Vendredi 31 mars et samedi 1er avril 2023

Forum Fribourg

JHAS 2023

Open space Cardiologie 01.04.2023

Dr. Med. Hadrien Beuret

HFR - Fribourg

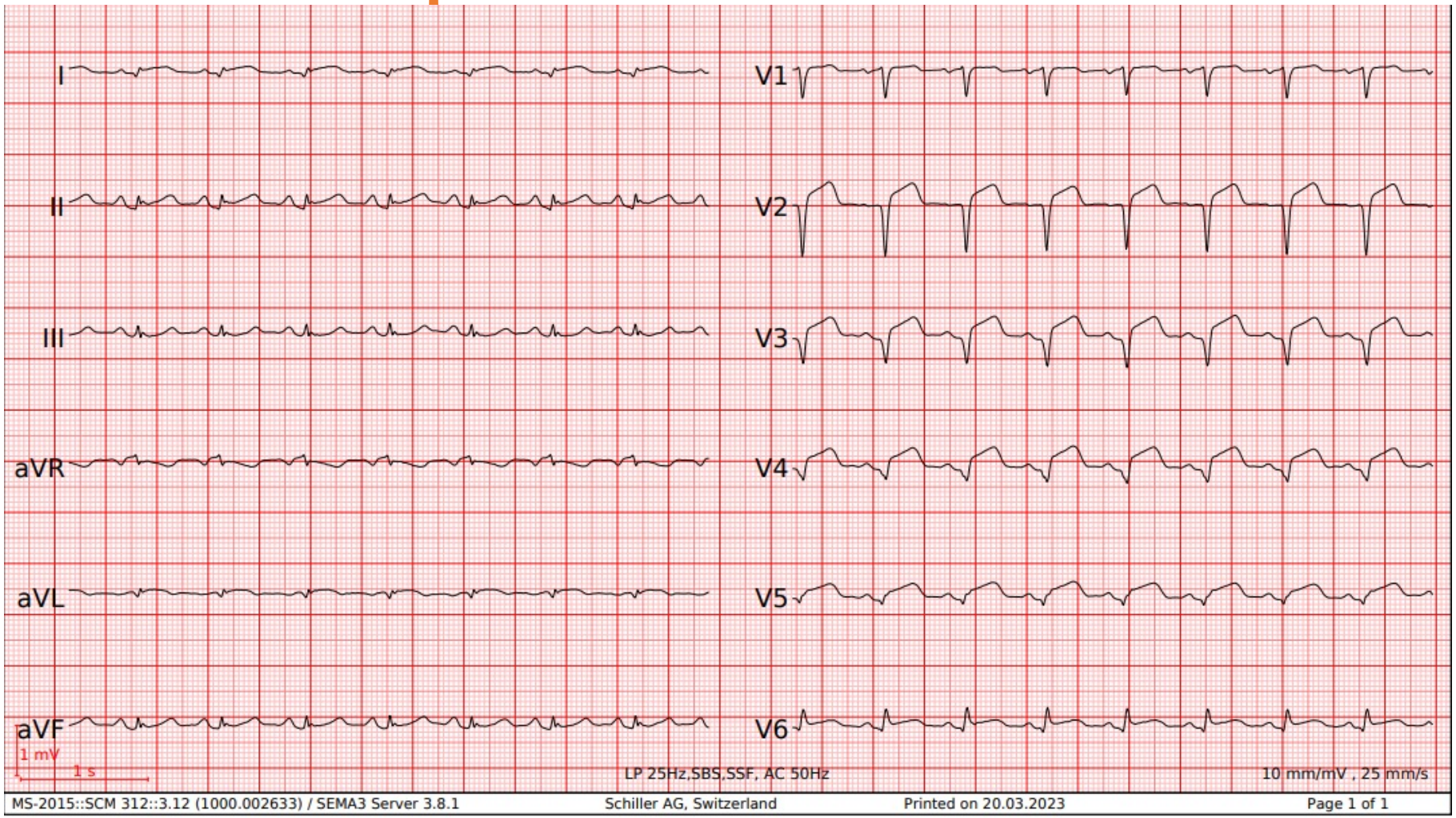
Déclaration d’intérêt

Pas de conflit d’intérêt

Plan

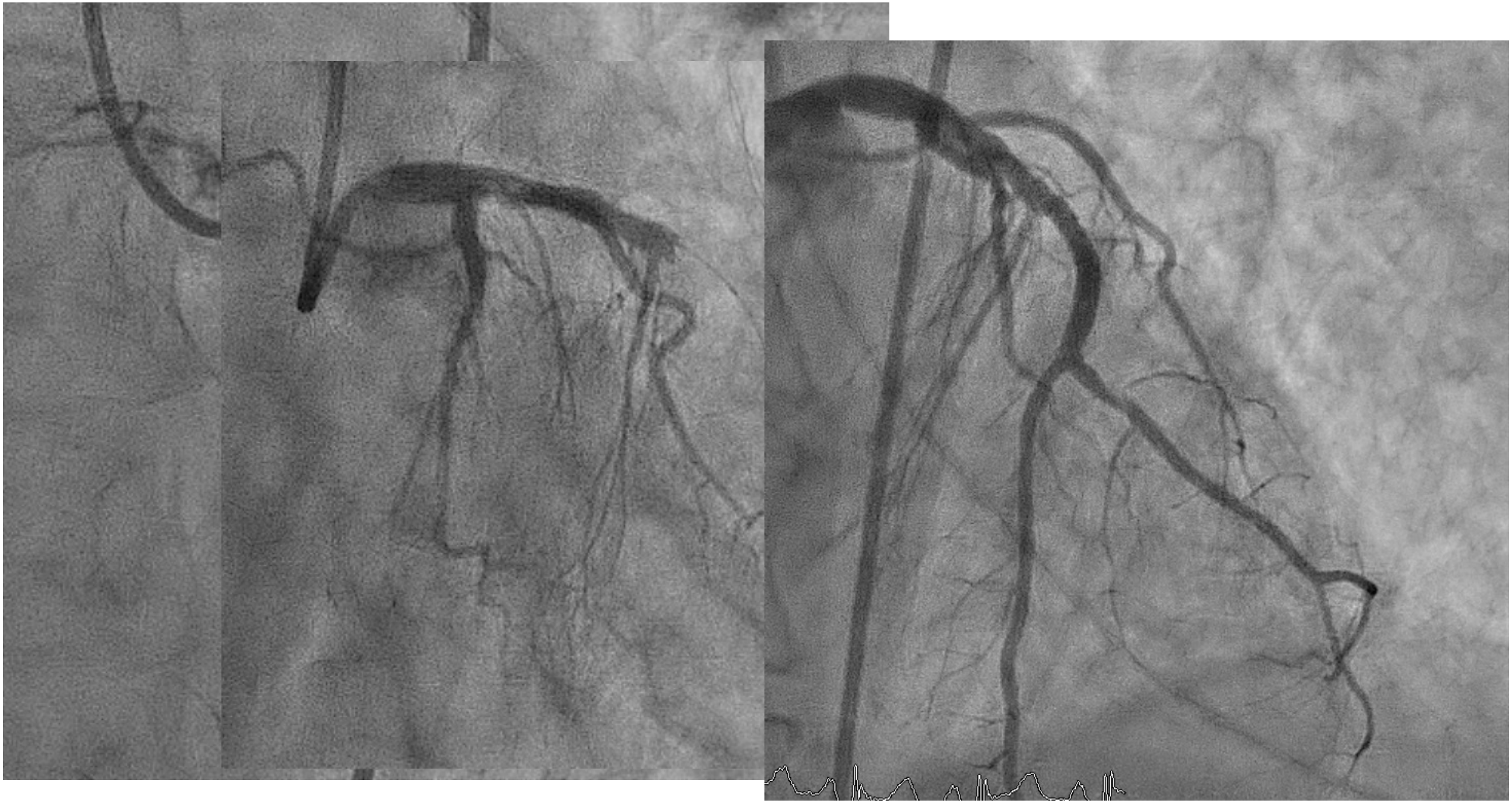
- Ischémie aigue
- HFrEF
- CRT
- ICD
- Lipides
- Quiz ECG

- Femme 60 ans, hypertension traitée, dyslipidémie non traitée
- Consulte en urgence à votre cabinet pour douleurs thoraciques depuis env. 10h
- TA 100/70 mmHg, symétrique, FC 95/min, sat 92% aa, FR 20/min.



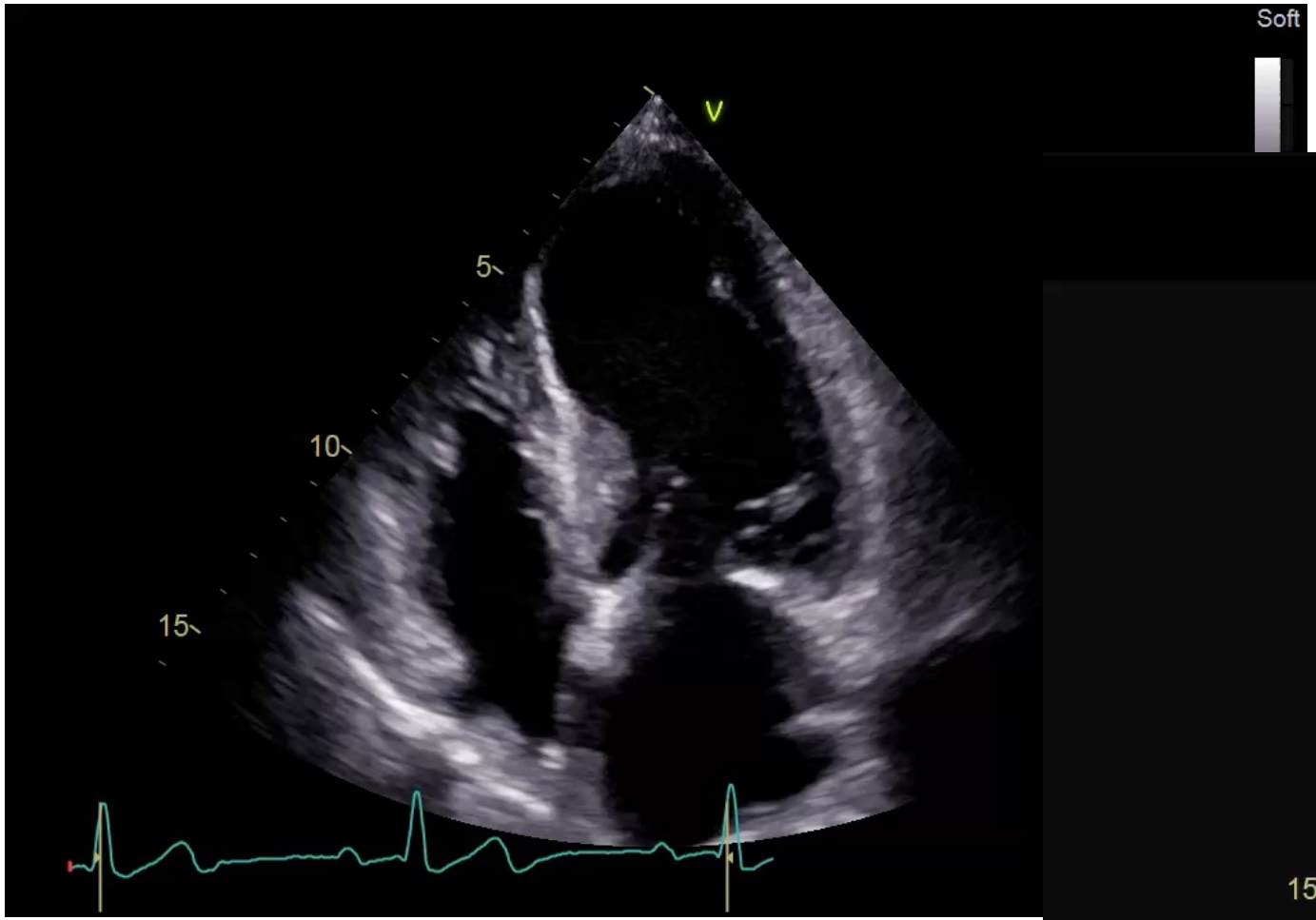
Que faites-vous ?

