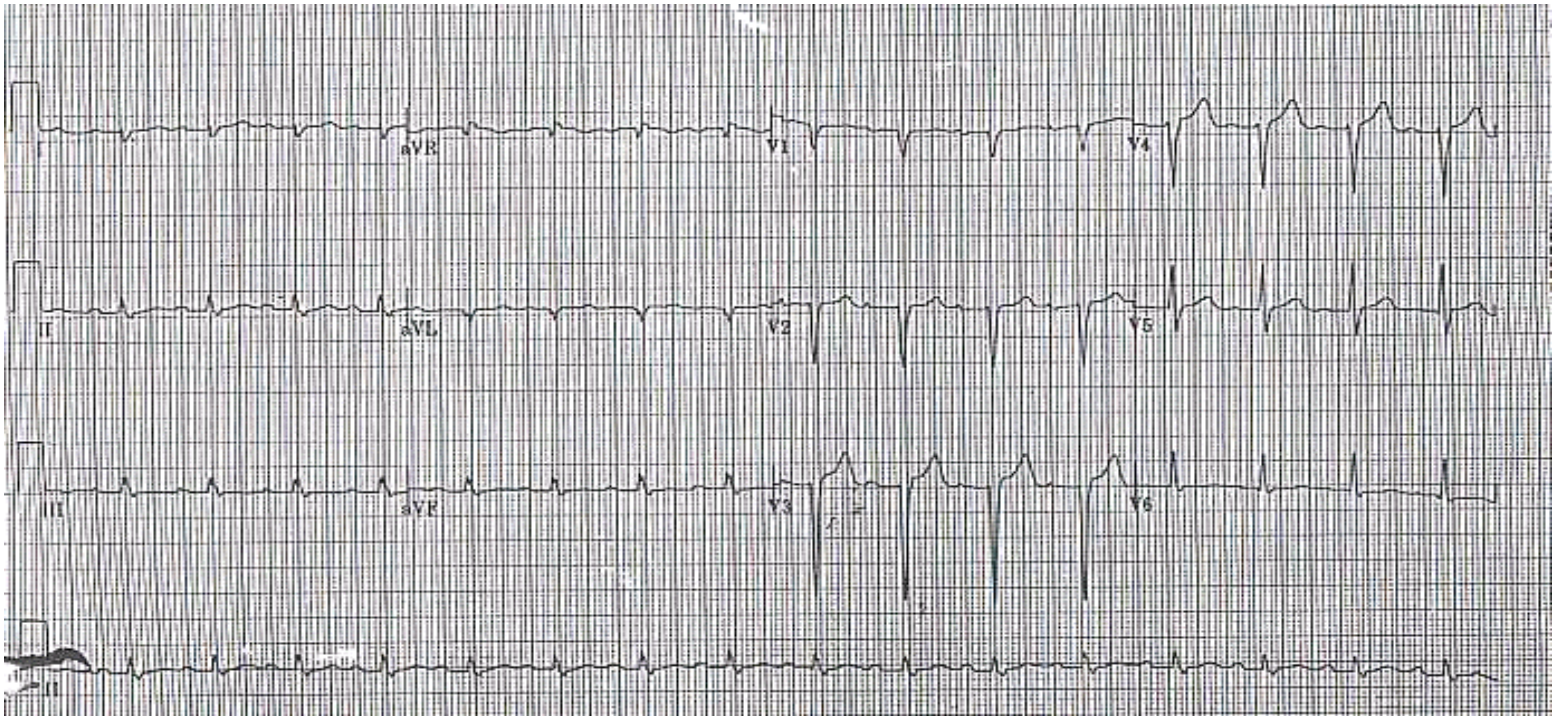
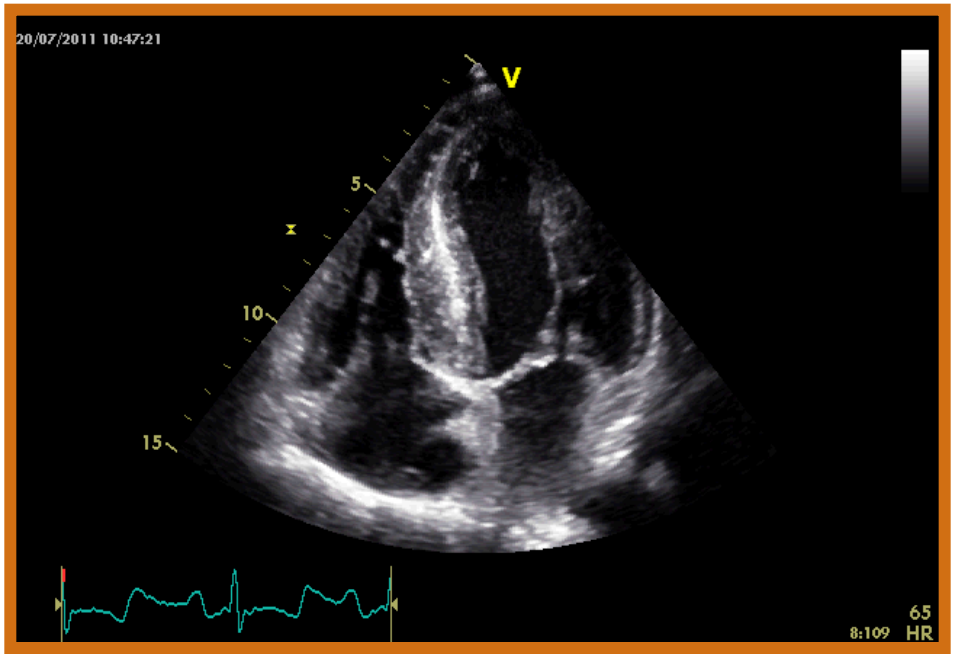
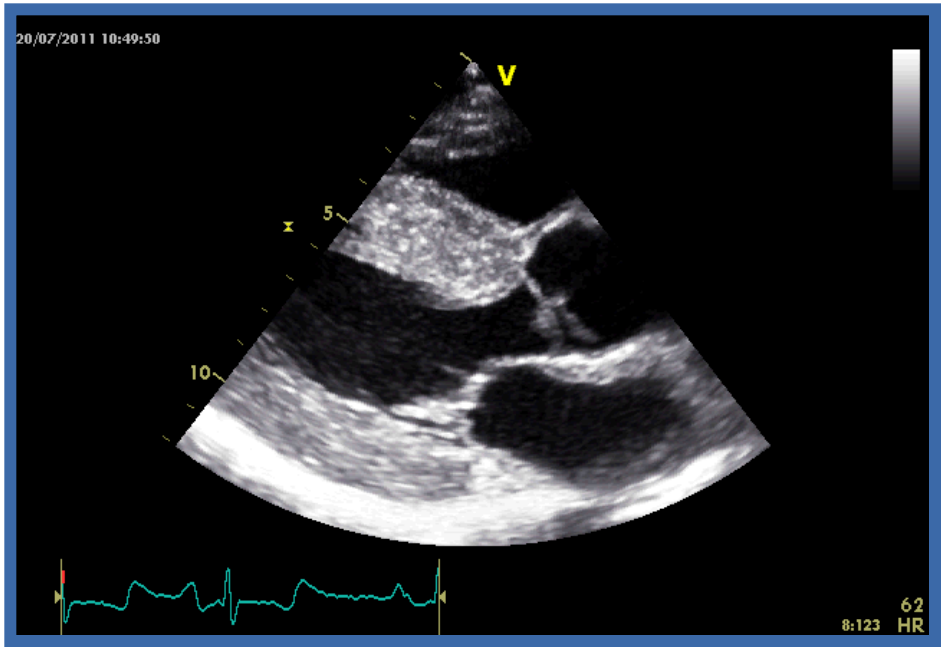
Case 2 : 50 year-old man – familial CM

1. 50 year-old man
2. Known HCM
3. Familial cardiomyopathy
4. Recent congestive HF

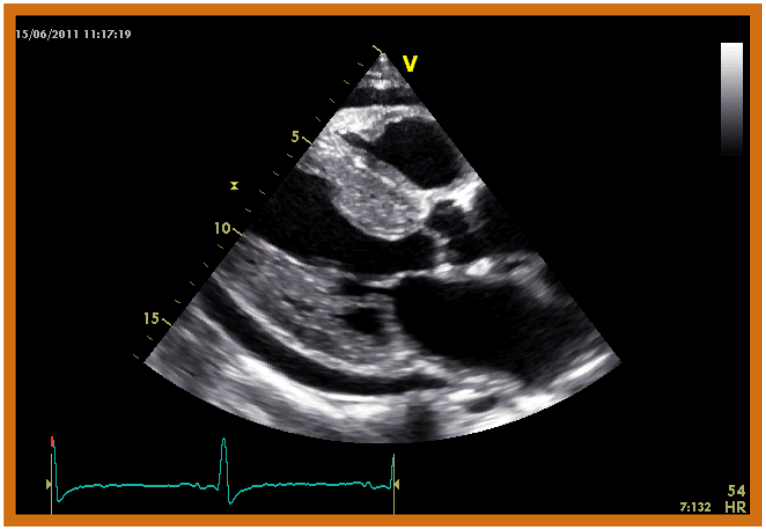


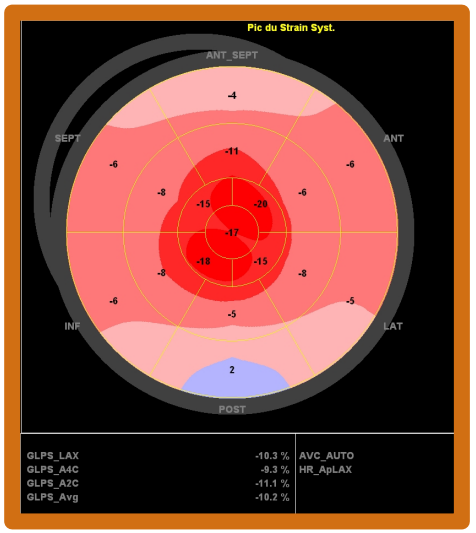
Case 2: 50 year-old man – familial CM

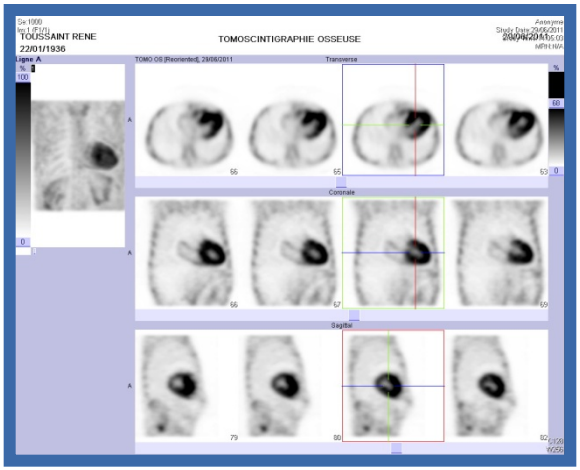


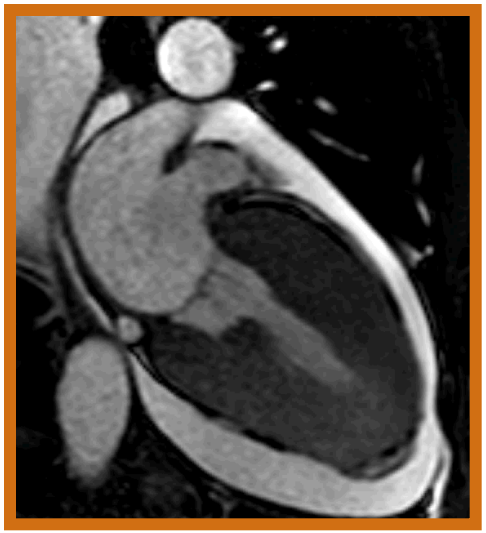


Cas clinique 2b: CM Familiale

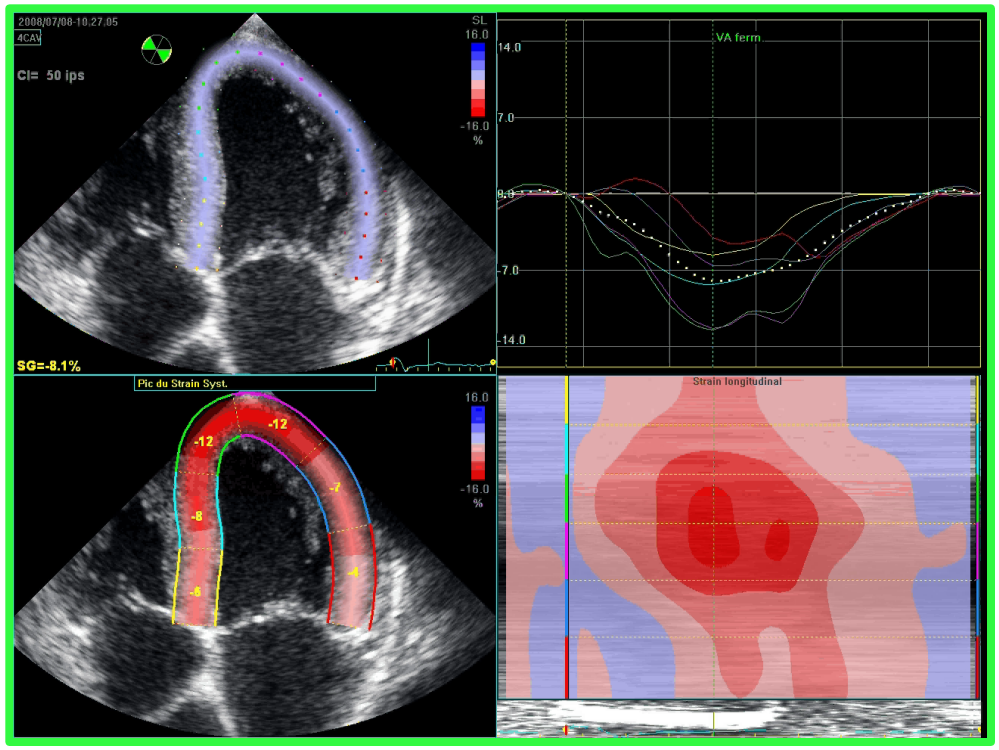


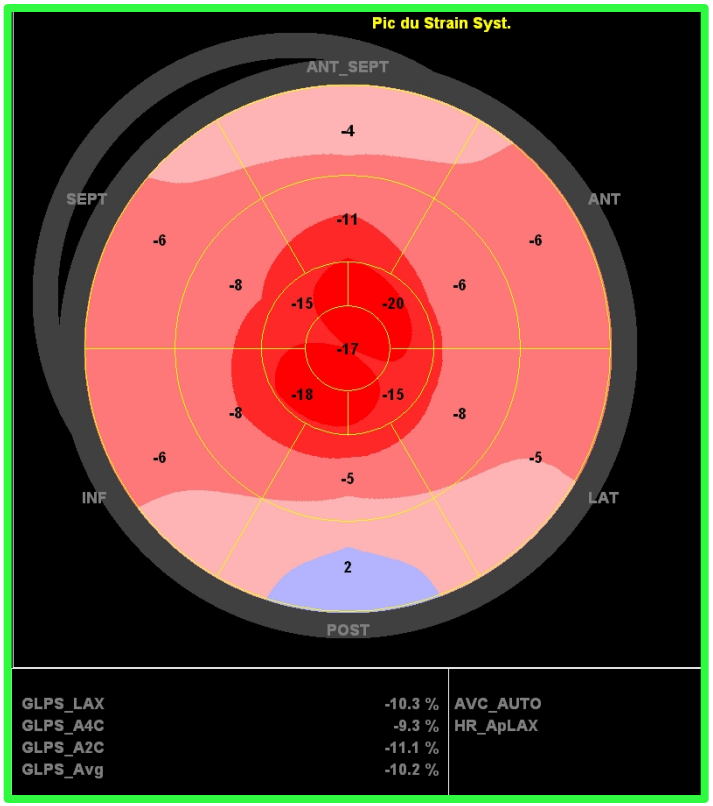






2D strain in cardiac amyloidosis





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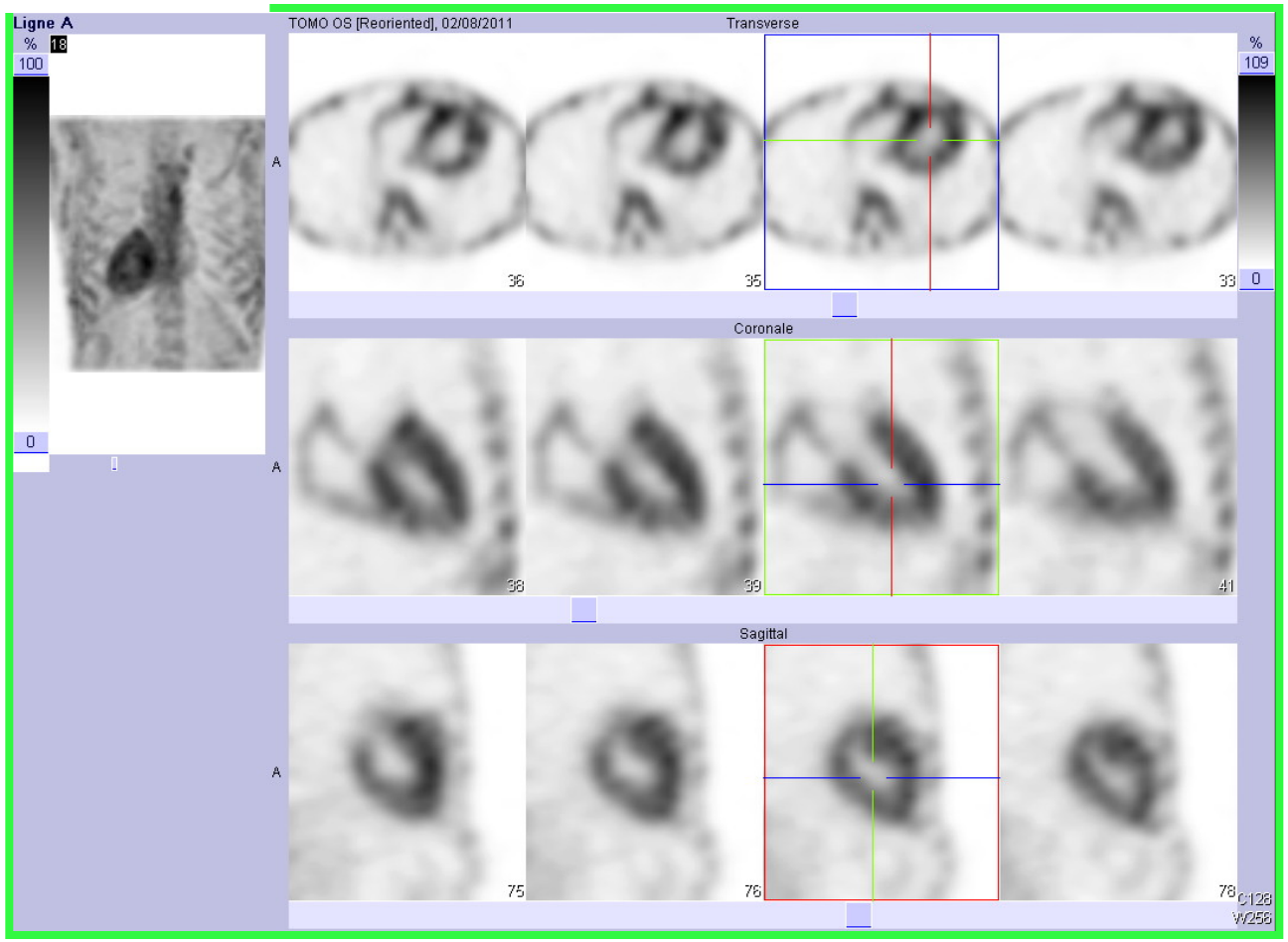
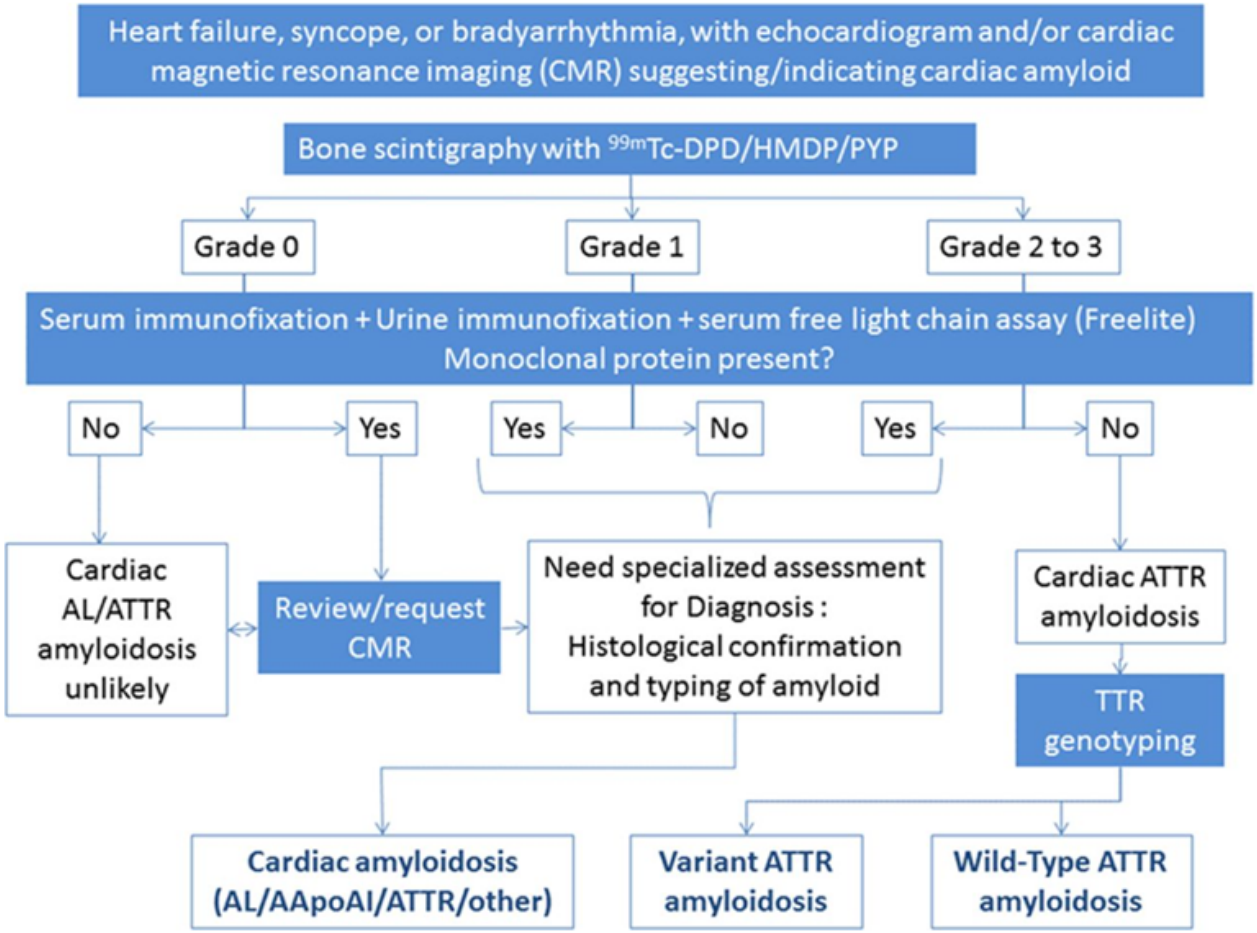
Case 2: Technetium scintigraphy

