Modifications structurales et fonctionnelles myocardiques dans l'HTA

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Pôle CVTE

GRENOBLE 1 UNIVERSITE JOSEPH FOURIER
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- Physiopathologie
- Définition de l'HVG
- Etiologie
- Méthode de détection: ECG/ETT/IRM

- HVG= rôle pronostic
- Peut-on agir?

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Physiopathologie

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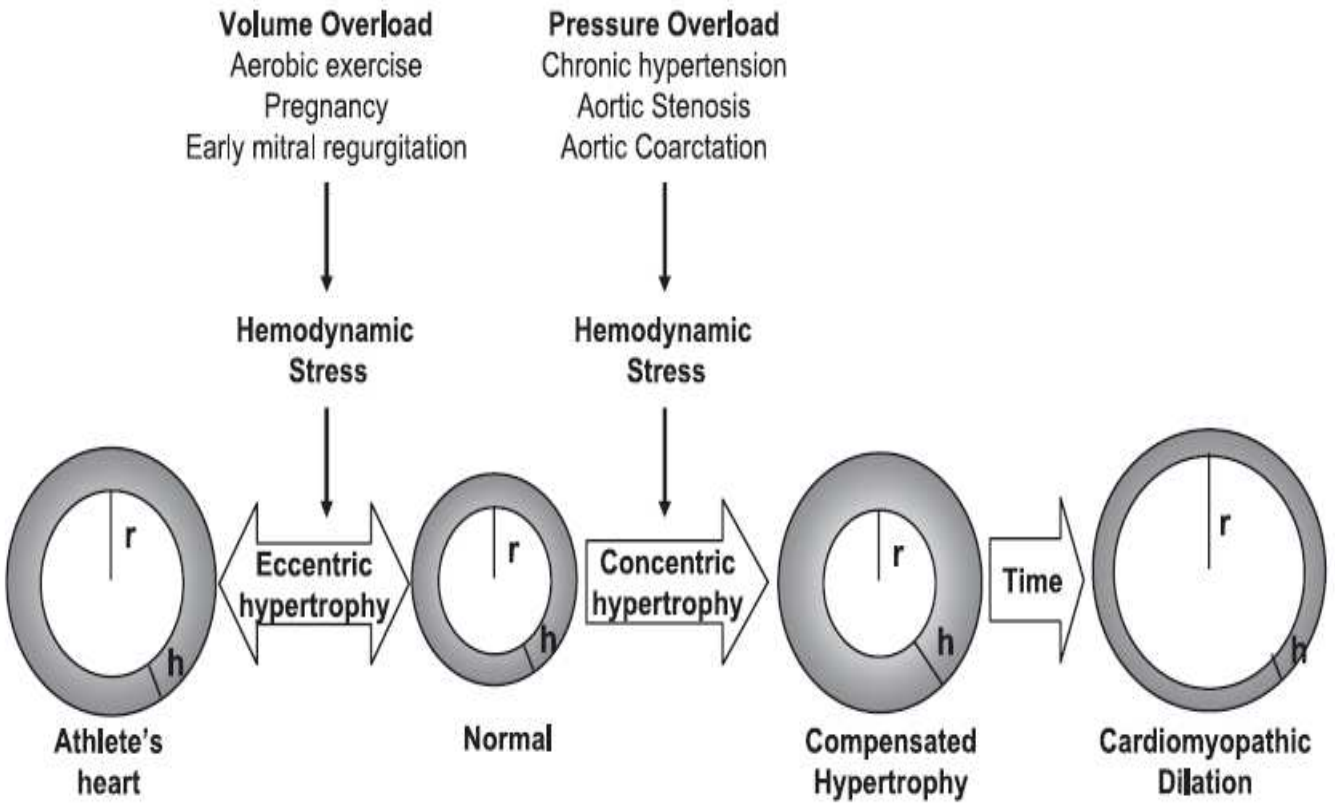
Hypertrophie ventriculaire gauche (HVG)

Augmentation de la masse VG liée à des **modifications de débit/post charge**

Physiologique :
- Croissance
- Sportif

Pathologique :
- HTA
- RA
- CMH (génétique)….

Hypertrophie ventriculaire gauche



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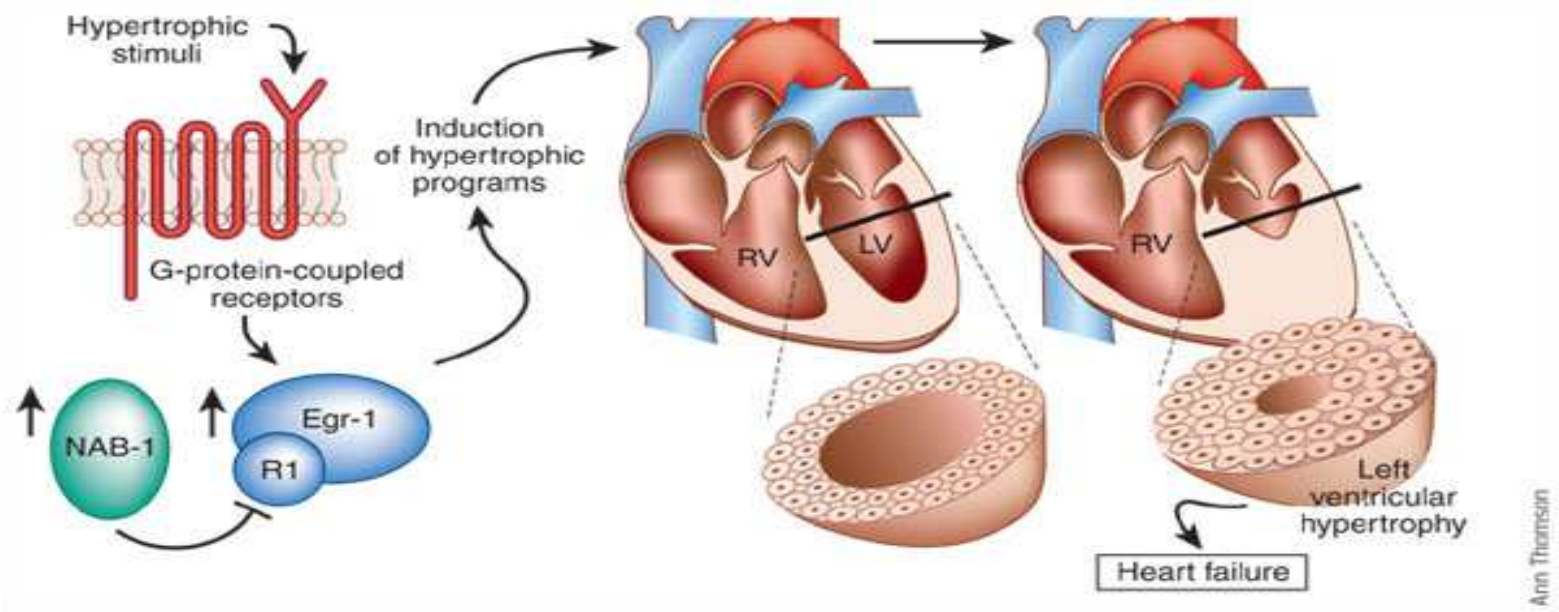
Physiopathologie

- Adaptation du VG à l ’augmentation de la post-charge
- Phénomène adaptatif complexe (Loi de Laplace → maintien constant du stress pariétal)



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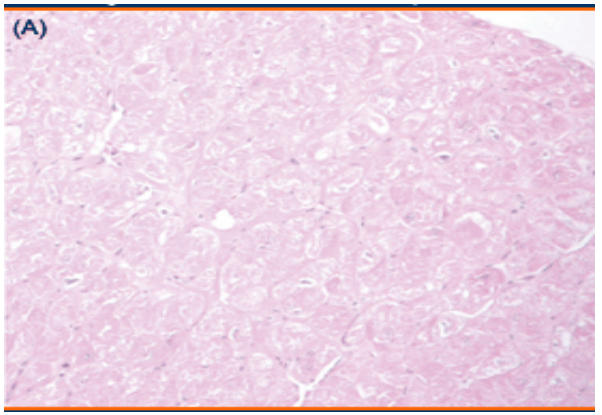
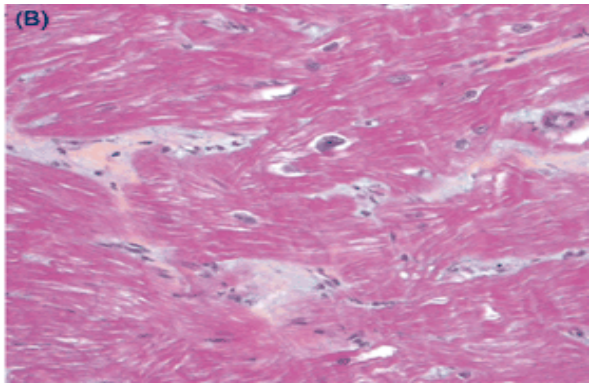
Physiopathologie de l'HVG

Cellular alterations
- Cardiomyocytes
  - Hypertrophy, atrophy, apoptosis, necrosis
- Non cardiomyocytes
  - Hyperplasia and apoptosis of fibroblasts
  - Hypertrophy and/or hyperplasia of vascular smooth muscle cells

Noncellular alterations
- Interstitial and perivascular fibrosis
- Microscopic scarring
- Medial thickening of coronary arterioles
- Diminished number of capillaries





La Fibrose est caractéristique du remodelage pathologique

Weber et al. NEJM 1999;341:753-5

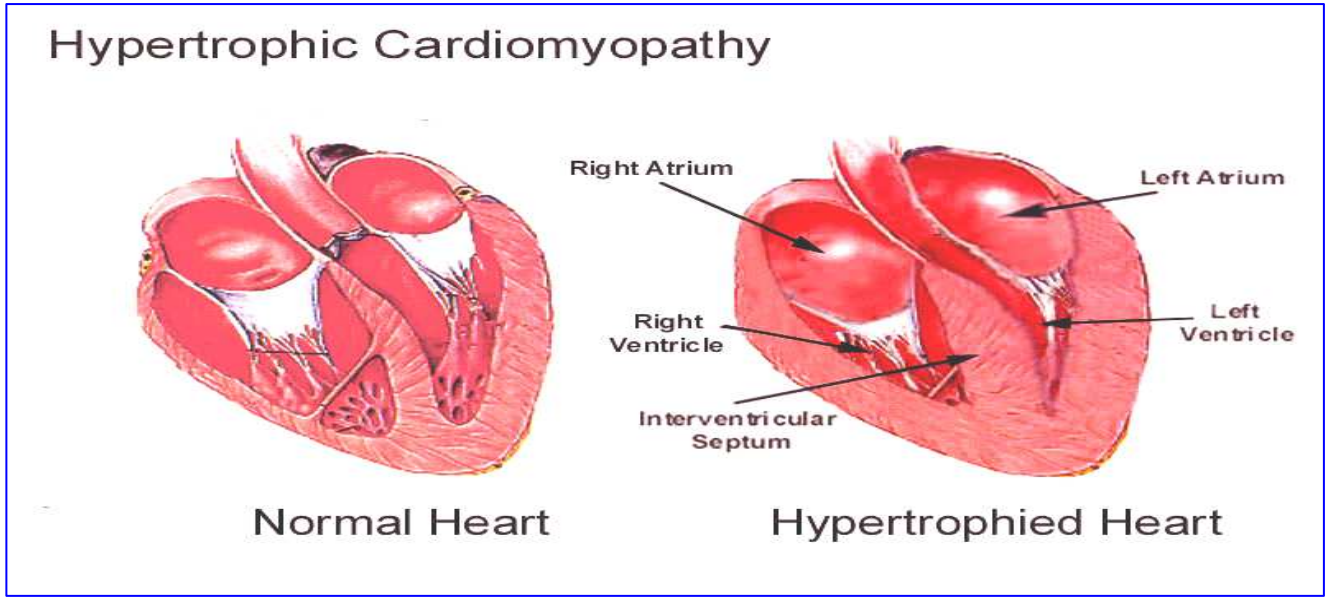
HTA

↓

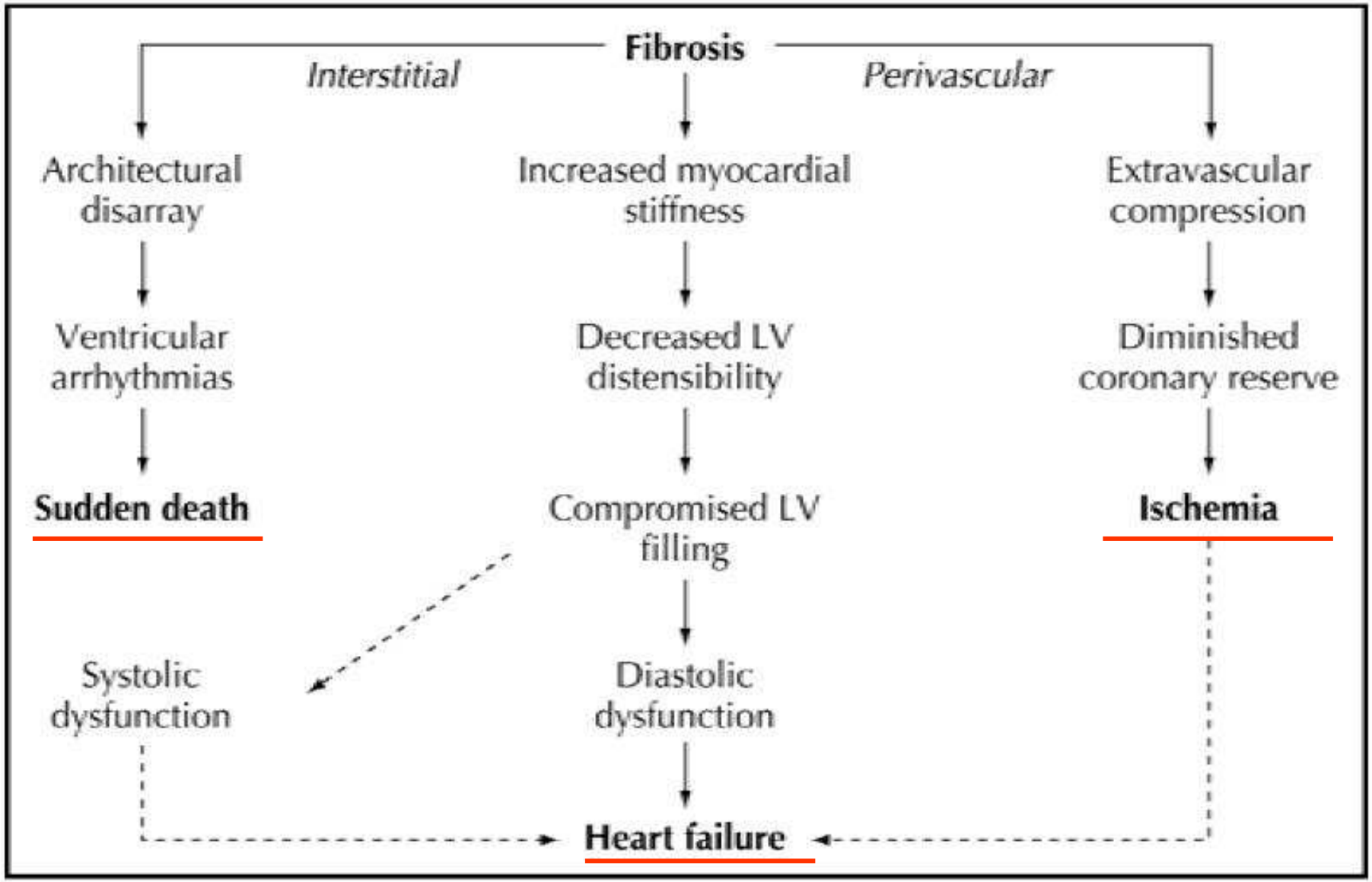
Augmentation post-charge

↙ ↓ ↘

HVG secondaire | Fibrose myocardique | Dilatation de l'OG avec FA



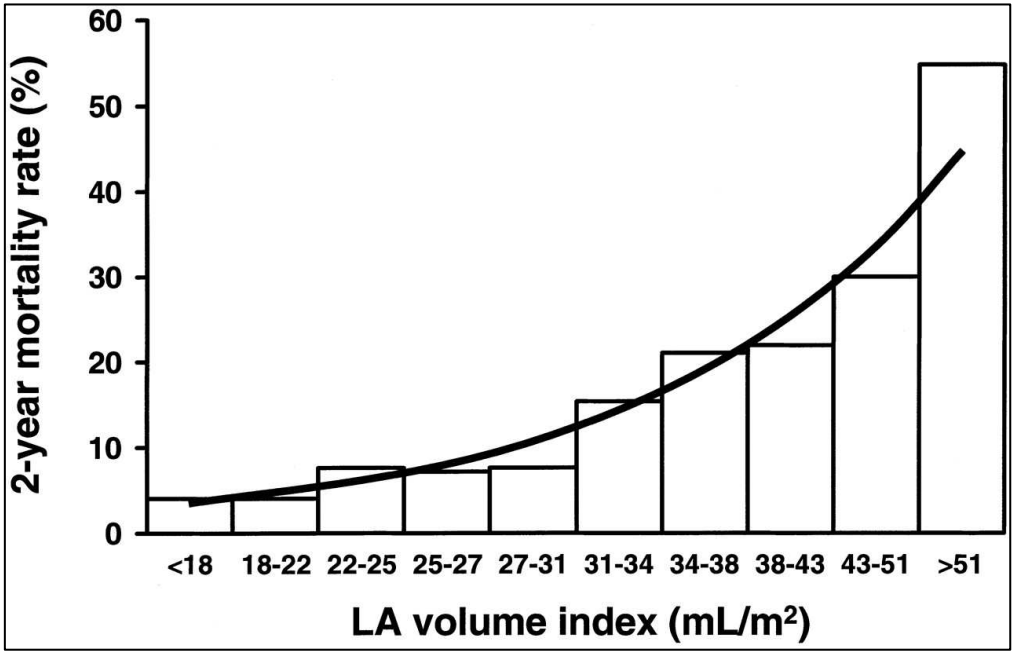
Fibrose et cardiopathie hypertensive



Remodelage de l ’OG

Importance du volume OG

- Prédicteur de la mortalité
- Association forte entre taille de l ’OG et risque de FA



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Moller et al. Circulation 2003; 107: 2207.
Parkash et al. Am H J 2004; 148: 649.