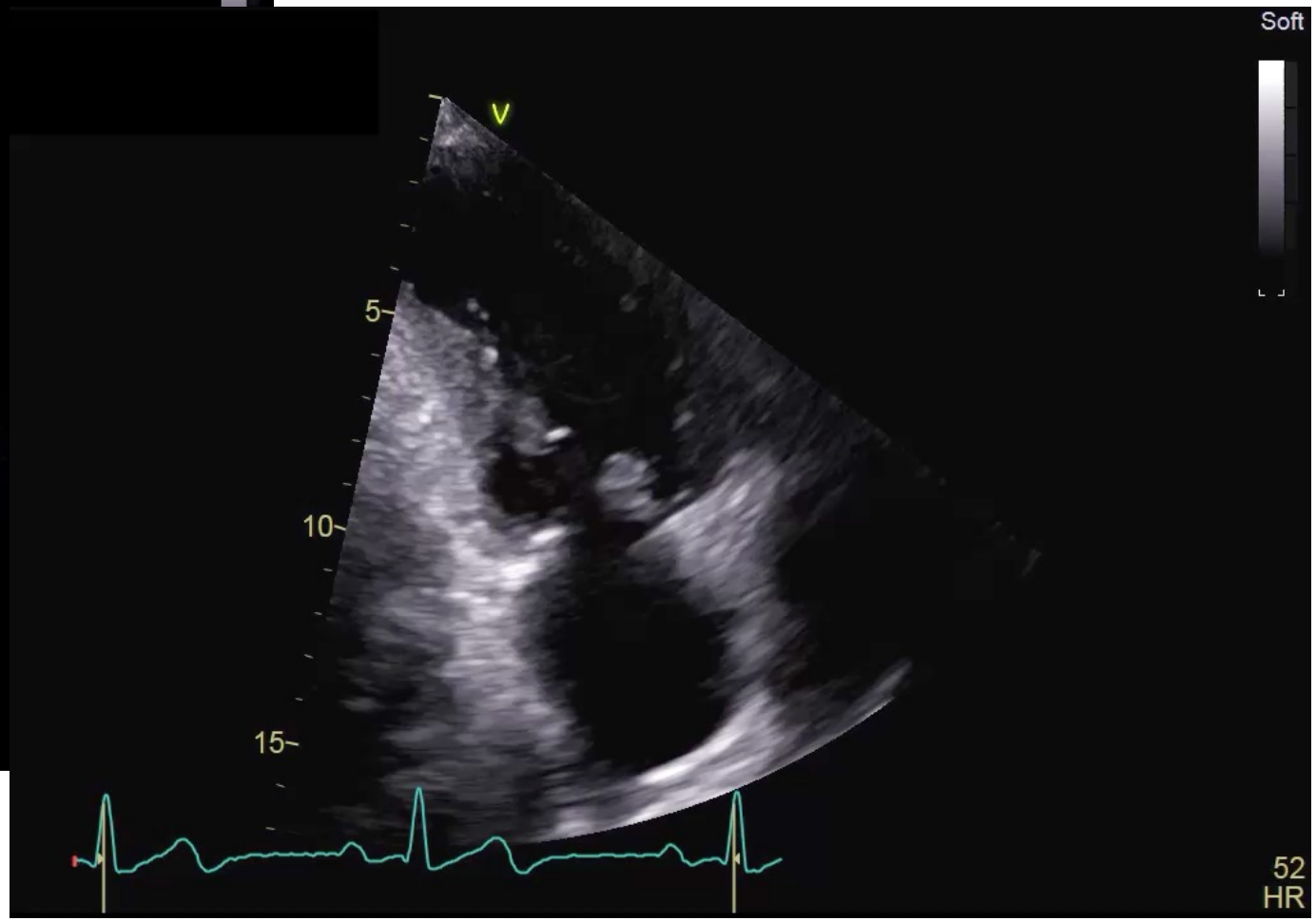
- ABC, O2 pour SpO2 > 90%
- Aspirine 150 – 300 mg p.o. ou 250 mg i.v.
- P2Y12 Inhib:
  - Ticagrelor (Brilique) LD 180 mg p.o., ou
  - Prasugrel (Efient) LD 60 mg p.o.
  - Si contre-indication (antécédant d'AVC/AIT, poids < 60 kg, âge > 75 ans, anémie, haut risque hémorragique) : Clopidogrel LD 600 mg p.o.
- Anticoagulation:
  - UFH (liquémine): 50-70 U/kg i.v (max 5000 U)
- Diminuer la pré/post-charge et la douleur:
  - Nitroglycérine (attention hypotension, STEMI inférieur et PDE-Inhib).
  - Furosemid (lasix)
  - Morphine
  - Bêtabloqueur (attention +++ dans les STEMI, risque de choc cardiogène)
  - (VNI/CPAP)
- Autres:
  - Atorvastatine 80 mg p.o.
  - Corriger les troubles électrolytiques, en particulier hypokaliémie et hypomagnésémie
- Transfert en urgence dans un centre avec PCI



Occlusion subaiguë IVA moyenne, PCI 1xDES, LVEDP 40 mmHg

Echographie - LVEF 30%





Insuffisance cardiaque à FEVG diminuée (HFrEF): Quels traitements pour la suite ?

Traitement médicamenteux HFrEF

Traitement médicamenteux HFrEF

Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Ventricular remodeling after MI

Pro-remodeling

Anti-remodeling

Sympathetic system

RAAS

ANP - BNP

Inflammation

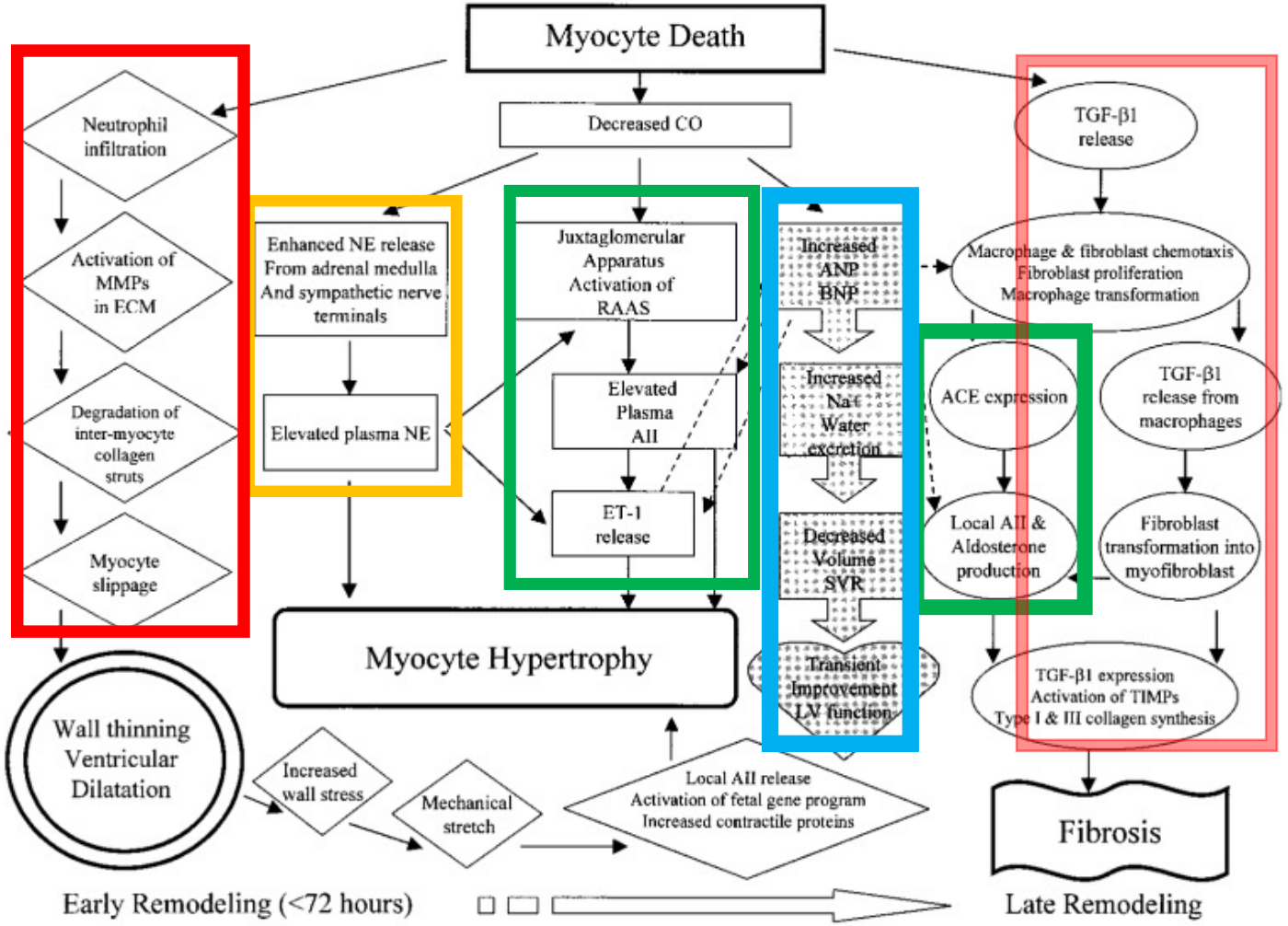


Figure 1. Diagrammatic representation of the many factors involved in the pathophysiology of ventricular remodeling. ECM indicates extracellular matrix; RAAS, renin-angiotensin-aldosterone system; CO, cardiac output; SVR, systemic vascular resistance; LV, left ventricular; and AII, angiotensin II.

Sutton MGSJ, *et al.* Left Ventricular Remodeling After Myocardial Infarction. *Circulation* 2000

ARNI – ENTRESTO – PARADIGM-HF TRIAL

Sacubitril–valsartan led to better outcomes than an ACE inhibitor in patients with stable HF and LVEF ≤ 40%

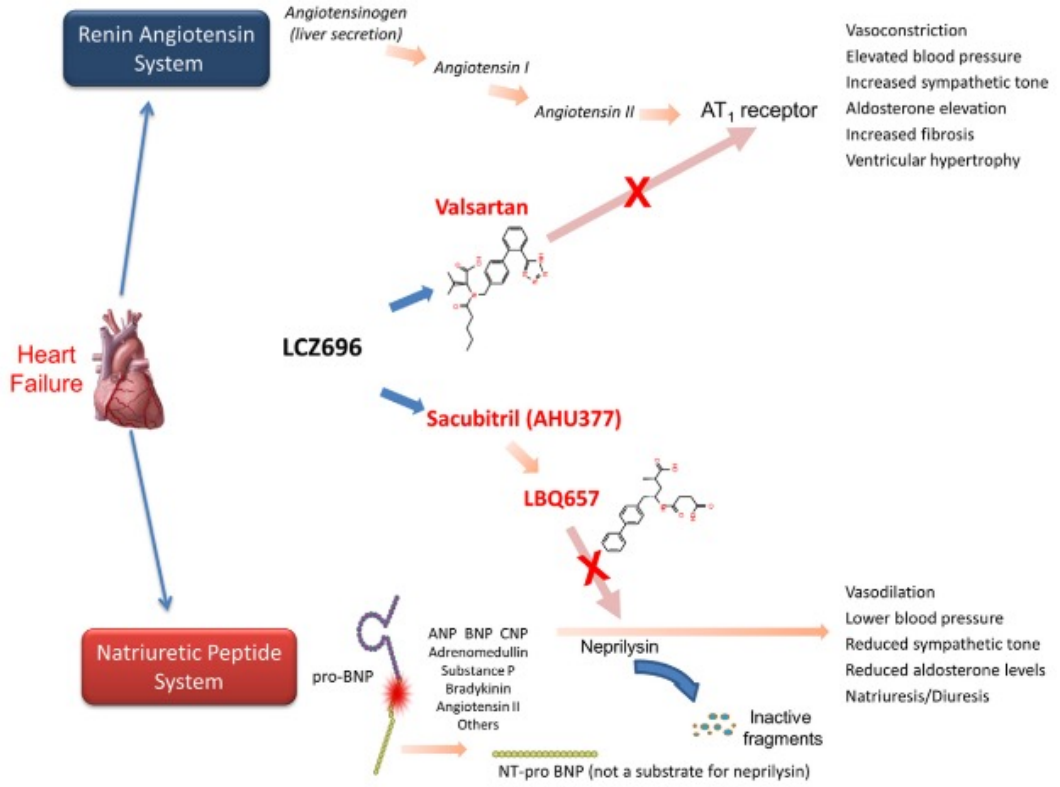
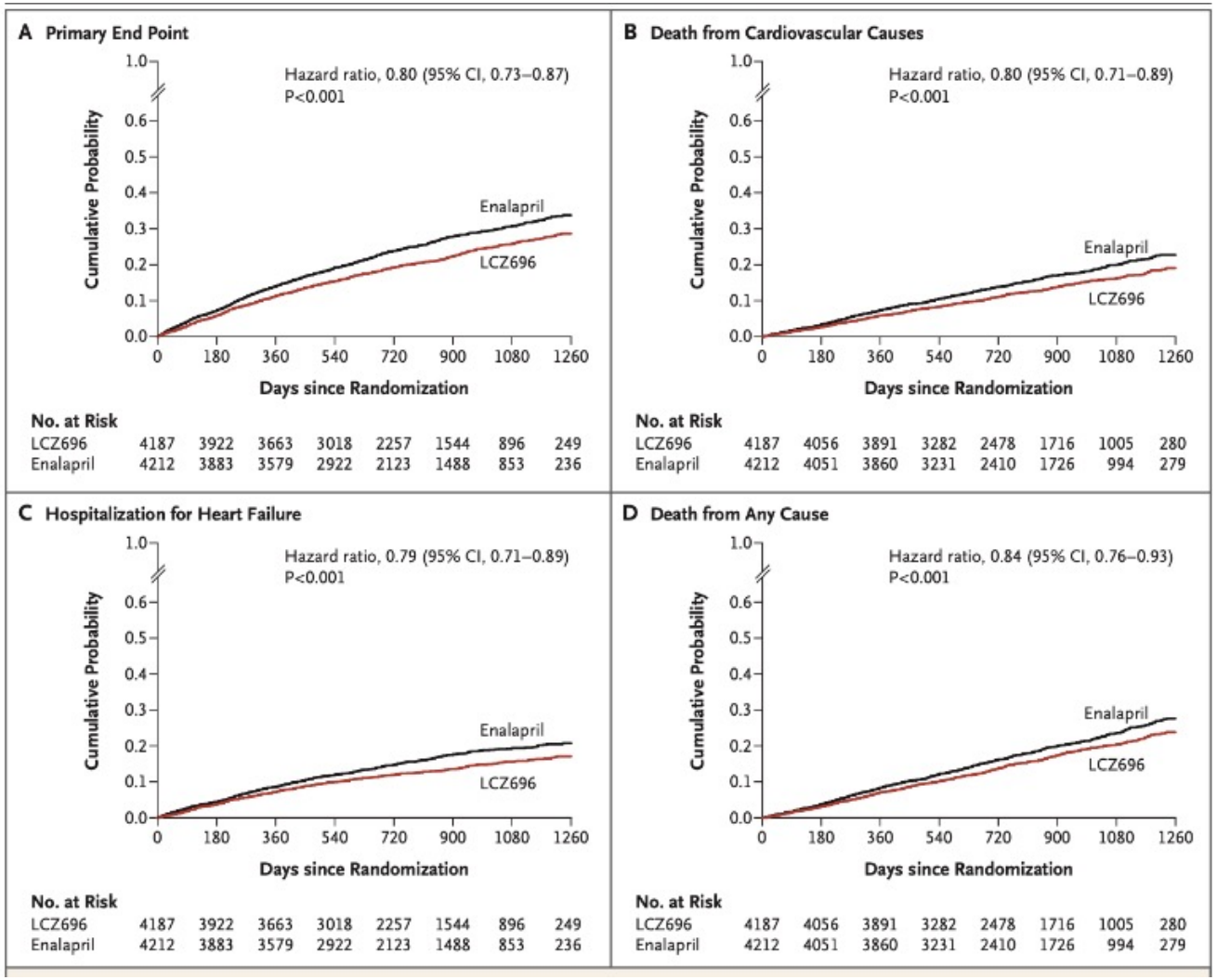


FIGURE 1 Schematic Showing the Mechanism of Action of LCZ696

Heart failure stimulates both the renin-angiotensin system and the natriuretic peptide system. LCZ696 is composed of 2 molecular moieties, the angiotensin receptor blocker valsartan and the neprilysin inhibitor prodrug sacubitril (AHU377). Valsartan blocks the angiotensin type I (AT_1) receptor. Sacubitril is converted enzymatically to the active neprilysin inhibitor LBQ657, which inhibits neprilysin, an enzyme that breaks down the breakdown of atrial natriuretic peptide (ANP), brain (or B-type) natriuretic peptide (BNP), and C-type natriuretic peptide (CNP), as well as other vasoactive substances. N-terminal pro-BNP (NT-proBNP) is not a substrate for neprilysin.