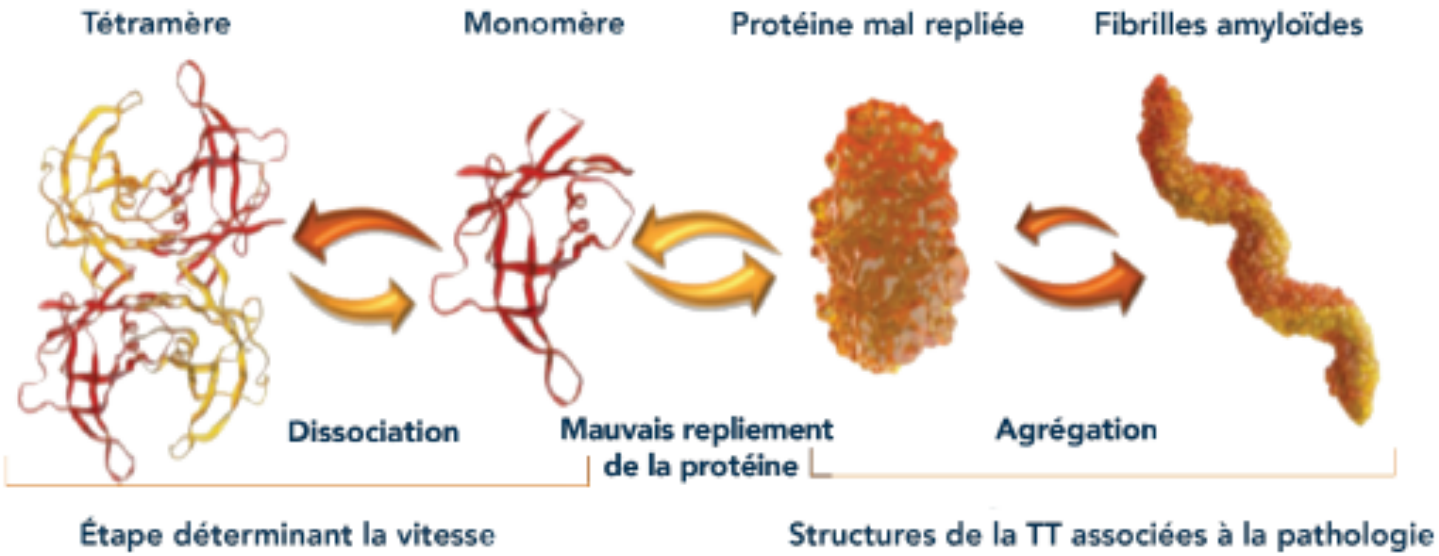


Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis

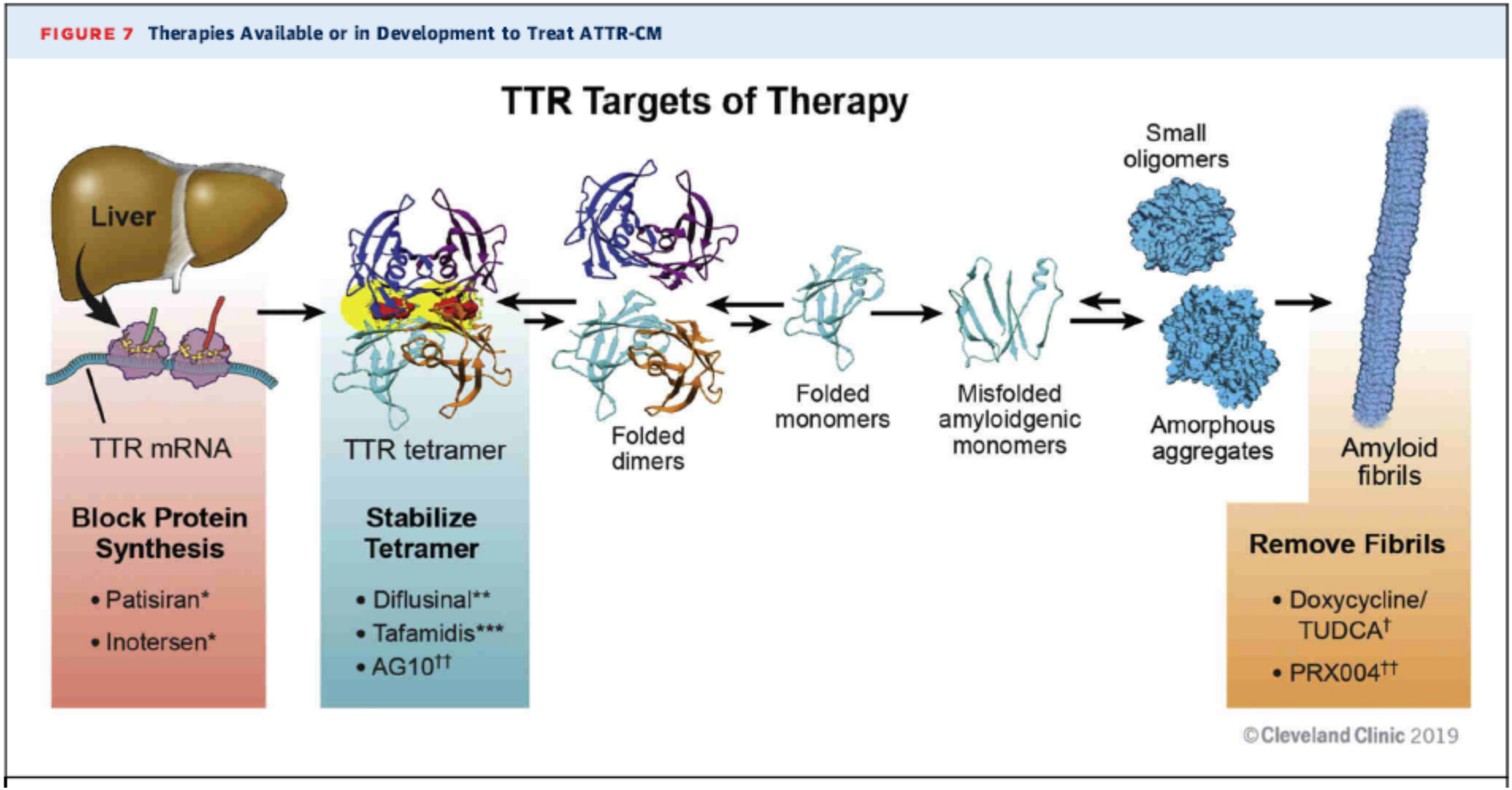
Gillmore JD - Circulation. 2016;133:2404-2412.



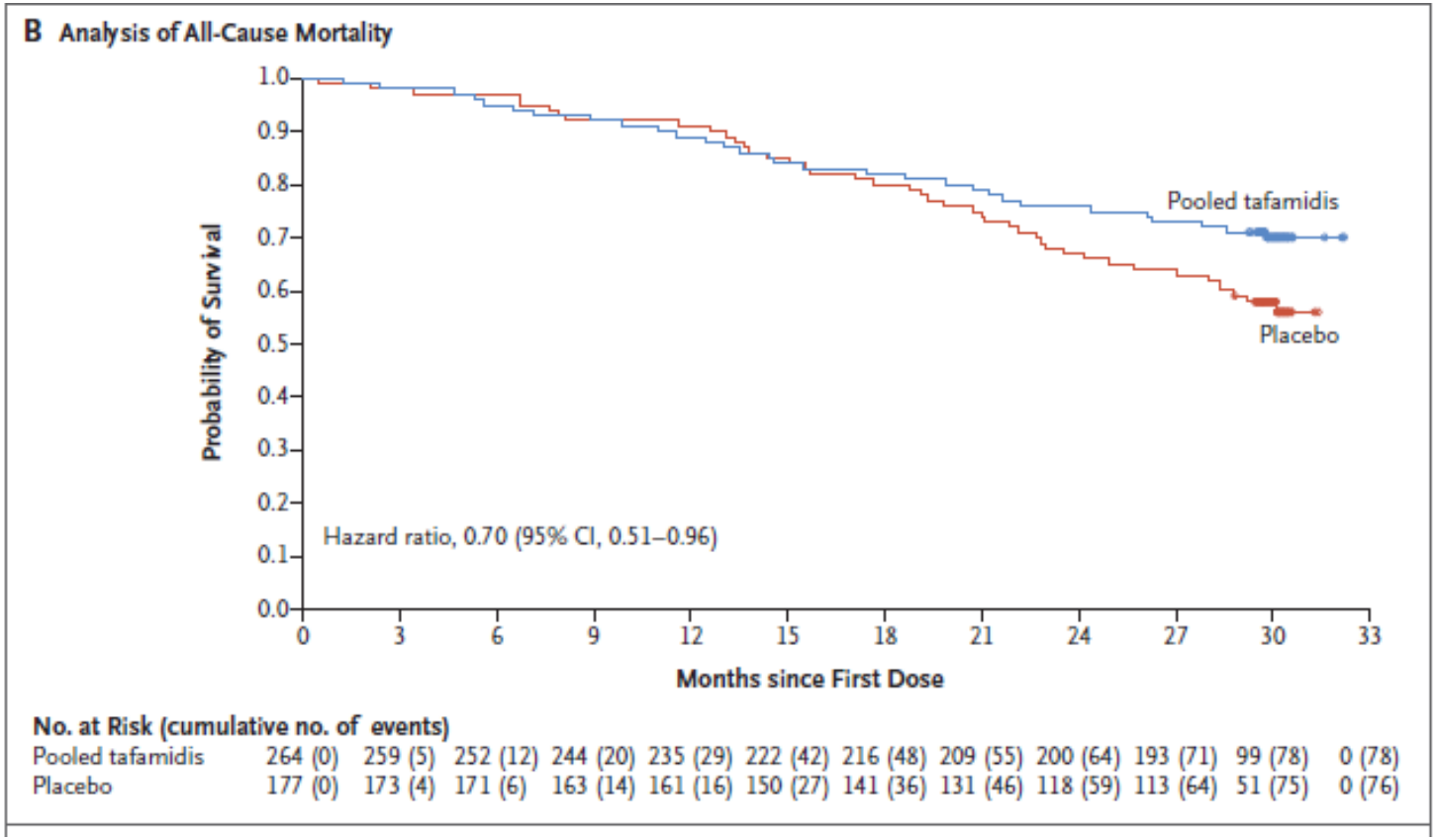
Physiopathologie :
Mécanisme de formation des fibrilles amyloïdes de TTR



Traitement de l'amylose TTR



Traitement médical des amyloses cardiaques? Tafamidis



Traitement médical des amyloses cardiaques? Tafamidis

Recommendations for the treatment of transthyretin amyloidosis-cardiac amyloidosis

Recommendations	Class[a]	Level[b]
Tafamidis is recommended in patients with genetic testing proven hereditary hTTR-CMP and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[979]	I	B
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[979]	I	B

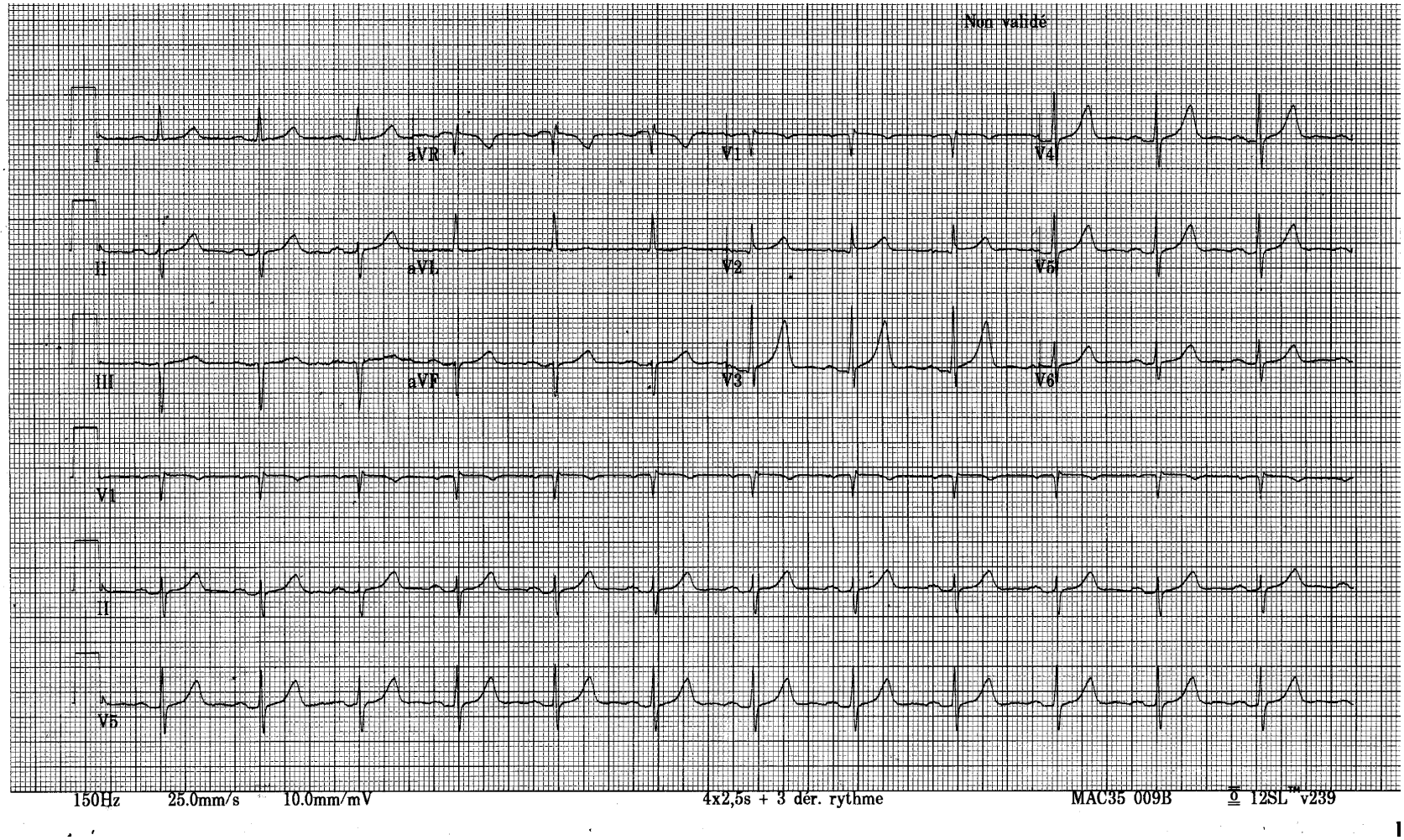
Complications

1. **Insuffisance cardiaque à FEVG conservée**
2. **Fibrillation auriculaire – troubles conductifs**
3. **Thromboses intracardiaques – embolies**
4. **Dysautonomie – hypotension artérielle**

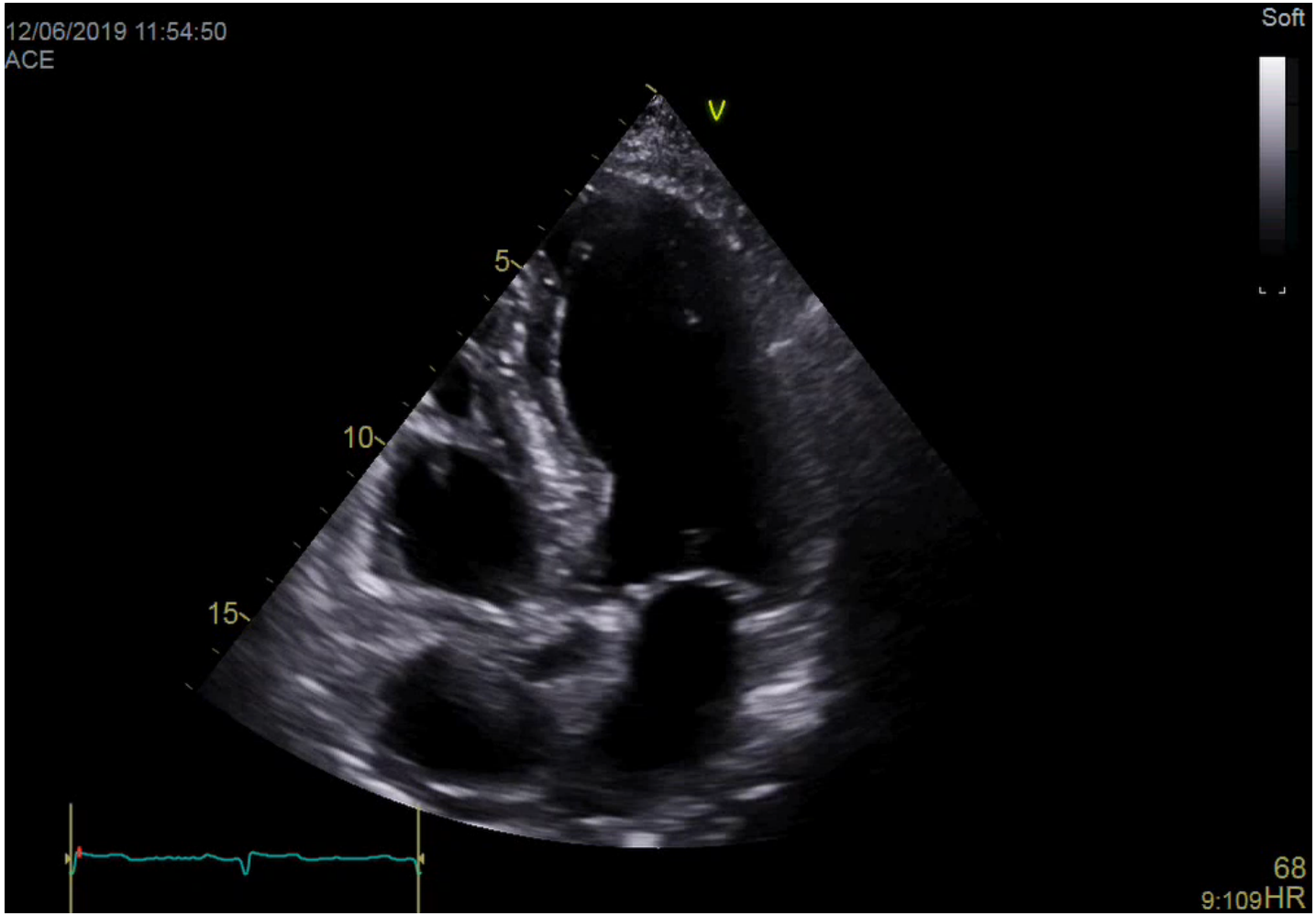
Traitement médical limité

1. diurétiques
2. IEC – Entresto – betabloquants mal supportés
3. anticalciques et digoxine contre-indiqués
4. pacemaker souvent necessaire
5. resynchronisation
6. greffe cardiaque (+/- hépatique)

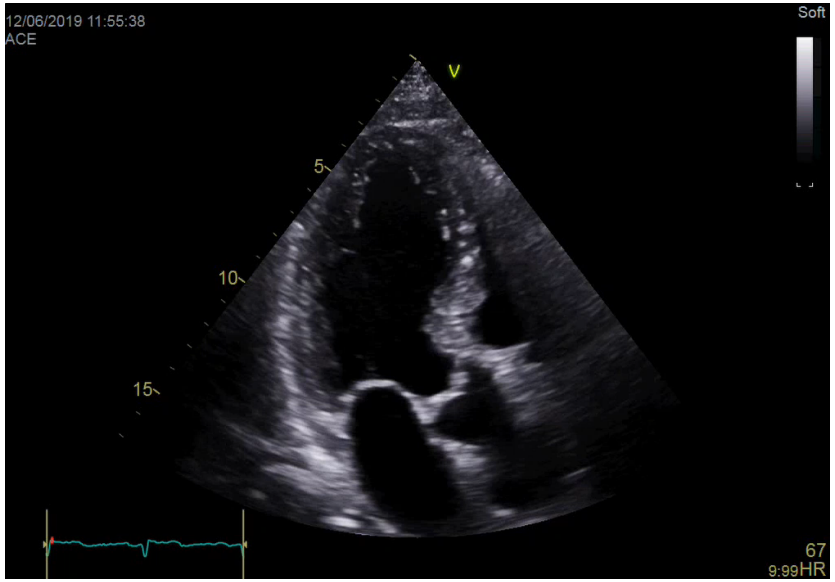
Cas clinique 3: CMH sarcomérique ou amylose ?

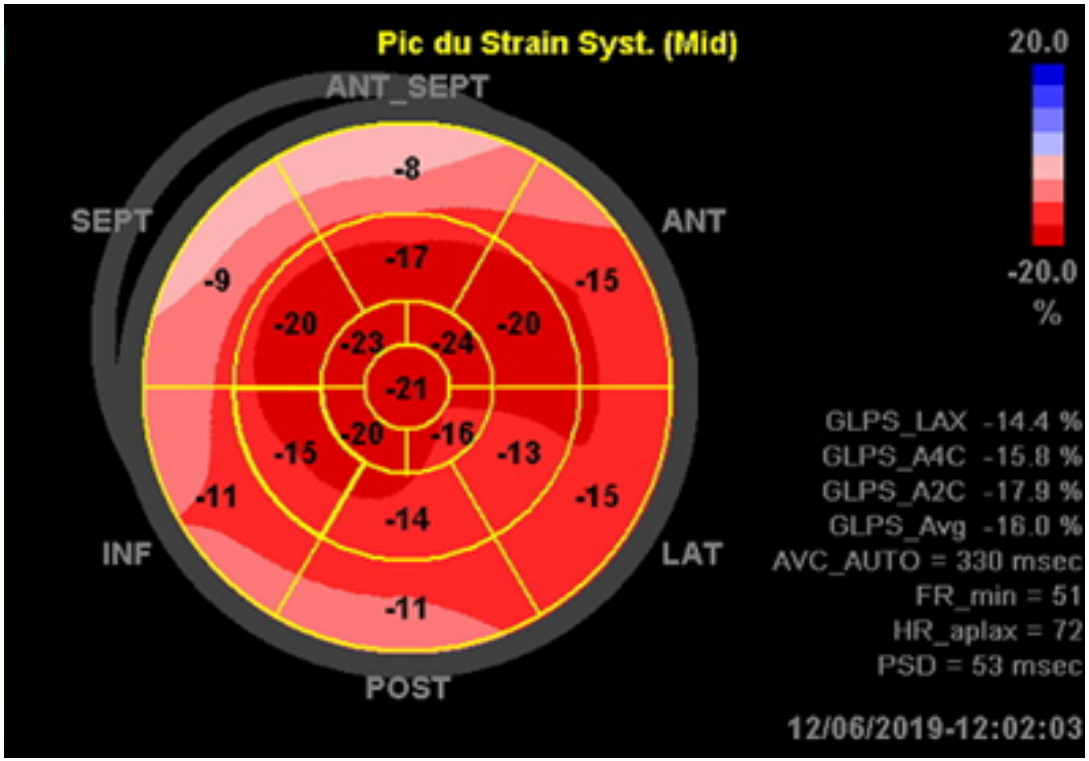


Cas clinique 3: CMH sarcomérique ou amylose ?