DEFINITION de l'HVG

-Augmentation de la masse VG

-Epaississement pariétal du VG> 11mm

-Pièges: faux tendons, trabéculations

-Topographie variable selon l'étiologie :
diffuse(HTA) ou localisée (CMH)

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Principales causes d'HVG

- **Primitives**

Cardiomyopathies hypertrophiques CMH

- **Secondaires**

-par augmentation de la post-charge

HTA
RA
Coarctation aortique

-par Infiltration myocardique

Amylose cardiaque
Granulomatose=sarcoïdose
Maladie de Fabry
Tumeurs cardiaques

-HVG physiologique du sportif

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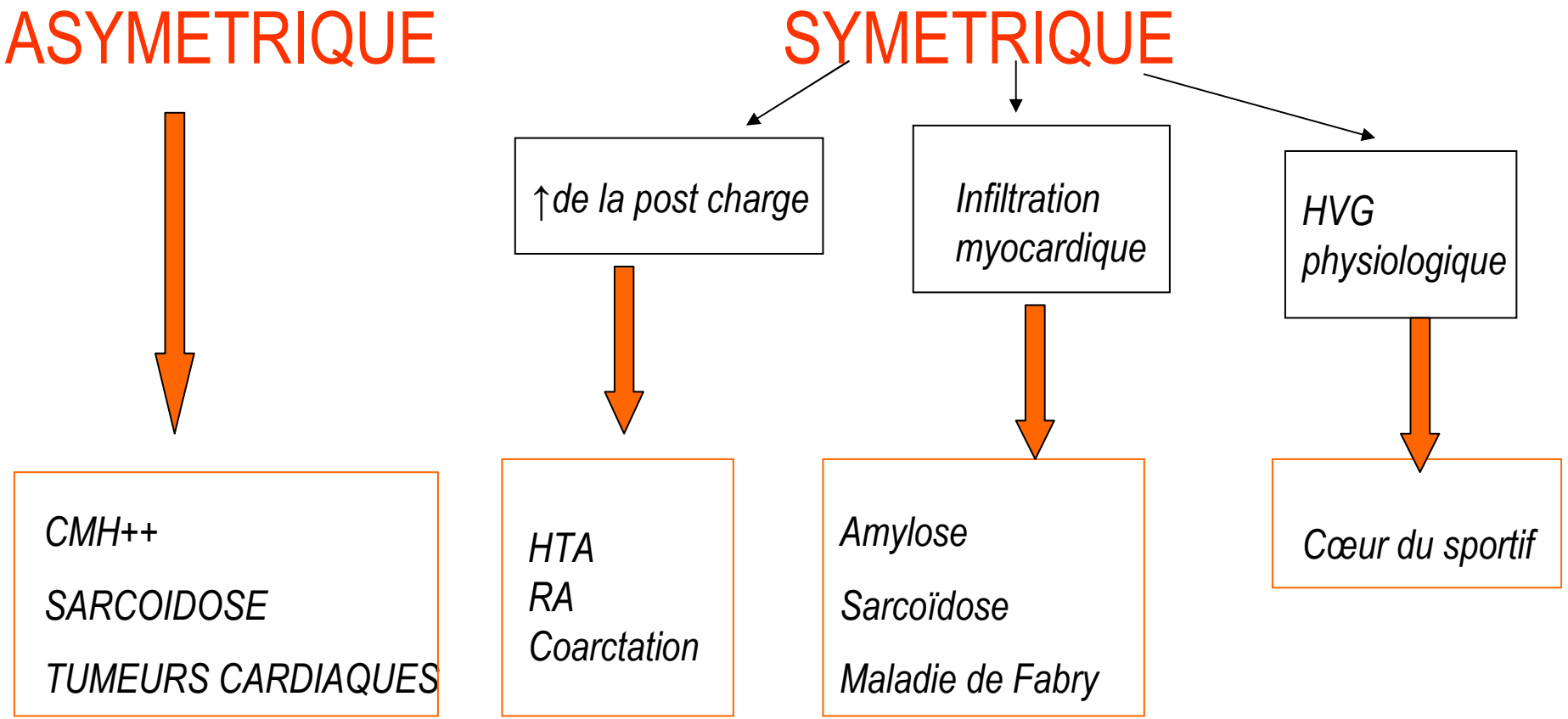
La distinction entre HVG asymétrique (focalisée) ou symétrique (diffuse) est primordiale car permet d'orienter vers une étiologie



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Détection de l'HVG

ECG

ETT

IRM

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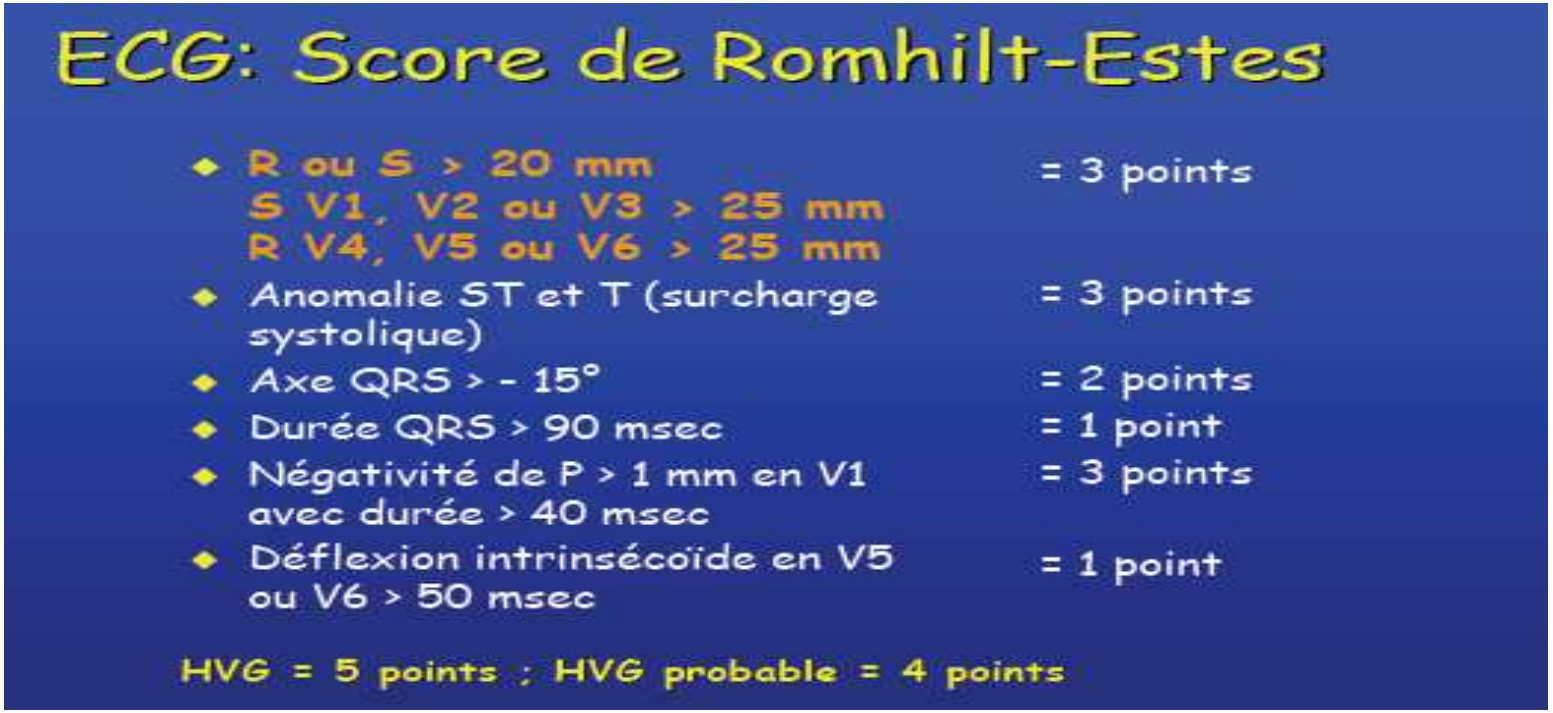
l ’ECG

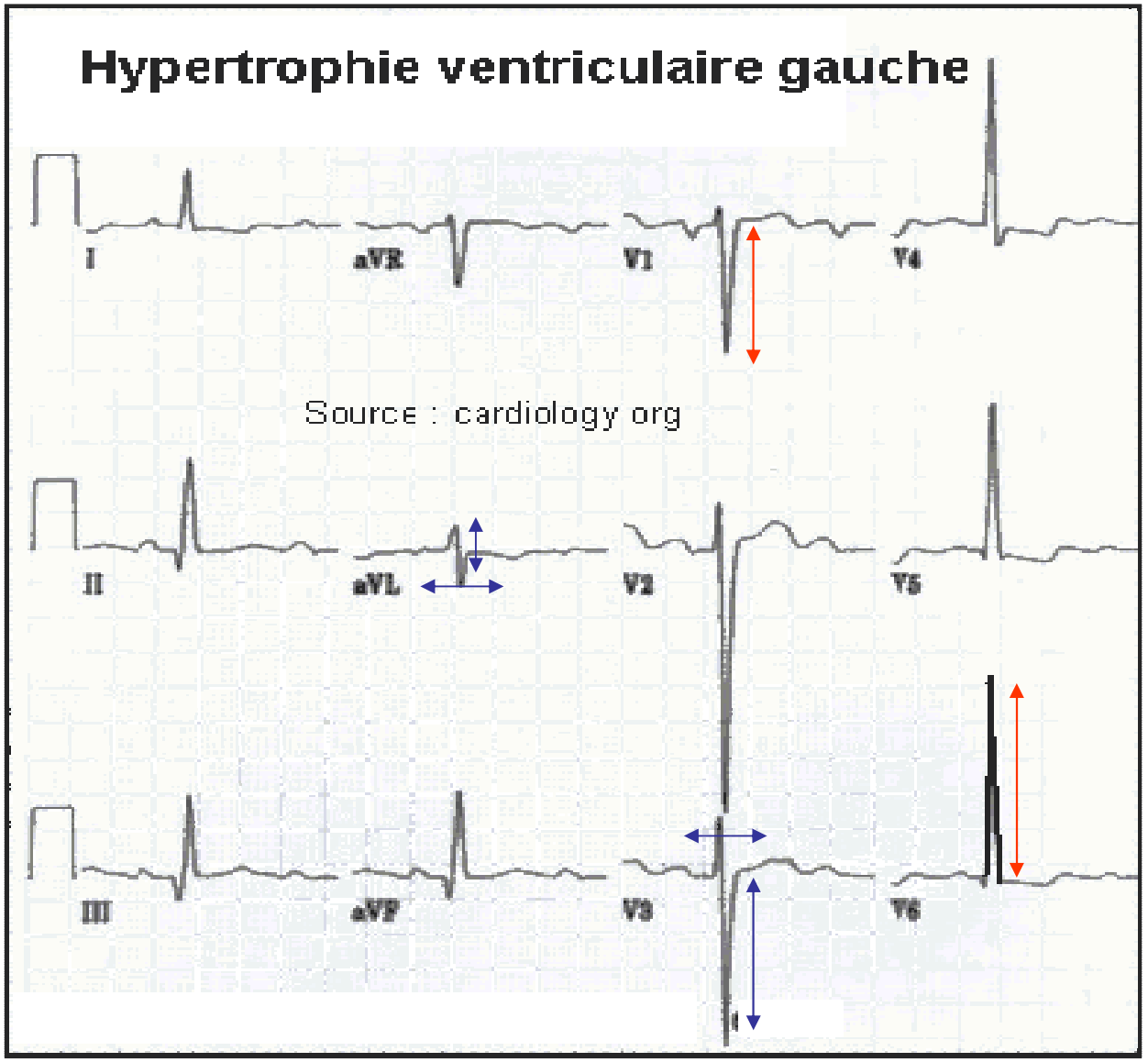
- Sokolow-Lyon : SV1 + RV5 ou RV6 ≥ 38 mm

- Cornell : SV3 + RVL > 28 mm (H) ou > 20 mm (F)

  Product > 2440 mm*ms



Hypertrophie ventriculaire gauche



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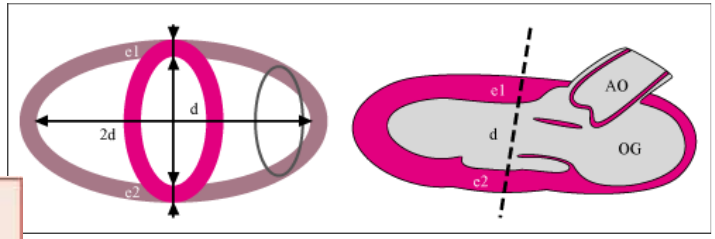
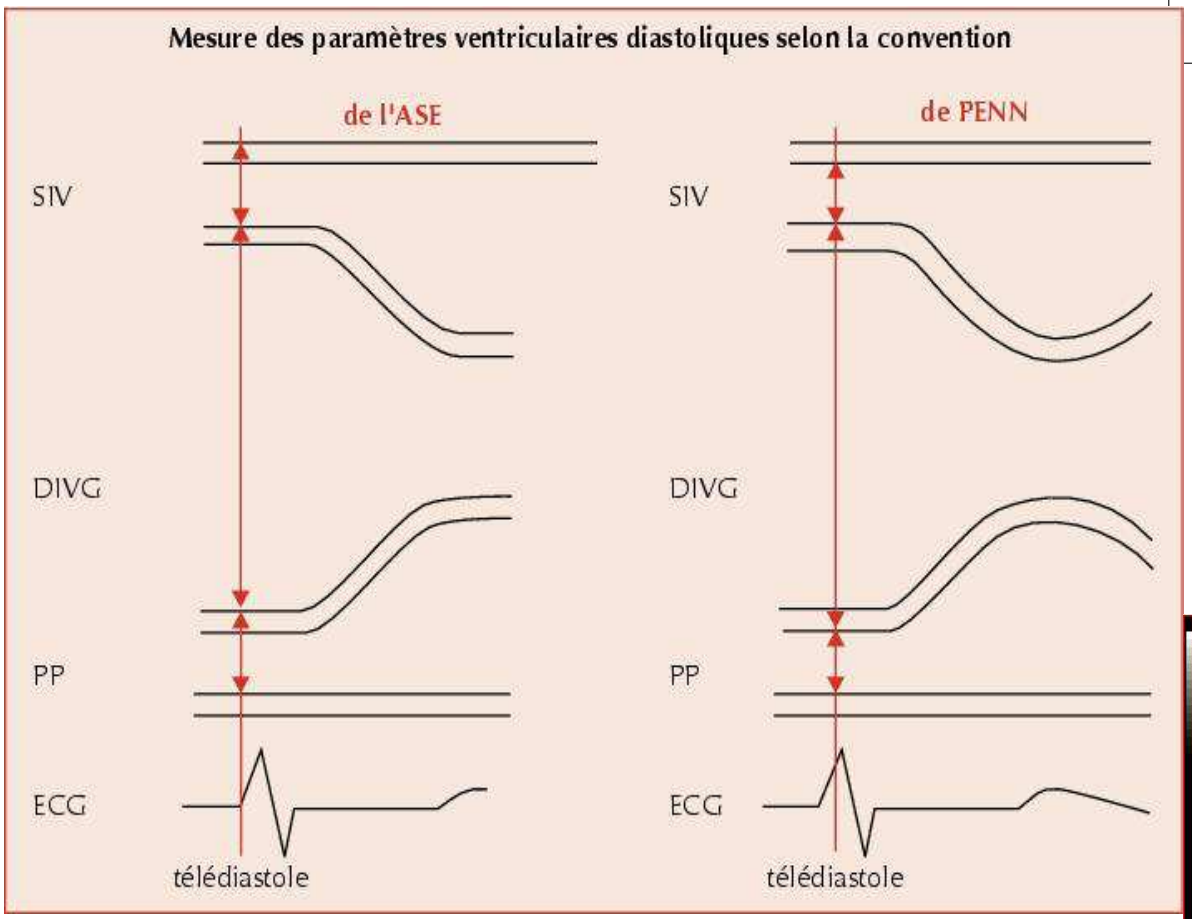
Sensitivity and specificity for selected ECG criteria of LVH

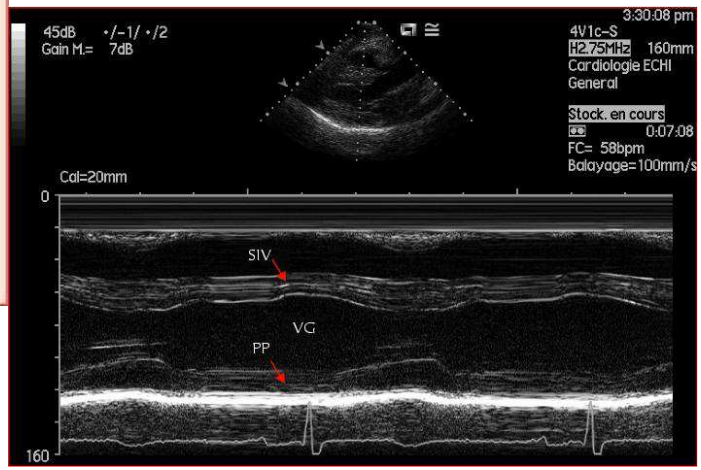
Criterion	Sensitivity (%)	Specificity (%)
- Sokolow Lyon Voltage	22	100
- Cornell Voltage Criteria	42	96
- Cornell Voltage Duration Criteria	51	95
- RaVL > 11 mm	11	100
- Romhilt-Estes > 4 points	54	85
- Romhilt-Estes > 5 points	33	94

l ’échocardiographie

- Mesure de la masse VG (TM)







Mesure de la masse VG

- MVG (g): $0.8[1.04[(DTDVG+SIV+PP)^3-DTDVG^3]]+0.6$ (ASE)
- MVG (g): $1.04\ [(DTDVG+SIV+PP)\ ^3-DTDVG^3]-13.6$ (Penn)

125 g/m² H ; 110 g/m² F (ESC-ESH 2007)

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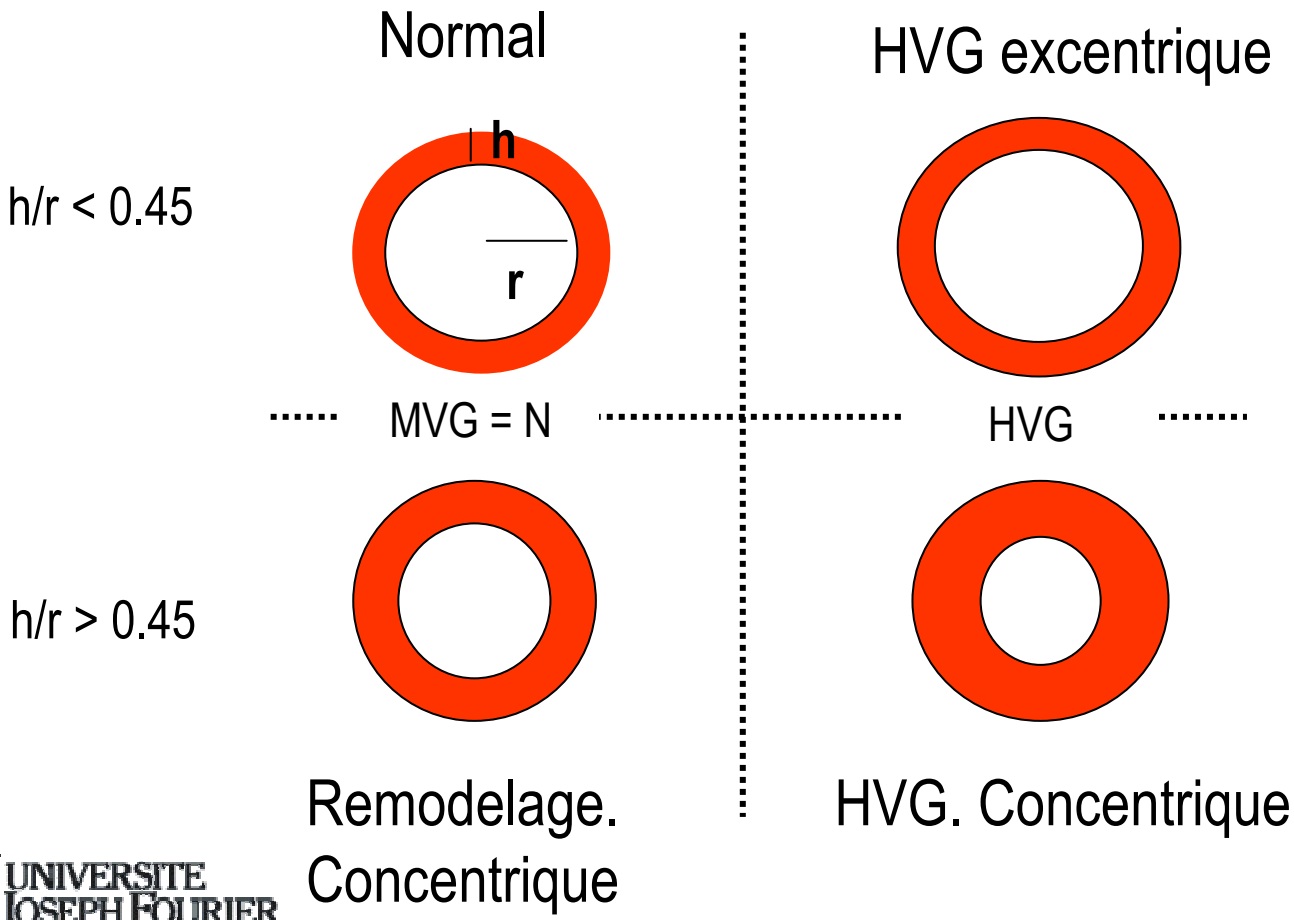
Autres apports de l'échocardiographie