Vardeny O*, et al.* Combined Neprilysin and Renin-Angiotensin System Inhibition for the Treatment of Heart Failure. *JACC: Heart Failure* 2014



McMurray JJV*, et al.* Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure. *New England Journal of Medicine* 2014

Les 4 médicaments en même temps ?

- OUI ! (si pas de contre-indication)
- ± diurétiques selon volémie
- Réévaluation régulière selon :
  - Tolérance clinique (vertiges, FC, TA, œdèmes etc)
  - Bilan biologique (K+, créatinine)

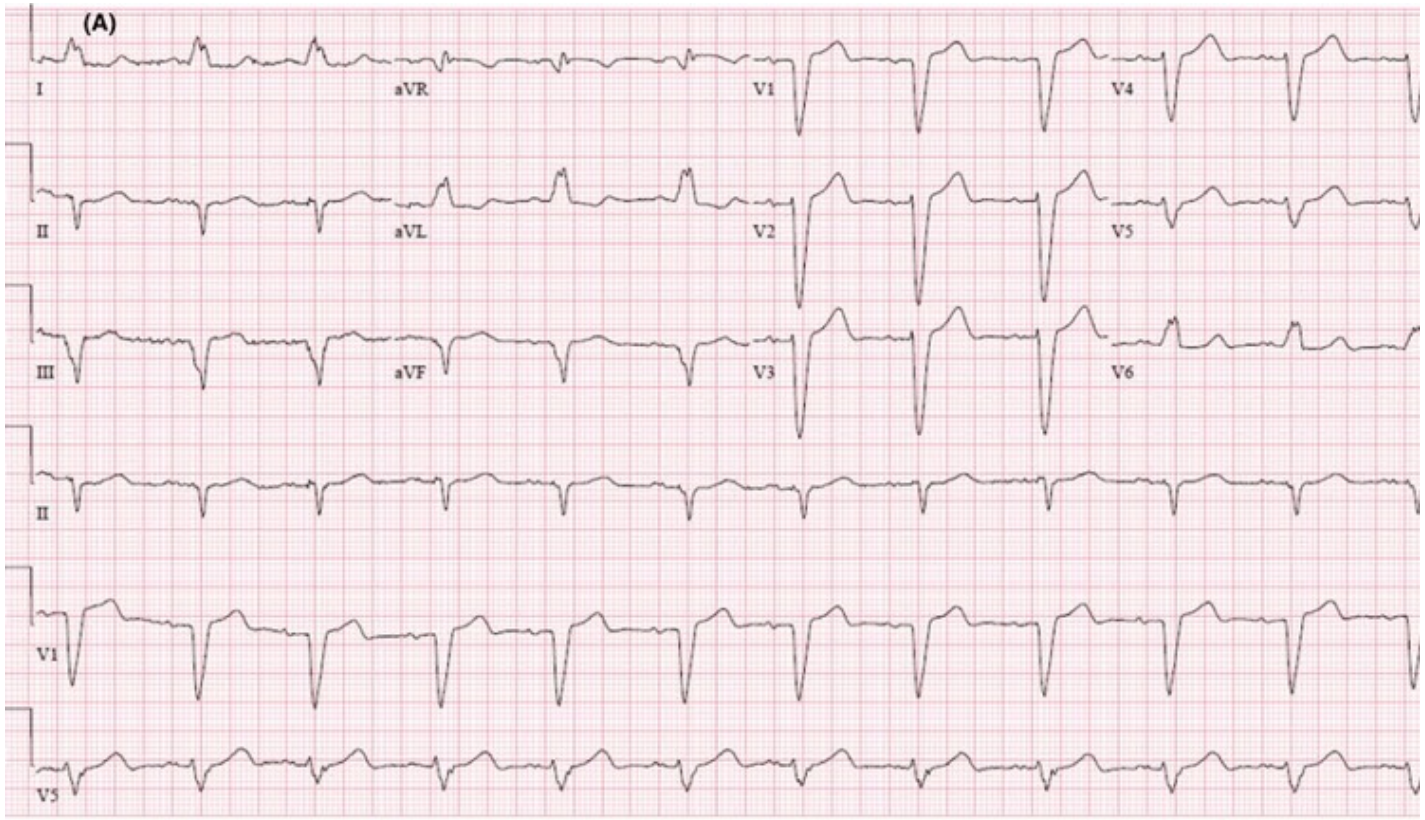
Visite à votre cabinet 1 mois post STEMI

- Dyspnée NYHA II stable, pas de douleur thoracique/vertiges/syncope
- TA 130/85 mmHg, FC 75/min, T° 36, FR 14/min
- Quelques râles de stase bi-pulmonaire, légers œdèmes membres inf.

- Médicaments:
  - Lisinopril 2.5mg/j, metoprolol 25mg/j, aldactone 12.5mg/j, jardiance 10mg/j
  - Aspirine 100 mg, efient 10 mg
  - Rosuvastatine 20 mg
  - Pantozol 20 mg

Visite à votre cabinet 1 mois post STEMI

- Labo: Hb 130 g/L, K+ 4.4 mmol/L, Creat 80 µmol/L, NT-ProBNP 1500 ng/L
- ETT: LVEF 35%
- ECG: sinusal, BBG 145 ms
- Holter: 2x TV non soutenues



- Que faire ?

Que faites-vous ? (plusieurs réponses possibles)

- Introduction d'un diurétique de l'anse (ex torasemide) ?
- Augmentation des doses de metoprolol + aldactone + lisinopril ?
- Changement lisinopril pour Entresto, + augmentation des doses de metoprolol et d'aldactone ?
- Arrêter la statine et l'efient ?
- Référer pour implantation d'une thérapie de resynchronisation (CRT-P) ?
- Référer pour implantation d'un défibrillateur implantable (ICD) ?
- Référer pour implantation d'un CRT-D ?
- Référer pour une transplantation cardiaque ?

Que faites-vous ? (plusieurs réponses possibles)

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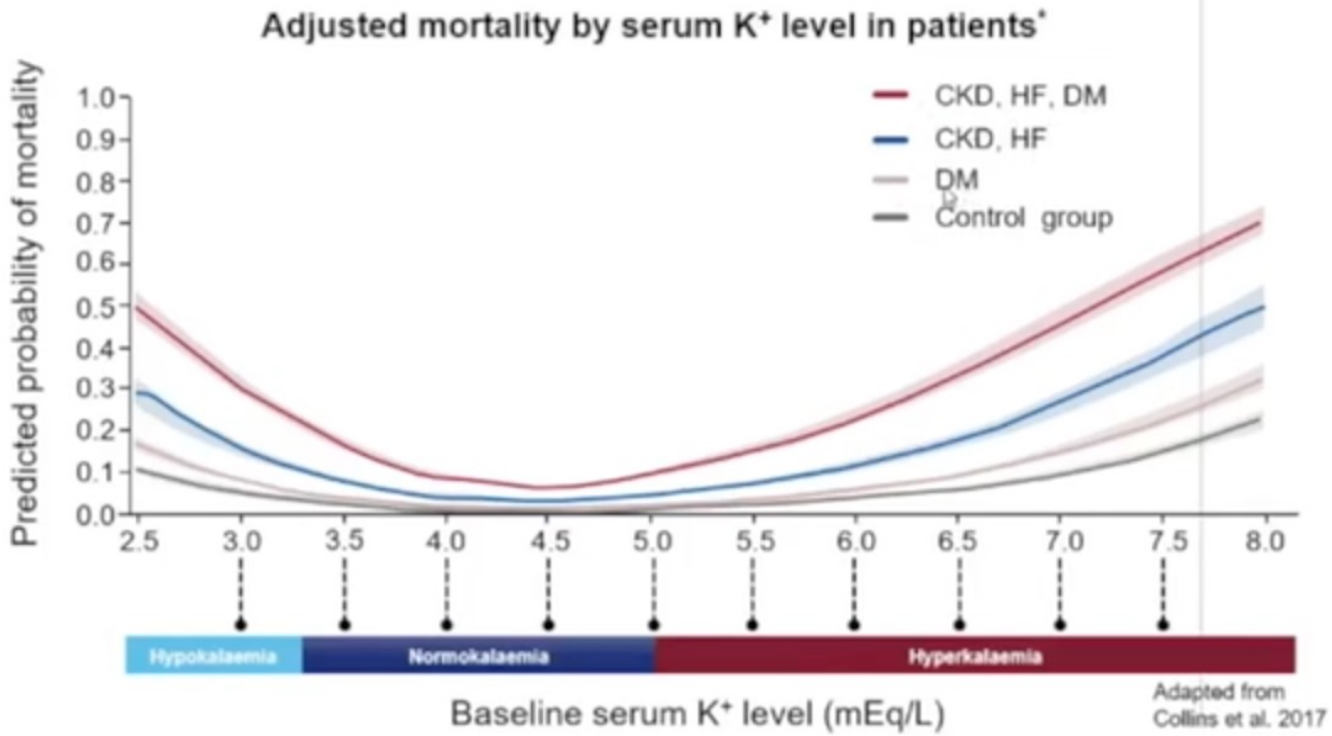
- Référer pour implantation d'un défibrillateur implantable (ICD) ?
- Référer pour implantation d'un CRT-D ?
- Référer pour une transplantation cardiaque ?

HFrEF Medication Management

- Start low, but don’t stay low ! Monter les doses et monitorer !!!
- Entresto:
  - Switch **IEC** -> Entresto : pause de 36 h (risque d’angio-oedème)
  - Switch **Sartan** -> Entresto : pas de pause nécessaire
  - Dose cible = 200 mg 2x/j (mais pas toujours atteignable)
- ARNI/ACE/ARB/MRA
  - Attention:
    - Hyperkaliémie:
      - K+ ≥ 5.0 mmol/L: monitor ++ and ad K+ binders
      - K+ ≥ 5.5 mmol/L: reduce dose / stop medication
      - K+ ≥ 6.0 mmol/L: stop medication !
    - GFR < 30 ml/min/1,73m^2 (contre-indication si GFR < 10 ml/min/1,73m^2)
    - Augmentation créatinine > 25-30% des valeurs de base
    - Hypotension **symptomatique / syncope**



ESC

1. Cooper *EJHF* 2019
2. Collins *Am J Nephrol*. 2017

K+ «sweet spot» : 4.0 – 5.0 mmol/L

Hyperkalemia may be risk marker rather than risk factor
Risk marker representing *non-RAASi use*

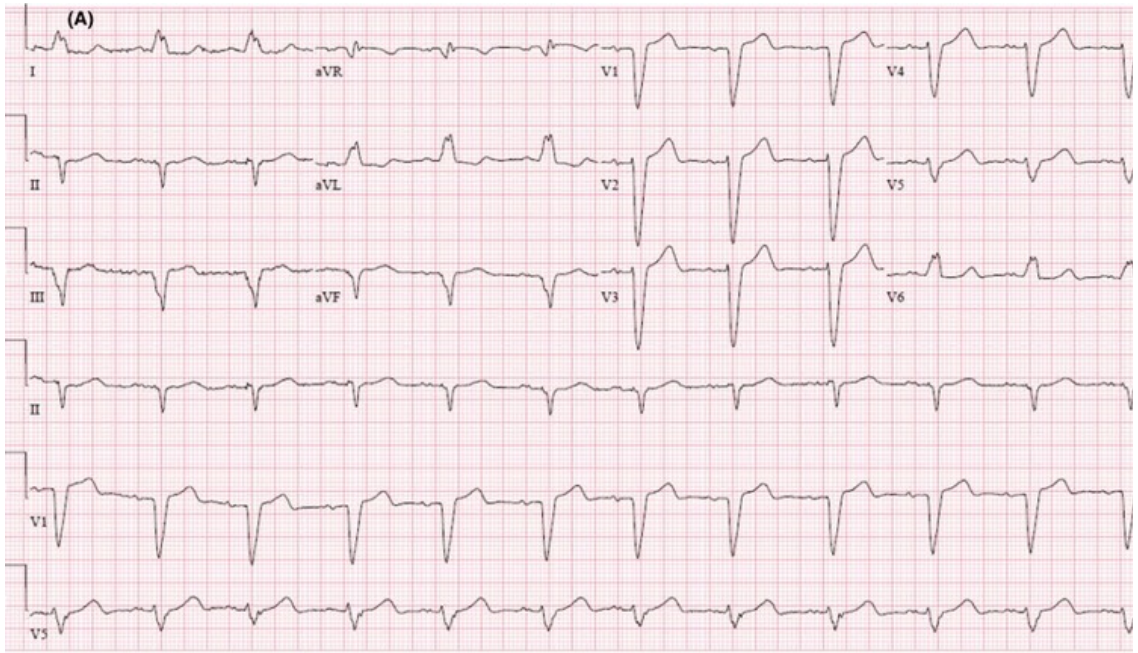
Figure 1 Hyperkalaemia is a risk marker for poor outcomes by leading to dose reduction or discontinuation of renin–angiotensin–aldosterone system inhibitors (RAASi).