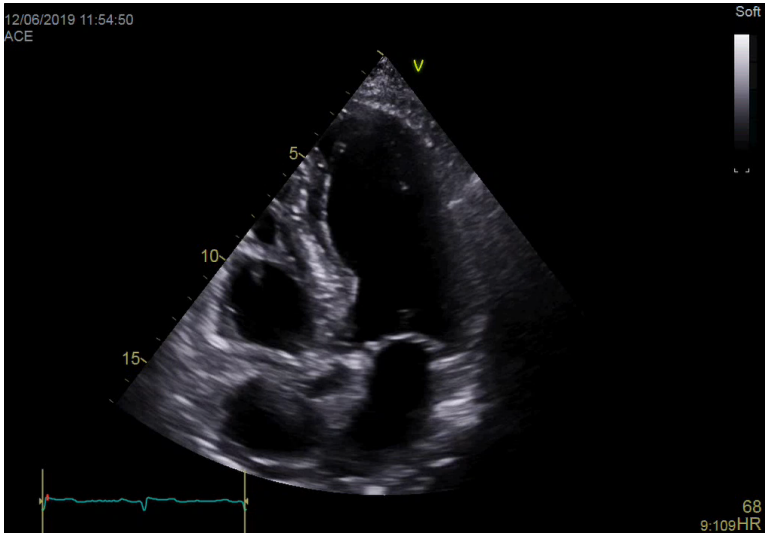


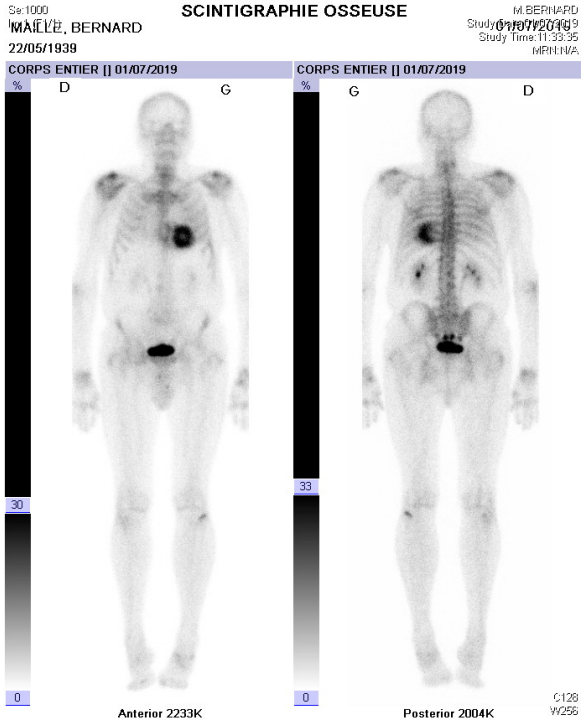
Cas clinique 3: CMH sarcomérique ou amylose ?



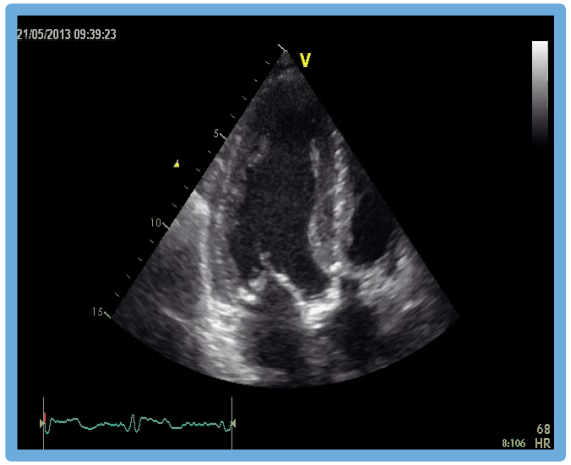


Cas clinique 3: CMH sarcomérique ou amylose ?

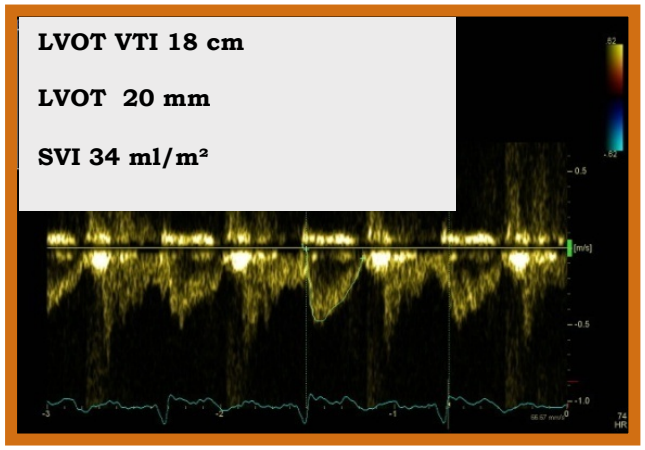




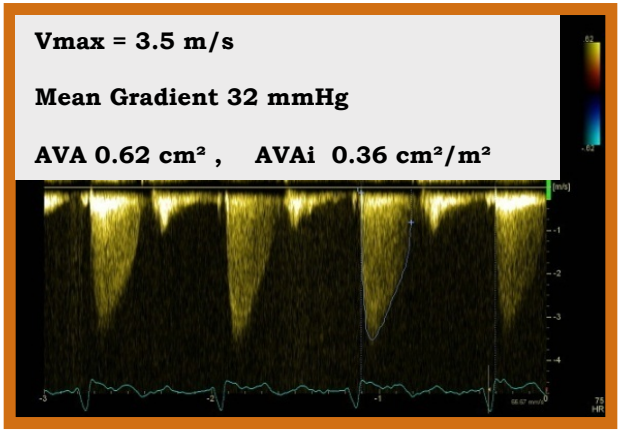
Cas 4: Sténose aortique BD BG



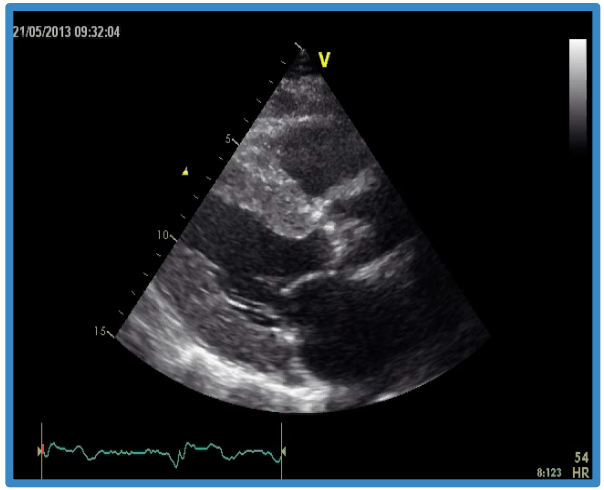
Normal LVEF

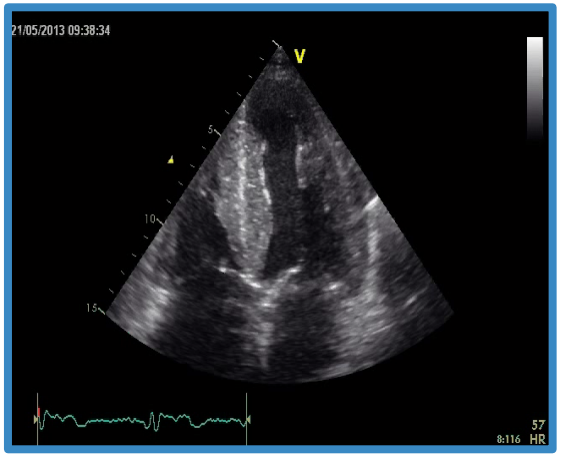


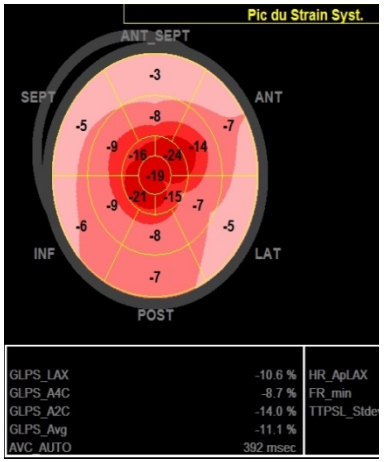
Low gradient



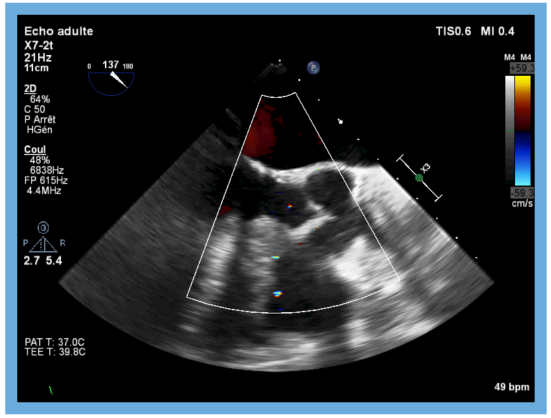
Low flow

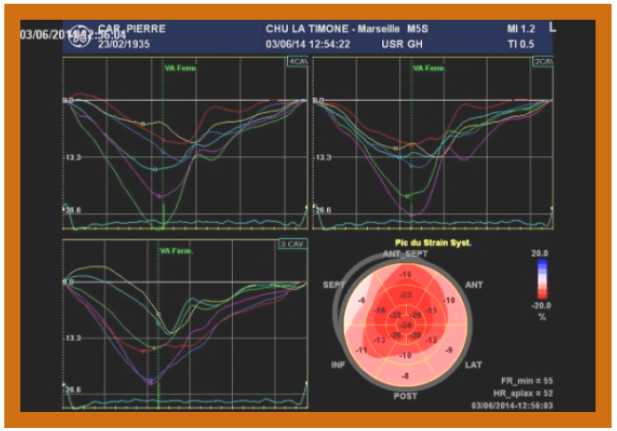


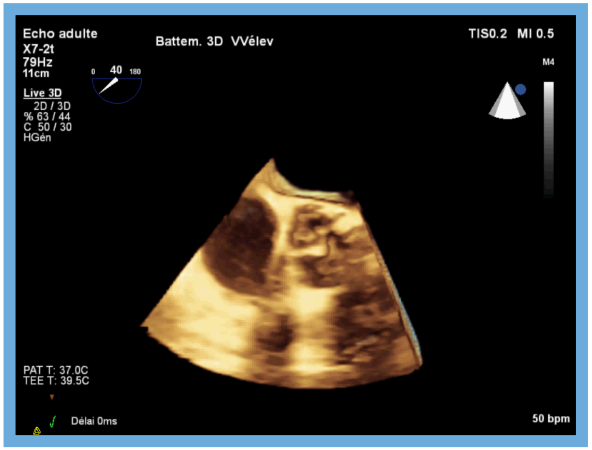


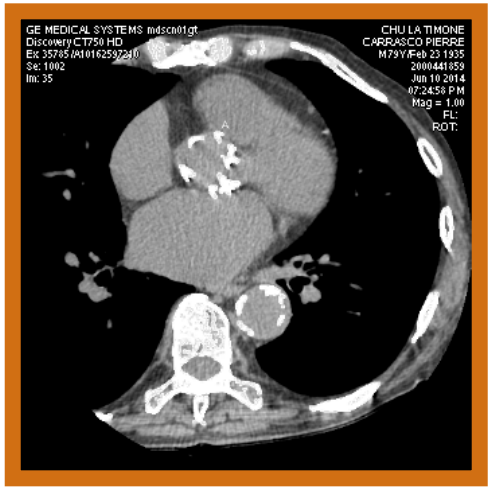


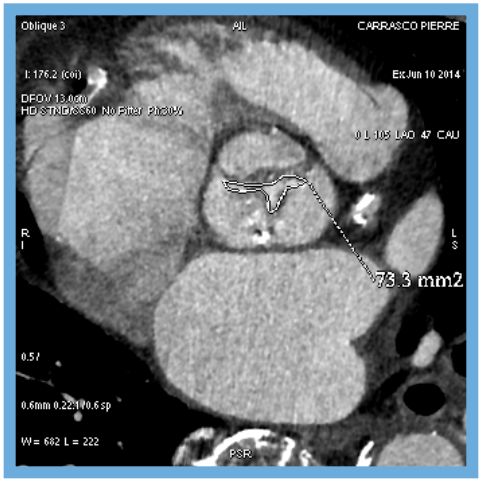
Multimodality Imaging in LFLG AS

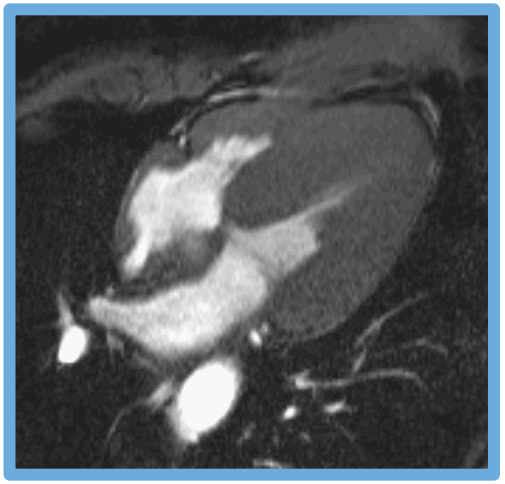




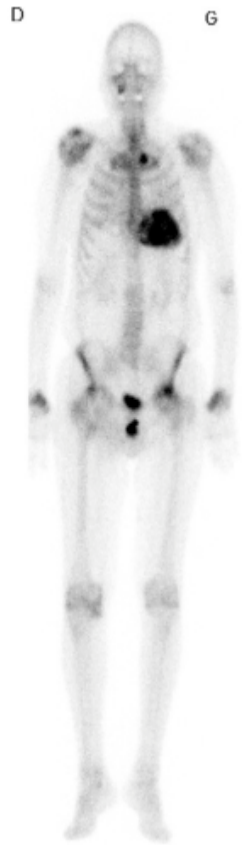








99mTc-HMDP scintigraphy



- **Severe cardiac uptake**
- **Suspected amyloidosis**

Quoi de neuf sur les cardiomyopathies ?

1. **Les centres de Cardiomyopathies**

2. **Cardiomyopathies hypertrophiques**

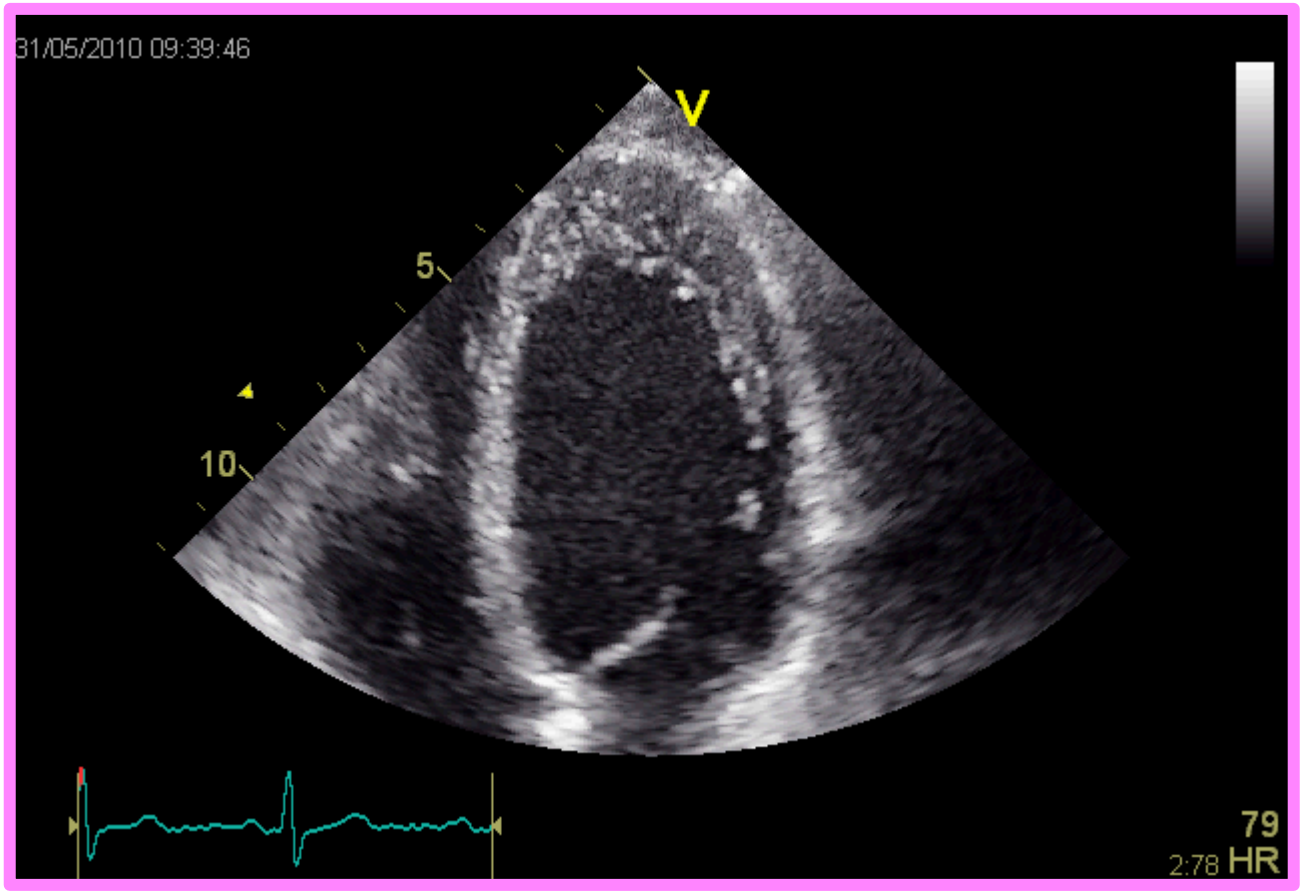
3. **Amylose**

4. ***Non compaction ventriculaire gauche***

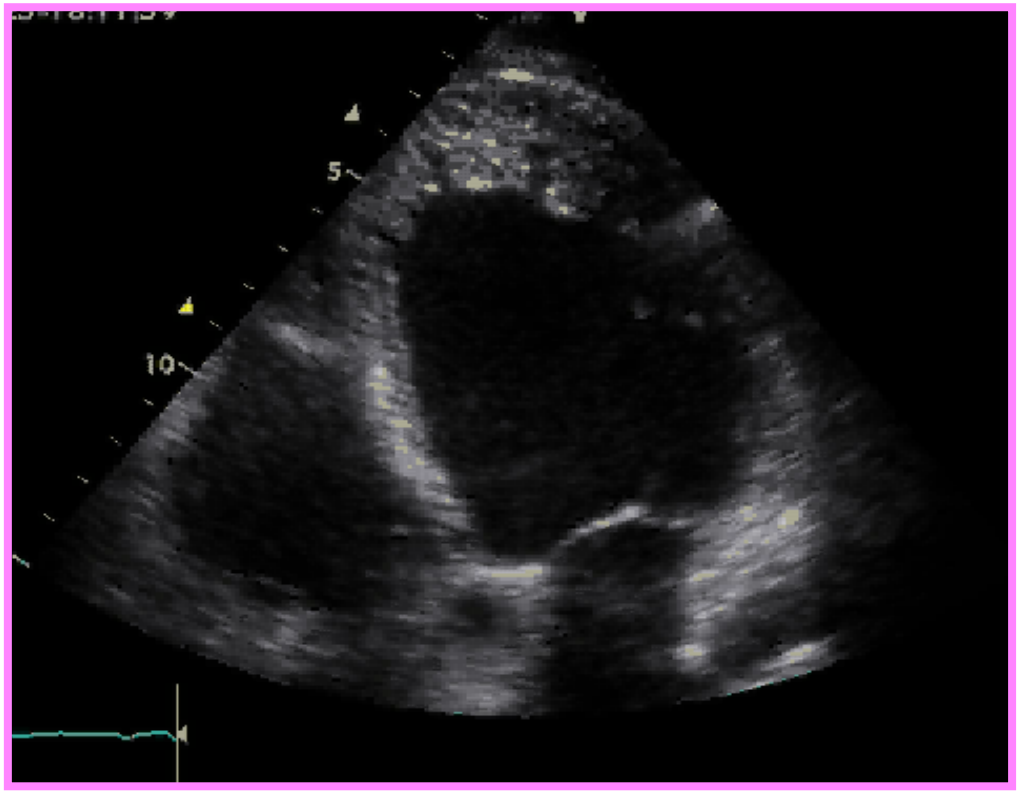
Cas Clinique n° 5

- femme de 30 ans
- pharmacienne
- dépistage car père porteur d'une cardiomyopathie ?
- examen cardiaque et ECG normaux

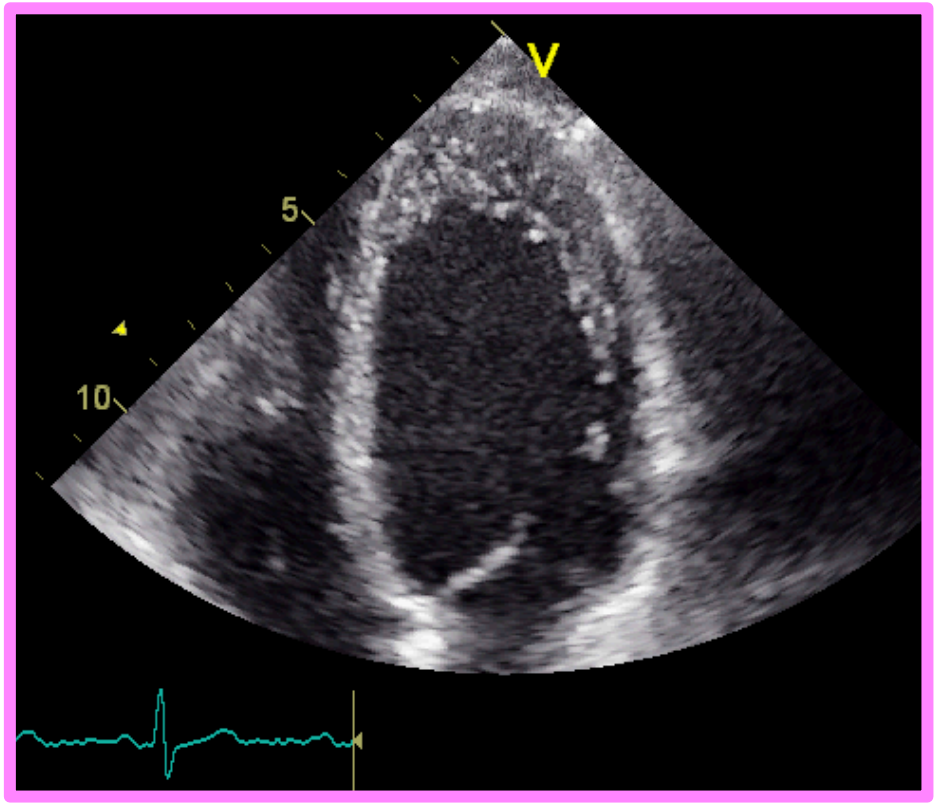
Cas Clinique n° 5



Cas Clinique n° 5



58 year-old man

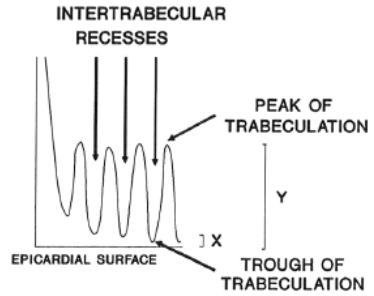


35 year-old woman

LVNC: Diagnostic criteria

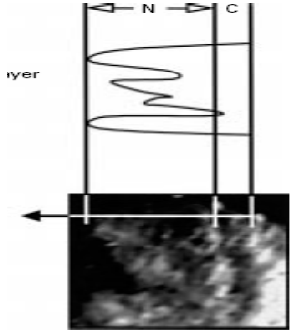
Chin 1990

1. multiple trabeculations
2. two-layer structure
3. X to Y ratio < 0.5
4. SA and apical views