Géométrie du VG



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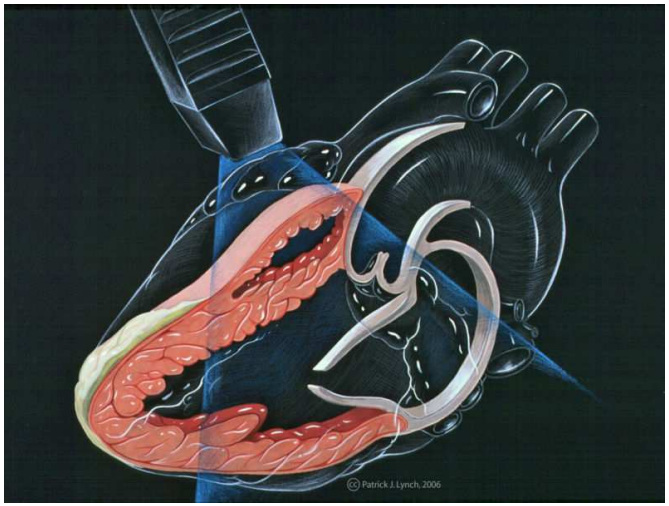
Autres apports de l'échocardiographie

-Diagnostic différentiel ++++

- Autres informations sur la structures et fonction cardiaque

fonction systolique et diastolique
troubles de la cinétique segmentaire
Taille des cavités
Pressions pulmonaires
Valvulopathies - aorte initiale
OG
Péricarde
AAA



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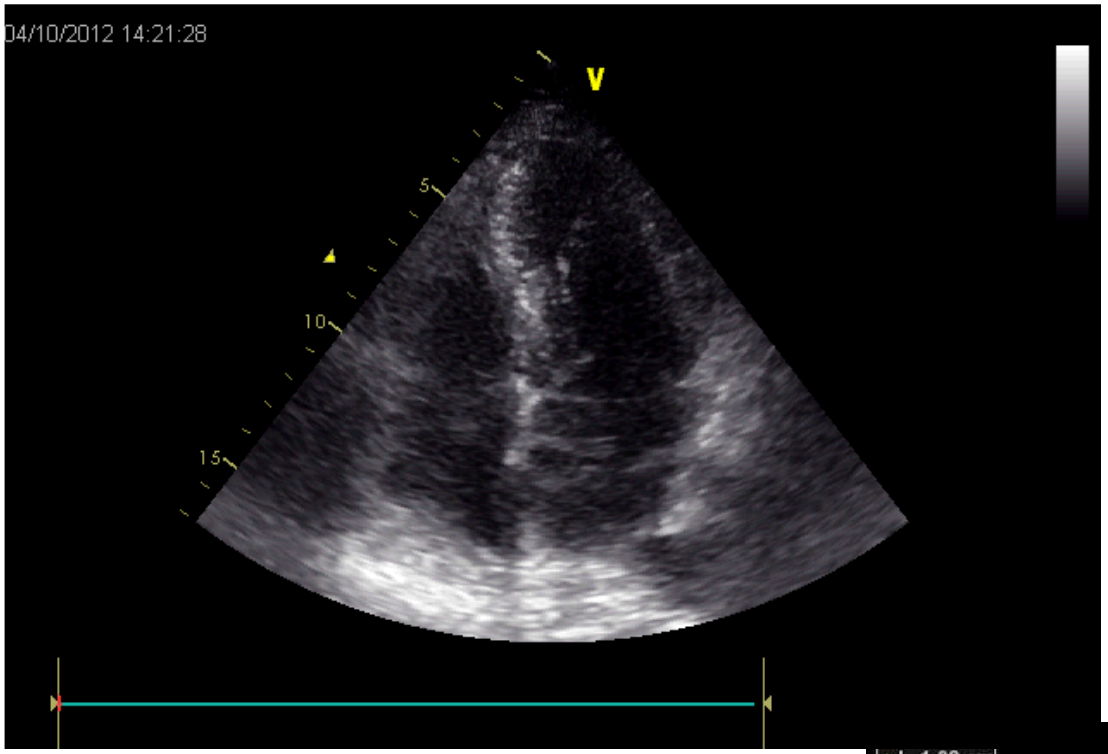
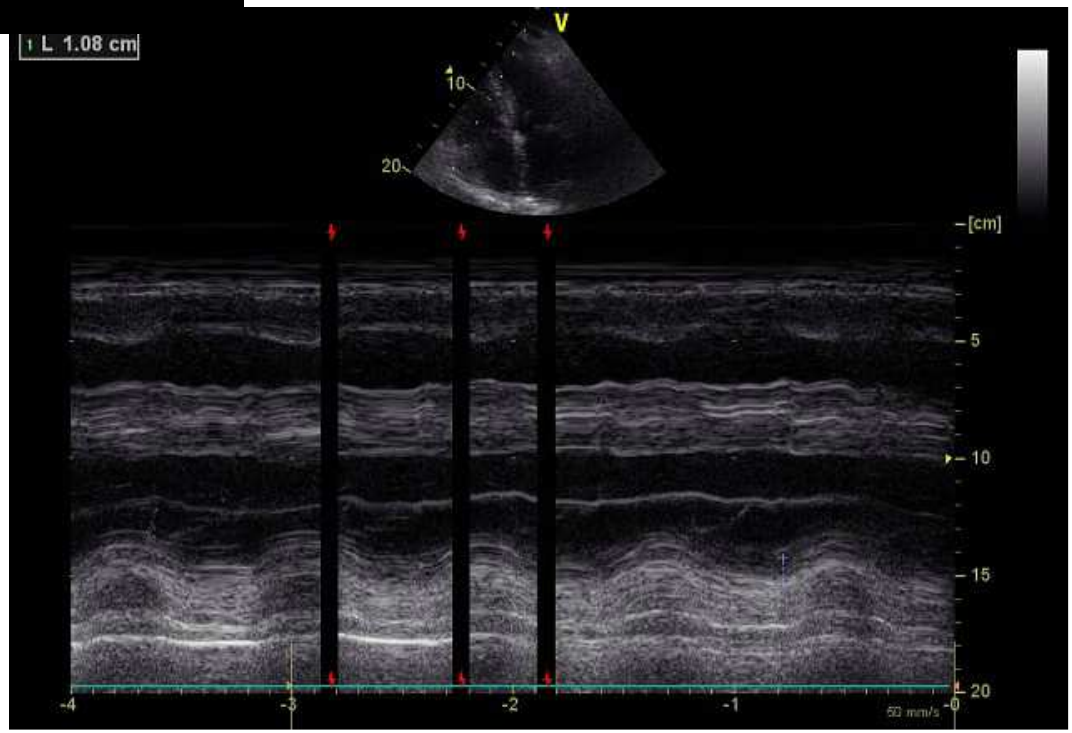


HTA



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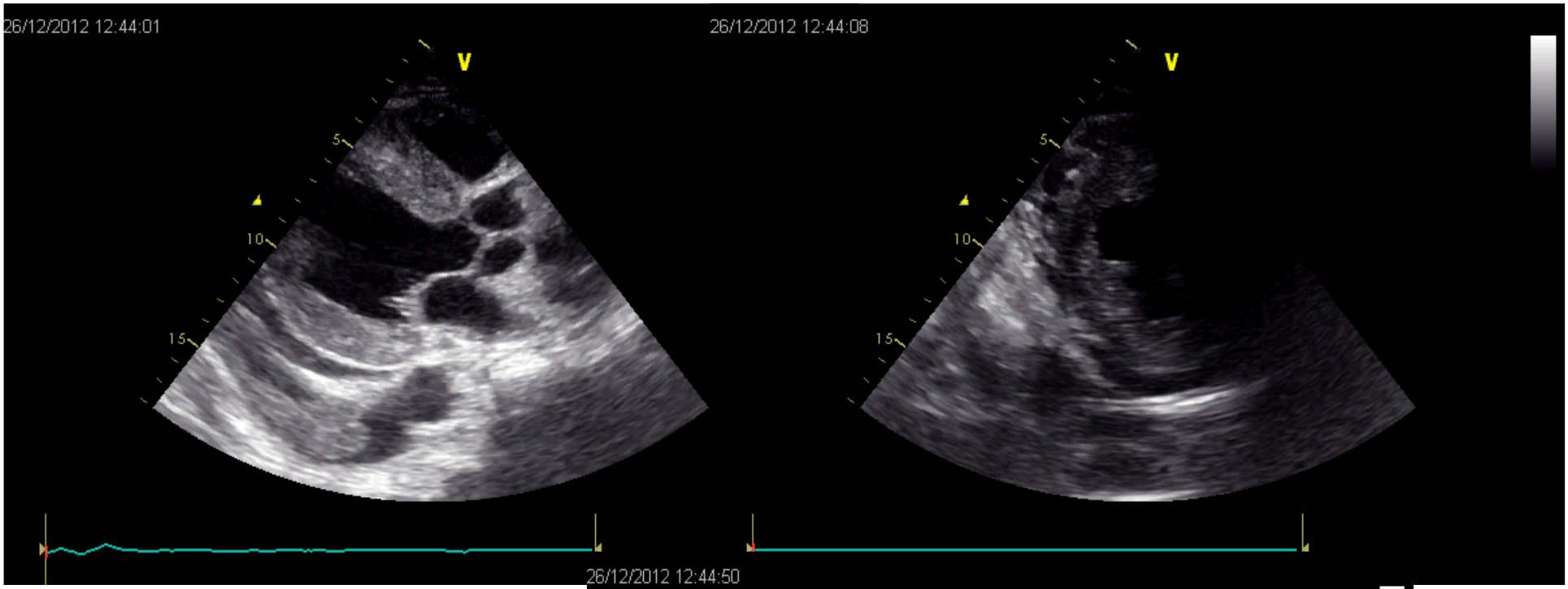

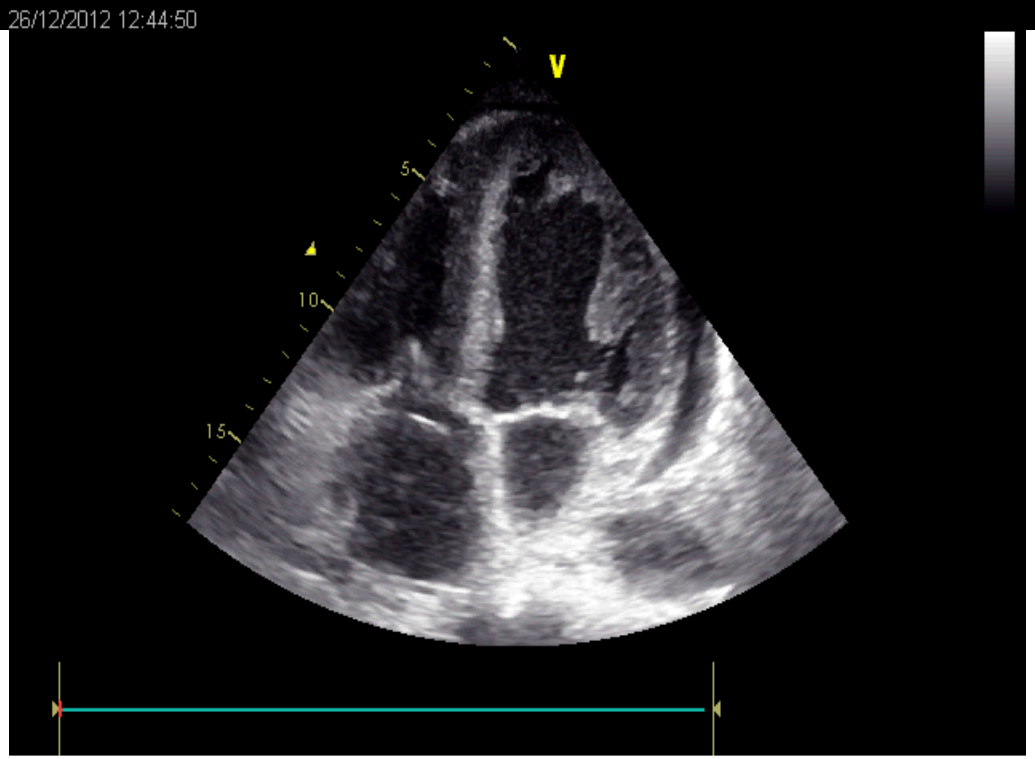

AMYLOSE

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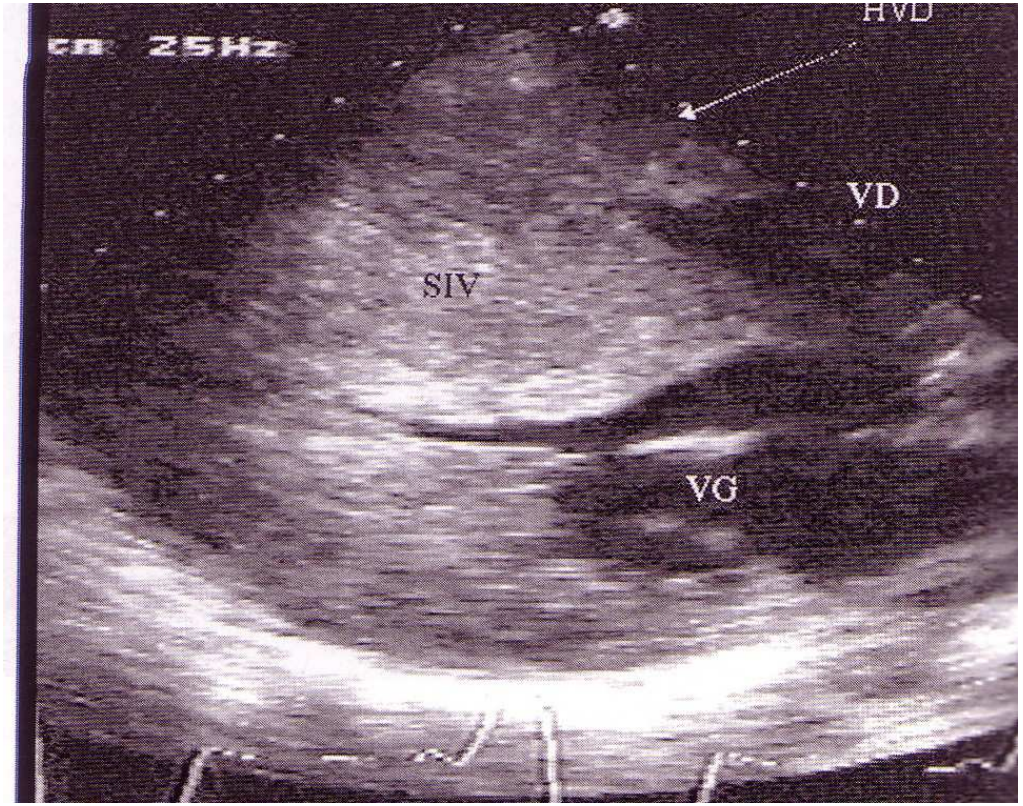

CMH

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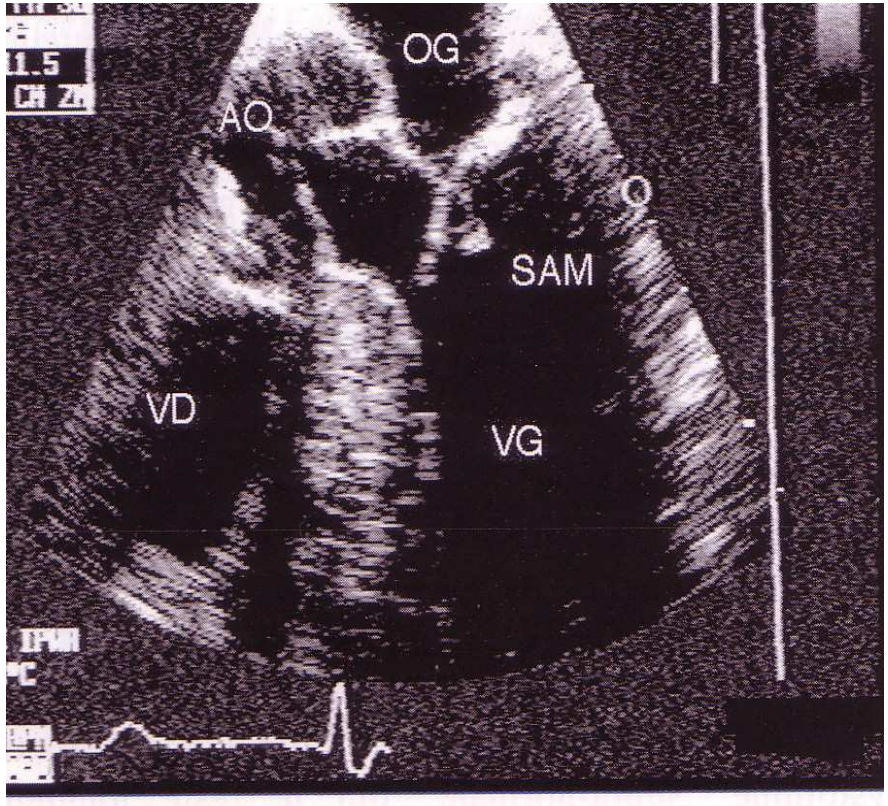
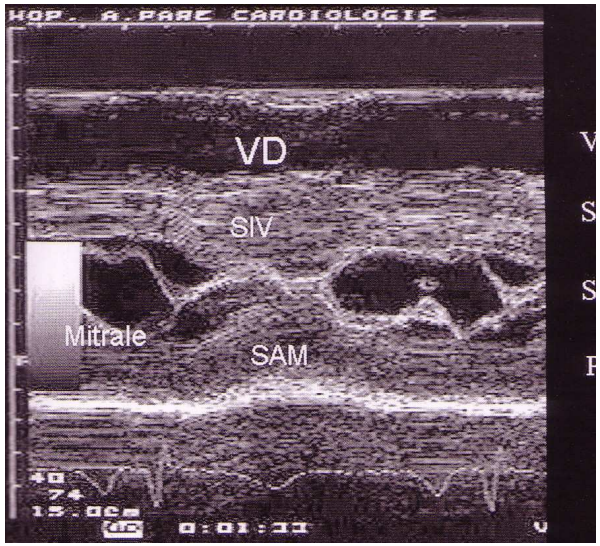
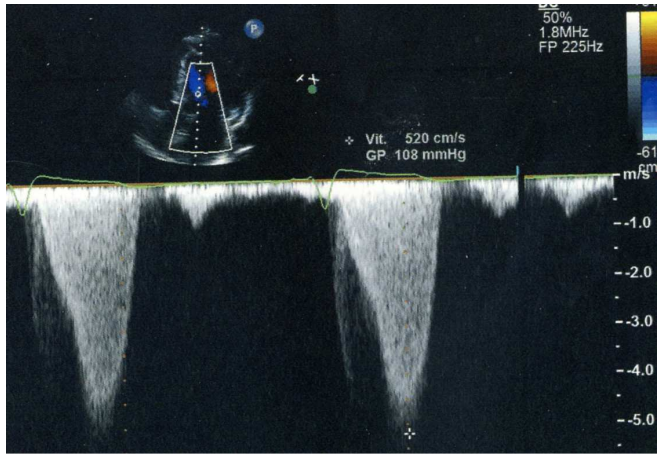
CMH OBSTRUCTIVE