Lund, EJHF 2018

Visite à votre cabinet 4 mois post STEMI

- Dyspnée NYHA II, légers vertiges quand se lève
- TA 100/60 mmHg, FC 55/min sinusal, euvolémique
- Médicaments:
  - Entresto 150 mg 2x/j, metoprolol 150 mg/j, aldactone 50 mg/j, jardiance 10 mg/j
  - Aspirine / Efient / Rosuvastatine / IPP
- Labo : K+ 4.5 mmol/L, Creat 80 µmol/L
- ECG: sinusal, BBG 145 ms
- ETT: LVEF 35%

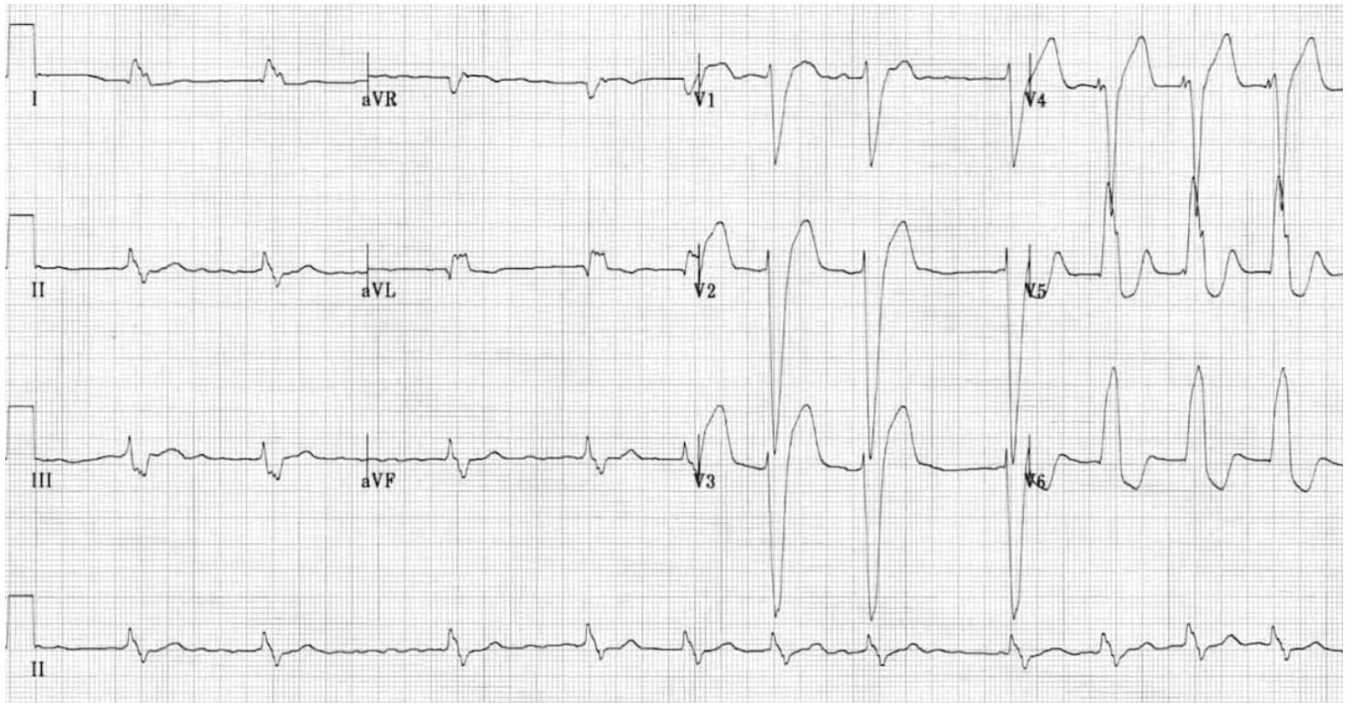
- Que faire ?



Dyssynchronous ventricular activation

Native or pacing-induced LBBB is hemodynamically disadvantageous:

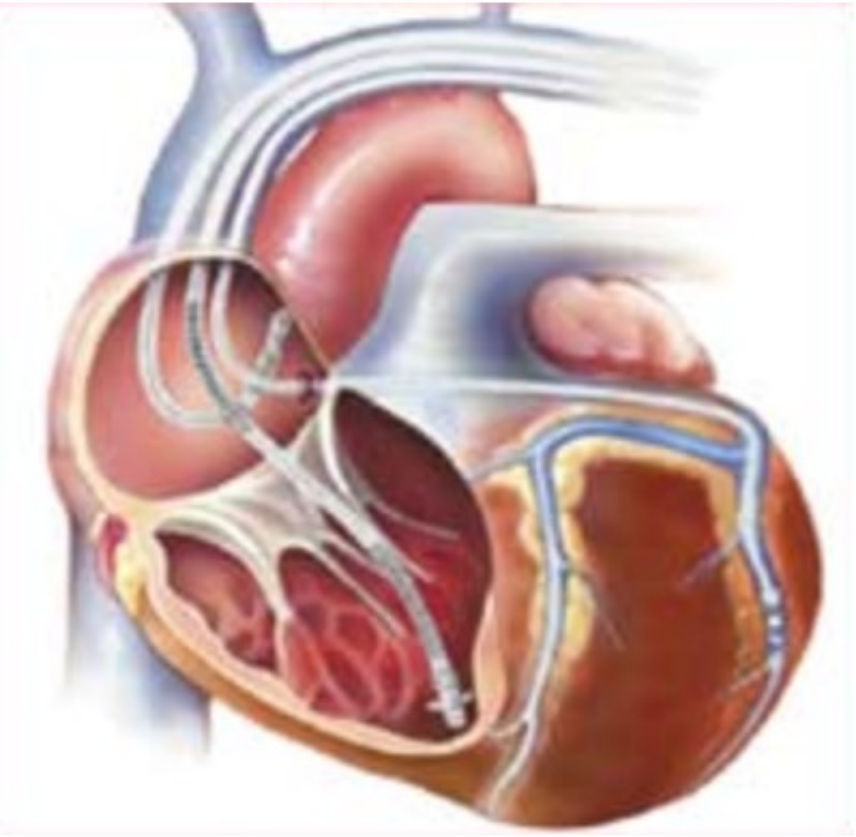
- Dyssynchrony -> reduced cardiac output
- Exacerbates functional mitral regurgitation
- Worsens LV dilatation

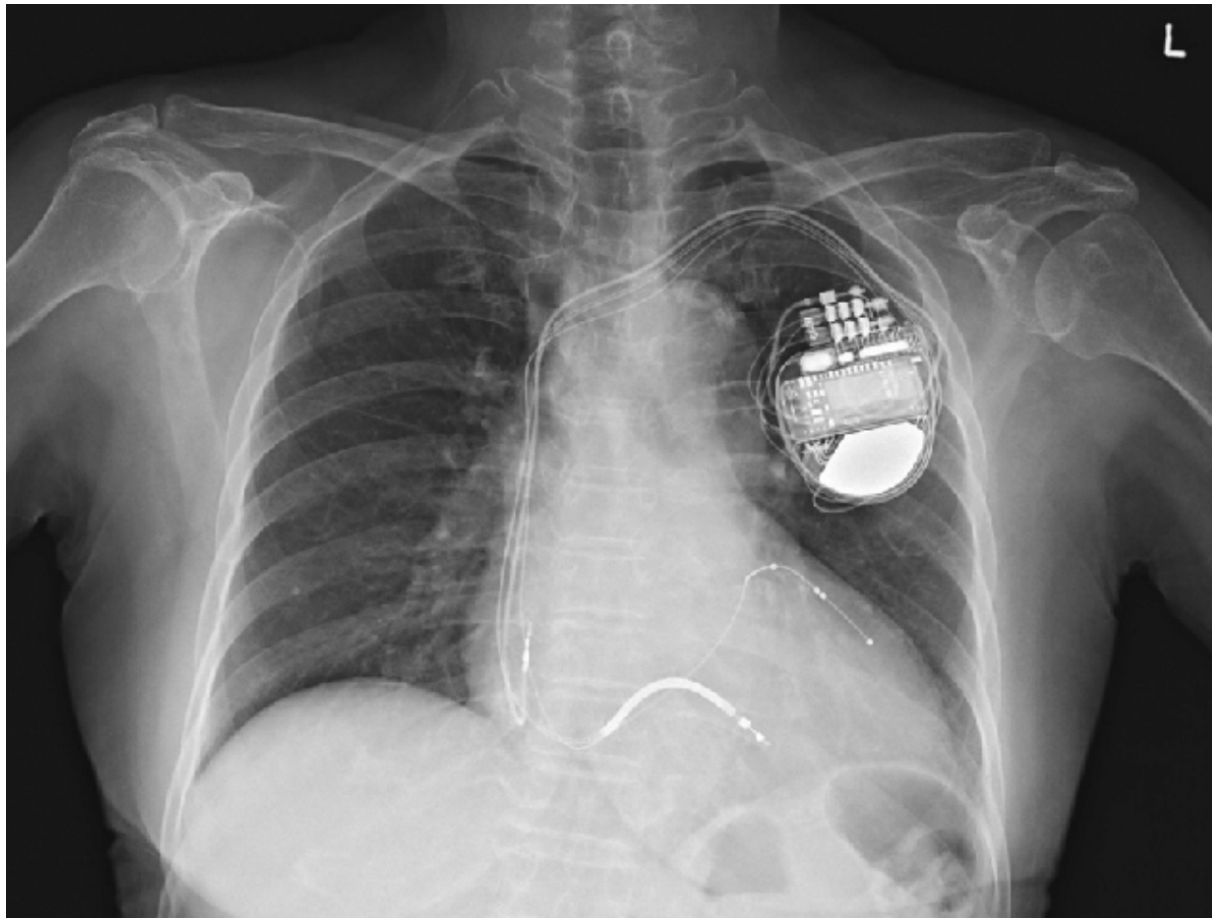


https://litfl.com/left-bundle-branch-block-lbbb-ecg-library/

Uptodate: Cardiac resynchronization therapy in heart failure: Indications and choice of system

Implantable Cardioverter-Defibrillator (ICD) and Cardiac Resynchronization Therapy (CRT)



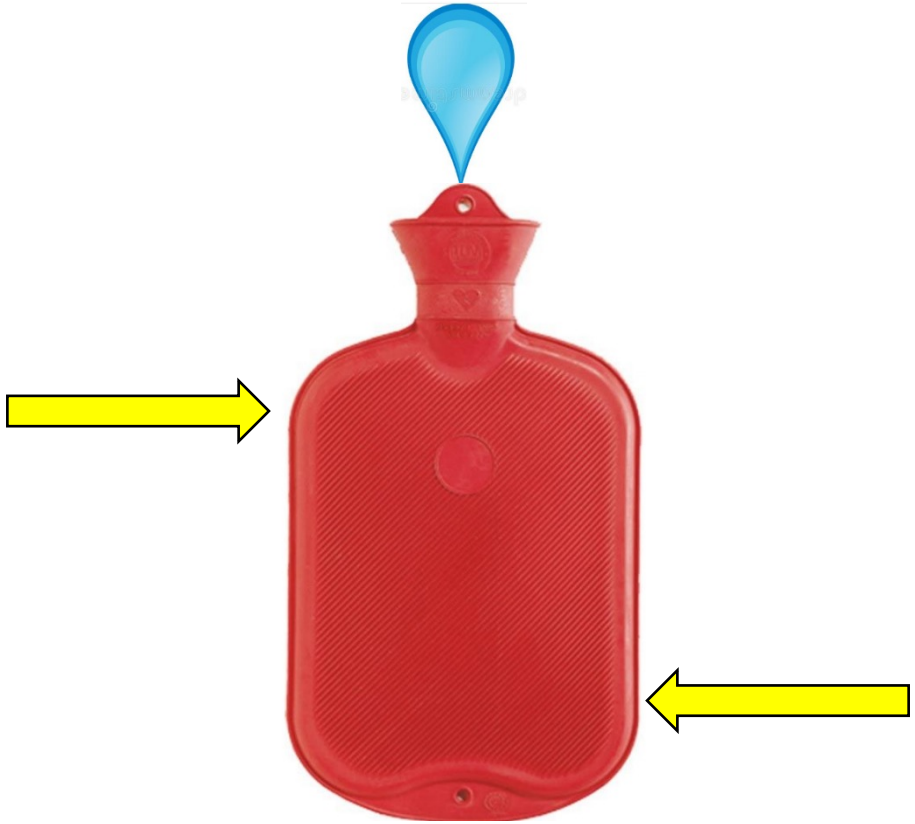


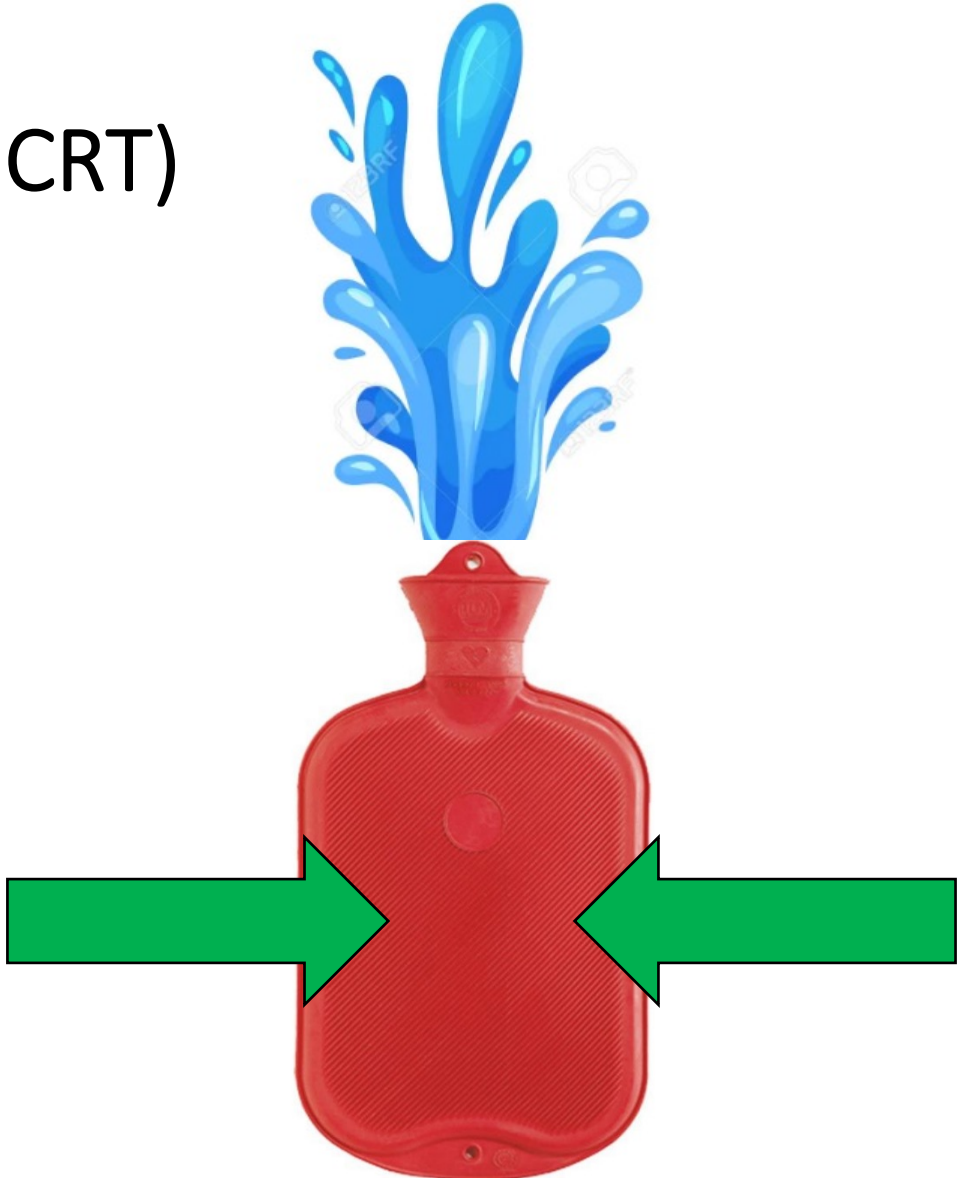
https://www.researchgate.net/figure/Chest-X-ray-after-cardiac-resynchronization-therapy-with-defibrillator-CRT-D_fig1_298422112
https://tcaheart.com/cardiac-resynchronization-therapy/

Cardiac resynchrony therapy (CRT)

- CRT-**p**acemaker (CRT-P)
- CRT-implantable cardioverter-**d**efibrillator (CRT-D)
- 3ème sonde placée dans une branche du sinus coronarien pour pacing du VG
- Effets sur le ventricule gauche:
  - Restaure la synchronie ventriculaire
  - «Reverse remodeling» - diminue la dilatation du VG
  - Augmente la contractilité myocardique sans augmenter la consommation en O2
  - Diminue la sévérité des insuffisances mitrales fonctionnelle
  - Augmentation de la FEVG

Cardiac resynchrony therapy (CRT)





Bloc de branche gauche:

- Contraction VG désynchronisée
- Volume d'éjection diminué

CRT:

- Contraction VG resynchronisée
- Augmentation du volume d'éjection

CRT – Quand y penser ?