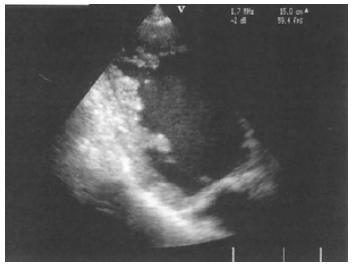
Jenni 2001

1. multiple trabeculations
2. deep recesses
3. two-layer structure
4. NC / C ratio > 2
5. Parasternal SA view

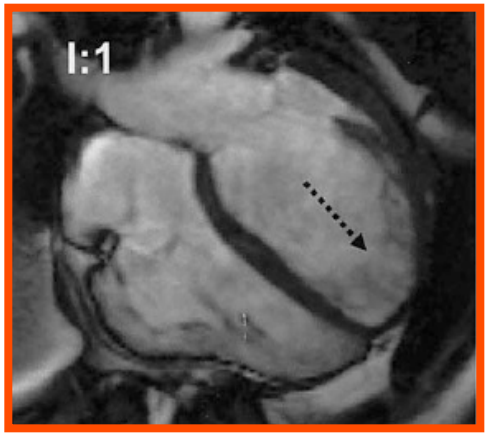


Stöllberger 2002

1. > 3 trabeculations
2. Apically to the PM
3. In 1 image plane
4. Intertrabecular spaces
5. Apical views

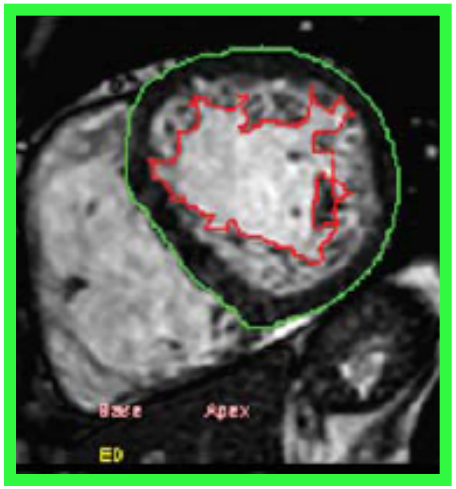


LVNC: MRI diagnostic criteria



Petersen 2005

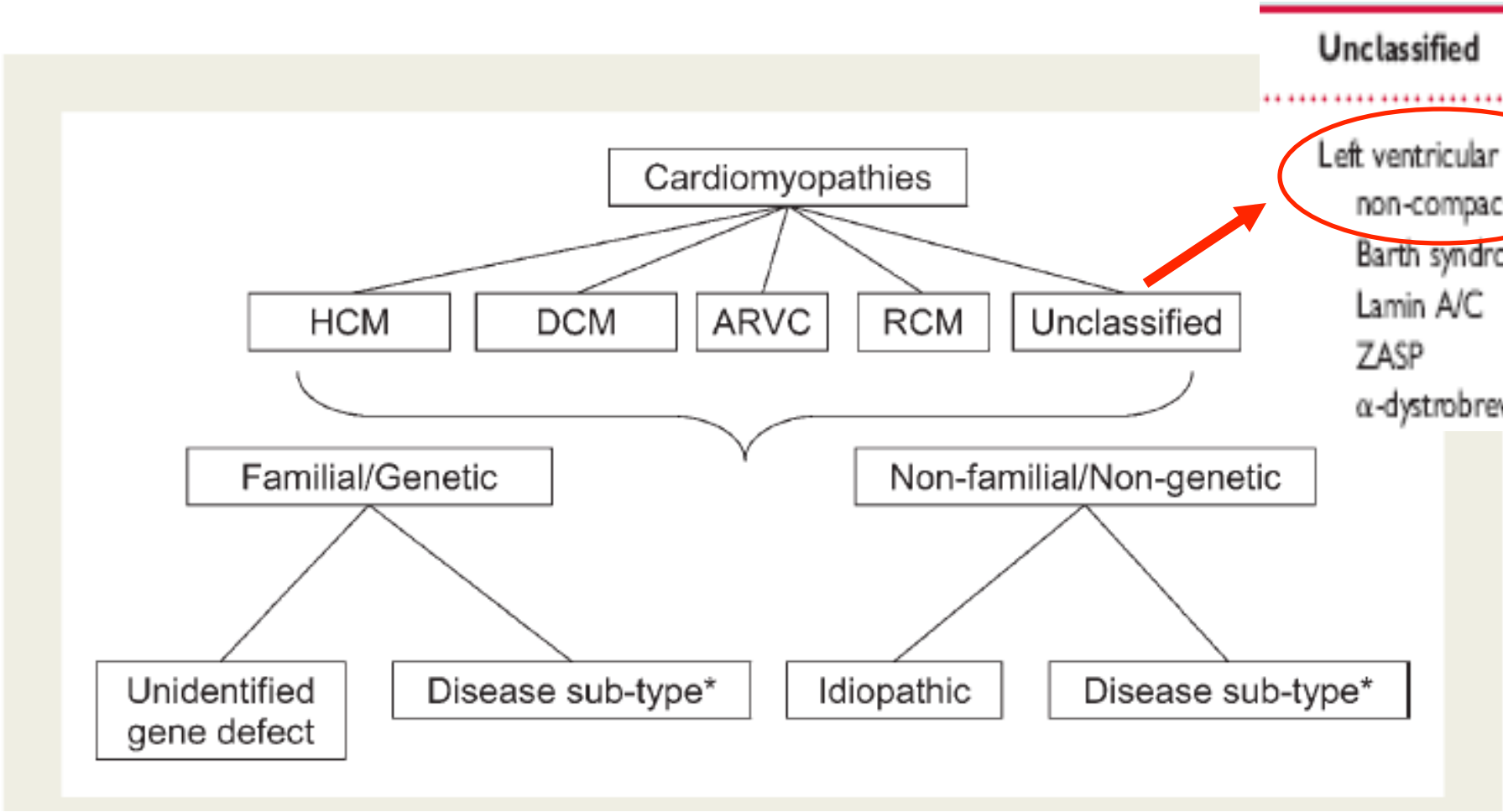
1. multiple trabeculations
2. NC / C ratio > 2.3
3. Diastolic measurement



Jacquier 2010

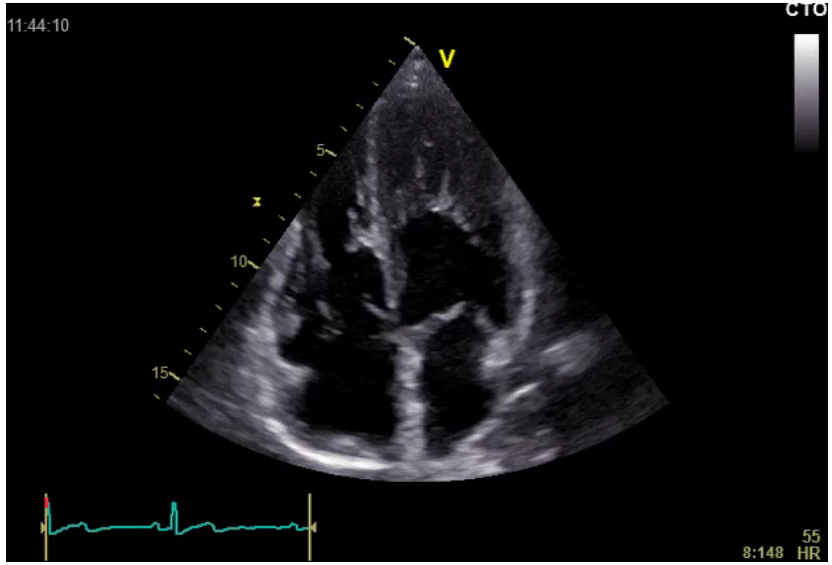
1. multiple trabeculations
2. Trabeculated LV mass
   > 20% of the global LV mass
3. Diastolic measurement

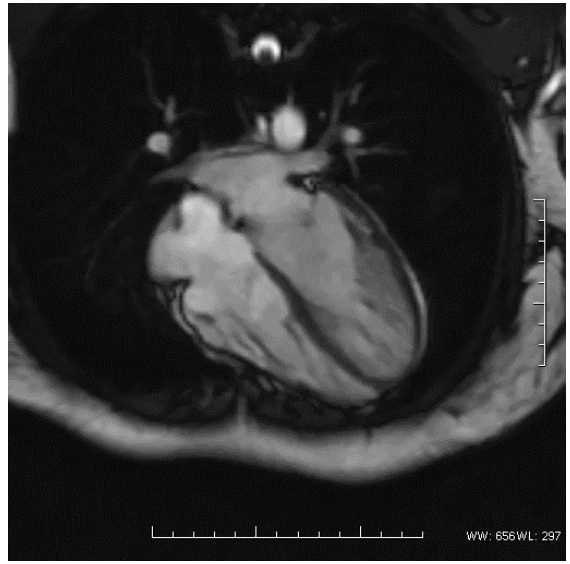
ESC Position Statement 2008



Non-compaction du ventricule gauche

Une cardiomyopathie distincte?





Non-compaction isolée du ventricule gauche

Summary

Isolated Non-Compaction of the Left Ventricle

Isolated non compaction of the left ventricle is a rare congenital cardiomyopathy linked to an arrest of normal myocardial embryogenesis.

We report two cases of isolated non compaction of the left ventricle discovered by echocardiography in 2 males of 30 and 55 years.The first had progressively worsening cardiac insufficiency, the second was being followed for an unexplained cardiomyopathy. In both cases, the diagnosis was able to be confirmed by transthoracic echocardiography, supported by MRI data.

Although present from birth, this condition can become apparent at various ages and is complicated by sudden death (principal cause of mortality), severe cardiac insufficiency, or thrombo-embolic accidents.

The diagnosis of left ventricular non compaction should be considered when faced with unexplained cardiac insufficiency in the adult. Arch Mal Cœur 2003 ; 96 : 339-43.

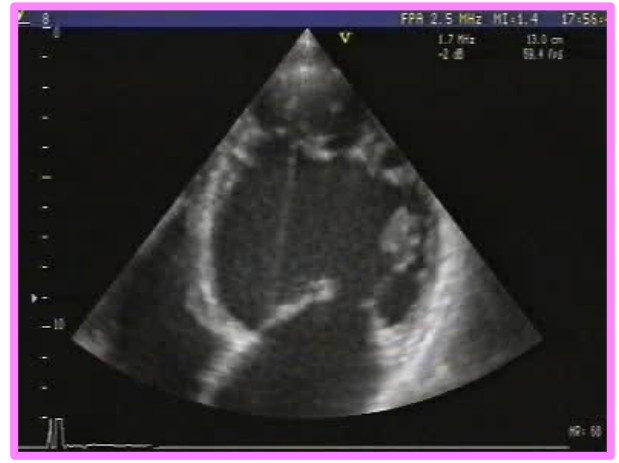
Résumé

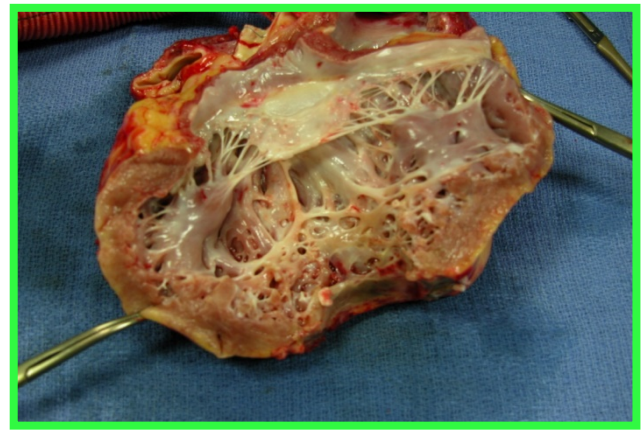
La non-compaction isolée du ventricule gauche est une cardiomyopathie congénitale rare liée à un arrêt de l'embryogenèse normale du myocarde.

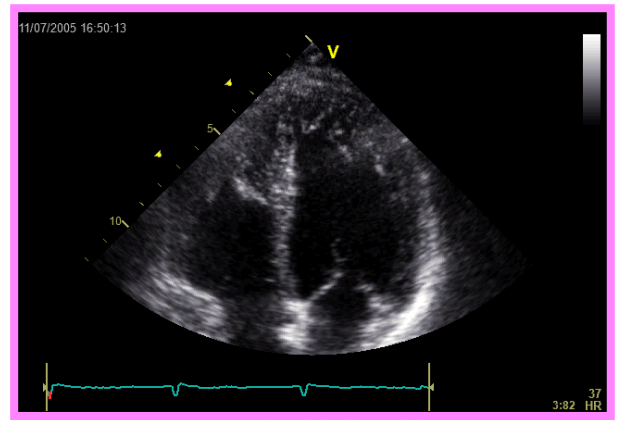
Nous rapportons 2 cas de non-compaction ventriculaire gauche découverts par l'échocardiographie chez 2 hommes de 30 et 55 ans. Le premier avait une insuffisance cardiaque d'aggravation progressive, le second était suivi pour une cardiomyopathie inexpliquée. Dans les 2 cas, le diagnostic a pu être affirmé par l'échocardiographie transthoracique, étayée par les données de l'IRM.

Bien que présente dès la naissance, cette affection peut se révéler à divers âges de la vie et se compliquer de mort subite (principale cause de mortalité), d'insuffisance cardiaque sévère ou d'accidents thrombo-emboliques.

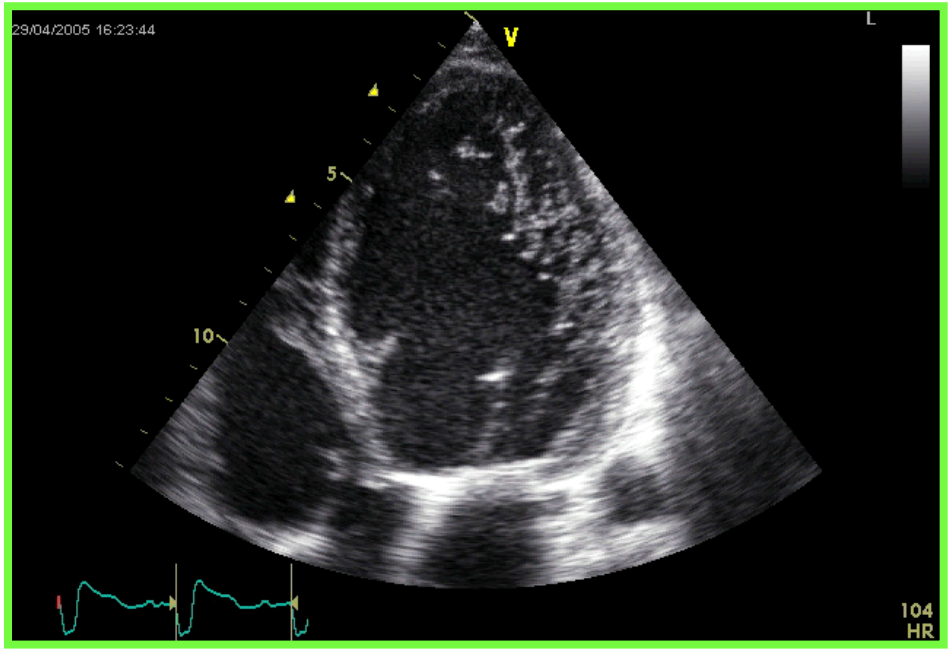
Le diagnostic de non-compaction ventriculaire gauche doit être évoqué devant une insuffisance cardiaque inexpliquée de l'adulte. Arch Mal Cœur 2003 ; 96 : 339-43.

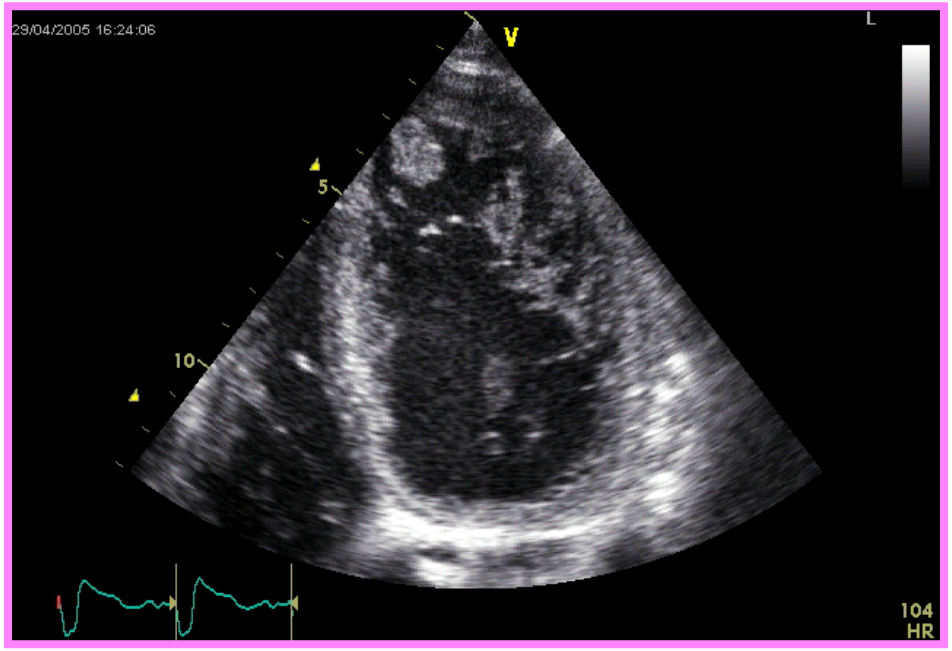






LVNC: typical echo findings





European Journal of Heart Failure Advance Access published December 29, 2010

European Journal of Heart Failure
doi:10.1093/eurjhf/hfq225

Isolated left ventricular non-compaction in adults: clinical and echocardiographic features in 105 patients. Results from a French Registry

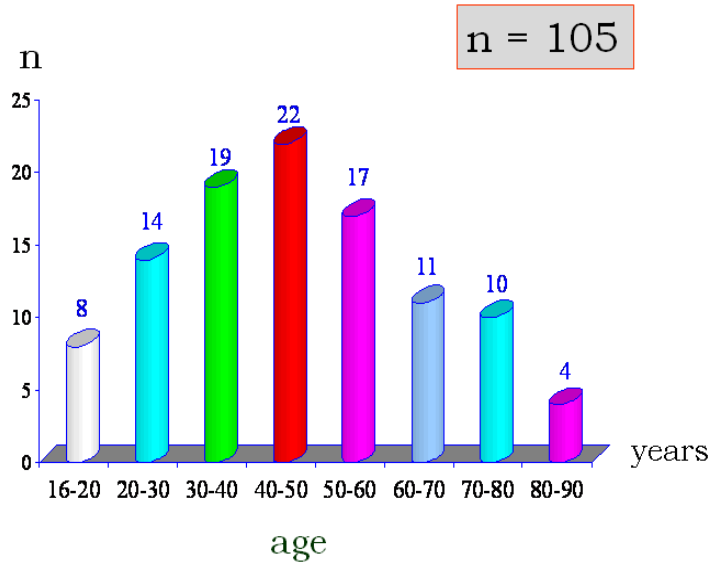
Gilbert Habib[1]*, Philippe Charron[2], Jean-Christophe Eicher[3], Roch Giorgi[4,5], Erwan Donal[6], Thierry Laperche[7], Dominique Boulmier[6], Cécile Pascal[8], Damien Logeart[9], Guillaume Jondeau[10], and Alain Cohen-Solal[9] On behalf of the Working Groups 'Heart Failure and Cardiomyopathies' and 'Echocardiography' of the French Society of Cardiology

The Adult LVNC French Register

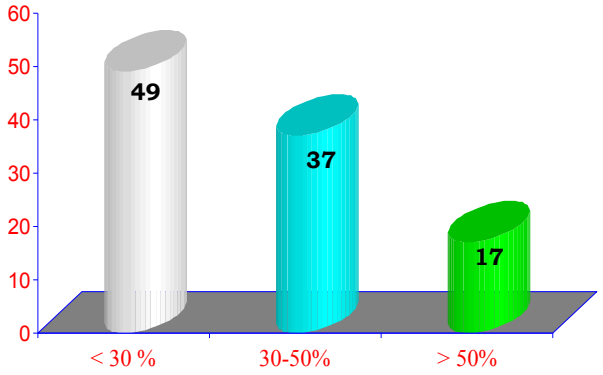
- 105 definite LVNC
- 49 doubtful cases
- 69 men, 36 women
- 18 - 86 years (45 +/-17)
- 25 (24%) > 60 year-old

Habib G - Eur J Heart Fail. 2011;13:177-85

Age

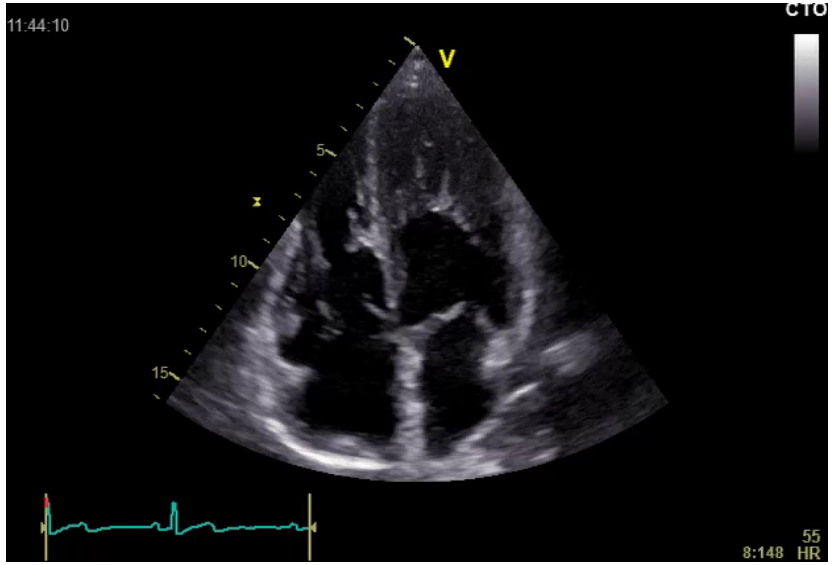


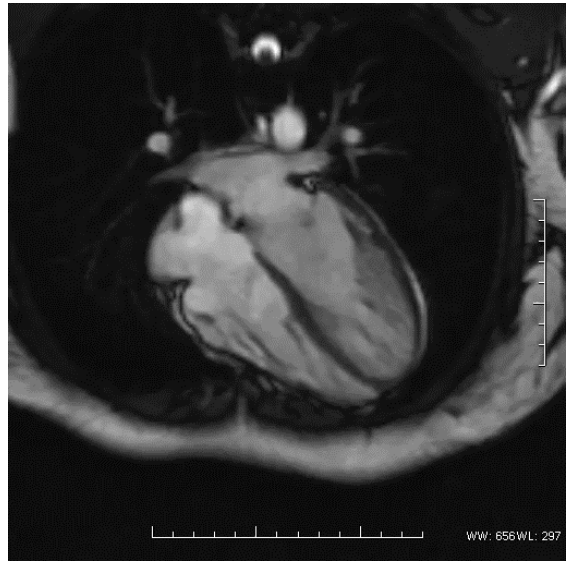
LVEF



Non-compaction du ventricule gauche

Une cardiomyopathie distincte?