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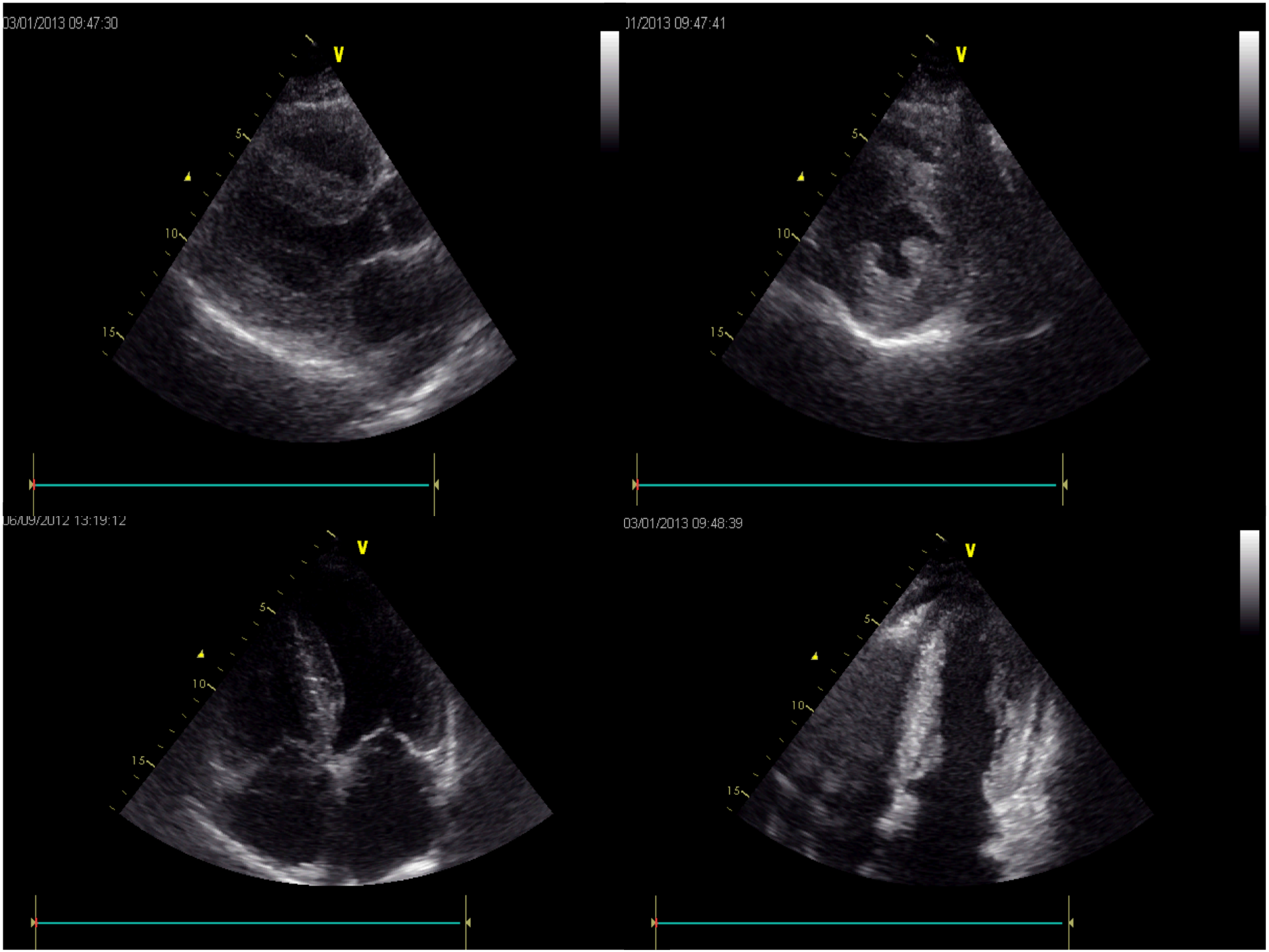
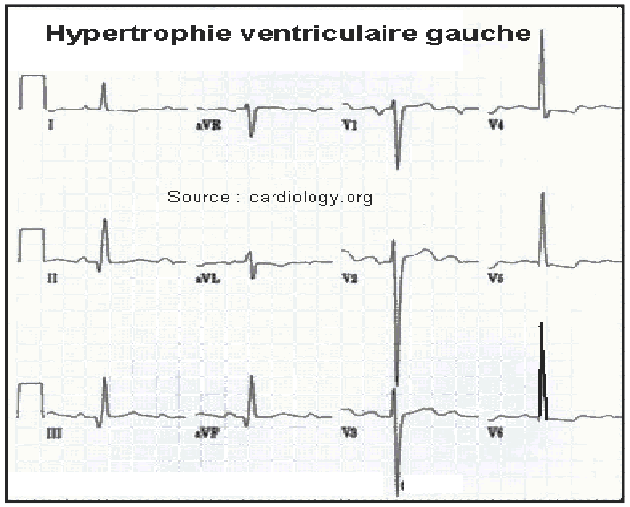
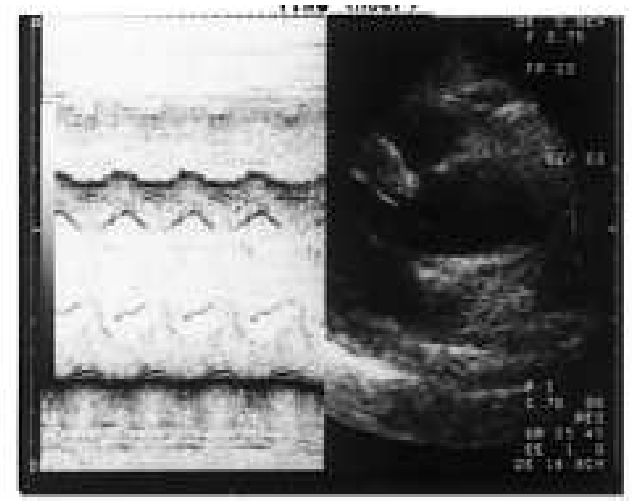

03/01/2013 09:47:30
V
5
10
15
01/2013 09:47:41
V
5
10
15
06/09/2012 13:19:12
V
5
10
15
03/01/2013 09:48:39
V
5
10
15

Prévalence de l ’HVG : Fonction de la méthode

430 hypertendus (H 54%), Suivi 3.2 ans, Critère combiné : MI, angina, stroke, etc.





Romhilt-Estes score ≥ 5 : 5.3%

LVMI > 125 g/m2 : 26.0%

HVG ECG moins fréquente que HVG Echo

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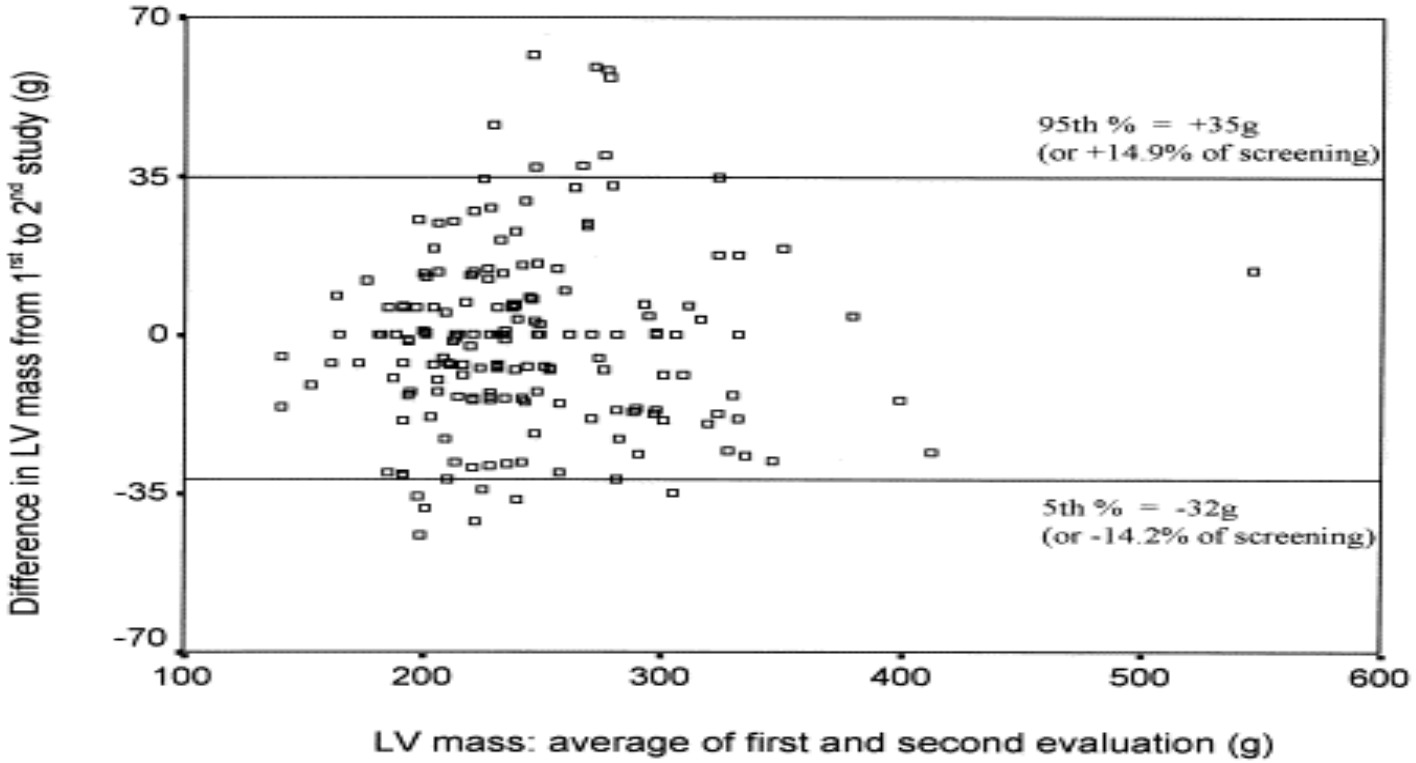
Verdecchia et al. Circulation 1998;97:48-54

Détection de l 'HVG/écho

Reproductibilité médiocre !



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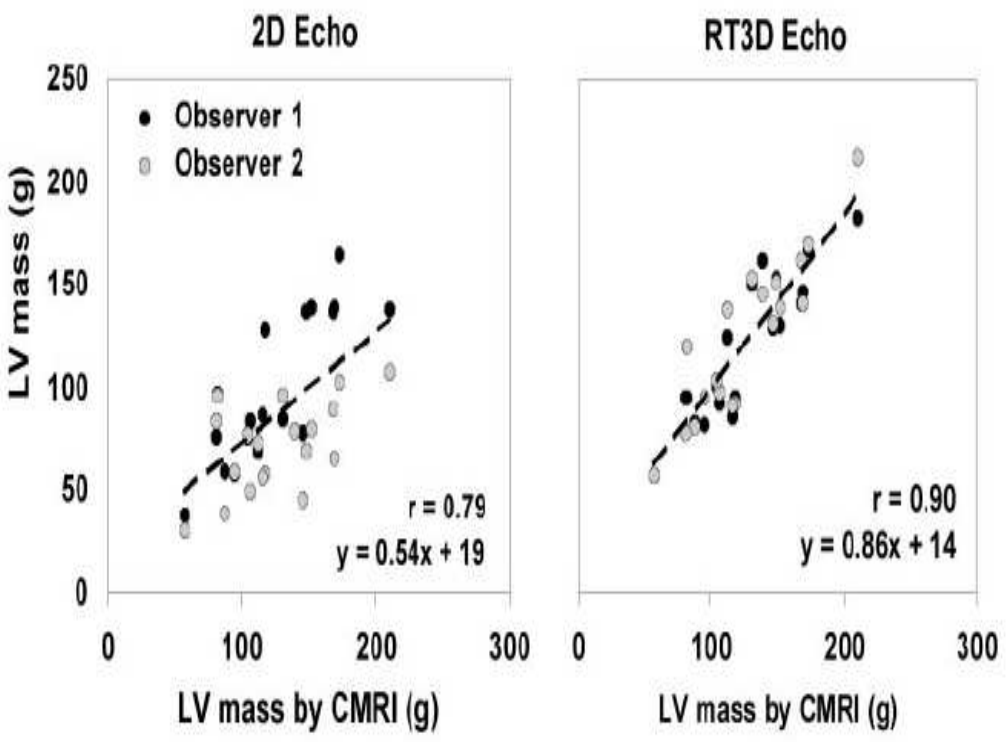
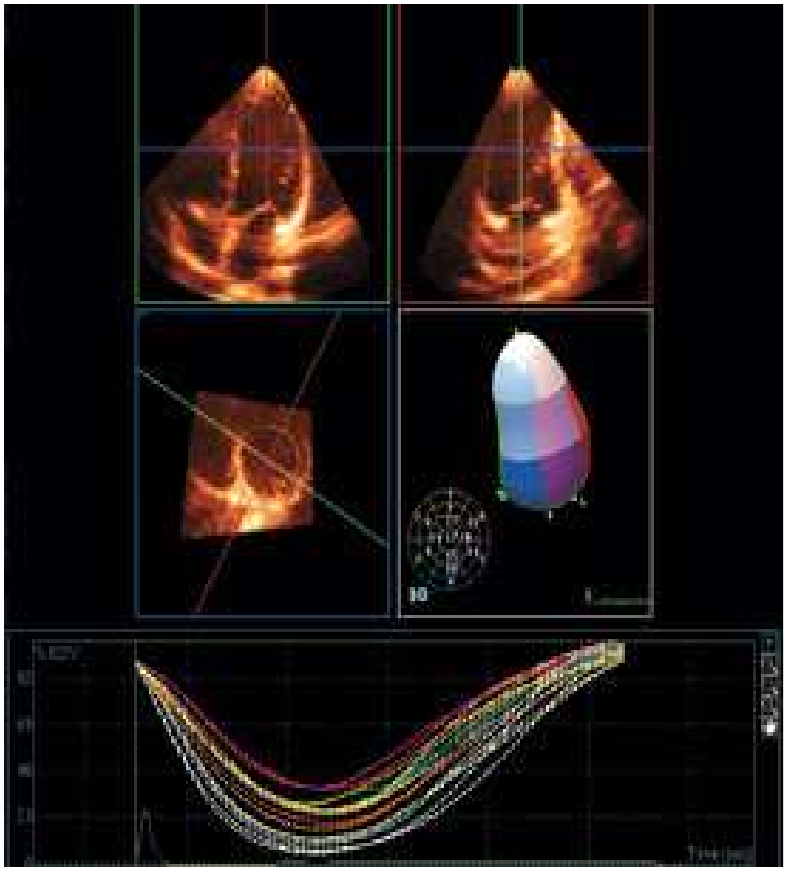
Palmieri V JACC 1999