- Patients symptomatiques d'insuffisance cardiaque (NYHA > I)
- Thérapie médicamenteuse optimale depuis ≥ 3 mois (= doses max tolérées)
- LVEF ≤ 35%
  - QRS ≥ 130 ms (si possible ≥ 150 ms)
  - Bloc de branche gauche (LBBB)
  - Non-LBBB - CRT à envisager
- LVEF > 35 – 50%
  - Patients nécessitant l'implantation d'un pacemaker pour une autre raison + nécessité de pacing anticipée > 40% (ex: AV-bloc, ablation NAV si FA)
  - QRS ≥ 150 ms + LBBB (native or paced) et symptômes réfractaires malgré OMT > 3 mois

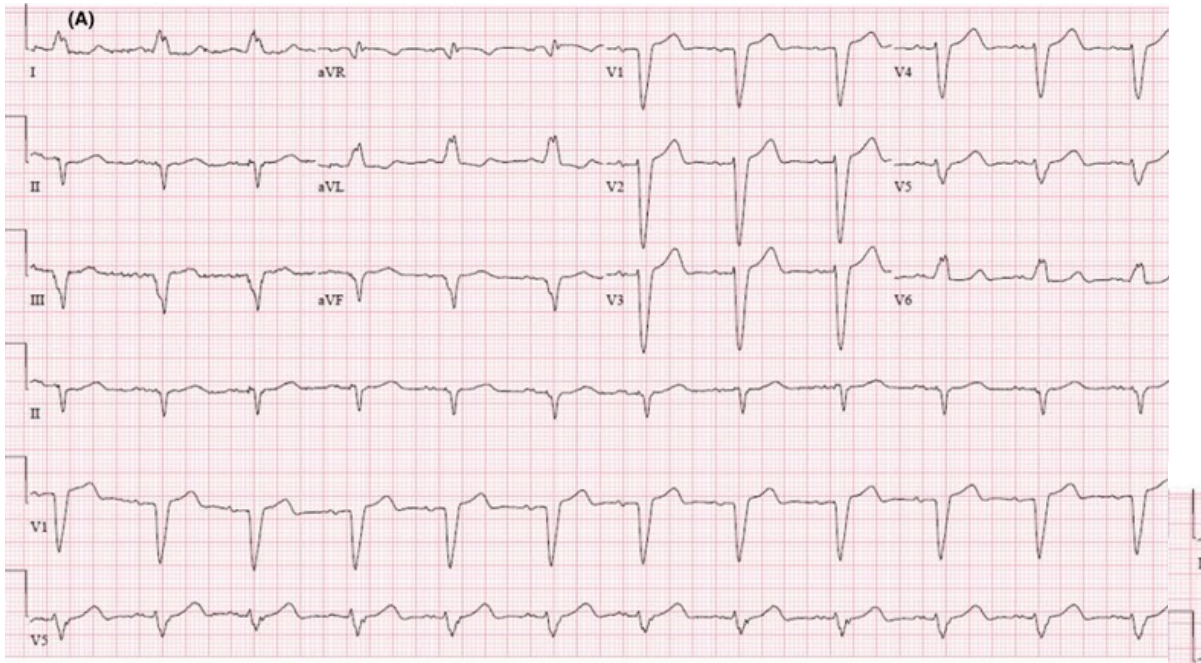
Recommendations for cardiac resynchronization therapy in patients in sinus rhythm

Recommendations	Class[a]	Level[b]
LBBB QRS morphology		
CRT is recommended for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	I	A
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.[37,39,40,254–266,283,284]	IIa	B
Non-LBBB QRS morphology		
CRT should be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration ≥150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[37,39,40,254–266,283,284]	IIa	B
CRT may be considered for symptomatic patients with HF in SR with LVEF ≤35%, QRS duration 130–149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.[273–278,281]	IIb	B
QRS duration		
CRT is not indicated in patients with HF and QRS duration <130 ms without an indication for RV pacing.[264,282]	III	A

CRT = cardiac resynchronization therapy; HF = heart failure; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; OMT = optimal medical therapy; SR = sinus rhythm.

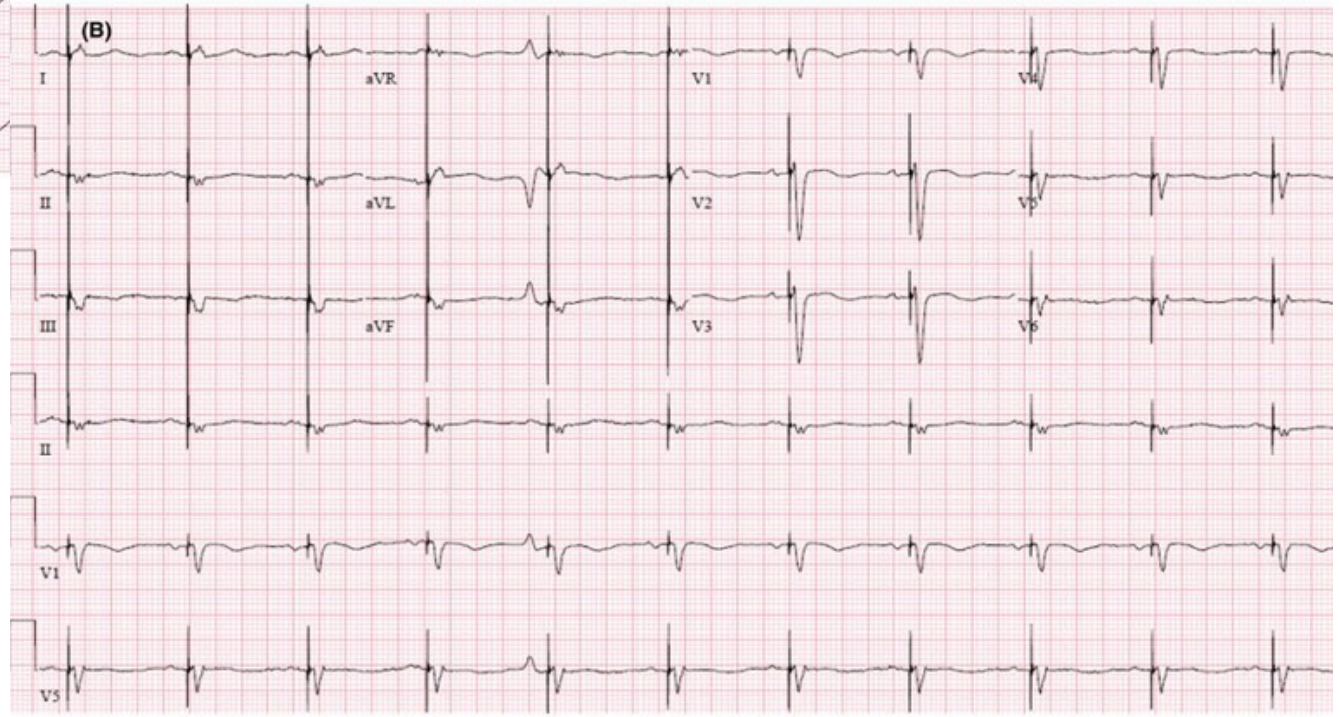
[a]Class of recommendation.

[b]Level of evidence.



LBBB

With CRT



https://www.researchgate.net/figure/Pre-and-post-CRT-P-ECG-A-Baseline-ECG-shows-normal-sinus-rhythm-with-left-bundle_fig2_341674534

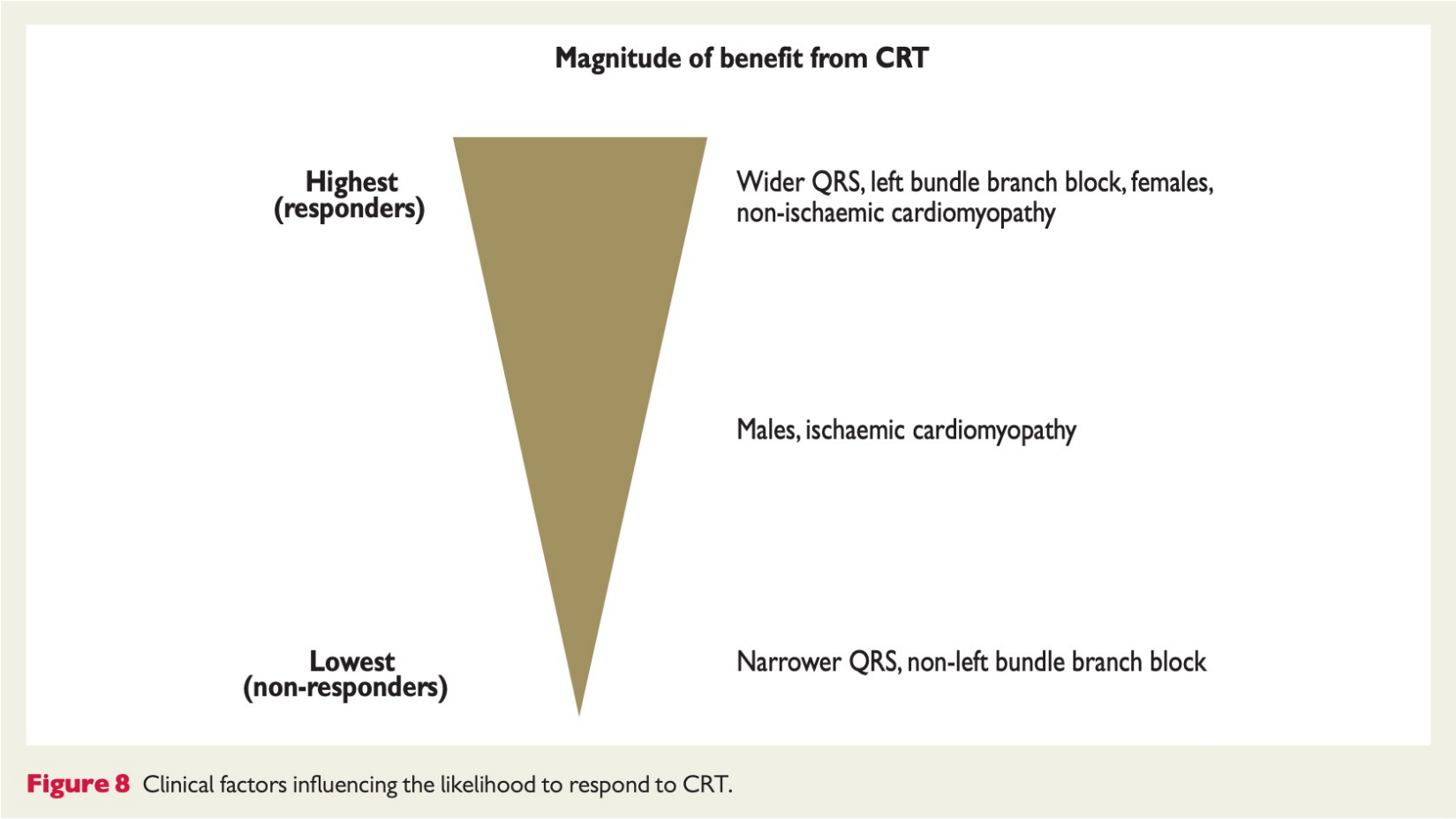


Figure 8 Clinical factors influencing the likelihood to respond to CRT.

2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

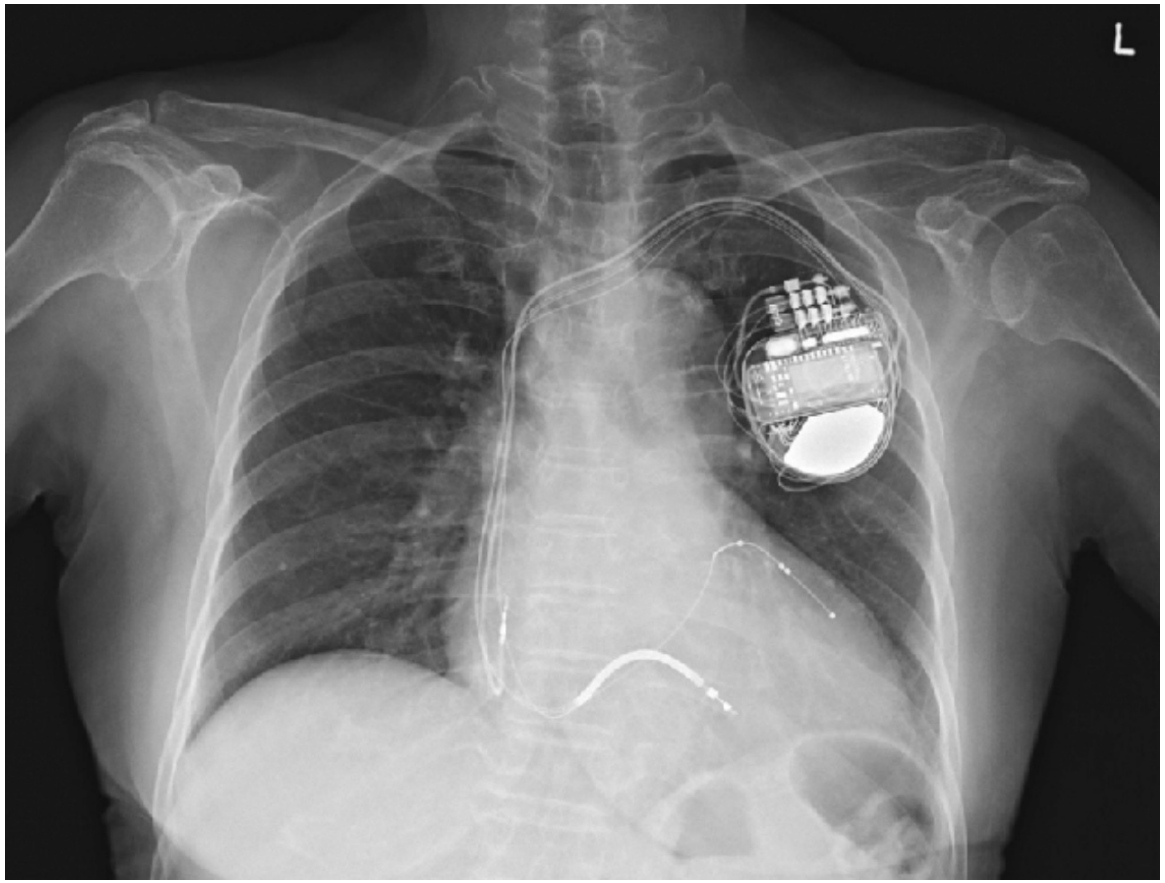
Probablement pas de bénéfice de la CRT:

- NYHA I et NYHA IV
- LVEF > 50%
- QRS < 120 ms

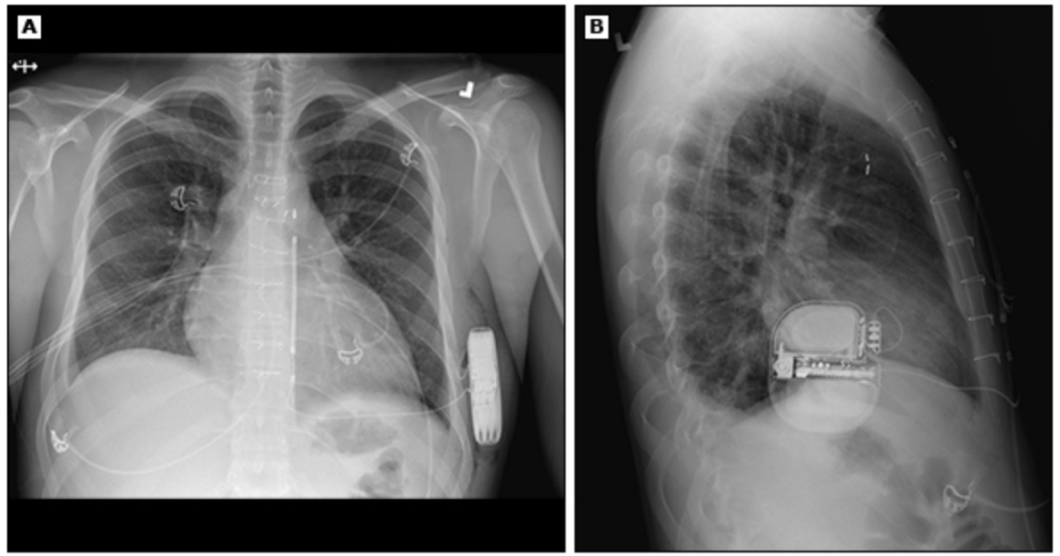
Implantable Cardioverter-Defibrillator (ICD) – Indications

- Prévention primaire:
  - NYHA II-III
  - LVEF ≤ 35% malgré traitement médicamenteux optimal > 3 mois
  - > 40 jours après l'infarctus
  - Espérance de vie > 1 an
- Prévention secondaire:
  - Survivant d'une arythmie ventriculaire avec instabilité hémodynamique
  - Espérance de vie > 1 an
  - > 48h après un syndrome coronarien aigu

2 possibilités : TV-ICD vs. S-ICD



Posteroanterior (PA) and lateral chest radiographs of a subcutaneous implantable cardioverter-defibrillator (S-ICD)



Posteroanterior (PA) and lateral chest radiographs of a subcutaneous implantable cardioverter-defibrillator (S-ICD) with the defibrillation lead visible adjacent to the sternum and the pulse generator in the axilla.

TV-ICD vs. S-ICD

Circulation

ORIGINAL RESEARCH ARTICLE

Efficacy and Safety of Appropriate Shocks and Antitachycardia Pacing in Transvenous and Subcutaneous Implantable Defibrillators: Analysis of All Appropriate Therapy in the PRAETORIAN Trial

Reinoud E. Knops, MD, PhD*; Willeke van der Stuijt, MD*; Peter Paul H.M. Delnoy, MD, PhD; Lucas V.A. Boersma, MD, PhD; Juergen Kuschyk, MD; Mikhael F. El-Chami, MD; Hendrik Bonnemeier, MD, PhD; Elijah R. Behr, MD; Tom F. Brouwer, MD, PhD; Stefan Kääb, MD, PhD; Suneet Mittal, MD; Anne-Floor B.E. Quast, MD, PhD; Lonneke Smeding, PhD; Jan G.P. Tijssen, PhD; Nick R. Bijsterveld, MD, PhD; Sergio Richter, MD; Marc A. Brouwer, MD, PhD; Joris R. de Groot, MD, PhD; Kirsten M. Kooiman, MPA; Pier D. Lambiase, MD, PhD; Petr Neuzil, MD, PhD; Kevin Vernooy, MD, PhD; Marco Alings, MD, PhD; Timothy R. Betts, MD; Frank A.L.E. Bracke, MD, PhD; Martin C. Burke, DO; Jonas S.S.G. de Jong, MD, PhD; David J. Wright, MD; Ward P.J. Jansen, MD, PhD; Zachary I. Whinnet, MD, PhD; Peter Nordbeck, MD; Michael Knaut, MD; Berit T. Philbert, MD; Jurren M. van Opstal, MD, PhD; Alexandru B. Chicos, MD; Cornelis P. Allaart, MD, PhD; Alida E. Borger van der Burg, MD, PhD; Jude F. Clancy, MD; Jose M. Dizon, MD; Marc A. Miller, MD; Dmitry Nemirovsky, MD; Ralf Surber, MD; Gaurav A. Upadhyay, MD; Raul Weiss, MD;

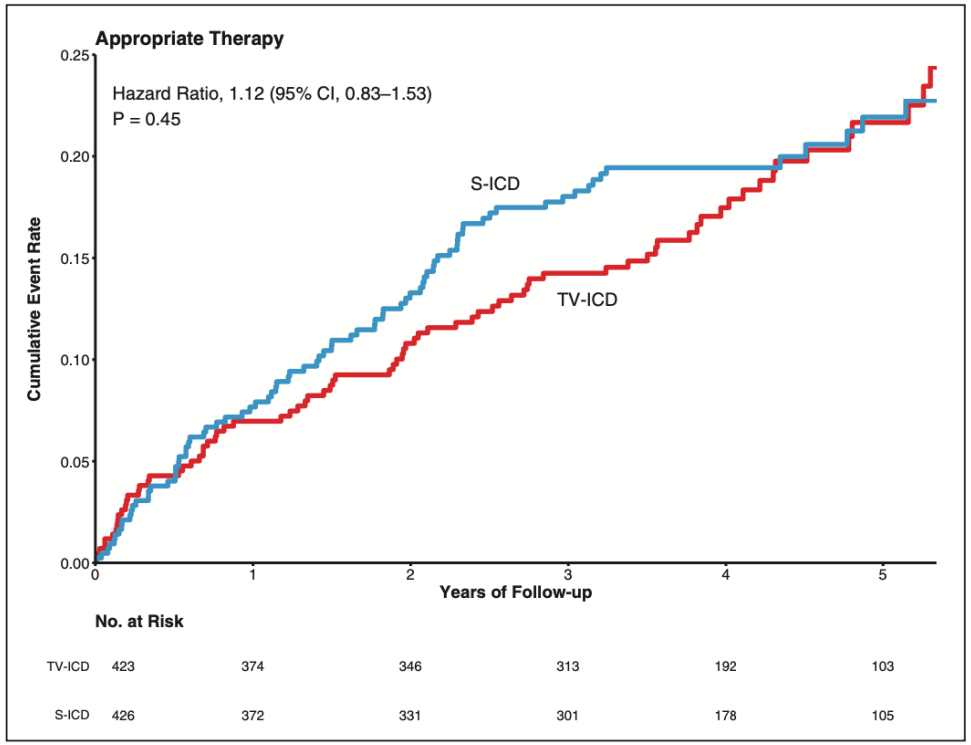
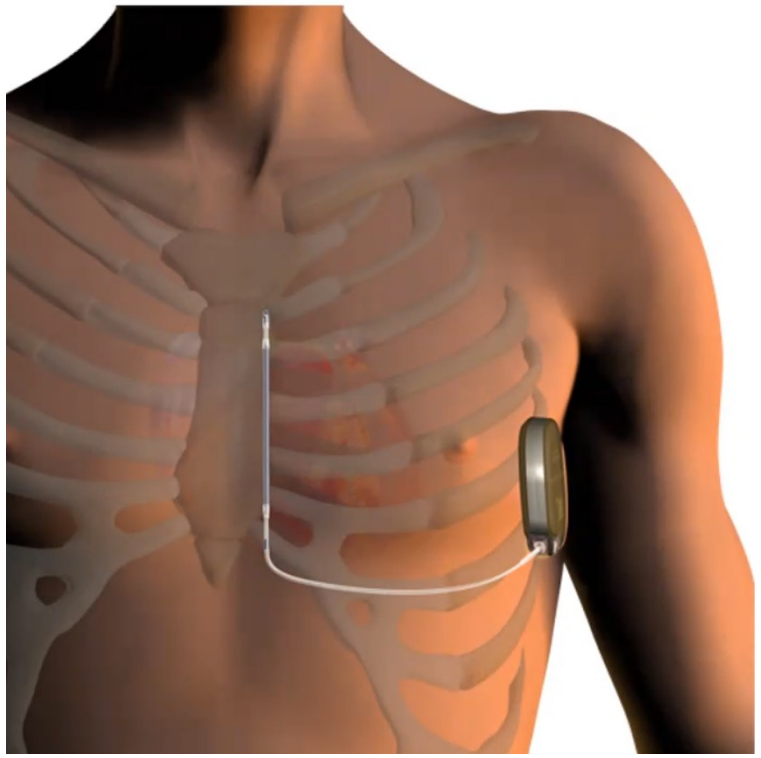


Figure 1. Kaplan-Meier curve of all patients with appropriate therapy in the PRAETORIAN trial.
CI indicates confidence interval; PRAETORIAN, A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter

Same efficacy:

- successfully terminating ventricular arrhythmias > 95%

TV-ICD vs. S-ICD



Avantages S-ICD:

- Moins de complications liées à l'implantation (tamponnade, pneumothorax, hémothorax)
- Moins d'usure de sondes
- Pas d'infection endovasculaire
  - Infection de poches (1-10%) – souvent traité conservativement sans devoir explanter le device

Désavantages S-ICD:

- Pas de pacing anti-tachycardie (ATP)
- Pas de pacing en cas de bradycardie (sauf transitoirement post-choc)
- Upgrade en pacemaker et/ou CRT pas possible
- Plus de chocs inappropriés (4-16%) – Importance du screening et discrimination QRS/onde T, myopotentiels

Antitachycardia pacing (ATP)

Knops et al

Appropriate Therapy in PRAETORIAN

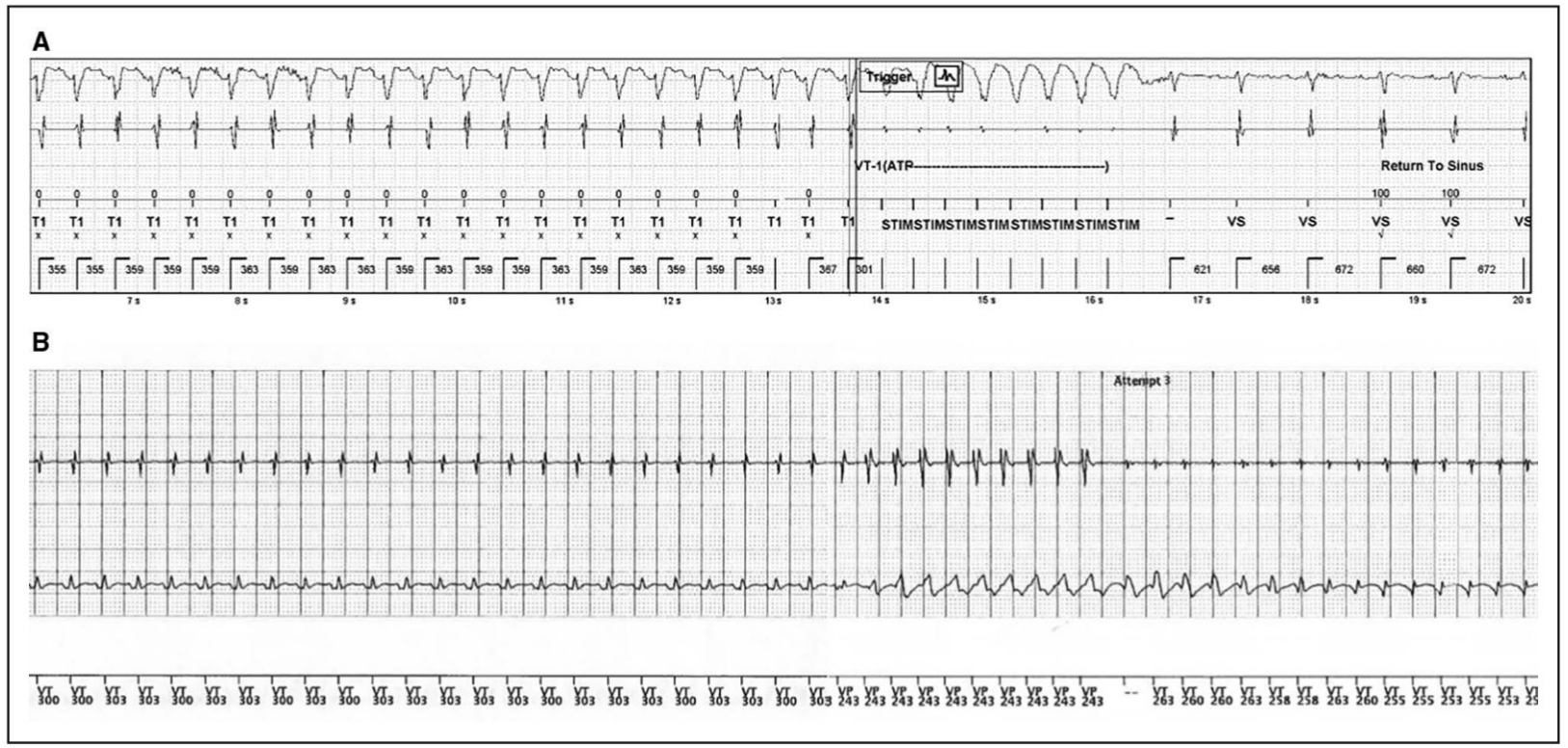


Figure 4. Successful conversion to sinus rhythm and acceleration of ventricular tachycardia after antitachycardia pacing. **A**, Successful conversion to sinus rhythm after antitachycardia pacing (ATP). **B**, Acceleration of ventricular tachycardia (VT) after ATP, ultimately terminated by a shock (shock not shown).