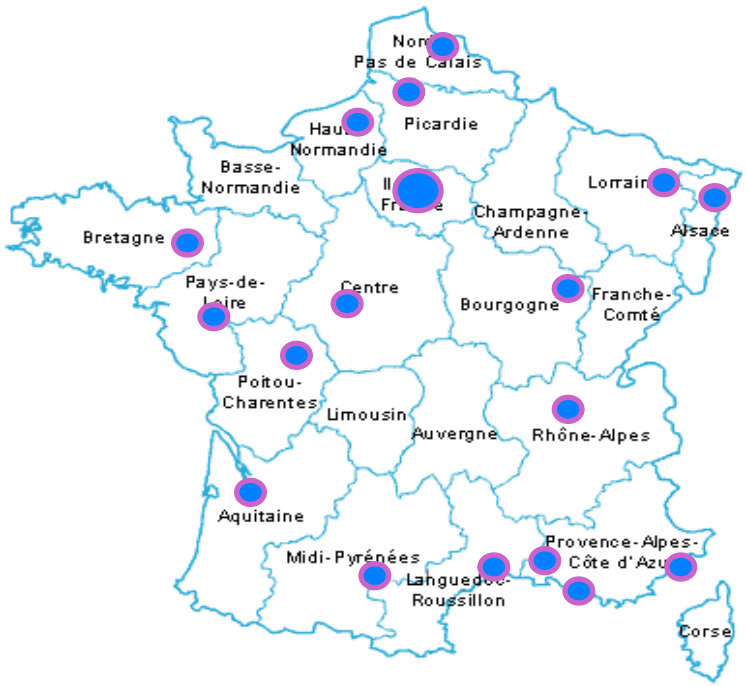
PHRC 2011 N°2011-20
Pronostic des adultes avec Non Compaction Isolée du Ventricule Gauche

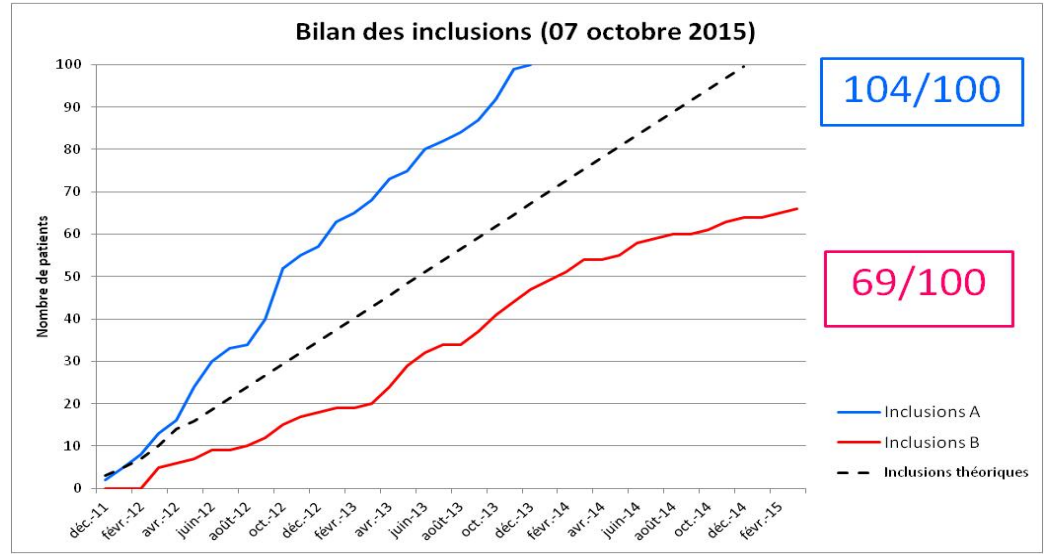
Investigateur principal : Pr Gilbert HABIB
Promoteur : DRCI de l'Assistance Publique des Hôpitaux de Marseille
Ingénieur coordinateur: Cécile LAVOUTE

Centre de Compétence
de Cardiomyopathies
CHU Timone, Marseille

- Etude multicentrique

(24 centres)





CLINICAL GENETICS
An International Journal of Genetics, Molecular and Personalized Medicine

Targeted panel sequencing and allelic spectrum in 95 unrelated adults with left ventricular non-compaction

Pascale Richard[1, 2], Flavie Ader[1], Maguelonne Roux[2], Erwan Donal[3], Jean-Christophe Eicher[4], Nadia Aoutil[1], Olivier Huttin[5], Damien Coisne[6], Guillaume Jondeau[7], Damien Logeart[8], Thierry Laperche[9], Anne-Claire Casalta[10], Nicolas Michel[10], Julie Haentjens[10], Laurence Faivre[11], Cecile Lavoute[10], Karine Nguyen[12], David-Alexandre Tregouët[2], Gilbert Habib[10,13*], Philippe Charron[14,15*]

Methods

Population

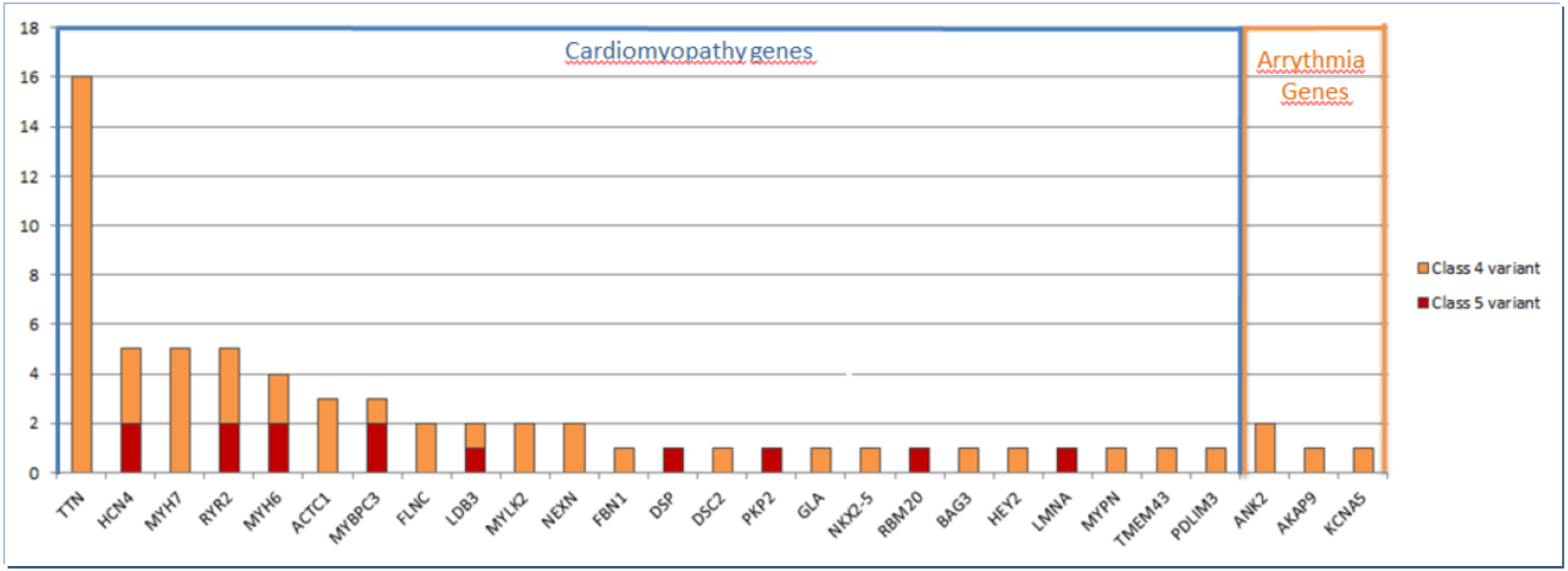
- 95 independent index cases with isolated LVNC
- From 13 French centers
- 56 M & 39 F
- Mean age 46 y. ±15

Molecular analyses

- NGS custom panel of 107 genes *(all the various cardiomyopathies and arrhythmia genes)*
- Nimblegen capture then Illumina MiSeq sequencing
- Criteria for pathogenicity: frequency < 10^{-4}, additional criteria: international guidelines *(ACMG 2015)*

Results

- 66 pathogenic or probably pathogenic variants, including 55 novel and private ones, were identified in 48 patients (50.5%) in 27 genes.
- The most prevalent mutated genes are *TTN*, then *MYH7, HCN4, MYH6, FLNC and RYR2*.
- 13 genes previously published associated with LVNC and 14 additional genes potentially involved for the first time in LVNC.



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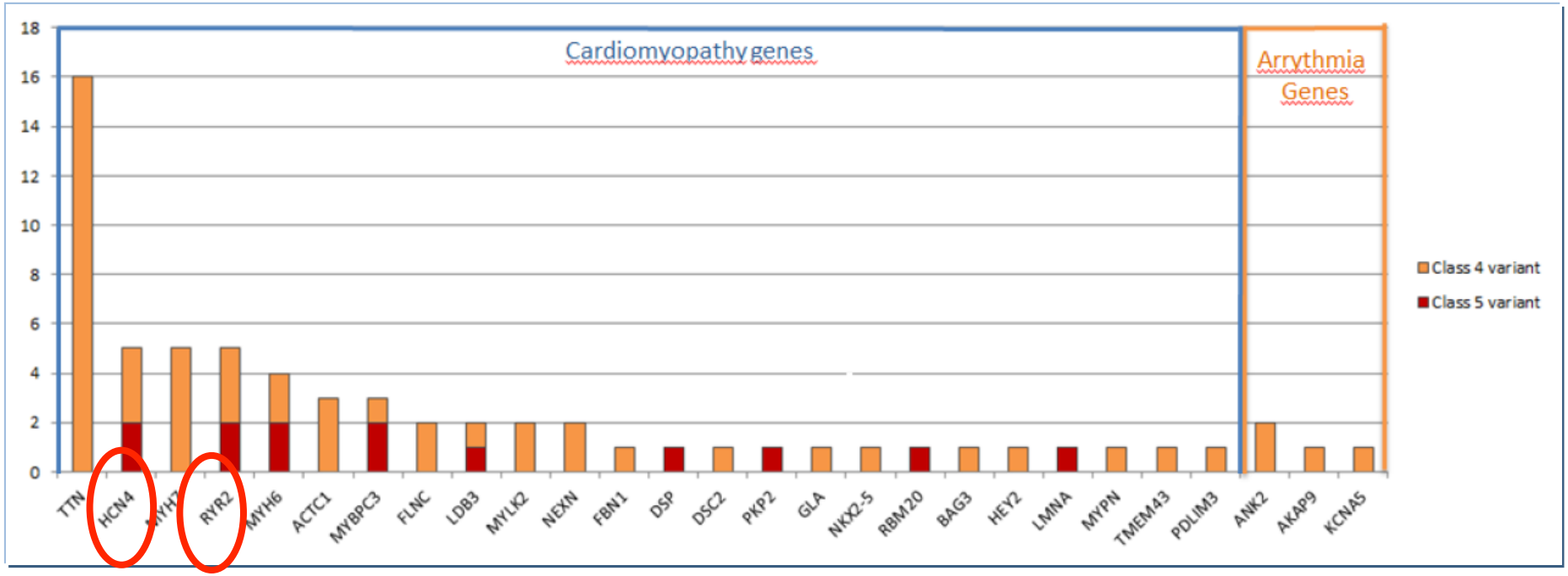


Corrélation génotype / phénotype

Journal of Cardiac Failure Vol. 27 No. 6 2021

Phenotype/Genotype Relationship in Left Ventricular Noncompaction: Ion Channel Gene Mutations Are Associated With Preserved Left Ventricular Systolic Function and Biventricular Noncompaction

Phenotype/Genotype of Noncompaction

MARIE CAMBON-VIALA, MD,[1,#] HILLA GERARD, MD,[1,#] KARINE NGUYEN, MD,[2,3,#] PASCALE RICHARD,[4,5] FLAVIE ADER, MD,[4,5] JEAN-FRANÇOIS PRUNY, MD,[13] ERWAN DONAL, MD,[6] JEAN-CHRISTOPHE EICHER, MD,[7] OLIVIER HUTTIN, MD,[8] CHRISTINE SELTON-SUTY, MD,[8] PASCALE RAUD-RAYNIER, MD,[9] GUILLAUME JONDEAU, MD,[10] NICOLAS MANSENCAL, MD,[11] CAROLINE SAWKA, MD,[12] ANNE-CLAIRE CASALTA, MD,[1] NICOLAS MICHEL, MD,[1] VALERIA DONGHI, MD,[1] HÉLèNE MARTEL, MD,[1] LAURENCE FAIVRE, MD,[12] PHILIPPE CHARRON, MD,[5,13,†] AND GILBERT HABIB, MD[1,14†]

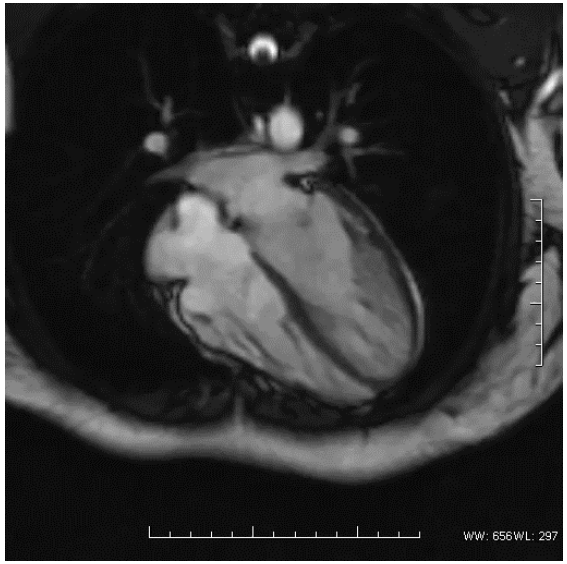
Aix*Marseille université

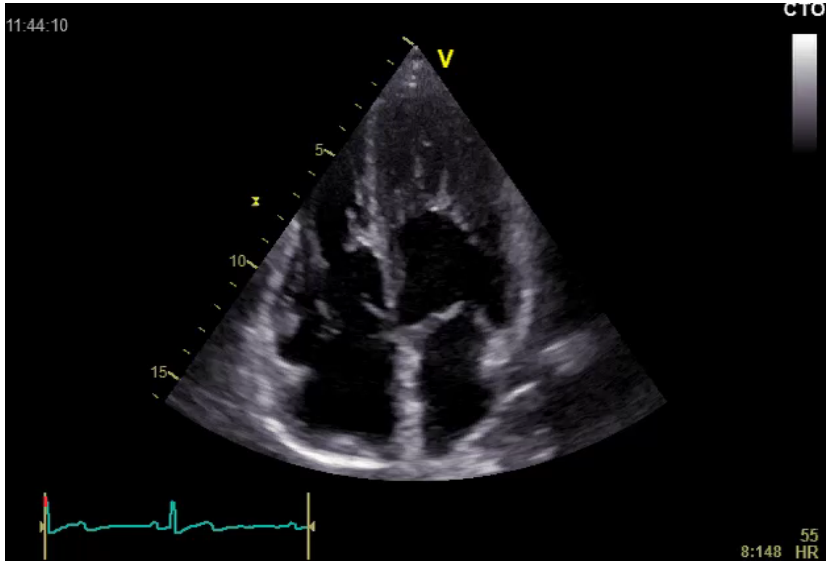
EACVI EUROPEAN ASSOCIATION OF CARDIOVASCULAR IMAGING

EUROPEAN SOCIETY OF CARDIOLOGY®

FACULTÉ DE MÉDECINE DE MARSEILLE

Biventricular non compaction?





Corrélation génotype / phénotype

	Ion channel genes mutations	Other patients	p	HCN4 mutated	Other patients	p
	n = 30 (27%)	*n = 81 (73%)*		*n = 19 (19%)*	*n = 81 (81%)*	
Male gender (%)	13 (43.3)	47 (58)	**0.15**	8 (42)	47 (58)	0.16
Age (mean ±sd, years)	38.5 ± 17.6	46.9 ± 15.9	**0.02**	41.8 ± 18.2	46.9 ± 15.9	0.28
Heart rate (mean ± sd, bpm)	54.2 ± 20.7	69.8 ± 14.5	**0.01**	45.9 ± 7.1	69.8 ± 14.5	**<0.001**
Left ventricular éjection fraction (%)	58.3 ± 11.2	42.0 ± 14.2	**<0.001**	59.3 ± 12.0	42.0 ± 14.2	**<0.001**
Indexed telediastolic volume (mean ±sd, mL/m2)	71.9 ± 20.9	86.9 ± 35.3	**0.01**	70.1 ± 22.7	86.9 ± 35.3	0.05
Indexed telesystolic volume (mean ±sd, mL/m2)	29.7 ± 16.2	53.2 ± 31.3	**<0.001**	28.8 ± 17.1	53.2 ± 31.3	**<0.001**
Cardiac index (mean ±sd, mL/min/m2)	2.6 ± 0.5	2.5 ± 0.8	0.59	2.4 ± 0.2	2.5 ± 0.8	0.31
NC/C diastole (mean ±sd)	2.5 ± 0.3	2.4 ± 0.4	0.58	2.7 ± 0.3	2.4 ± 0.4	0.07
NC/C systole (mean ±sd)	1.9 ± 0.5	2.2 ± 0.3	**0.02**	1.9 ± 0.4	2.2 ± 0.3	**0.03**
Number of non-compacted segments (mean±sd)	5.4 ± 1.9	5.3 ± 1.5	0.83	5.4 ± 1.5	5.3 ± 1.5	0.92
Biventricular non-compaction (%)	17 (53.1)	15 (18.5)	**<0.001**	11 (58.9)	15 (18.5)	**<0.001**

Corrélation génotype / phénotype

	Ion channel genes mutations *n = 30 (27%)*	Other patients *n = 81 (73%)*	p	HCN4 mutated *n = 19 (19%)*	Other patients *n = 81 (81%)*	p
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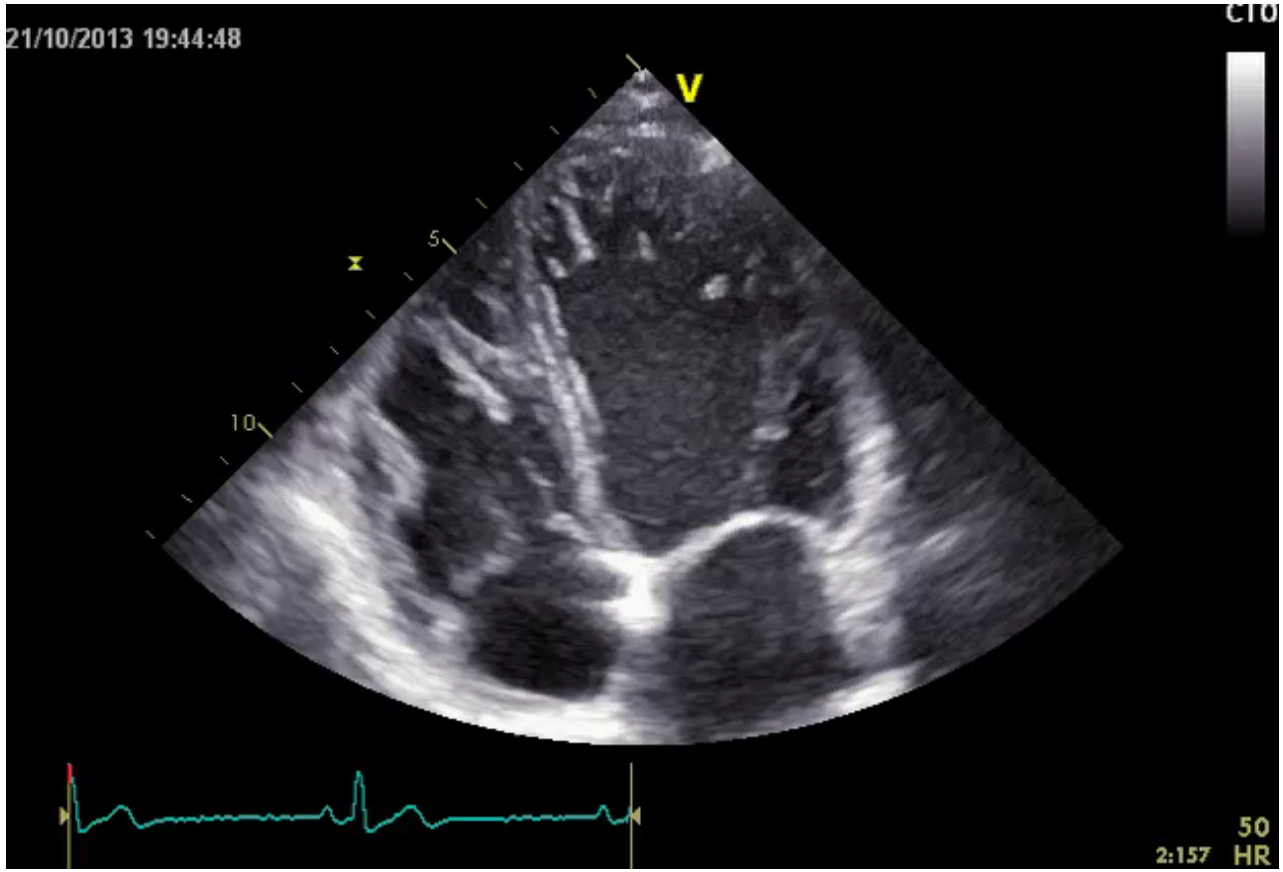
Association between ion channel gene mutations and biventricular non compaction

Corrélation génotype / phénotype

	Ion channel genes mutations	Other patients	p	HCN4 mutated	Other patients	p
	n = 30 (27%)	*n = 81 (73%)*		*n = 19 (19%)*	*n = 81 (81%)*	
Male gender (%)	13 (43.3)	47 (58)	**0.15**	8 (42)	47 (58)	0.16
Age (mean ±sd, years)	38.5 ± 17.6	46.9 ± 15.9	**0.02**	41.8 ± 18.2	46.9 ± 15.9	0.28
Heart rate (mean ± sd, bpm)	54.2 ± 20.7	69.8 ± 14.5	**0.01**	45.9 ± 7.1	69.8 ± 14.5	**<0.001**
Left ventricular éjection fraction (%)	58.3 ± 11.2	42.0 ± 14.2	**<0.001**	59.3 ± 12.0	42.0 ± 14.2	**<0.001**
Indexed telediastolic volume (mean ±sd, mL/m2)	71.9 ± 20.9	86.9 ± 35.3	**0.01**	70.1 ± 22.7	86.9 ± 35.3	0.05
Indexed telesystolic volume (mean ±sd, mL/m2)	29.7 ± 16.2	53.2 ± 31.3	**<0.001**	28.8 ± 17.1	53.2 ± 31.3	**<0.001**
Cardiac index (mean ±sd, mL/min/m2)	2.6 ± 0.5	2.5 ± 0.8	0.59	2.4 ± 0.2	2.5 ± 0.8	0.31
NC/C diastole (mean ±sd)	2.5 ± 0.3	2.4 ± 0.4	0.58	2.7 ± 0.3	2.4 ± 0.4	0.07
NC/C systole (mean ±sd)	1.9 ± 0.5	2.2 ± 0.3	**0.02**	1.9 ± 0.4	2.2 ± 0.3	**0.03**
Number of non-compacted segments (mean±sd)	5.4 ± 1.9	5.3 ± 1.5	0.83	5.4 ± 1.5	5.3 ± 1.5	0.92
Biventricular non-compaction (%)	17 (53.1)	15 (18.5)	**<0.001**	11 (58.9)	15 (18.5)	**<0.001**