Echo 3D





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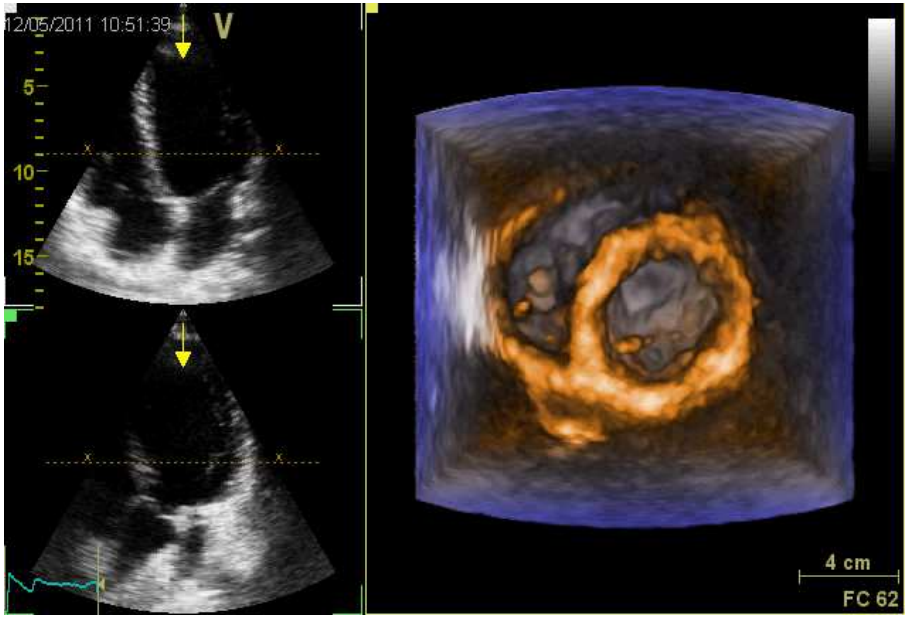
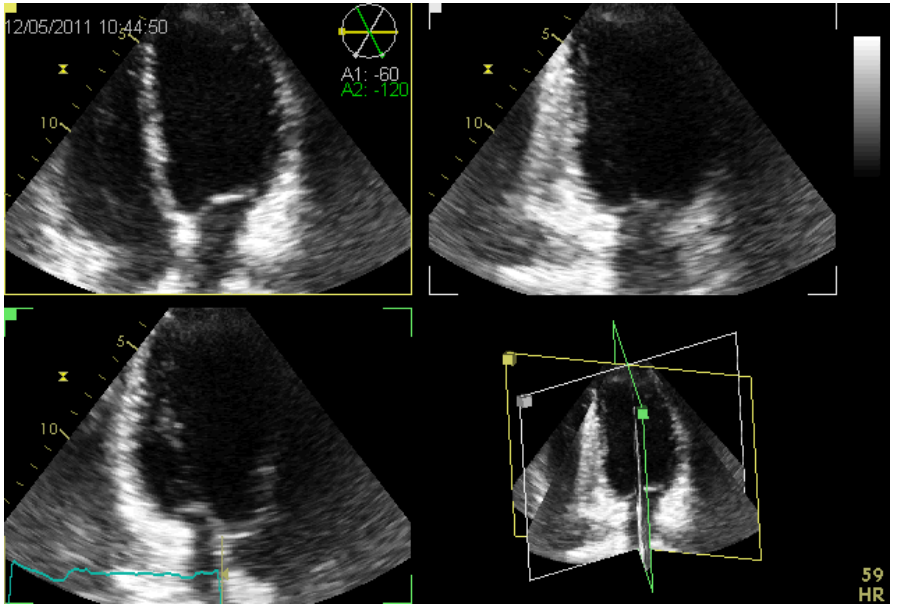
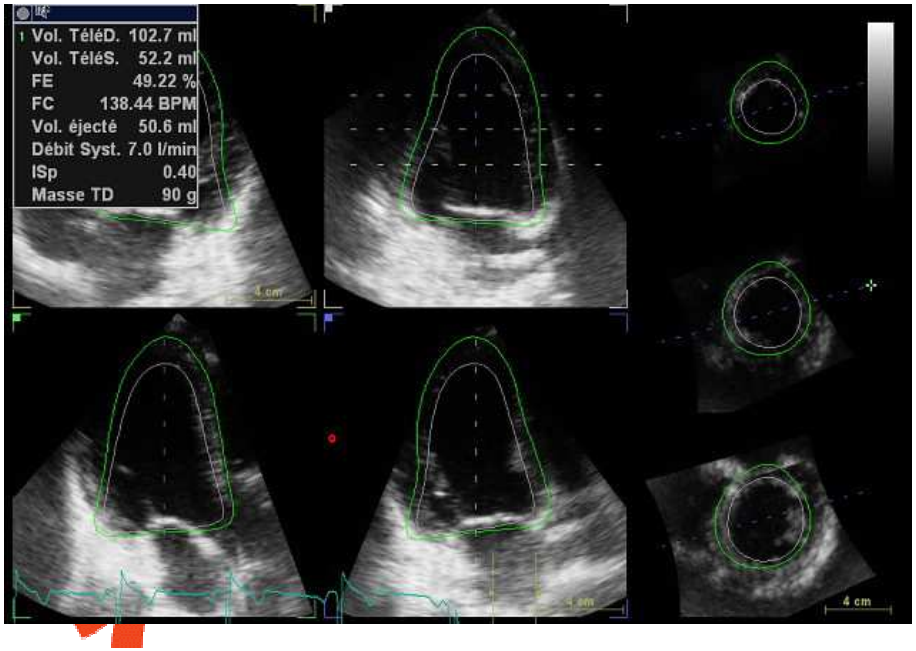
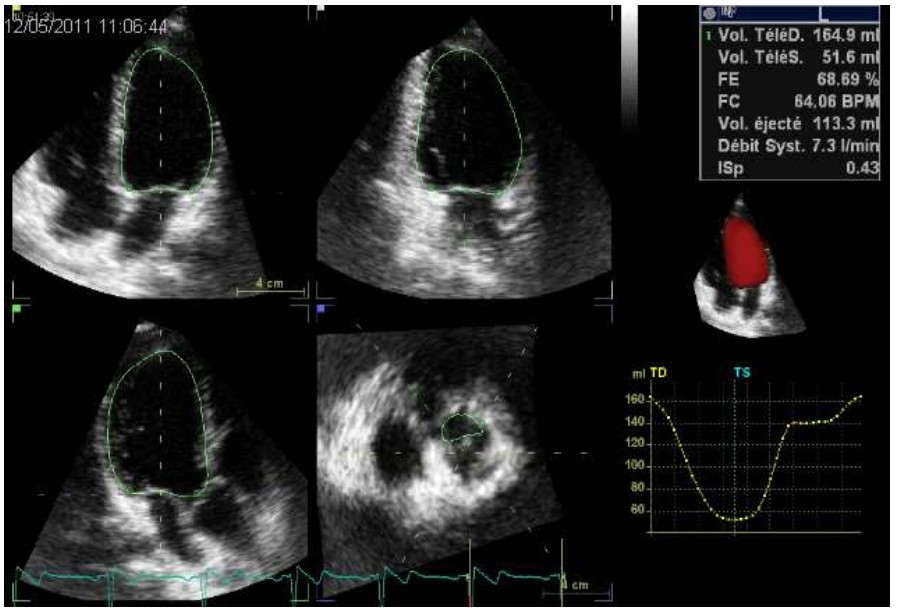
Mor-avi et al. Circulation 2004;110:1814-1818


12/05/2011 10:51:39
V
4 cm
FC 62


12/05/2011 10:44:50
A1: -60
A2: -120
59
HR


Vol. TéléD. 102.7 ml
Vol. TéléS. 52.2 ml
FE 49.22 %
FC 138.44 BPM
Vol. éjecté 50.6 ml
Débit Syst. 7.0 l/min
ISp 0.40
Masse TD 90 g


12/05/2011 11:06:44
Vol. TéléD. 164.9 ml
Vol. TéléS. 51.6 ml
FE 68.69 %
FC 84.06 BPM
Vol. éjecté 113.3 ml
Débit Syst. 7.3 l/min
ISp 0.43
ml TD
TS
160
140
120
100
80
60

IRM

- **Examen de référence pour l'étude de la FEVG et des volumes VG**
- Masse myocardique fiable et reproductible
- Localisation et quantification précise des zones hypertrophiées
- Etude de l'ensemble du VG et des autres structures anatomiques cardiaques, de la perfusion myocardique, de la fonction diastolique
- Séquences de rehaussement tardifs très utiles au **diagnostic étiologique**

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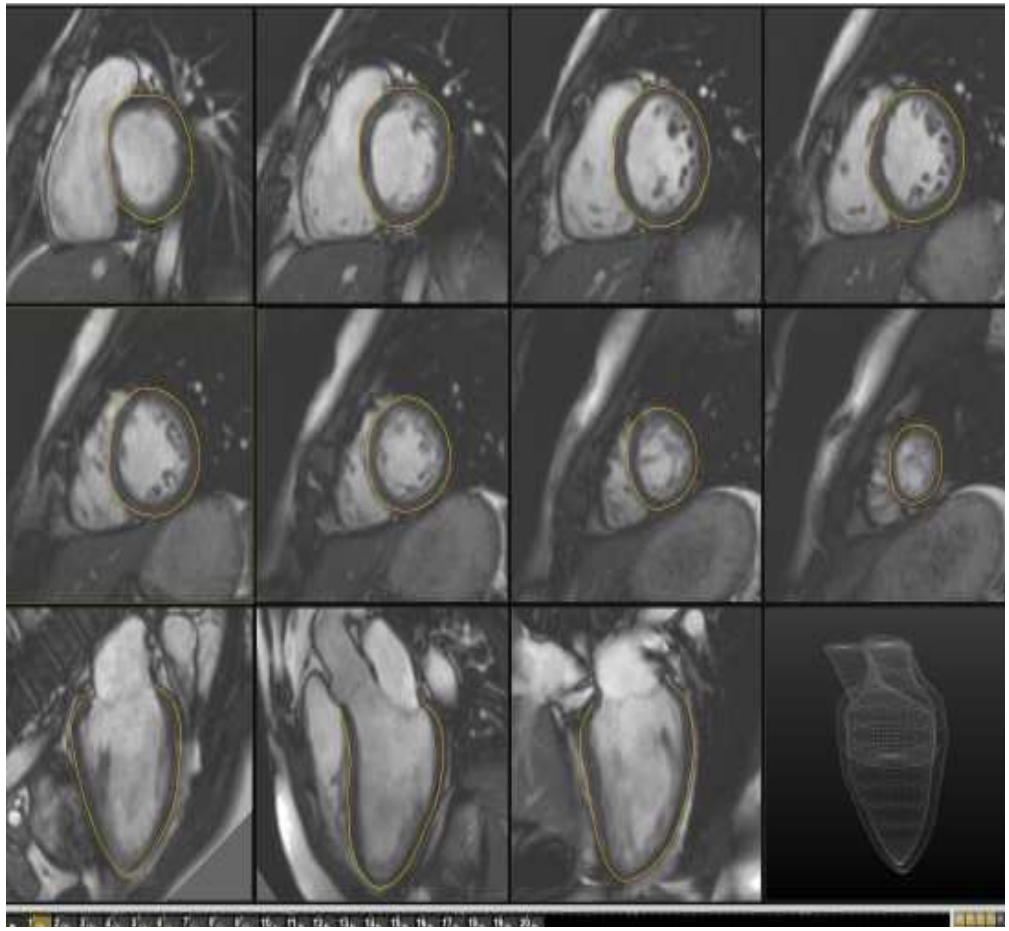
IRM

L ’IRM

Reproductibilité excellente

≈ 8 g entre deux examens



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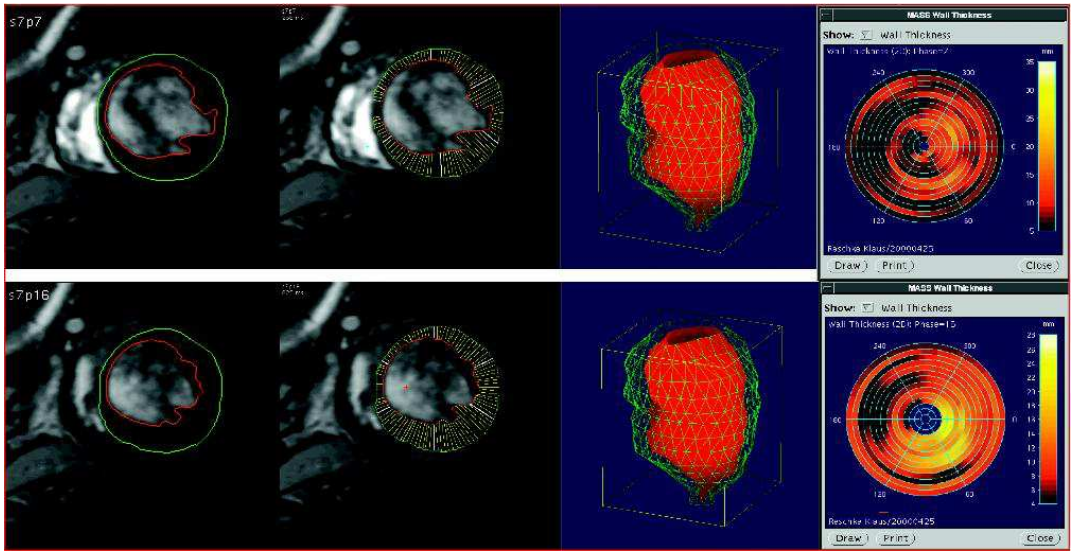
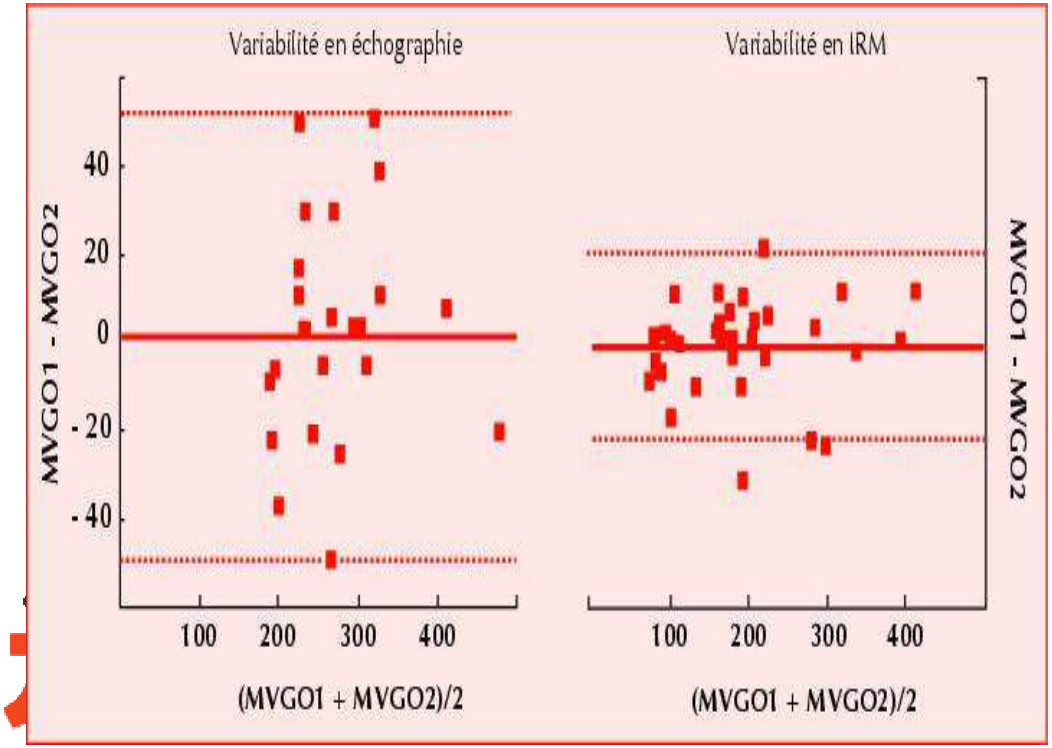
Recommandation SFC/SFR 2009


s7p7
s7p16
MASS Wall Thickness
Show:
Wall Thickness
Draw
Print
Close


Variabilité en échographie
Variabilité en IRM
MVGO1 - MVGO2
40
20
0
- 20
- 40
100
200
300
400
(MVGO1 + MVGO2)/2
MVGO1 - MVGO2

HVG
rôle pronostic

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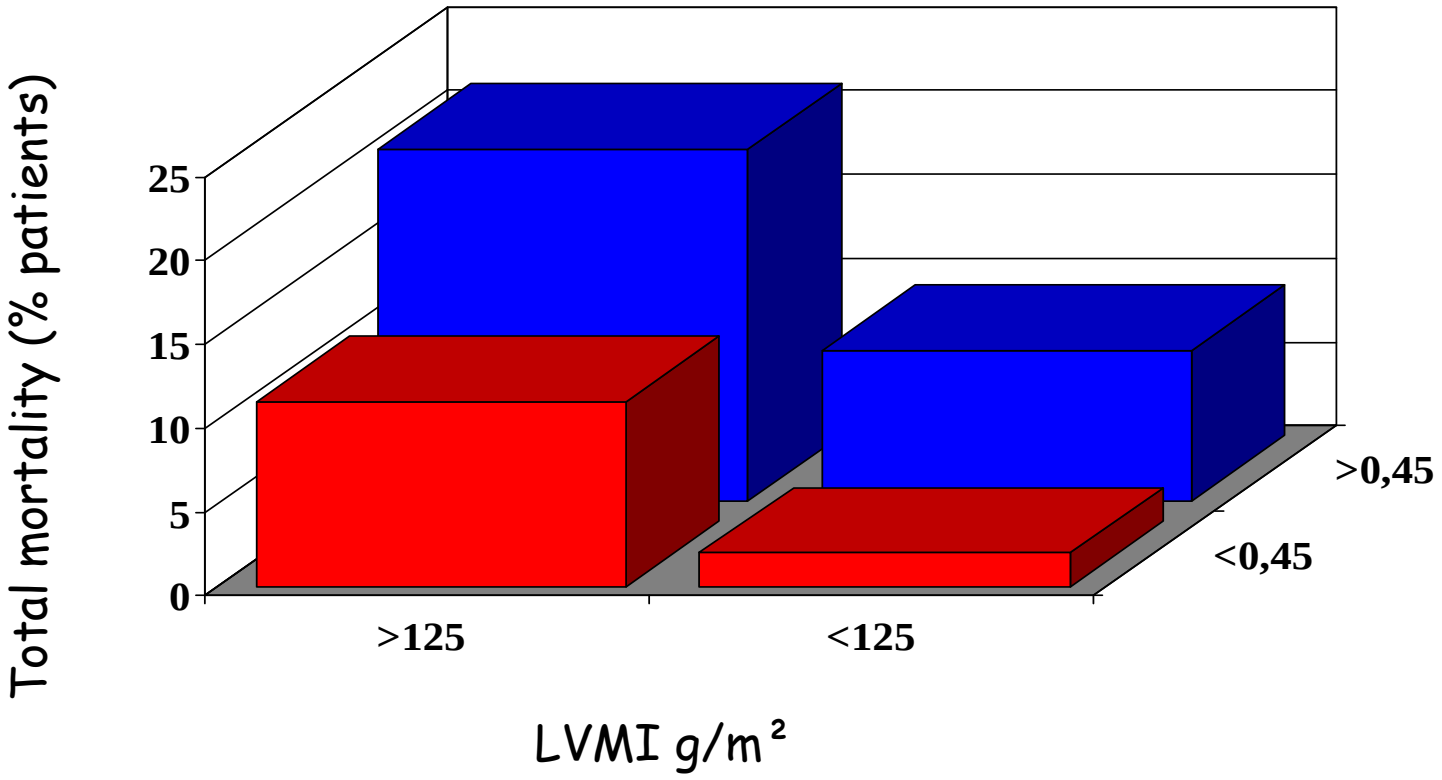
Fonction du type d'HVG