- Uniquement possible avec TV-ICD.
- Permet de terminer env. 50% des TV monomorphes (et d'éviter un choc)

S-ICD – Pour quels patients ?

- Patients jeunes (<45 ans), qui auront probablement besoin de plusieurs remplacement de boitiers durant leur vie (ex: HCM, Brugada, ARVC etc)
- Patients à haut risque de bactériémie (ex: hémodialyse, immunosuppression, cathéters à long terme)
- Problèmes d'accès veineux
- Antécédant de complications avec TV-ICDs / endocardites

Visite à votre cabinet 12 mois post STEMI

- Va bien, pas de plainte
- TA 110/70 mmHg, FC 65/min, euvolémique
- Médicaments:
  - Entresto 200 mg 2x/j, metoprolol 150 mg/j, aldactone 50 mg/j, jardiance 10mg/j
  - Aspirine 100 mg, efient 10 mg
  - Rosuvastatine 20 mg
  - Pantozol 20 mg
- La patiente veut diminuer le nombre de ses médicaments, que lui proposez-vous ?

La patiente veut diminuer le nombre de ses médicaments, que lui proposez-vous ?

- Entresto 200 mg 2x/j, metoprolol 150 mg/j, aldactone 50 mg/j, jardiance 10mg/j
- Aspirine 100 mg, efient 10 mg
- Rosuvastatine 20 mg ?
- Pantozol 20 mg

- Et la statine ???

- The key events in the initiation of ASCVD are the retention and accumulation of cholesterol-rich apoB containing lipoproteins within the arterial intima at sites of predilection for plaque formation.
- LDL-C is causally associated with the risk of ASCVD, and that lowering LDL-C reduces the risk of ASCVD proportionally to the absolute achieved reduction in LDL-C.

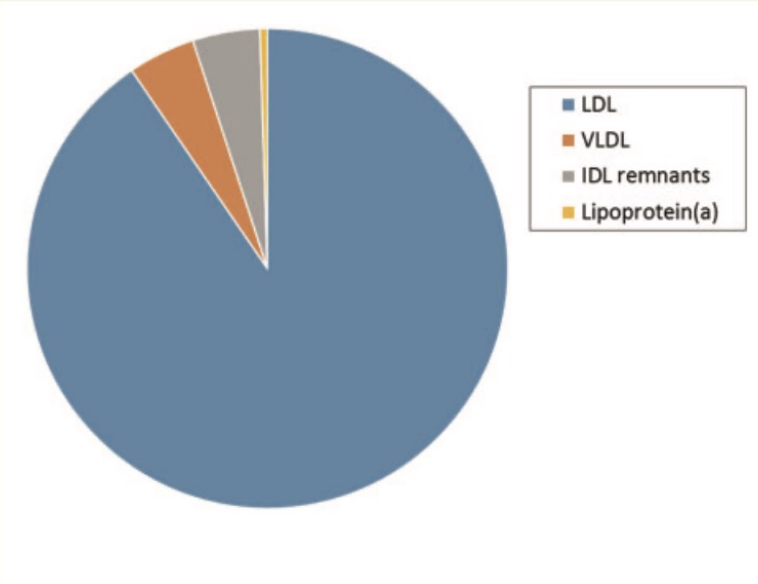


Figure 1 Relative concentration of apolipoprotein B (ApoB) contained in circulating lipoproteins in normolipidaemic individuals. ApoB content was calculated in nanomoles per litre using 500 000 as the defined molecular mass [i.e. low-density lipoprotein (LDL) 100 mg/dL or 2000 nmol/L, very low-density lipoprotein (VLDL) 5 mg/dL or 100 nmol/L, intermediate density lipoprotein (IDL) remnants 5 mg/dL or 100 nmol/L and lipoprotein(a) 10 nmol/l*]. *Based on population median.

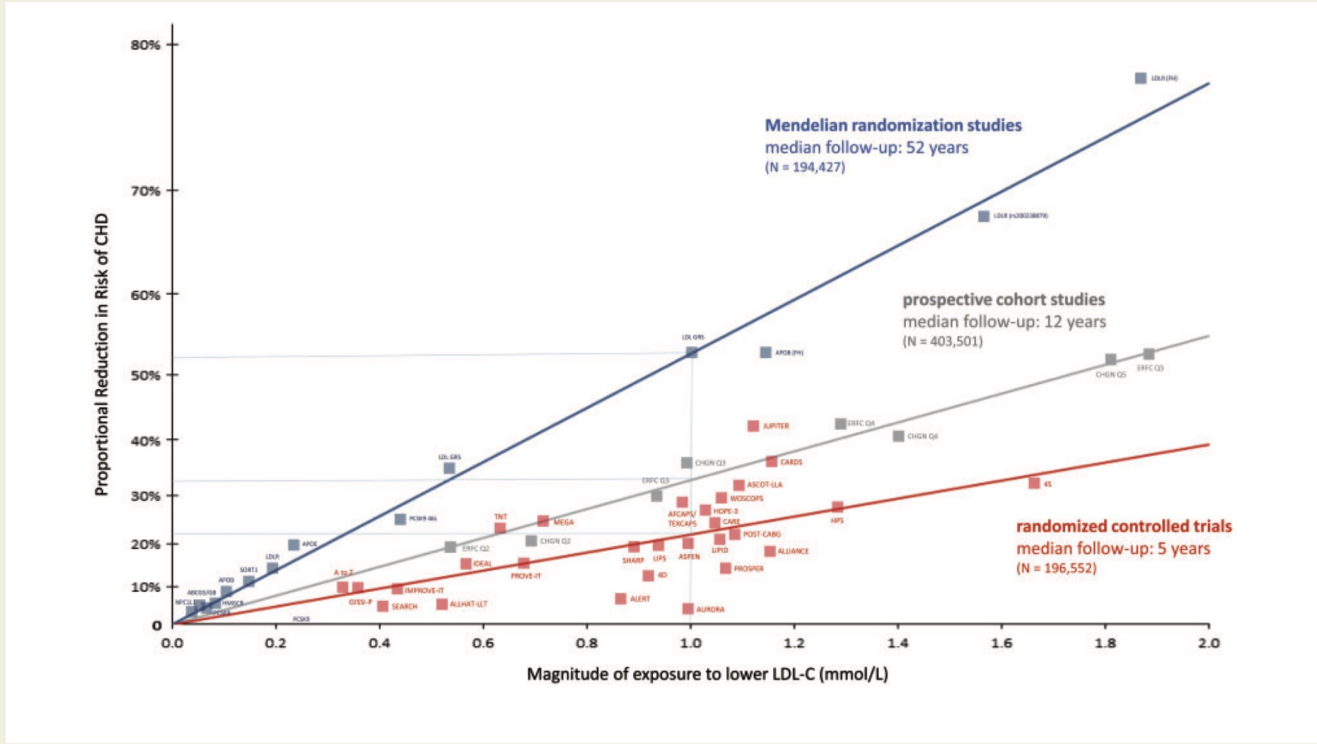


Figure 2 Log-linear association per unit change in low-density lipoprotein cholesterol (LDL-C) and the risk of cardiovascular disease as reported in meta-analyses of Mendelian randomization studies, prospective epidemiologic cohort studies, and randomized trials. The increasingly steeper slope of the log-linear association with increasing length of follow-up time implies that LDL-C has both a causal and a cumulative effect on the risk of cardiovascular disease. The proportional risk reduction (*y* axis) is calculated as 1-relative risk (as estimated by the odds ratio in Mendelian randomization studies, or the hazard ration in the prospective epidemiologic studies and randomized trials) on the log scale, then exponentiated and converted to a percentage. The included meta-analyses were identified from (i) MEDLINE and EMBASE using the search terms meta-analysis, LDL, and 'cardiovascu-

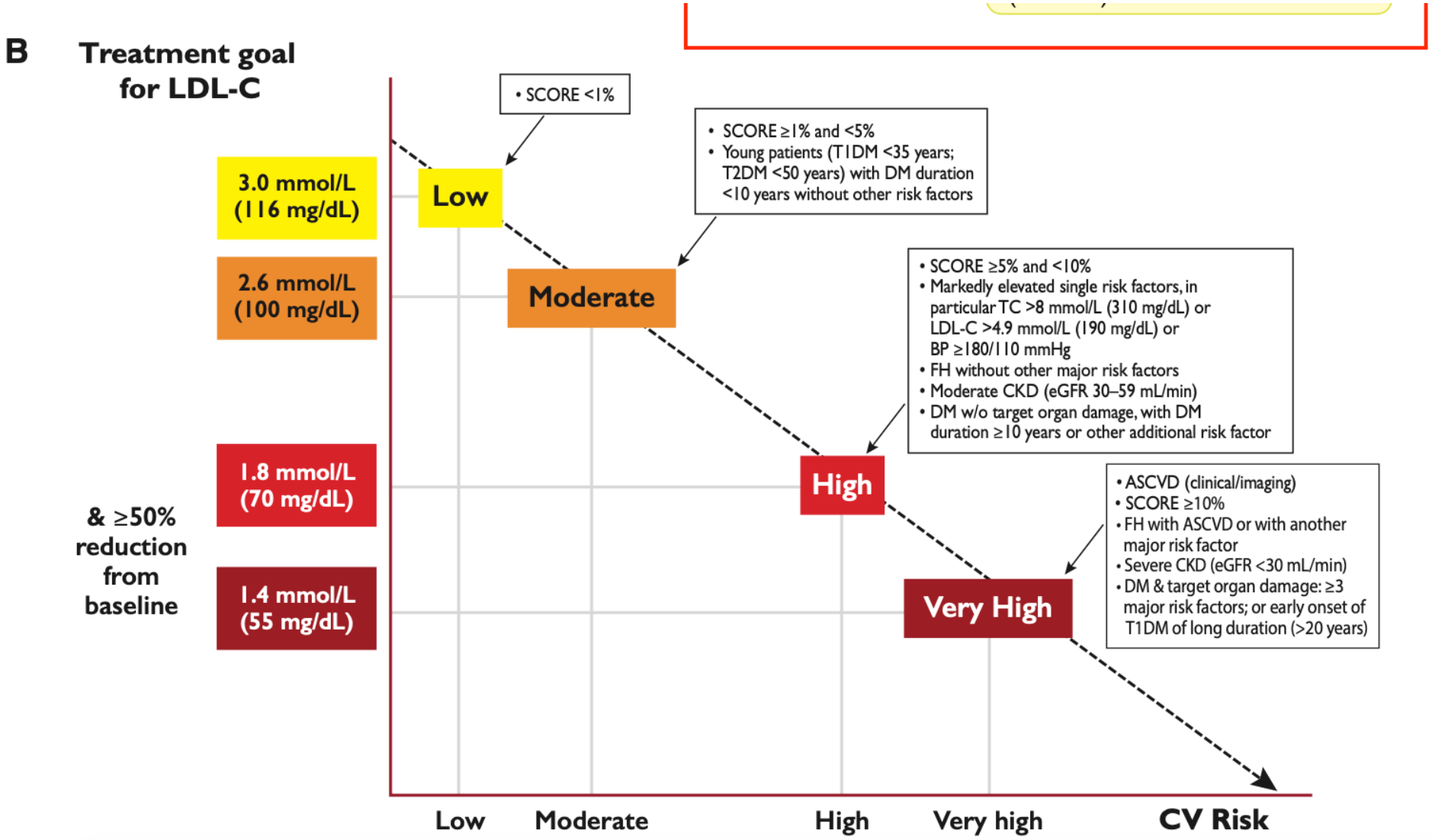
Ference BA et al., Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J, 2017

Lipides – quelles cibles pour notre patiente ?

Recommendations for lipid-lowering therapy in very-high-risk patients with acute coronary syndromes

Recommendations	Class[a]	Level[b]
In all ACS patients without any contraindication or definite history of intolerance, it is recommended that high-dose statin therapy is initiated or continued as early as possible, regardless of initial LDL-C values.[438,440,442]	I	A
Lipid levels should be re-evaluated 4–6 weeks after ACS to determine whether a reduction of ≥50% from baseline and goal levels of LDL-C <1.4 mmol/L (<55 mg/dL) have been achieved. Safety issues need to be assessed at this time and statin treatment doses adapted accordingly.	IIa	C
If the LDL-C goal is not achieved after 4–6 weeks with the maximally tolerated statin dose, combination with ezetimibe is recommended.[33]	I	B
If the LDL-C goal is not achieved after 4–6 weeks despite maximal tolerated statin therapy and ezetimibe, the addition of a PCSK9 inhibitor is recommended.[119,120]	I	B
In patients with confirmed statin intolerance or in patients in whom a statin is contraindicated, ezetimibe should be considered.	IIa	C
For patients who present with an ACS and whose LDL-C levels are not at goal, despite already taking a maximally tolerated statin dose and ezetimibe, the addition of a PCSK9 inhibitor early after the event (during hospitalization for the ACS event if possible) should be considered.	IIa	C

LDL-C : quelles cibles ?



2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Diminuer le LDL-C – quels médicaments ?