Association between HCN4 mutation and the complex phenotype associating sinus bradycardia and biventricular non compaction



Ion channel mutations, particularly HCN4, should be systematically searched in patients with LVNC associated with either bradycardia or biventricular noncompaction

PRONOSTIC DES ADULTES PORTEURS D'UNE NON COMPACTION ISOLÉE DU VENTRICULE GAUCHE :

RÉSULTATS D'UNE ÉTUDE PROSPECTIVE MULTICENTRIQUE

Hilla Gérard-Pettel

Soutenance de thèse – 29.10.2020

D.E.S Cardiologie et Médecine Vasculaire

Faculté de Médecine

Aix*Marseille Université

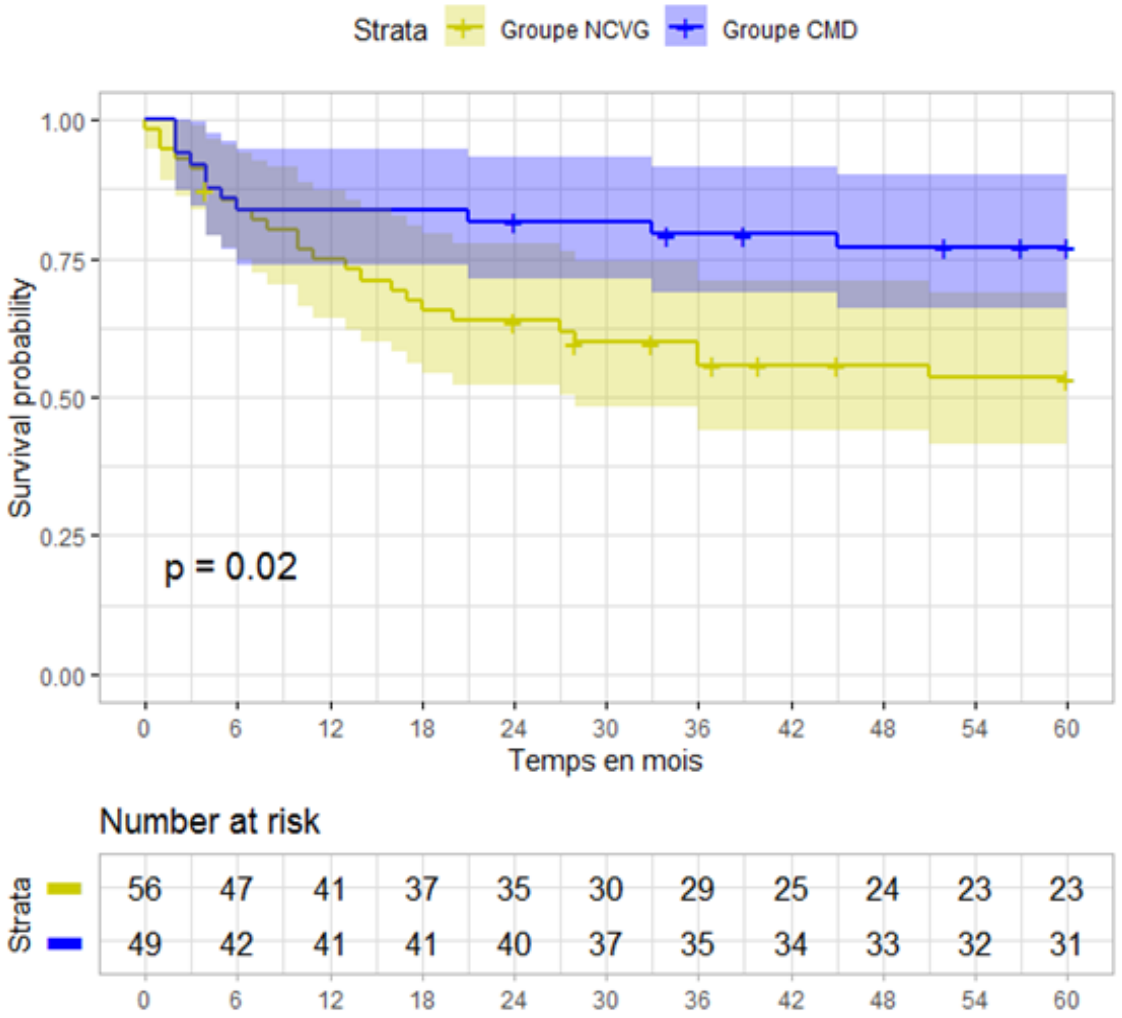
Critère de jugement principal et secondaire

Critère de jugement principal combiné – à 2 ans de suivi

- Décès cardio-vasculaire
- Transplantation cardiaque
- Hospitalisation pour insuffisance cardiaque
- Hospitalisation pour évènement embolique
- Hospitalisation pour complication rythmique

Critères de jugement secondaire

- Survenue d'un des éléments du critère combiné
- Aggravation des volumes ventriculaires et de la FEVG



CJP à 5 ans

- NCVG : N = 56
- CMD : N= 49 (- 2)

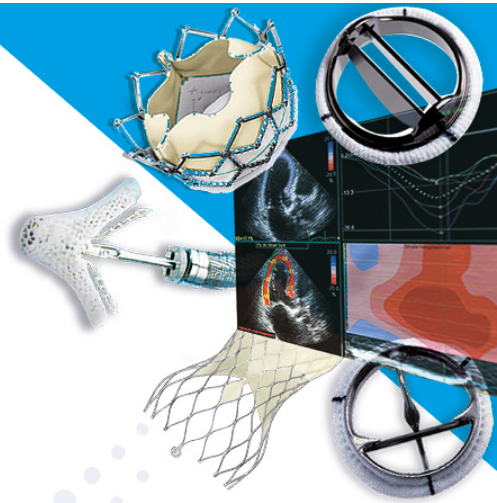
CJP atteint

- NCVG : 33 (58.9%)
- CMD : 18 (36.7%)

Conclusions

1. classifications imparfaites
2. rôle majeur de l'échographie et de l'IRM
3. intérêt de la biopsie endomyocardique et de la génétique
4. intérêt d'une prise en charge multidisciplinaire
5. une cardiomyopathie peut en cacher une autre
6. rechercher les étiologies ayant une conséquence pronostique ou thérapeutique
7. intérêt des centres de cardiomyopathies

CARDIO VALVES



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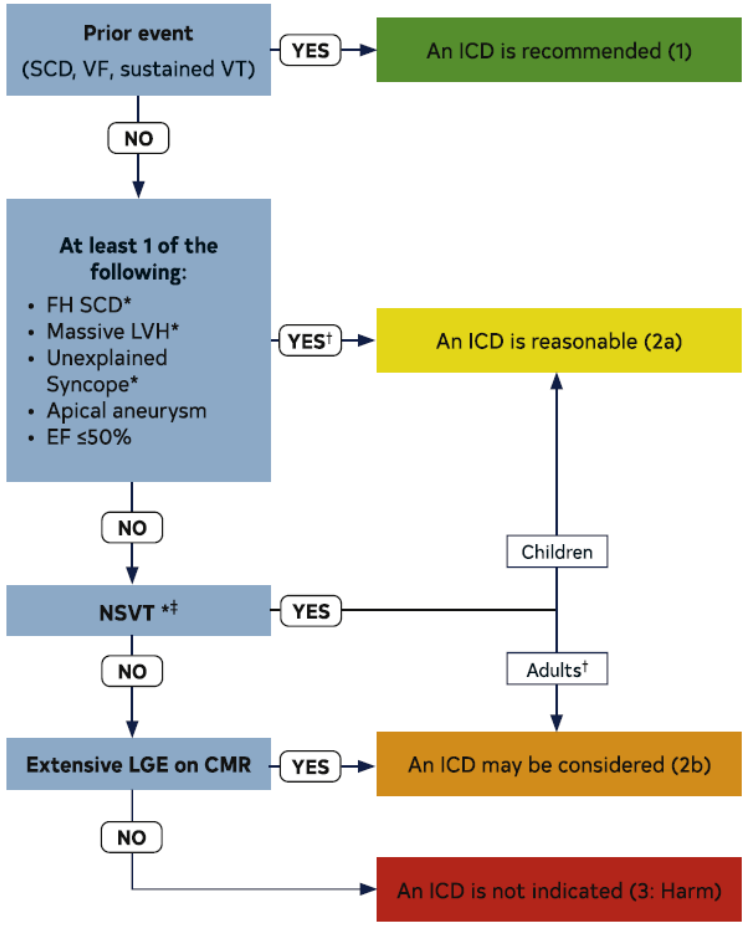
CMH: indications du défibrillateur

FIGURE 3 ICD Patient Selection



Algorithme décisionnel « américain »
ACC /AHA guidelines 2020

Algorithme décisionnel « Européen »

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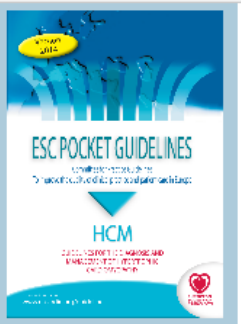
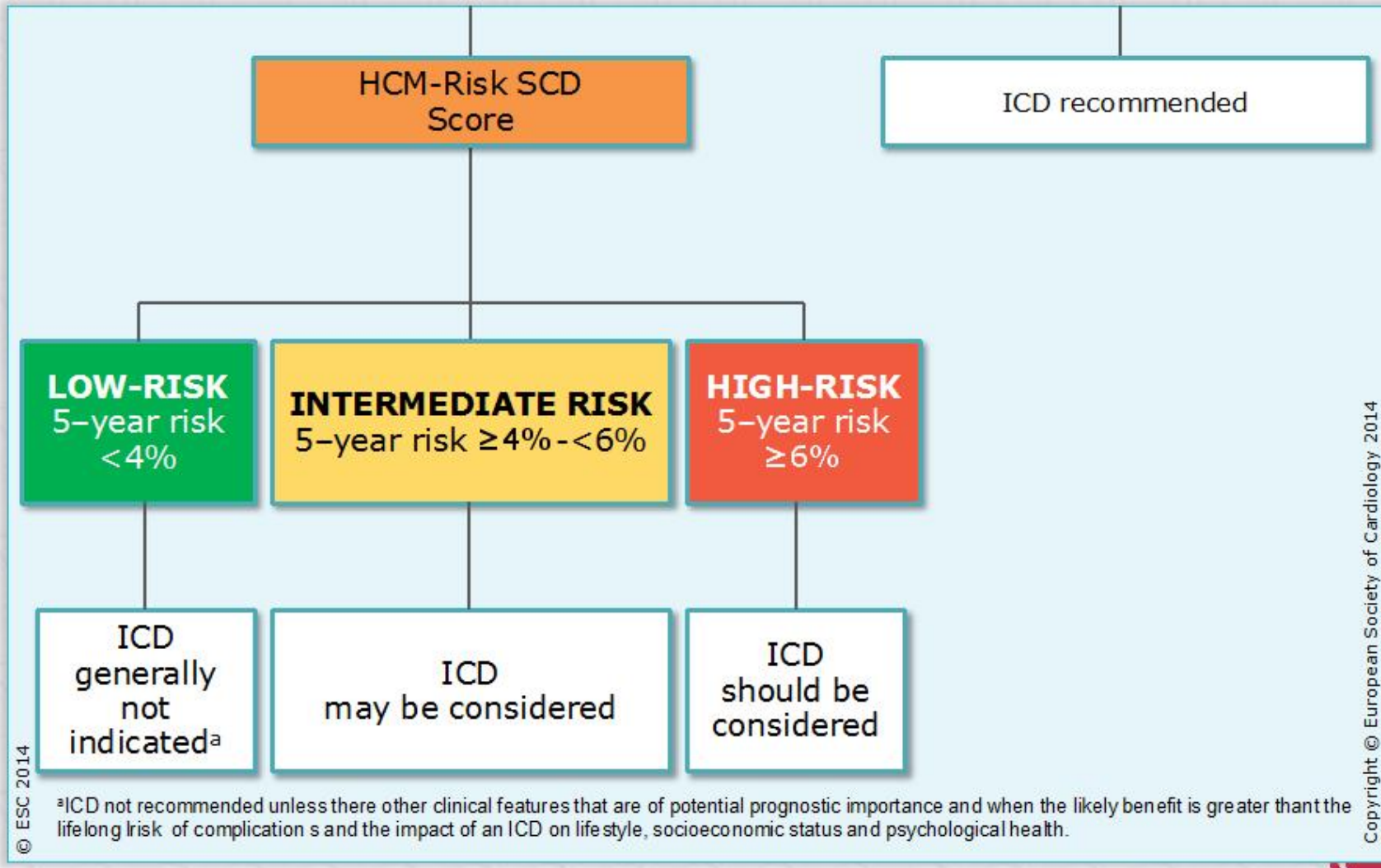
HCM Risk-SCD Calculator



Age	19 **Years**	*Age at evaluation*
Maximum LV wall thickness	35 **mm**	*Transthoracic Echocardiographic measurement*
Left atrial size	38 **mm**	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	50 **mmHg**	*The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients should be determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity*
Family History of SCD	(•) No ( ) Yes	*History of sudden cardiac death in 1 or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).*
Non-sustained VT	( ) No (•) Yes	*3 consecutive ventricular beats at a rate of 120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	(•) No ( ) Yes	*History of unexplained syncope at or prior to evaluation.*

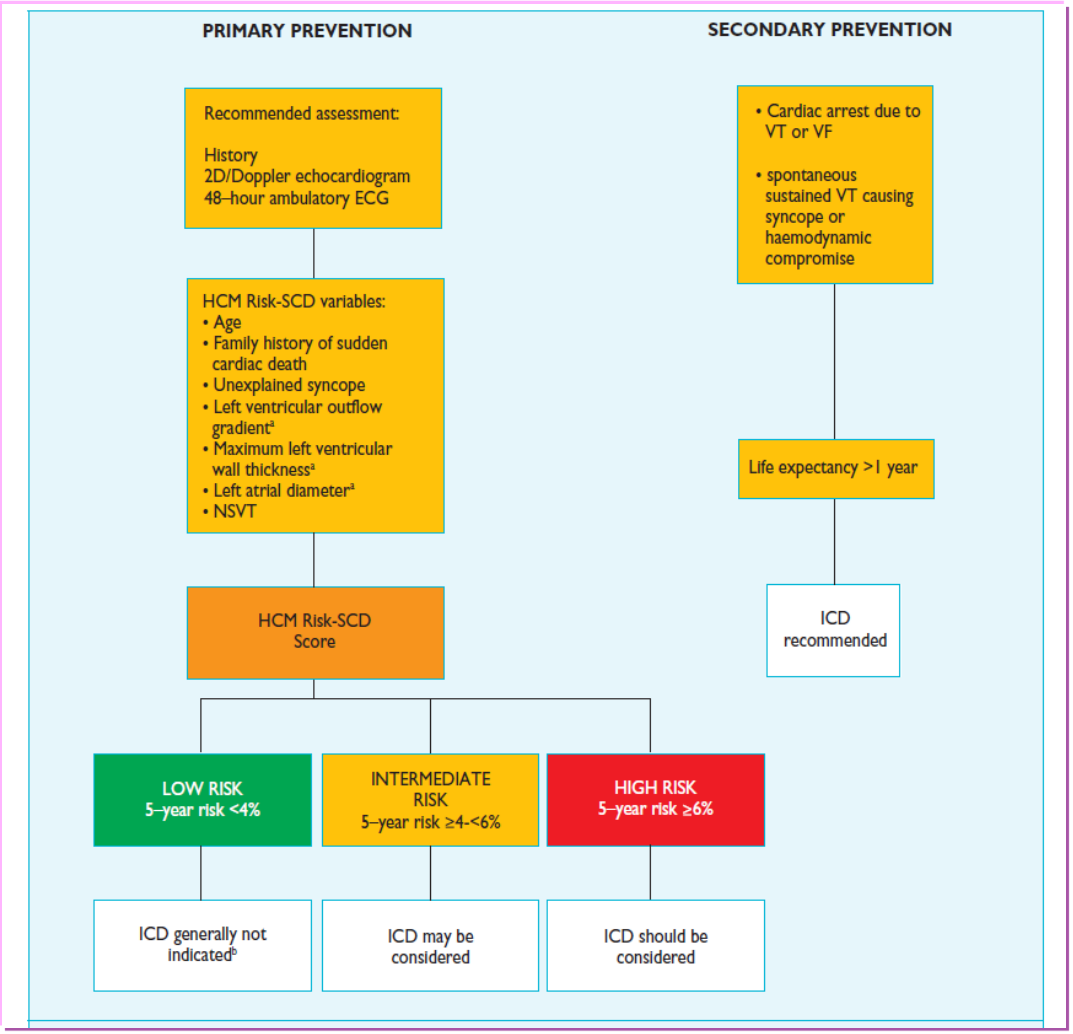
Risk of SCD at 5 years (%):	7.53
ESC recommendation:	ICD should be considered

Flow chart for ICD implantation

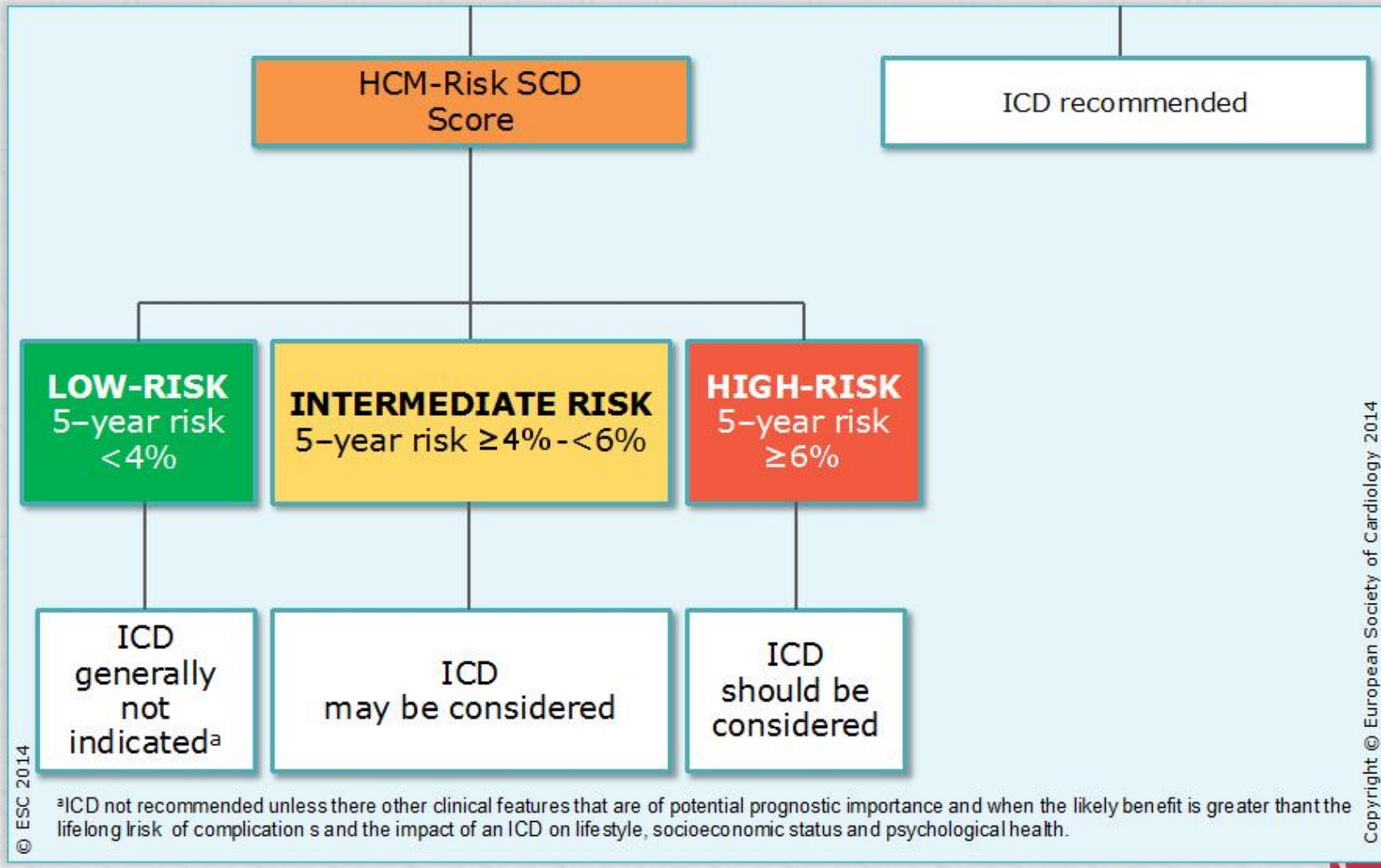


European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Algorithme décisionnel « Européen »