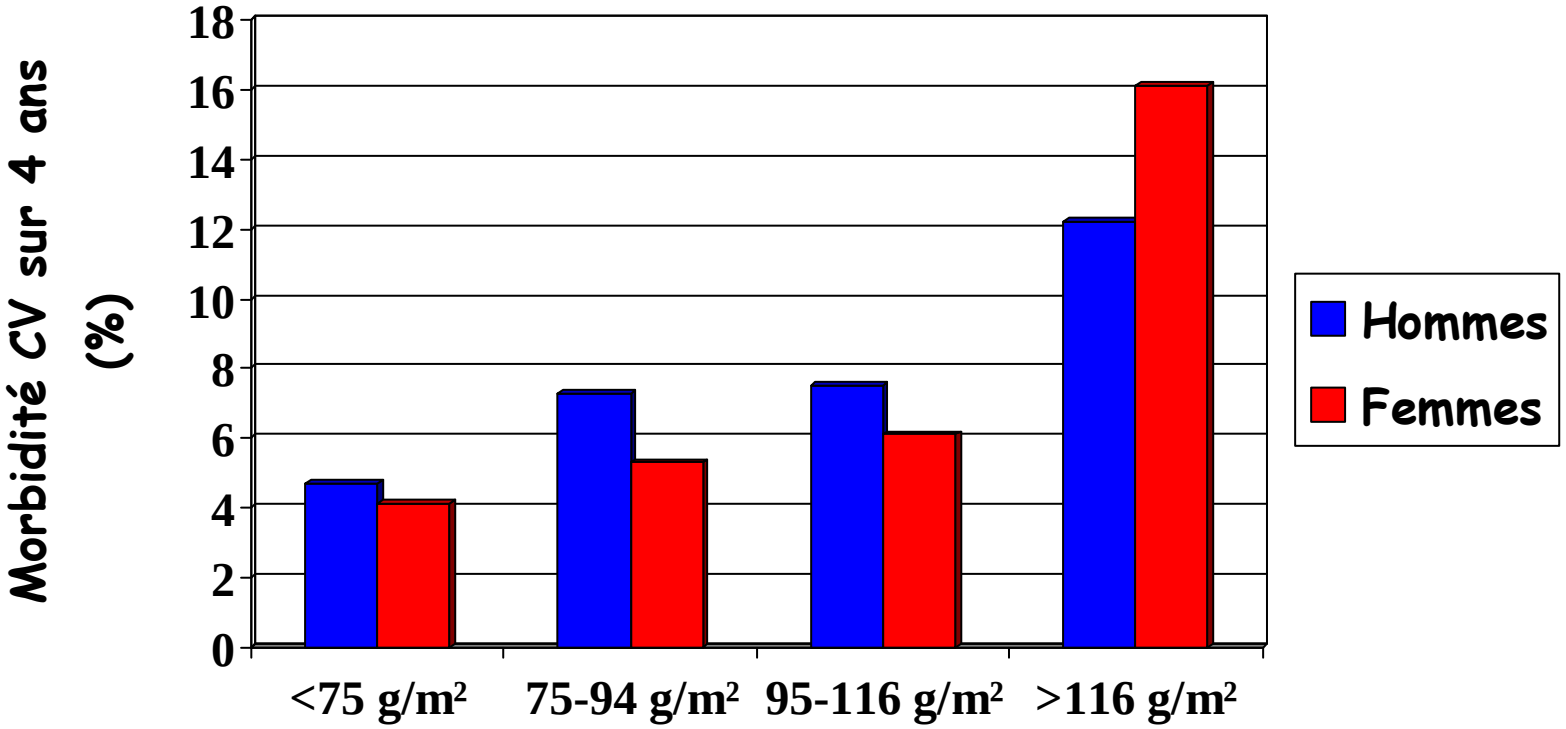
253 hypertendus, Follow-up : 10,2 ans



Koren et al. Ann Intern Med. 1991 1;114:345-52

Rôle pronostique de l ’HVG

N = 3200 sujets
morbidité CV et mortalité



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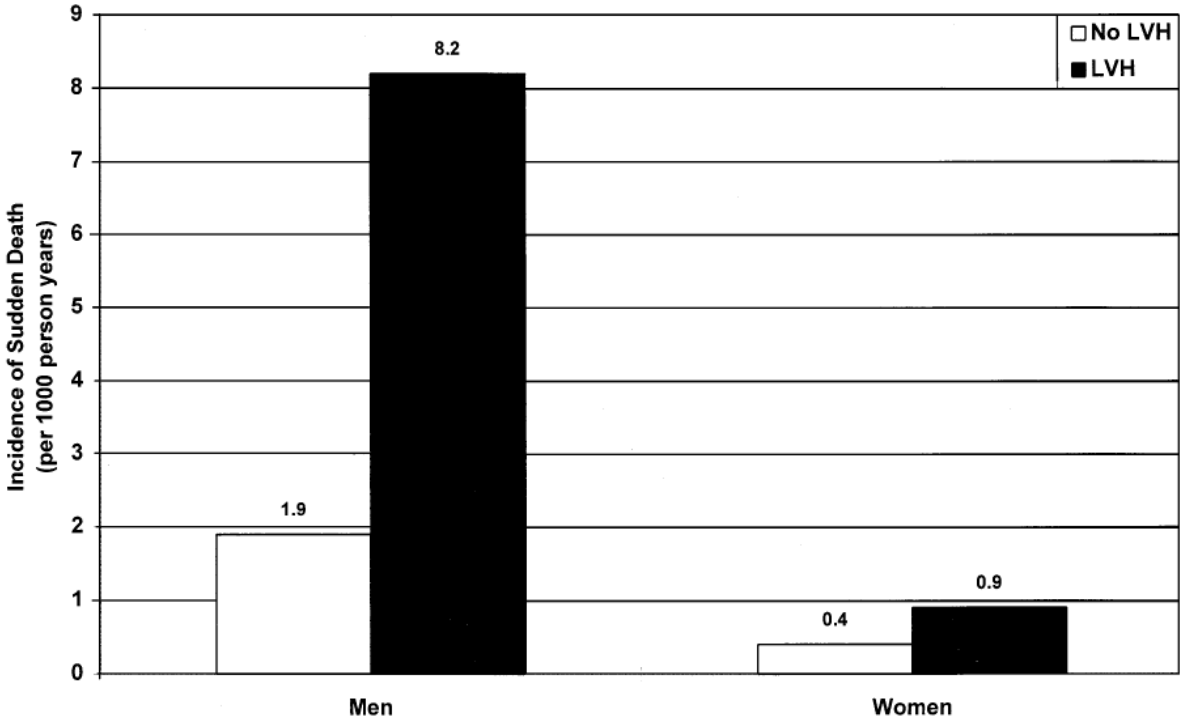
Levy et al. N Engl J Med. 1990;322:1561-6

Rôle pronostique de l ’HVG

HVG et mort subite, 3661 sujets, Framingham, 14 ans de suivi



Increased LV mass and hypertrophy are associated with increased risk for sudden death after accounting for known risk factors

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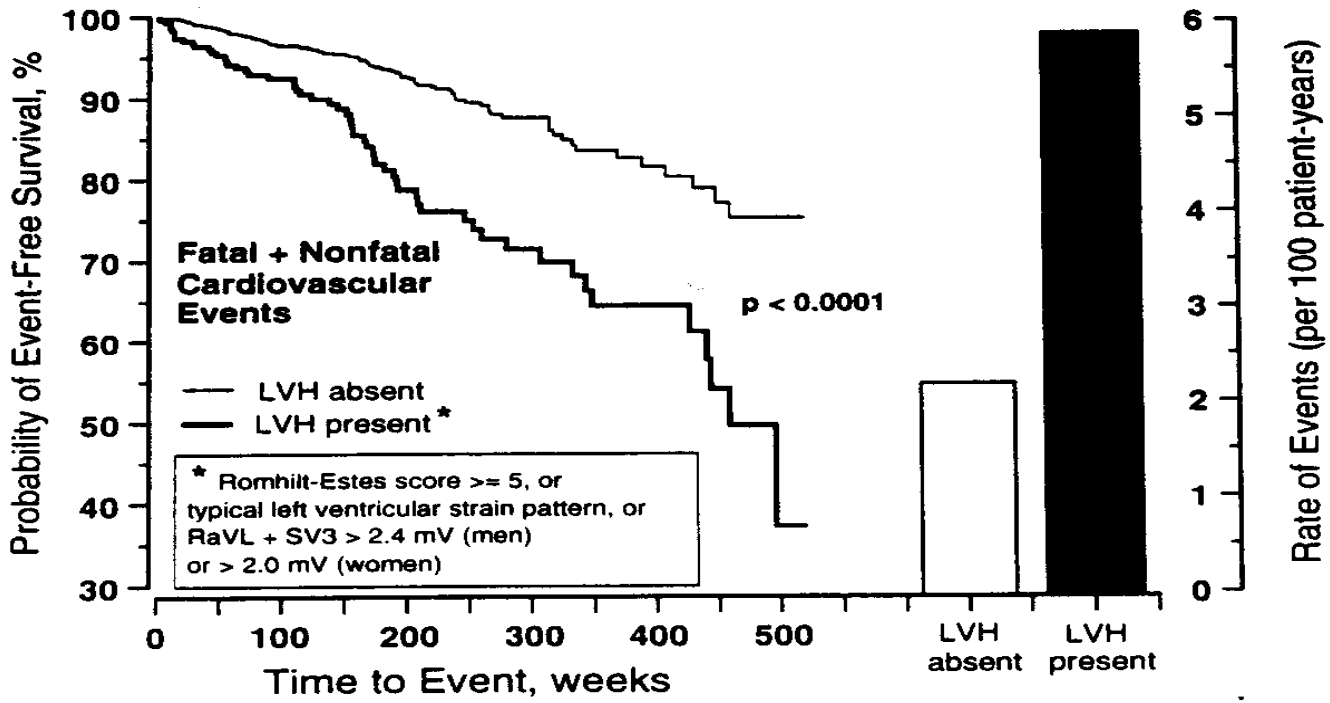
Haider et al. JACC 1998;32:1454-9

Rôle pronostique de l ’HVG

N = 1717 hypertendus, Suivi = 3,3 ans, Evnmts = Coronaires, AVC,AOMI, IC, IRC, OACR



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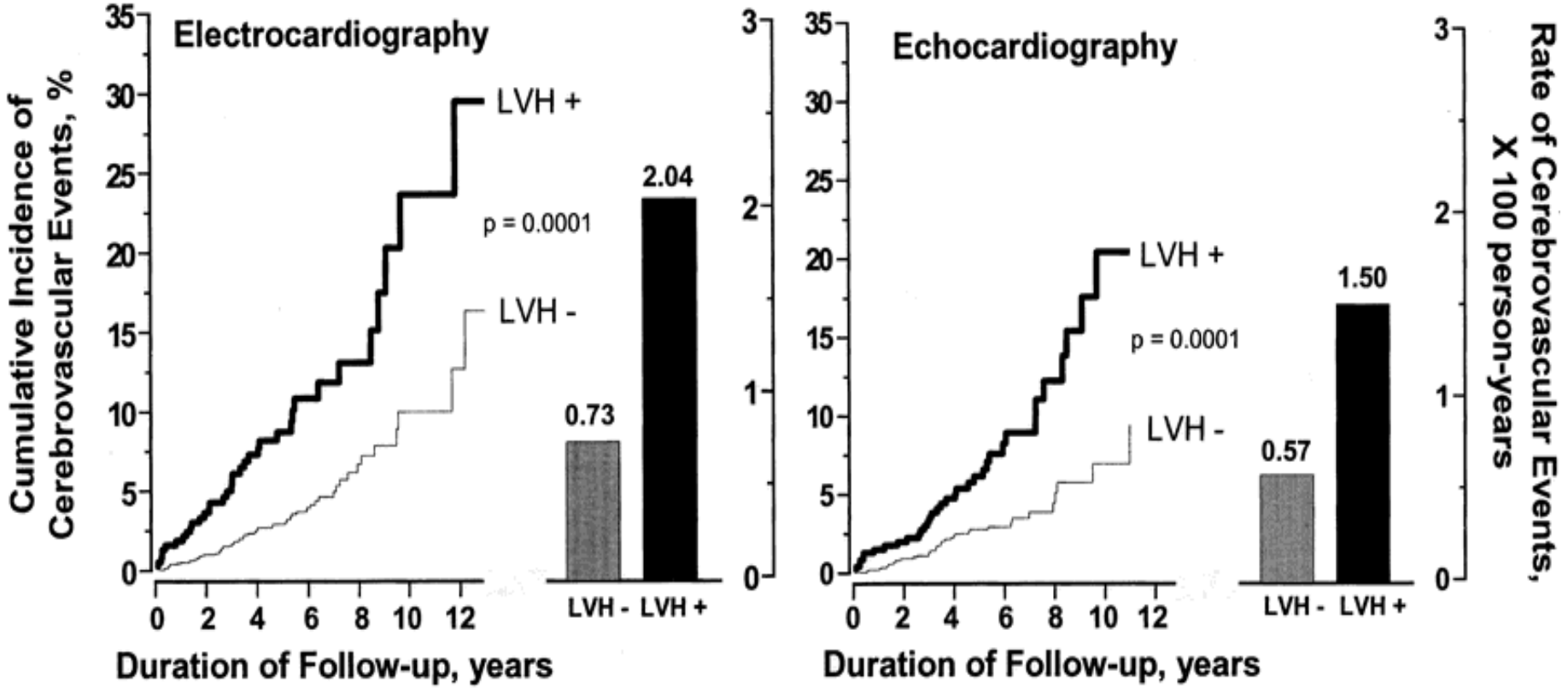
Verdecchia et al. Circulation 1998;97:48-54

HVG et risque cérébral

N= 2363 hypertendus Suivi = 5ans



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Verdecchia et al Circulation 2001 23;104:2039-44

MESA STUDY

- But: évaluer la relation de la masse VG **/IRM** et la survenue d'évènements CV
- 5098 patients, suivi de 4 ans

=>Augmentation de la masses VG (du remodelage concentrique à l'HVG concentrique) (IRM) est fortement associé à la survenue d'évènements CV

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Bluemke et al. J Am Coll Cardiol. 200816;52(25):2148-55

Peut on agir ?

Régression de l'HVG avec le traitement

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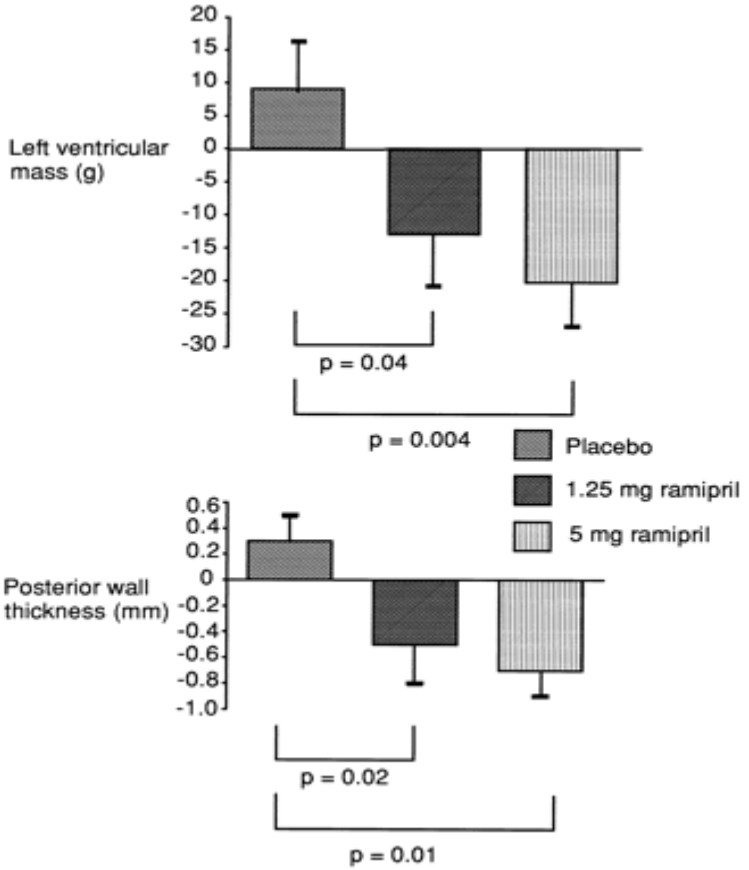
étude HYCAR : effet du ramipril

115 hypertendus
furosemide 20 mg/d - ramipril 1,25 ou 5 mg / placebo
Suivi 6 mois
Evolution

- de la masse VG (écho)
- Pas de différence de PA



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Lièvre M et al. Hypertension. 1995 ; 25:92-7

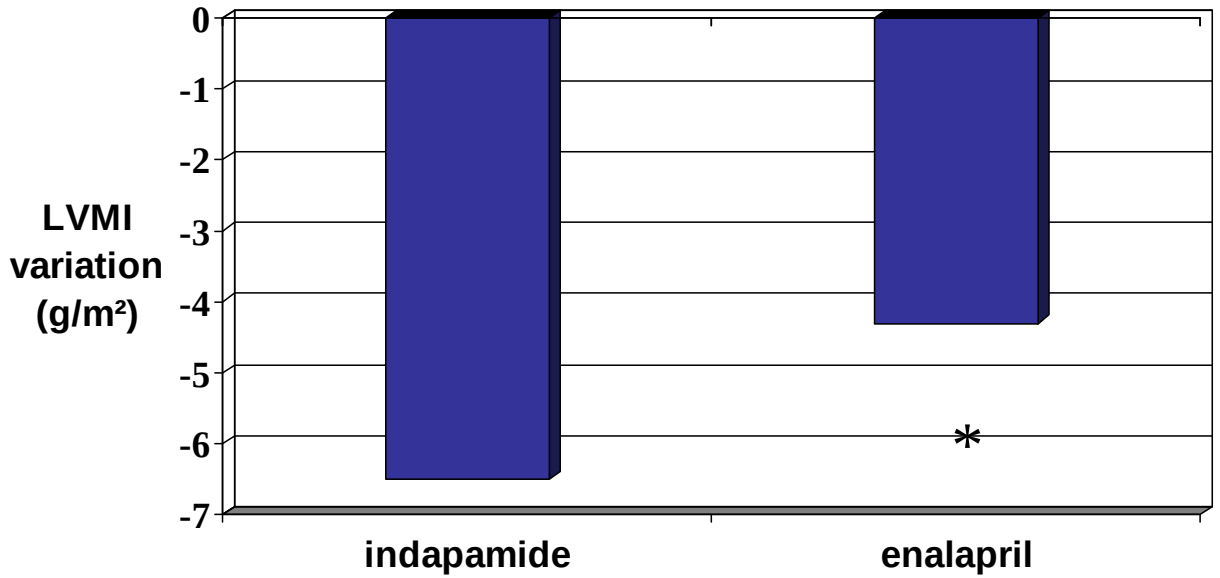
Etude LIVE : indapamide vs enalapril

411 hypertendus avec HVG

indapamide 1,5 mg/j vs enalapril 20 mg/

Suivi 48 sem avec évolution de la masse VG (écho)

Pas de différence de PA avec les deux TTT



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Gosse P et al . J Hypertens. 2000 ;18:1465-75

Etude HOPE

Reduction of Cardiovascular Risk by Regression of Electrocardiographic Markers of Left Ventricular Hypertrophy by the Angiotensin-Converting Enzyme Inhibitor Ramipril

James Mathew, MD, FCCP; Peter Sleight, MD, FRCP; Eva Lonn, MD, MSc; David Johnstone, MD; Janice Pogue, PhD; Qilong Yi, PhD; Jackie Bosch, MS; Bruce Sussex, MD, FRCPC; Jeffrey Probstfield, MD; Salim Yusuf, MBBS, DPhil, FRCP; for the Heart Outcomes Prevention Evaluation (HOPE) Investigators

Background—Electrocardiographic markers of left ventricular hypertrophy (LVH) predict poor prognosis. We determined whether the ACE inhibitor ramipril prevents the development and causes regression of ECG-LVH and whether these changes are associated with improved prognosis independent of blood pressure reduction.

Methods and Results—In the Heart Outcomes Prevention Evaluation (HOPE) study, patients at high risk were randomly assigned to ramipril or placebo and followed for 4.5years. ECGs were recorded at baseline and at study end. We compared prevention/regression and development/persistence of ECG-LVH in the two groups and related these changes to outcomes. At baseline, 676 patients had LVH (321 in the ramipril group and 355 in the placebo group) and 7605 patients did not have LVH (3814 in the ramipril group and 3791 in the placebo group). By study end, 336 patients in the ramipril group (8.1%) compared with 406 in the placebo group (9.8%) had development/persistence of LVH; in contrast, 3799 patients in the ramipril group (91.9%) compared with 3740 in the placebo group (90.2%) had regression/prevention of LVH ($P=0.007$). The effect of ramipril on LVH was independent of blood pressure changes. Patients who had regression/prevention of LVH had a lower risk of the predefined primary outcome (cardiovascular death, myocardial infarction, or stroke) compared with those who had development/persistence of LVH (12.3% versus 15.8%, $P=0.006$) and of congestive heart failure (9.3% versus 15.4%, $P<0.0001$).