Flow chart for ICD implantation



European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

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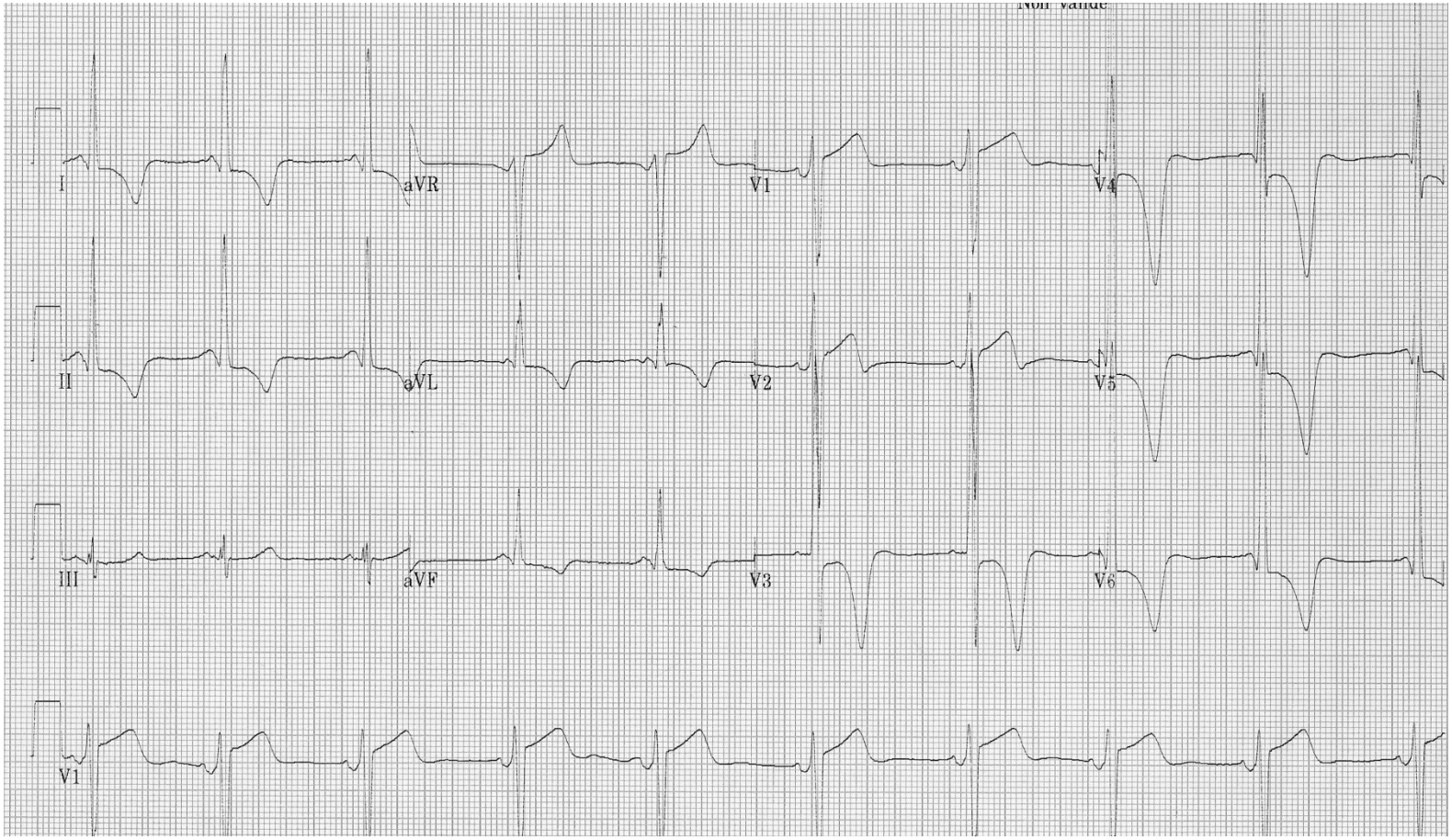
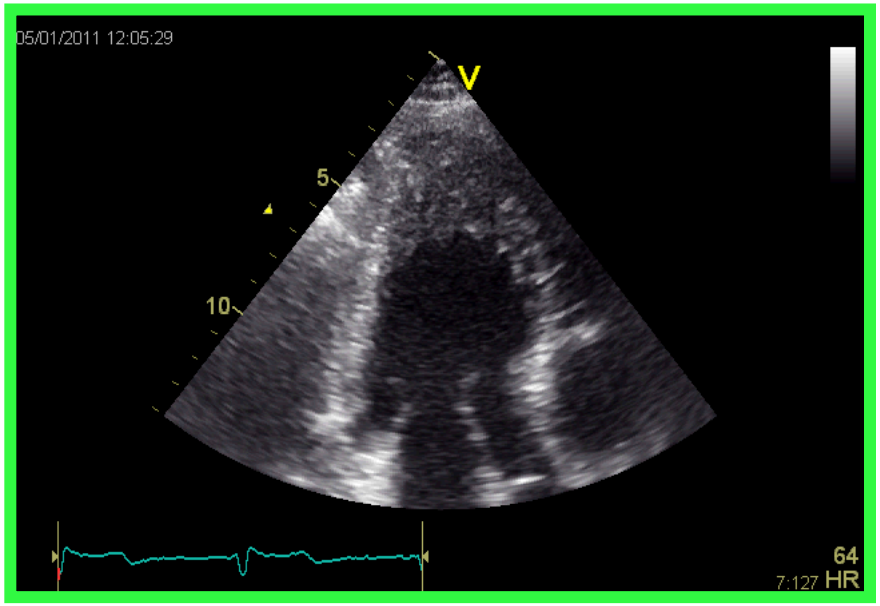
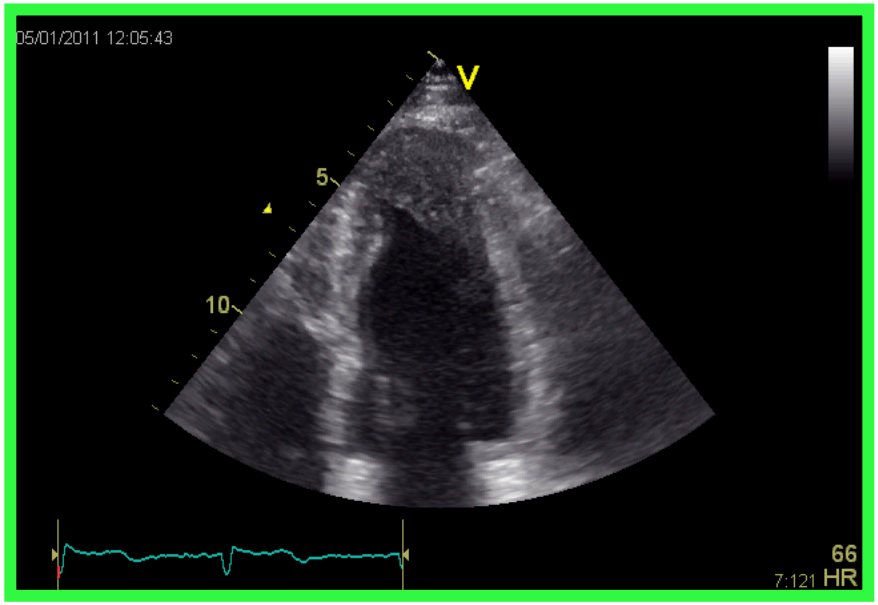
Case 5: Familial HCM

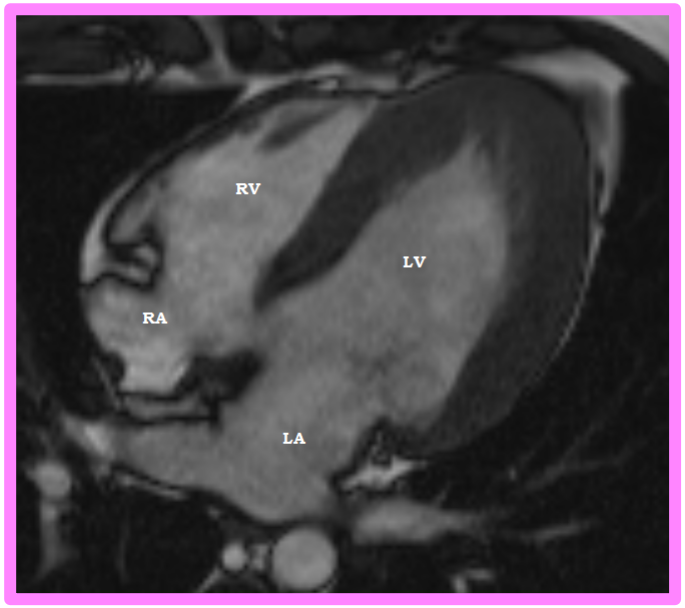


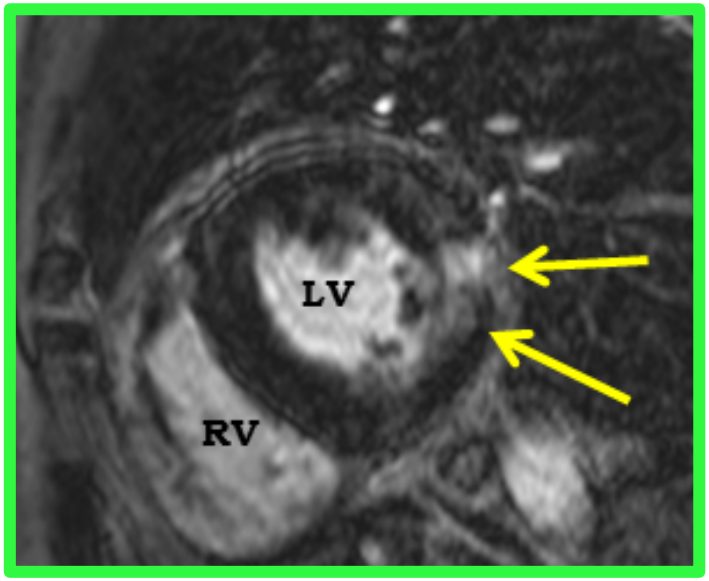
Case 5: Familial HCM





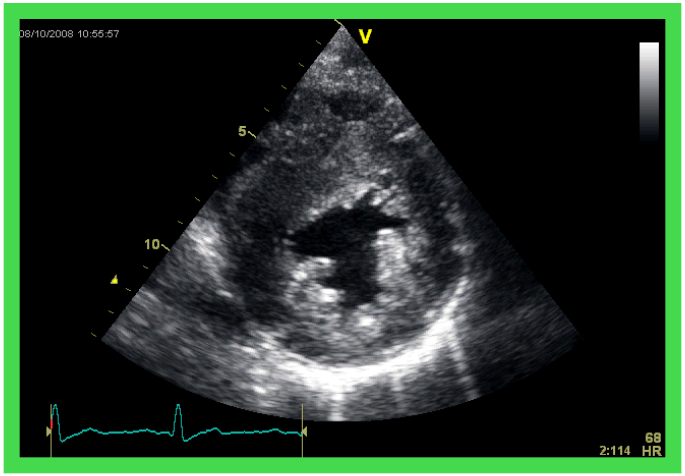
Case 5: Familial HCM





Quand penser à la maladie de Fabry ?

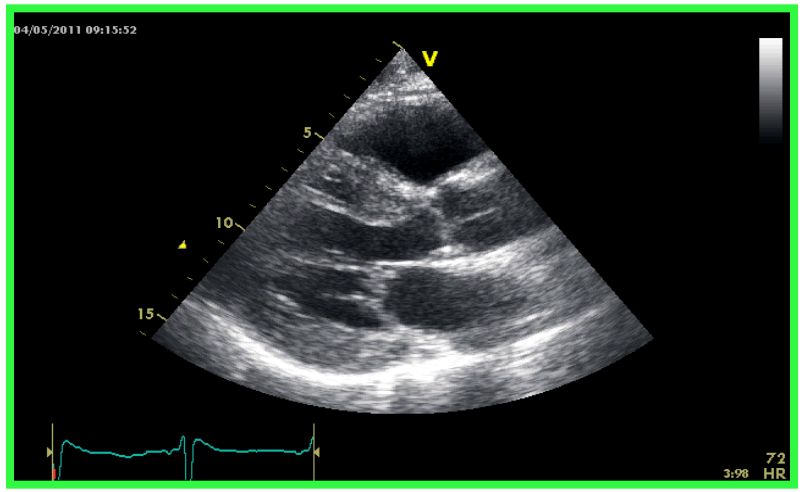
- CM hypertrophique “bizarre”
- HVG concentrique symétrique
- pas d’obstruction
- pas d’HTA
- atypies échographiques

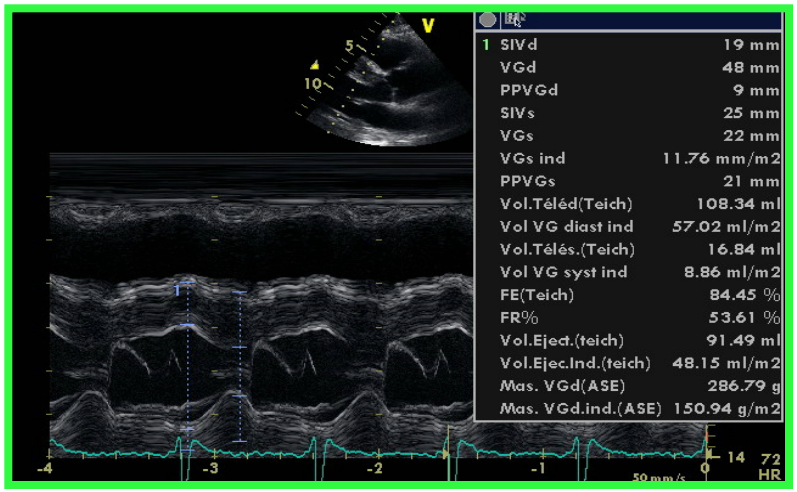


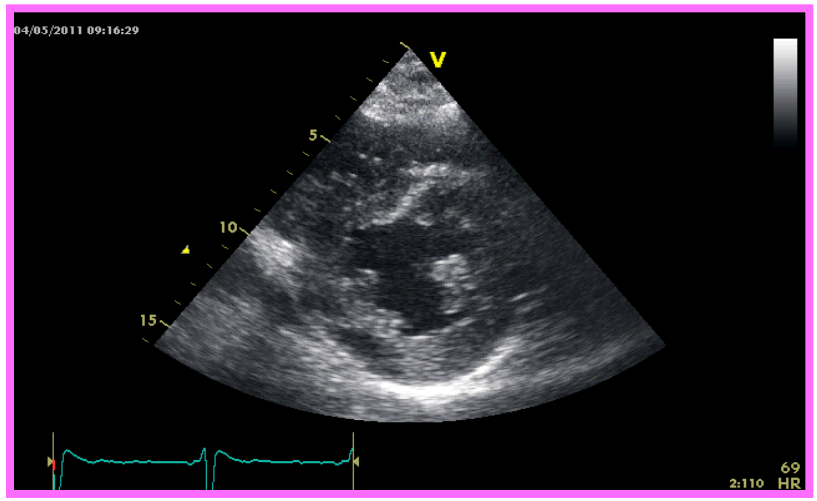
CMH

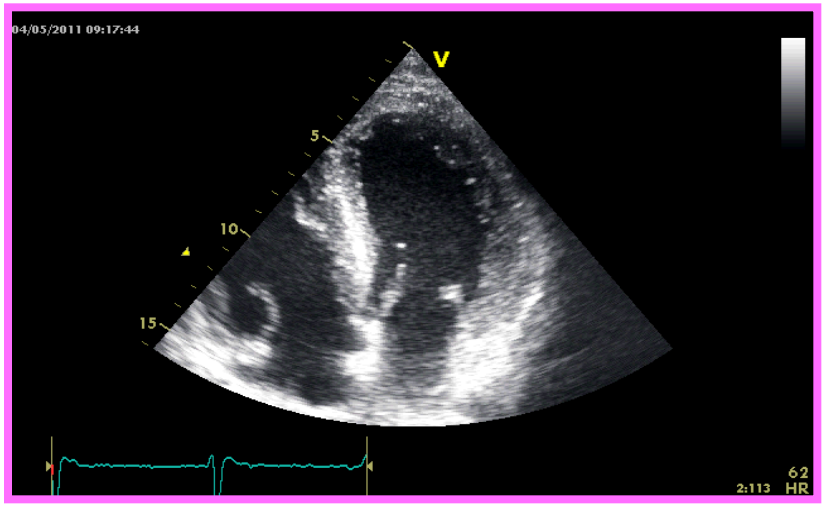
Cardiomyopathie hypertrophique

Maladie de Fabry: aspects écho

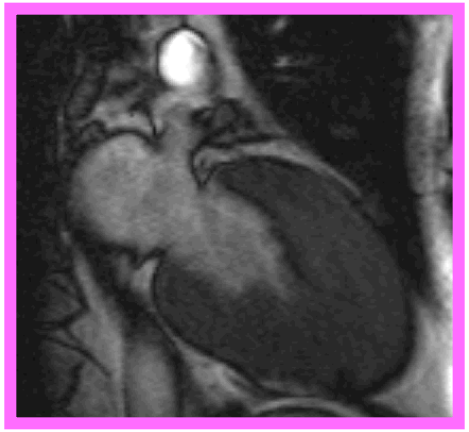


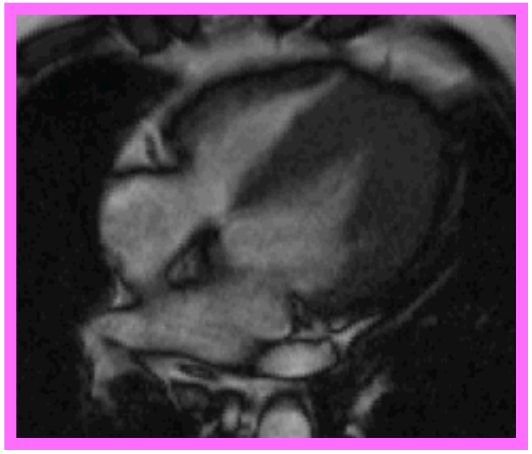


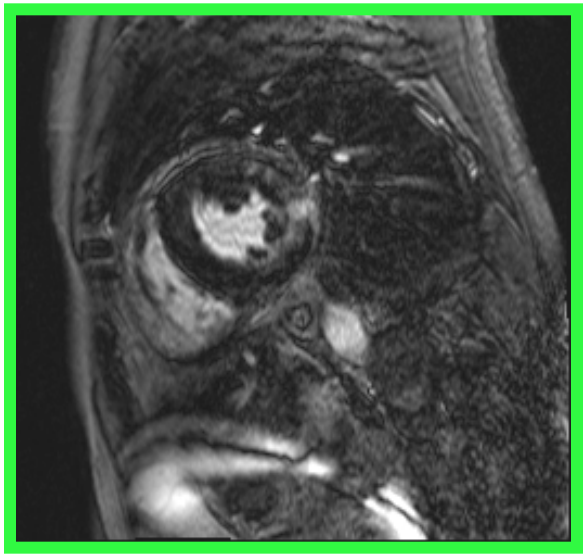


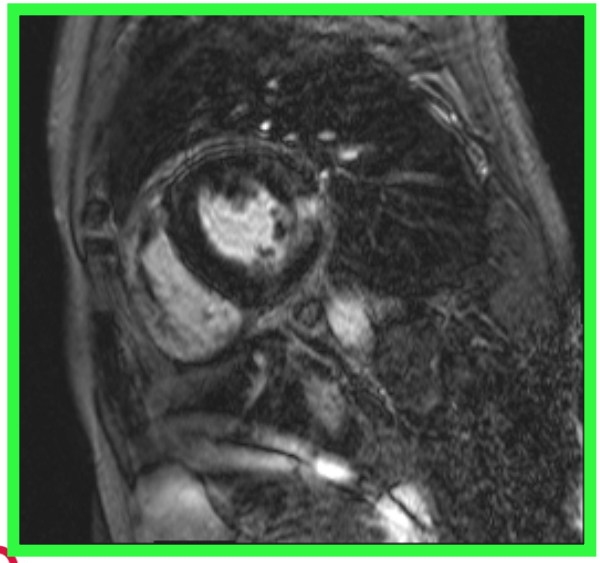


Fabry: apport de l'IRM





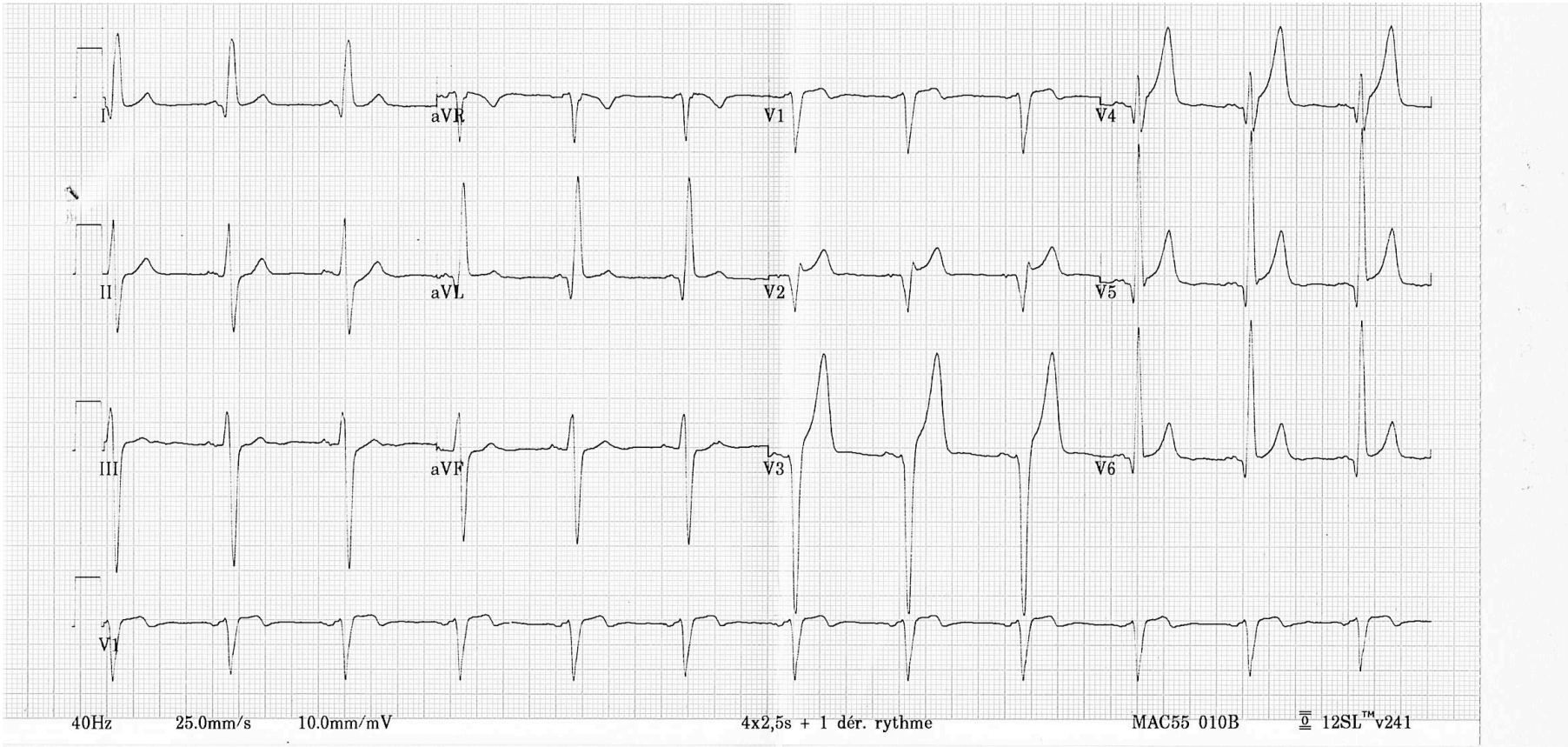




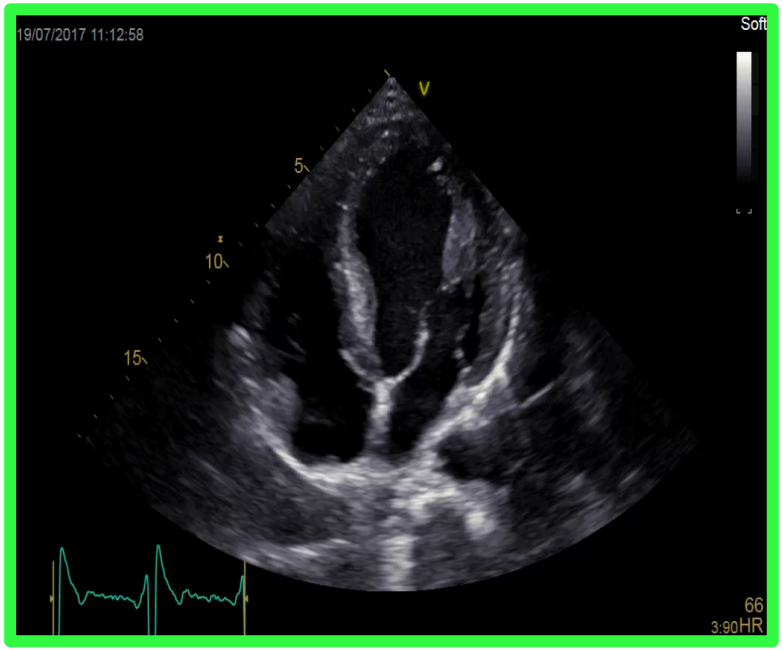
Cas 6: Variant Cardiaque

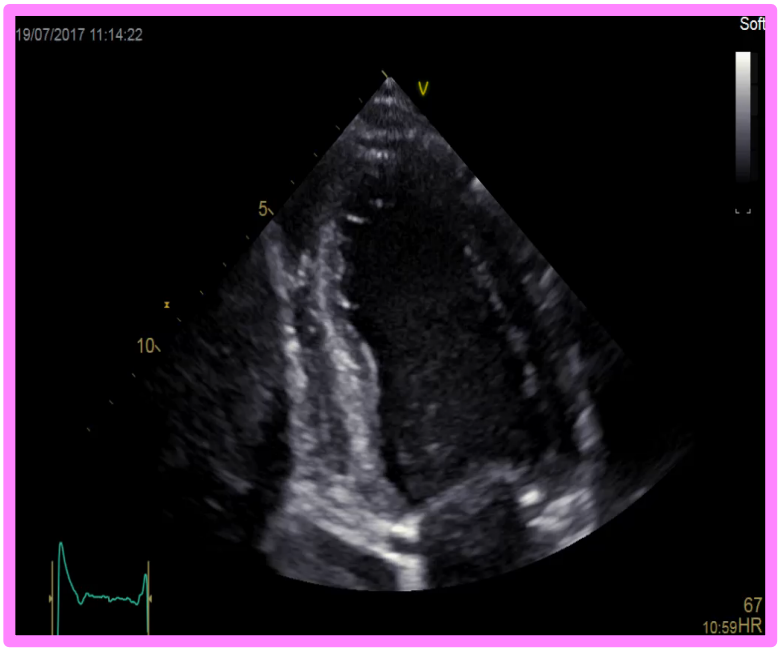
- Homme de 46 ans
- Bilan de routine chez patient sportif (6H/ semaine vélo) asymptomatique
- Famille: décès père 65 ans (IDM?)- décès mère 6 mois après naissance
- Mutation GLA hémizygote p.A215S (c.644A>G)
- Lyso GB3= 5,4 ng/ml (N<1,8 ng/ml) - alpha gal < 2,8 (N>15,3)