Conclusions—The ACE inhibitor ramipril decreases the development and causes regression of ECG-LVH independent of blood pressure reduction, and these changes are associated with reduced risk of death, myocardial infarction, stroke, and congestive heart failure. (*Circulation*. 2001;104:1615-1621.)

Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol

Methods We did a double-masked, randomised, parallel-group trial in 9193 participants aged 55–80 years with essential hypertension (sitting blood pressure 160–200/95–115 mm Hg) and LVH ascertained by electrocardiography (ECG). We assigned participants once daily losartan-based or atenolol-based antihypertensive treatment for at least 4 years and until 1040 patients had a primary cardiovascular event (death, myocardial infarction, or stroke). We used Cox regression analysis to compare regimens.

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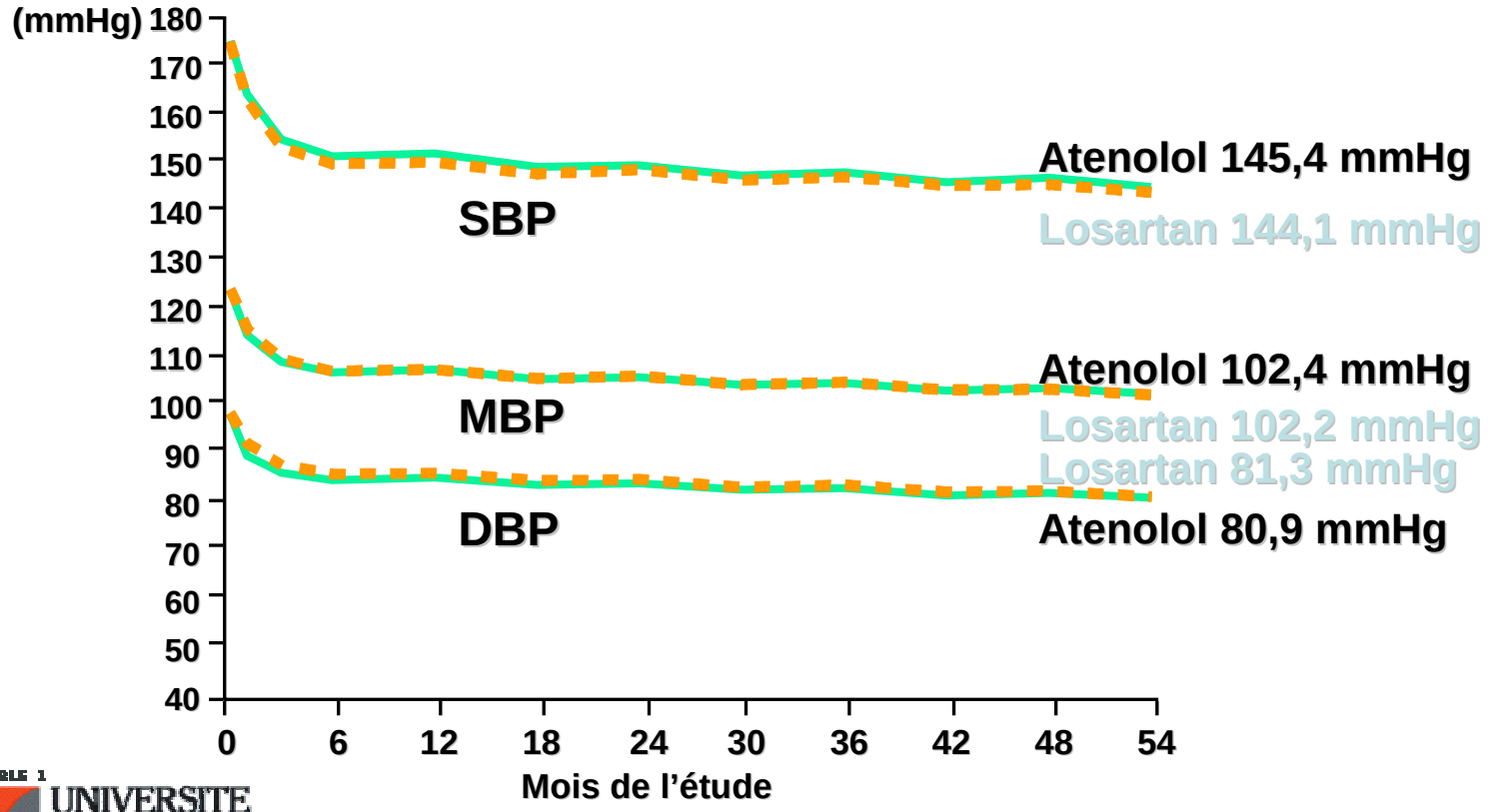
Björn Dahlöf et al. Lancet 2002; 359: 995–1003

Etude LIFE : Losartan vs Atenolol

N= 9193 hypertendus, HVG +, Suivi moyen = 4,8 ans



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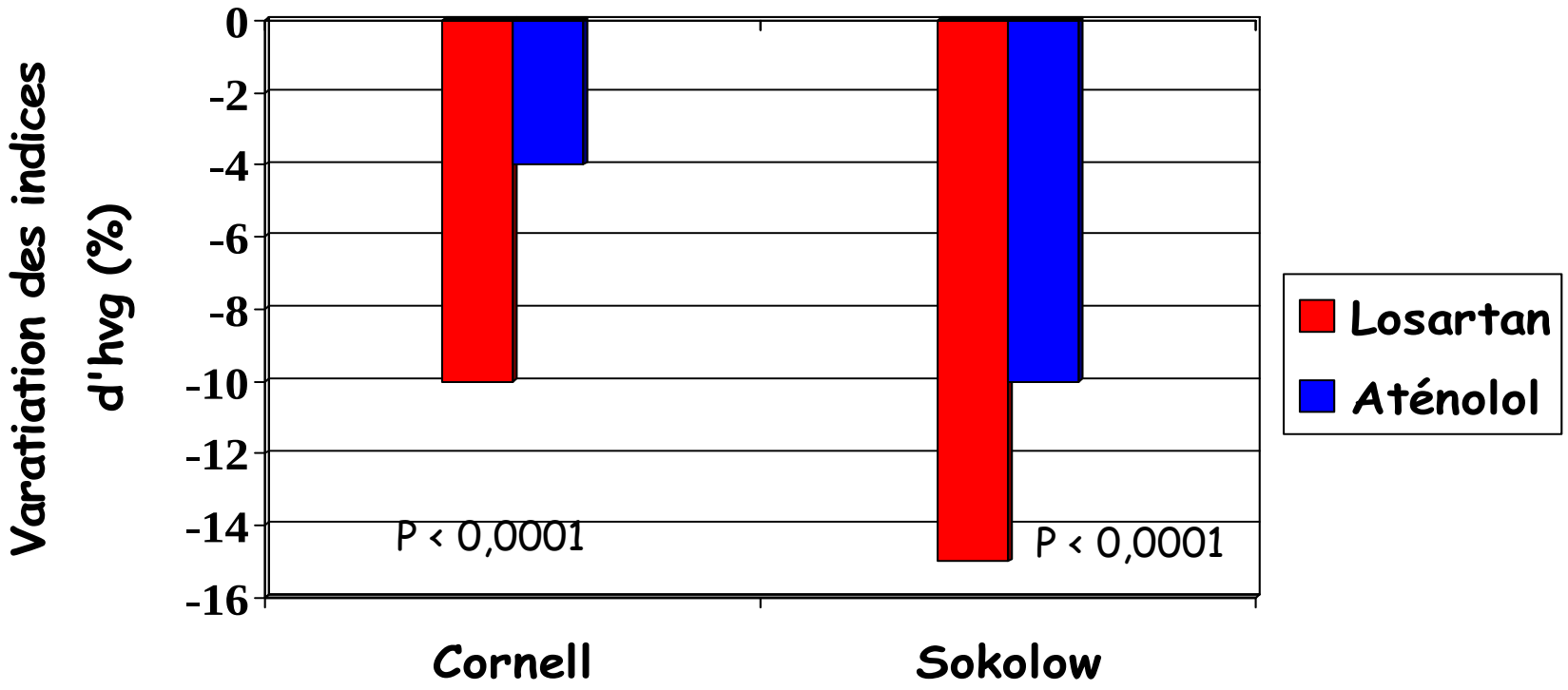
Björn Dahlöf et al. Lancet 2002; 359: 995–1003

LIFE : Losartan vs Atenolol



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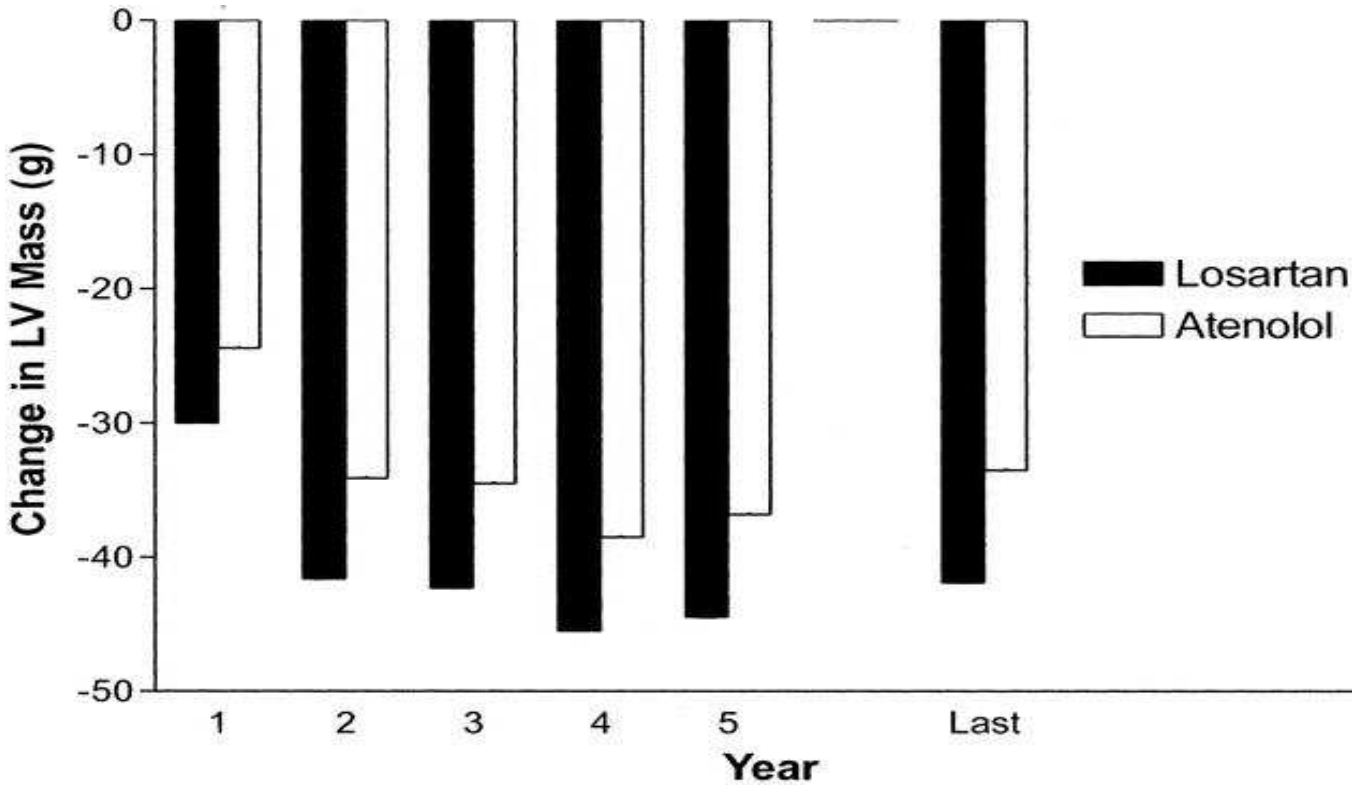
Björn Dahlöf et al. Lancet 2002; 359: 995–1003

LIFE : Losartan vs Atenolol



Losartan -21.7±21.8 vs Atenolol –17.7 ±19.6 g/m²

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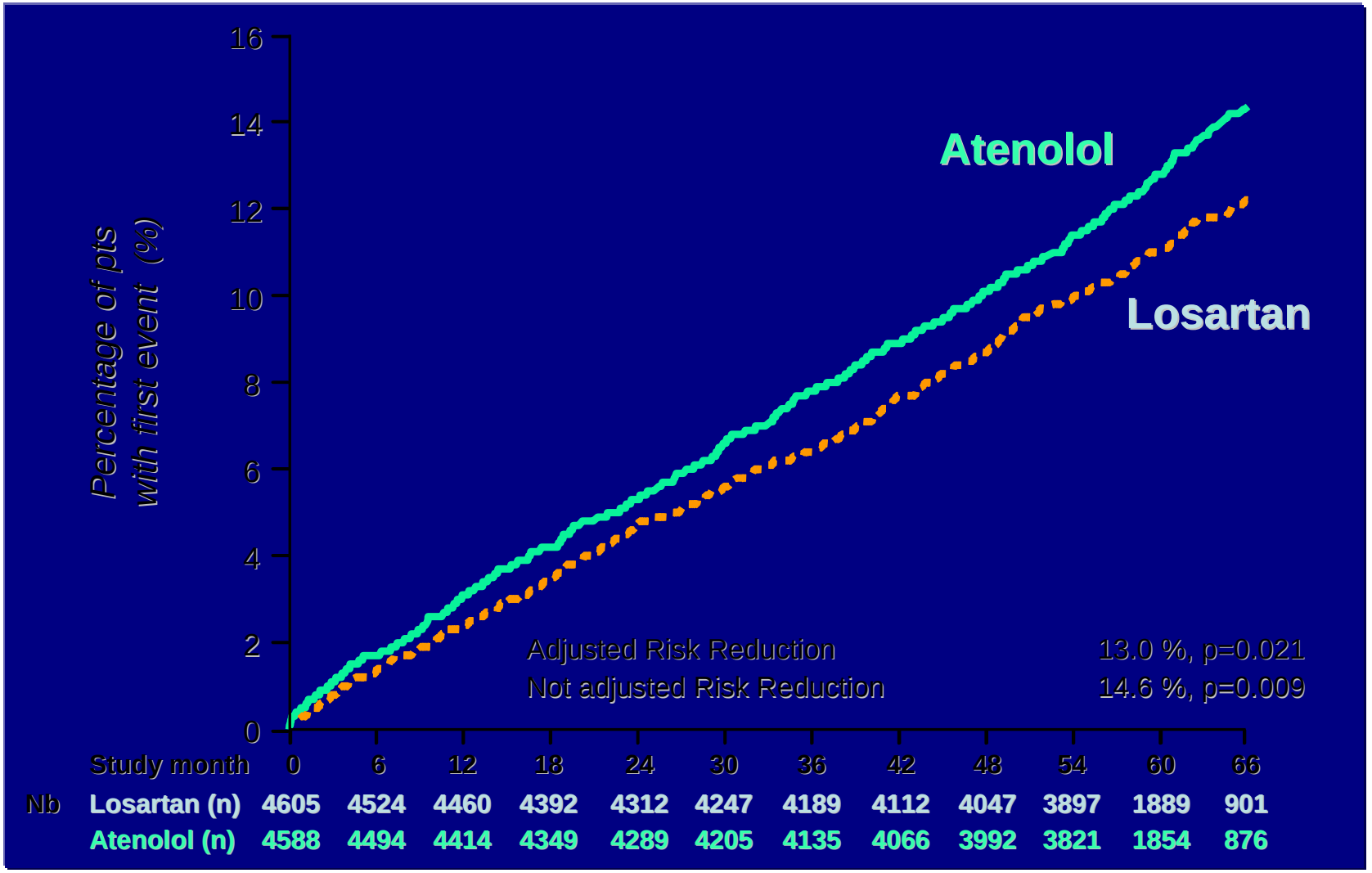
Devereux RB et al. Circulation 2004 ;110 :1456-62

LIFE – Primary end point

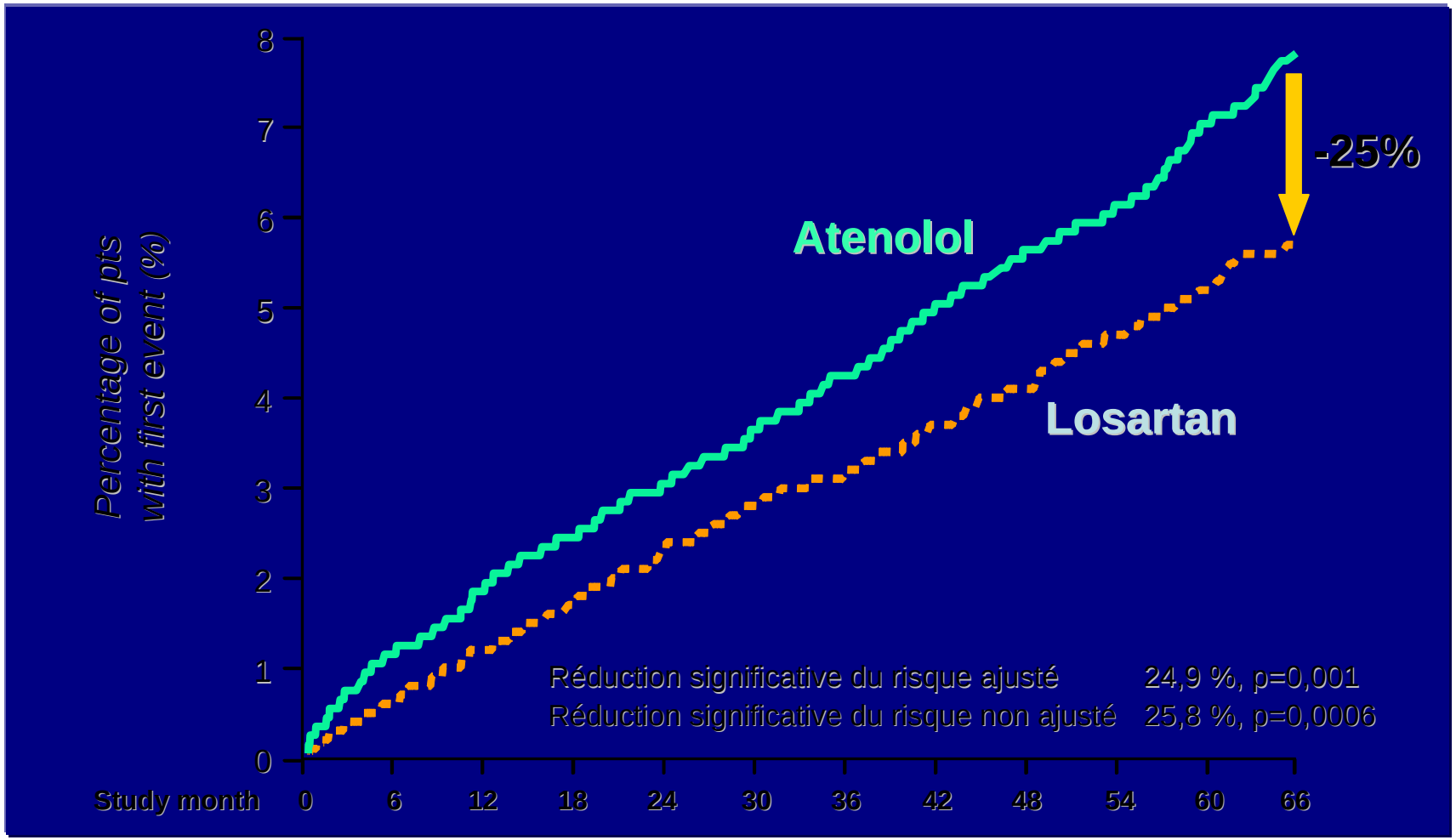
Combined endpoint: CV death, stroke and MI



Björn Dahlöf et al. Lancet 2002; 359: 995–1003

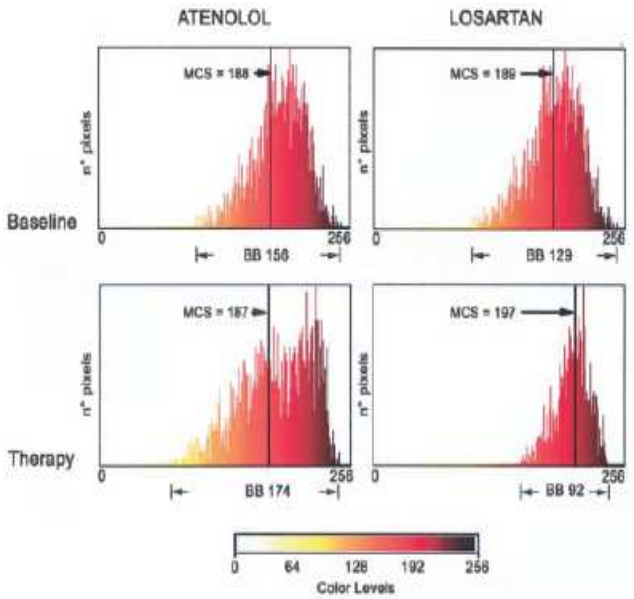
LIFE – Stroke

Fatal and non fatal stroke



Björn Dahlöf et al. Lancet 2002; 359: 995–1003

La régression de la fibrose



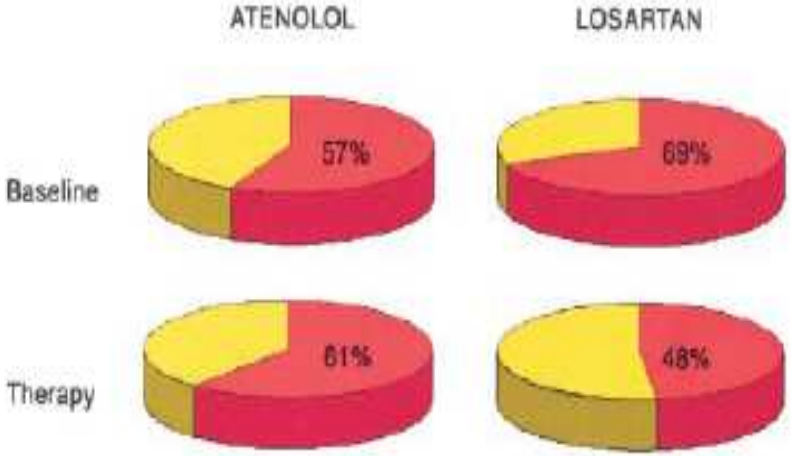


Figure 2. Prevalence of excessive fibrosis (defined as BB ≥100 color levels) in atenolol- and losartan-treated patients at baseline and after 36-week treatment. Note prevalence of excessive fibrosis was unchanged by atenolol and decreased by losartan.

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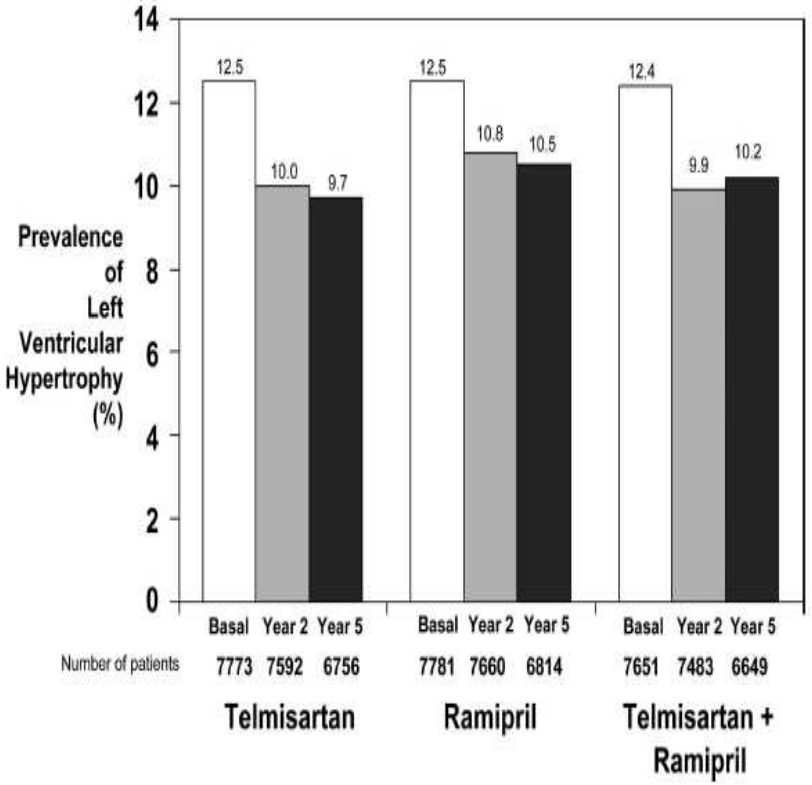
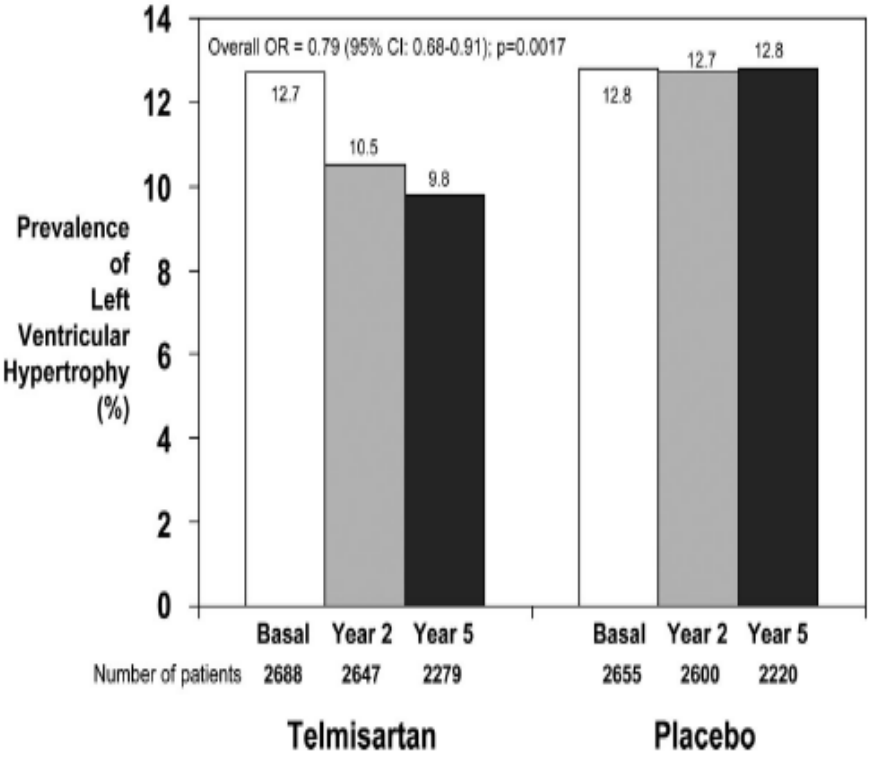
Ciulla et al. Circulation. 2004;110:552-557

Etudes
ONTARGET and TRANSCEND





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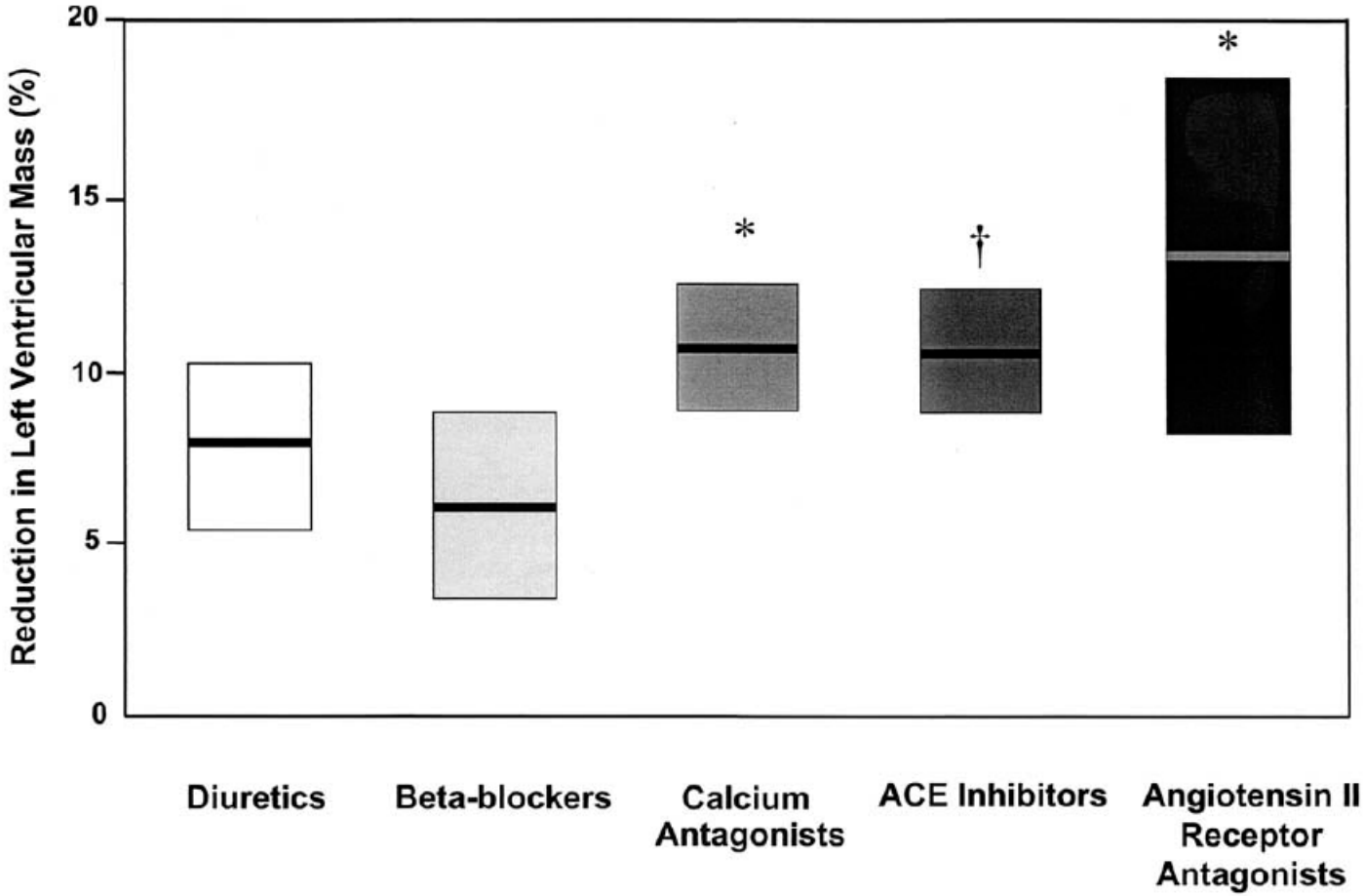
Verdecchia et al. Circulation. 2009; 120:1380-1389

Effet des traitements sur l ’HVG



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Klingbeil et al. Am J Med. 2003;115:41-6

Effect of the Direct Renin Inhibitor Aliskiren, the Angiotensin Receptor Blocker Losartan, or Both on Left Ventricular Mass in Patients With Hypertension and Left Ventricular Hypertrophy

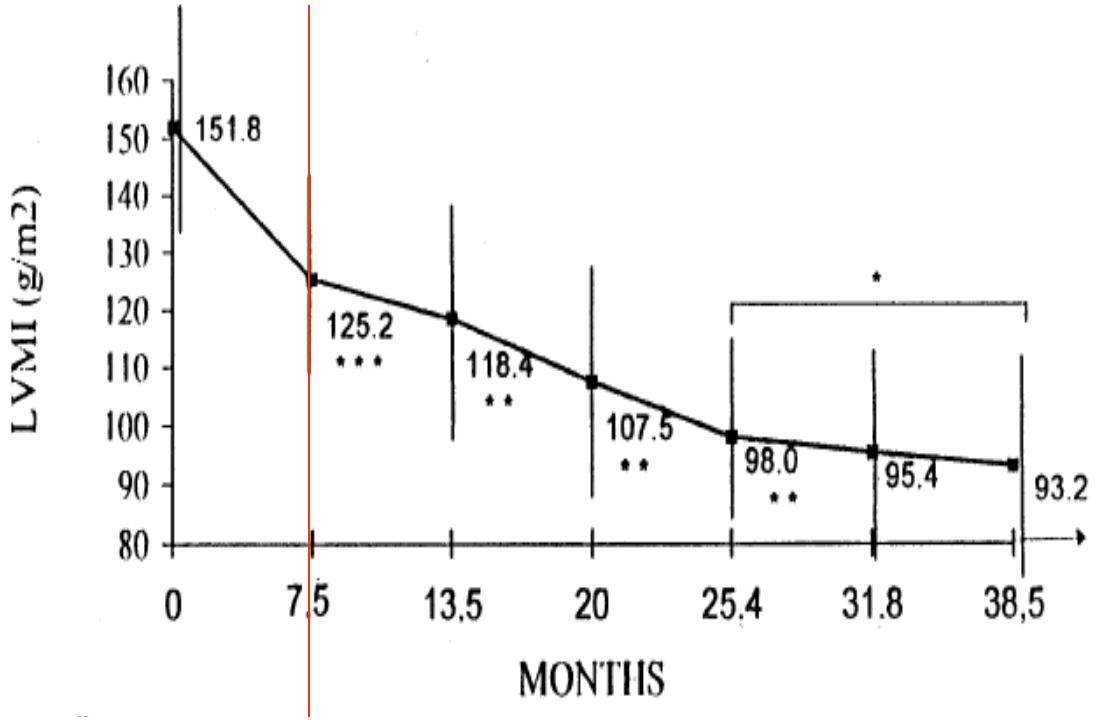
Scott D. Solomon, MD; Evan Appelbaum, MD; Warren J. Manning, MD; Anil Verma, MD; Tommy Berglund, MD; Valentina Lukashevich, MD; Cheraz Cherif Papst, MS; Beverly A. Smith, RN; Björn Dahlöf, MD, PhD; for the Aliskiren in Left Ventricular Hypertrophy (ALLAY) Trial Investigators

Background—Left ventricular (LV) hypertrophy, a marker of cardiac end-organ damage, is associated with an increased risk of cardiovascular morbidity and mortality. Inhibitors of the renin-angiotensin-aldosterone system may reduce LV mass to a greater extent than other antihypertensive agents. We compared the effect of aliskiren, the first orally active direct renin inhibitor, the angiotensin-receptor blocker losartan, and their combination on the reduction of LV mass in hypertensive patients.

Methods and Results—We randomized 465 patients with hypertension, increased ventricular wall thickness, and body mass index >25 kg/m^2 to receive aliskiren 300 mg, losartan 100 mg, or their combination daily for 9 months. Patients were treated to standard blood pressure targets with add-on therapy, excluding other inhibitors of the renin-angiotensin-aldosterone system and β-blockers. Patients underwent cardiovascular magnetic resonance imaging for assessment of LV mass at baseline and at study completion. The primary objective was to compare change in LV mass index from baseline to follow-up in the combination and losartan arms; the secondary objective was to determine whether aliskiren was noninferior to losartan in reducing LV mass index from baseline to follow-up. Systolic and diastolic blood pressures were reduced similarly in all treatment groups (6.5±14.9/3.8±10.1 mm Hg in the aliskiren group; 5.5±15.6/3.7±10.7 mm Hg in the losartan group; 6.6±16.6/4.6±10.5 mm Hg in the combination arm; $P<0.0001$ within groups, $P=0.81$ between groups). LV mass index was reduced significantly from baseline in all treatment groups (4.9-, 4.8-, and 5.8 g/m^2 reductions in the aliskiren, losartan, and combination arms, respectively; $P<0.0001$ for all treatment groups). The reduction in LV mass index in the combination group was not significantly different from that with losartan alone ($P=0.52$). Aliskiren was as effective as losartan in reducing LV mass index ($P<0.0001$ for noninferiority). Safety and tolerability were similar across all treatment groups.

Conclusions—Aliskiren was as effective as losartan in promoting LV mass regression. Reduction in LV mass with the combination of aliskiren plus losartan was not significantly different from that with losartan monotherapy, independent of blood pressure lowering. These findings suggest that aliskiren was as effective as an angiotensin receptor blocker in attenuating this measure of myocardial end-organ damage in hypertensive patients with LV hypertrophy. (***Circulation.*** **2009;119:530-537.)**

Régression de l'HVG : en combien de temps?



Franz et al. AJH 1999; 11: 631-9

CONCLUSION

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HTA

- Une des causes principales d'HVG

- À l'hypertrophique myocytaire secondaire à l'élévation de la post charge s'ajoute une fibrose interstitielle et des anomalies de microcirculation coronaire

HTA

- Au niveau morphologique:

HVG symétrique avec épaisseur myocardique variable
(du remodelage concentrique à l' hypertrophie concentrique)

masse VG augmentée chez 28% des patients HTA de race blanche et
62%des patients de race noire

- Au niveau fonctionnel

-fonction systolique le plus souvent normale (en l'absence de cardiopathie ischémique associée)

-fonction diastolique perturbée à des degrés variables

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HTA

- **L'IRM** est nettement plus sensible que l'**ETT** pour dépister une HVG chez les patients Hypertendus (SE ETT 30%) qui elle-même est nettement plus sensible que l'**ECG**(Se 5 à 10%)

- Chez les patients hypertendus, l'HVG secondaire est **facteur indépendant de morbidité et de mortalité**, prédisposant à l'insuffisance cardiaque, aux troubles du rythme ventriculaire, aux AVC ischémiques , à la FA.

Conclusion HVG

- Faut il chercher une HVG chez l'hypertendu ?

OUI

- Pourquoi ?

Un **marqueur de risque**, un excellent critère intermédiaire une possible cible thérapeutique, un facteur de risque ?

- Comment ?

ECG ou ETT ou IRM

- Faut il la traiter *?*

Oui avec ARA II ou inh calcique

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Merci pour votre attention …