Cas 6: Variant Cardiaque: ECG

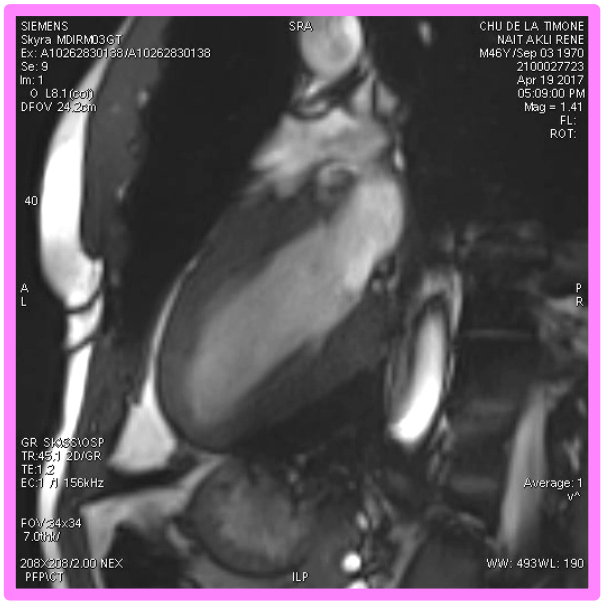


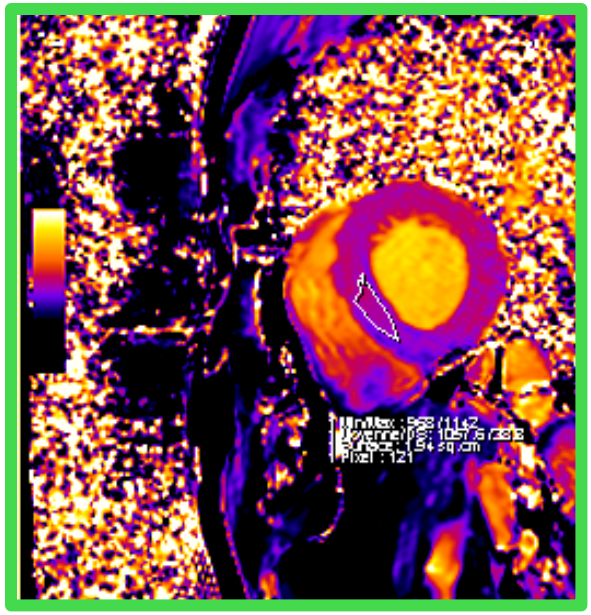
Cas 6: Variant Cardiaque: échocardiographie

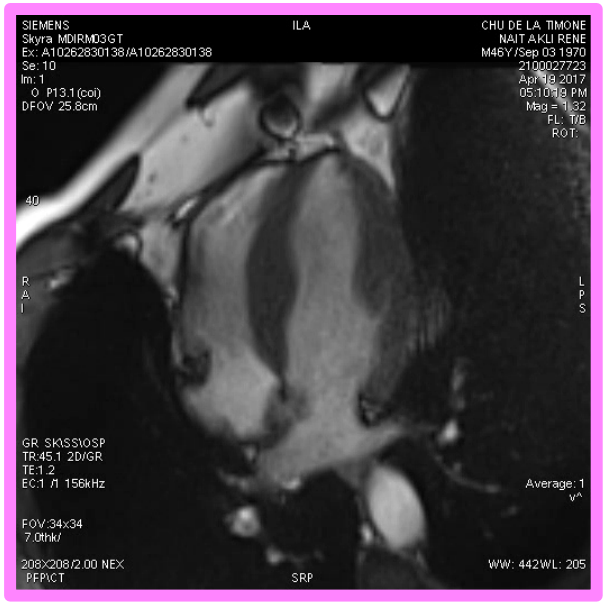




Cas 6: Variant Cardiaque: IRM







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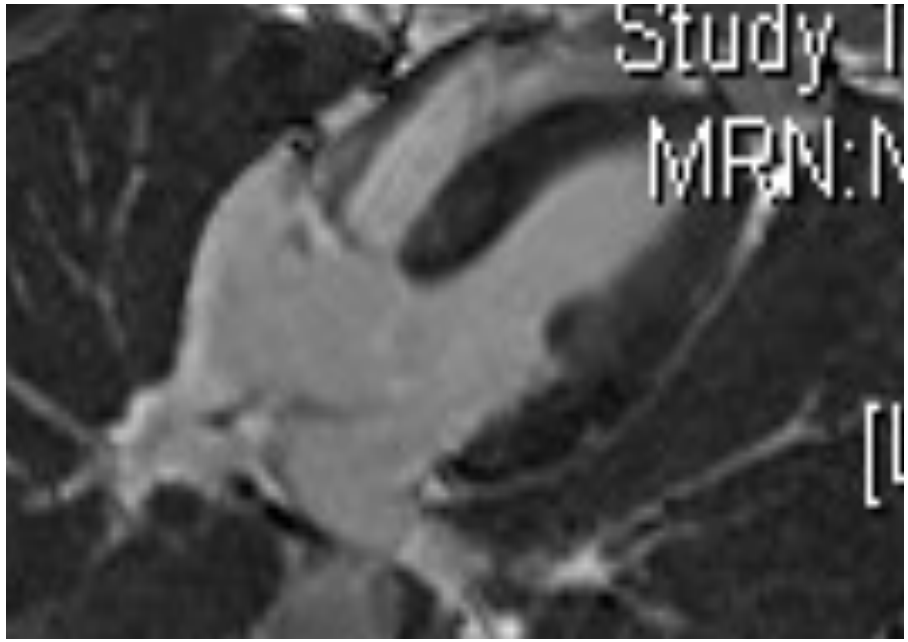
Cas 6: Variant Cardiaque: IRM

CONCLUSION

Hypertrophie diffuse et homogène du myocarde ventriculaire gauche qui doit en premier lieu faire rechercher une cause secondaire (hypertension artérielle?).

Une maladie de surcharge comme la maladie de Fabry pourrait être également évoquée.

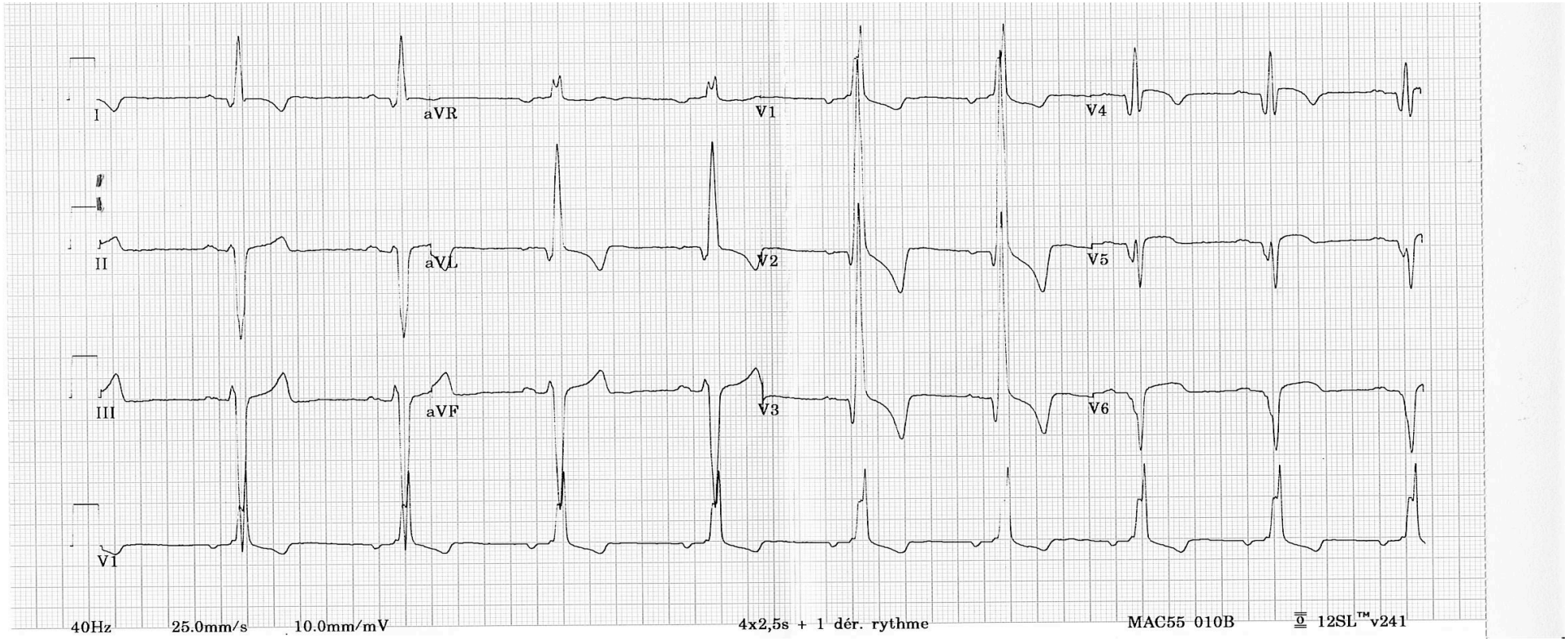
Cette IRM est également compatible avecle diagnostic de CMH mais le caractère diffus de cette hypertrophie est atypique



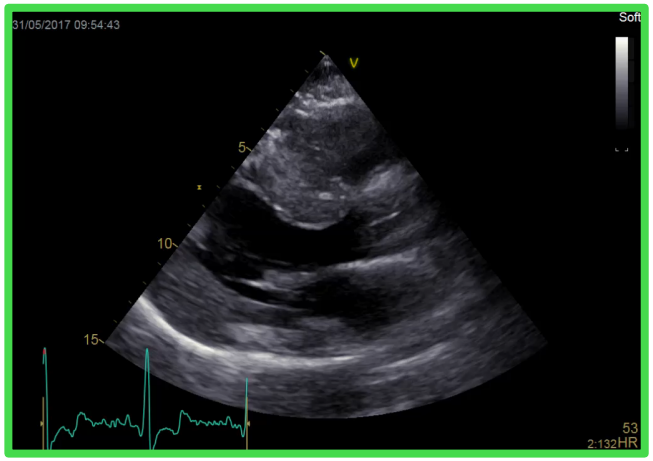
Cas Clinique n° 7: maladie de Fabry

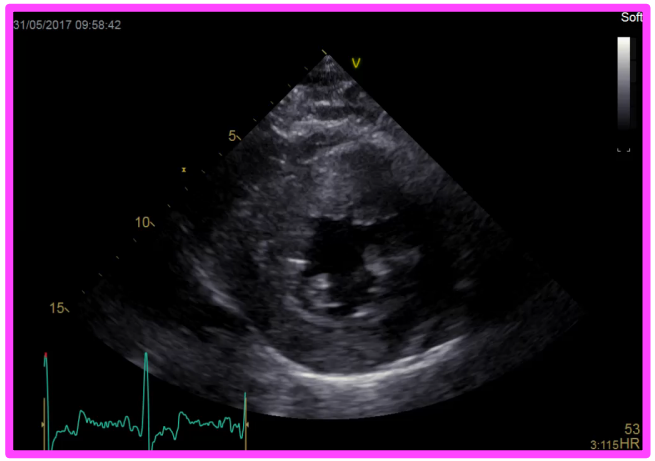
- Homme de 61 ans
- Bilan de paresthésies -> découverte HTA et HVG
- Atcd digestifs anciens, troubles visuels récents non explorés.
- Lipothymies, frère CMH?
- Mutation GLA hémizygote p.S238N (c.713G>A)
- Lyso GB3= 6 ng/ml (N<1,8 ng/ml) - alpha gal < 0,8 (N> 15,3)

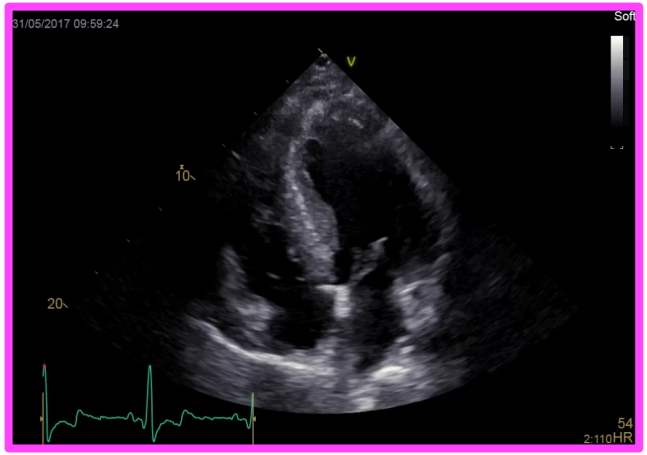
Cas Clinique n° 7: maladie de Fabry

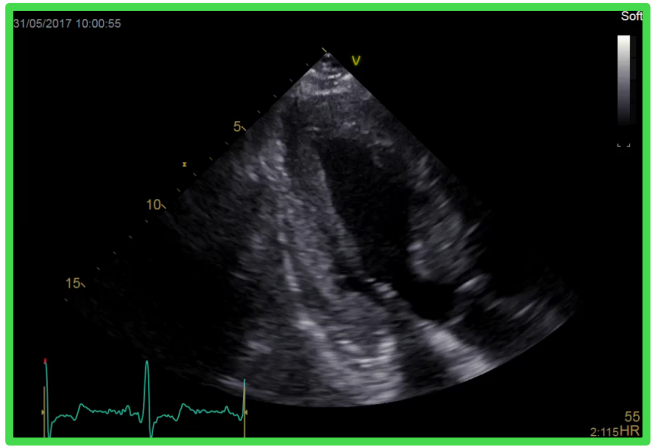


Cas Clinique n° 7: maladie de Fabry









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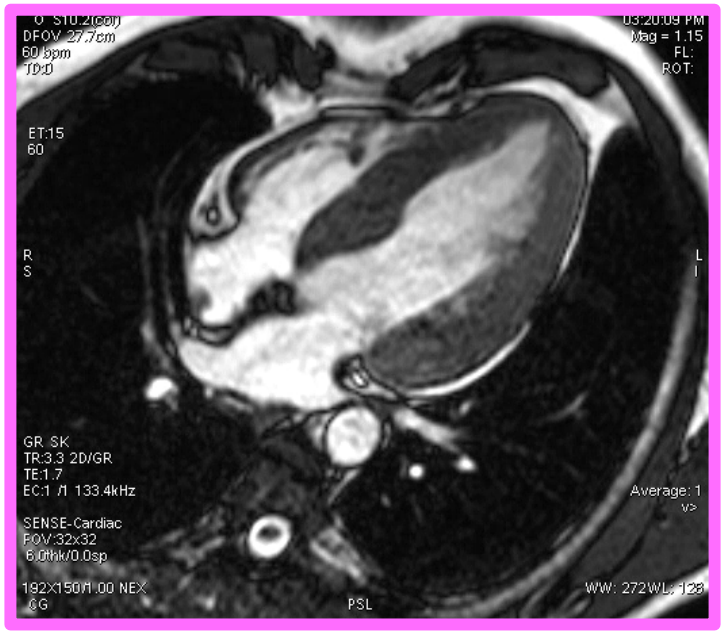
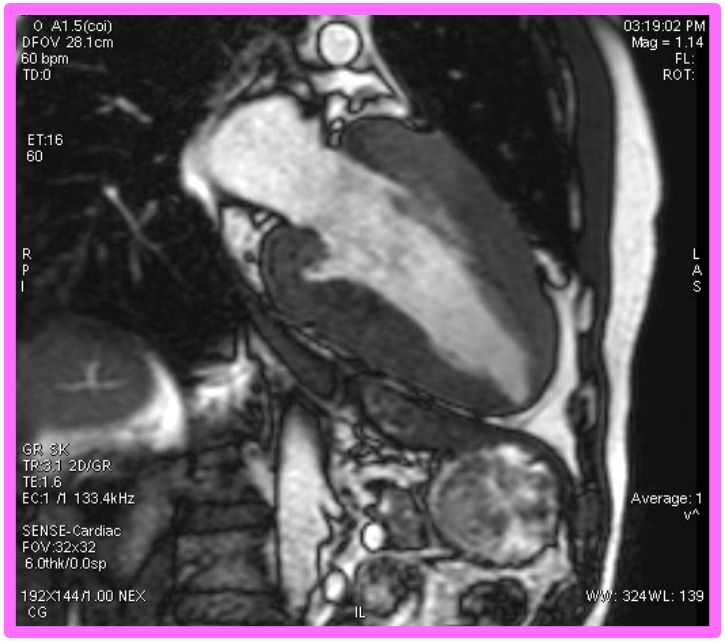
Cas Clinique n° 7: maladie de Fabry





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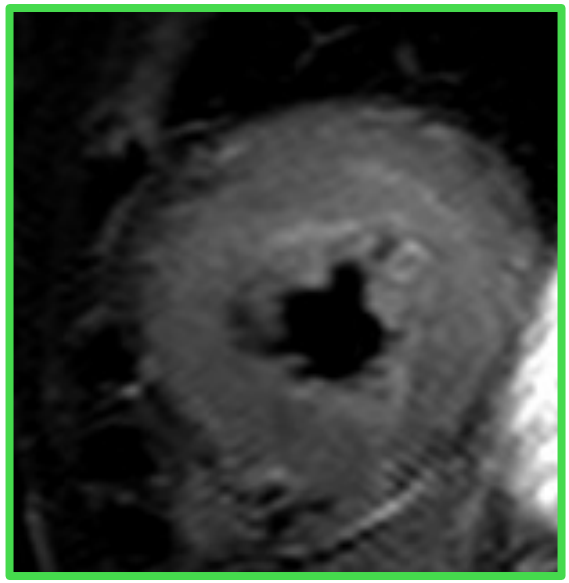
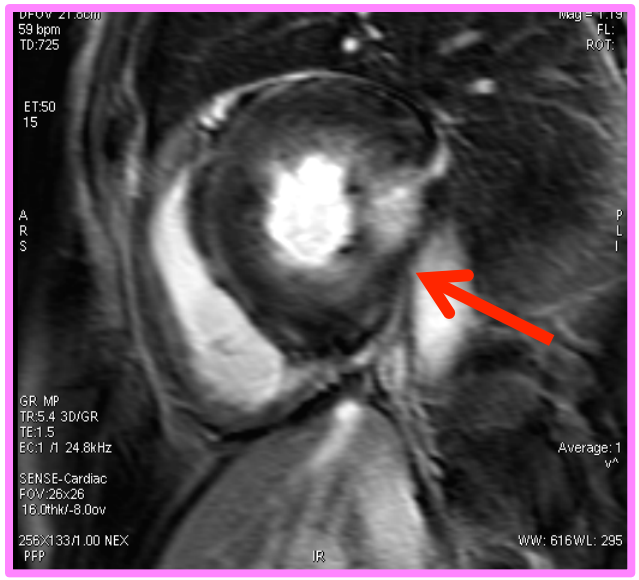
Cas Clinique n° 7: maladie de Fabry





prises de contraste intra myocardiques diffuses prédominant en antérolatéral mais visibles également en septal et inférieur et prise de contraste en motte intra myocardique latéro-basale.

ESC Position Statement 2008

	HCM	DCM	ARVC	RCM	Unclassified
Fa	Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Left ventricular non-compaction
	Sarcomeric protein mutations	Sarcomeric protein mutations (see HCM)	Intercalated disc protein mutations	Sarcomeric protein mutations	Barth syndrome
	ß myosin heavy chain	Z-band	Plakoglobin	Troponin I (RCM +/− HCM)	Lamin A/C
	Cardiac myosin binding protein C	Muscle LIM protein	Desmoplakin	Essential light chain of myosin	ZASP
	Cardiac troponin I	TCAP	Plakophilin 2	Familial amyloidosis	α-dystrobrevin
	Troponin-T	Cytoskeletal genes	Desmoglein 2	Transthyretin (RCM + neuropathy)	
	α-tropomyosin	Dystrophin	Desmocollin 2	Apolipoprotein (RCM + nephropathy)	
	Essential myosin light chain	Desmin	Cardiac ryanodine receptor (RyR2)	Desminopathy	
	Regulatory myosin light chain	Metavinculin	Transforming growth factor-β3 (TGFβ3)	Pseuxanthoma elasticum	
	Cardiac actin	Sarcoglycan complex		[illegible]	
	α-myosin heavy chain	CRYAB		Anderson–Fabry disease	
	Titin	Epicardin		Glycogen storage disease	
	Troponin C	Nuclear membrane			
	Muscle LIM protein	Lamin A/C			
	Glycogen storage disease (e.g. Pompe; PRKAG2, [illegible])	Emerin			
	Lysosomal storage diseases (e.g. Anderson–Fabry, Hurler's)	Mildly dilated CM			
	Disorders of fatty acid metabolism	Intercalated disc protein mutations (see ARVC)			
	Carnitine deficiency	Mitochondrial cytopathy			
	Phosphorylase B kinase deficiency				
	Mitochondrial cytopathies				
	Syndromic HCM				
	Noonan's syndrome				
	LEOPARD syndrome				
	Friedreich's ataxia				
	Beckwith–Wiedermann syndrome				
	Swyer's syndrome				
	Other				
	Phospholamban promoter				
	Familial amyloid				