Statines

PCSK9-Inhibitors

Ezetimibe

Mécanismes d'action

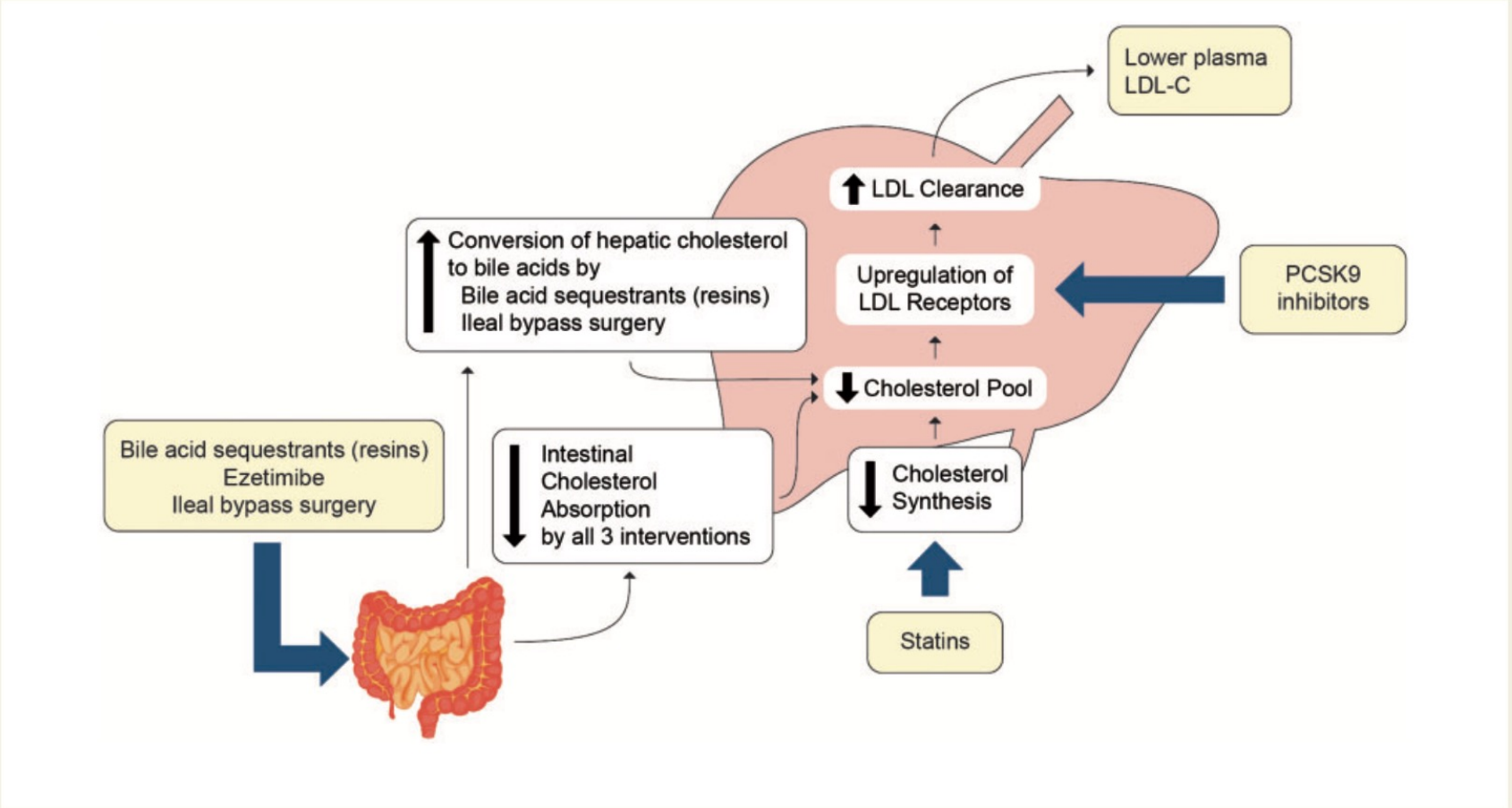


Figure 4 Schematic figure showing that all therapies that act predominantly to lower low-density lipoprotein (LDL) act via the LDL receptor pathway to up-regulate LDL receptors and thus increase LDL clearance.

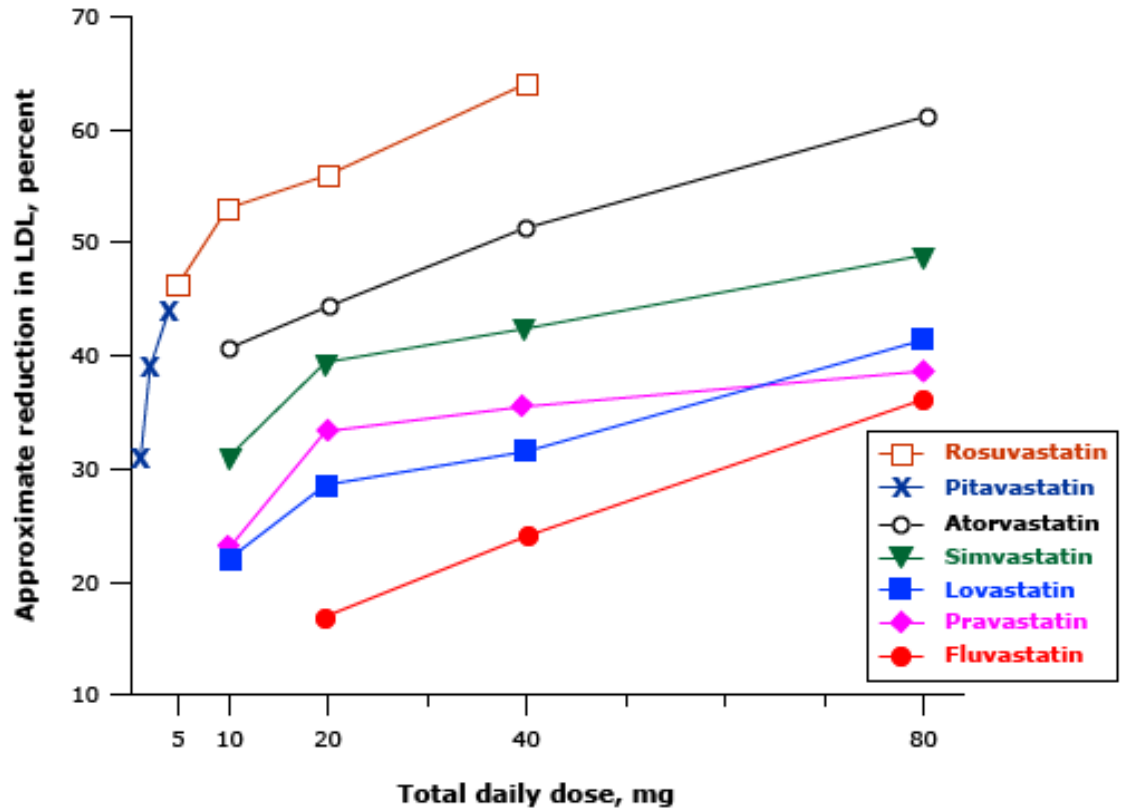
Ference BA et al., Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J, 2017

Intensity of lipid-lowering treatment

Treatment	Average LDL-C reduction
Moderate-intensity statin	≈30%
High-intensity statin	≈50%
High-intensity statin plus ezetimibe	≈65%
PCSK9 inhibitor	≈60%
PCSK9 inhibitor plus high-intensity statin	≈75%
PCSK9 inhibitor plus high-intensity statin plus ezetimibe	≈85%

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Comparison of the efficacy of statin drugs



Comparison of the percent reduction in serum LDL cholesterol with various statin drugs.

LDL: low-density lipoprotein.

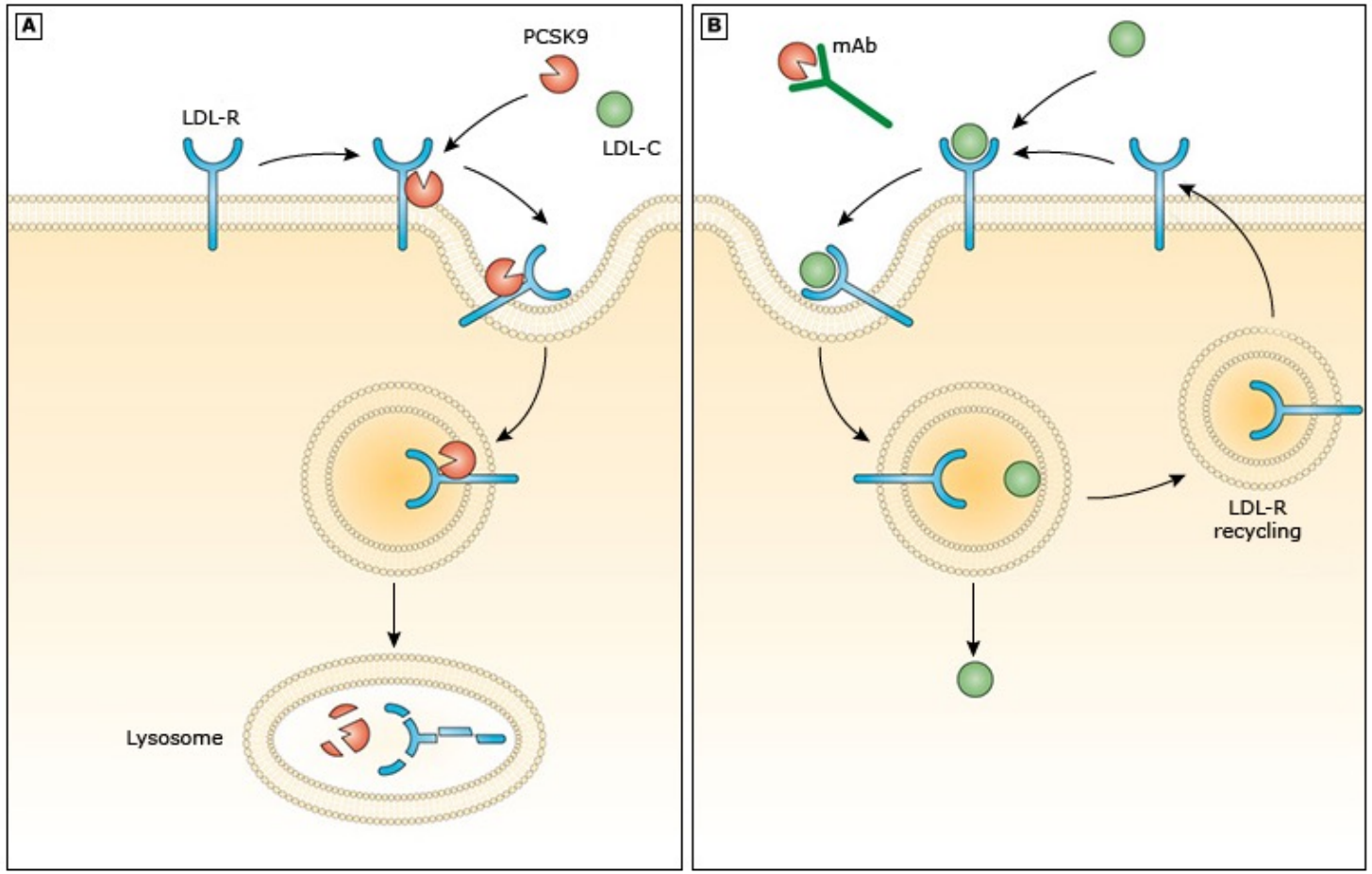
UpToDate®

Proprotein convertase subtilisin/kexin type 9 (PCSK9) - Inhibitors

3 drogues, 2 mécanismes d'action:

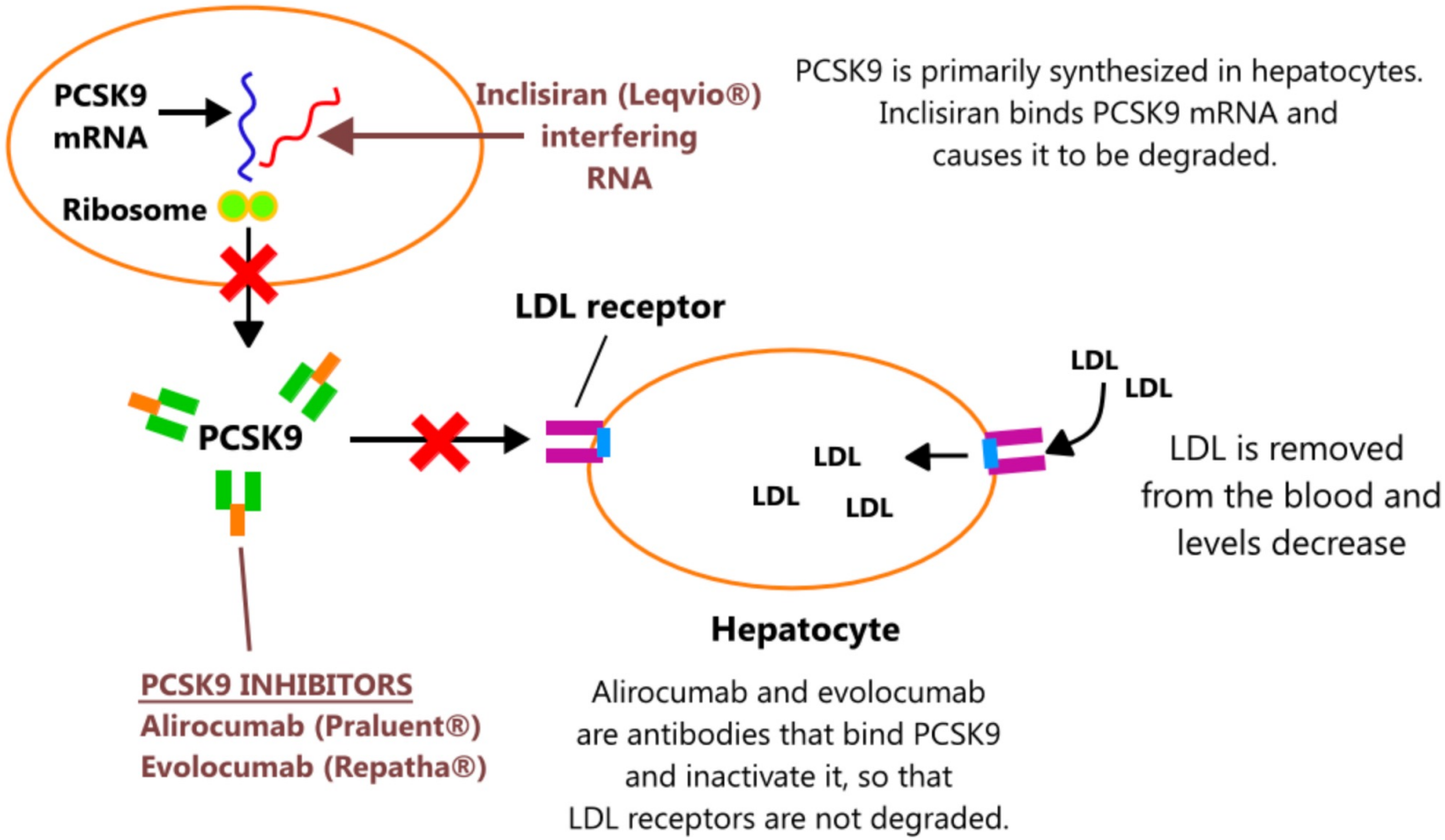
- L'alirocumab (Praluent) et l'evolocumab (Repatha) sont des anticorps monoclonaux qui lient le PCSK9 sérique, favorisant sa dégradation.
- L'inclisiran (Leqvio) est un petit ARN interférant (pARNi), qui interfère avec le mRNA codant pour la PCSK9 et diminution sa production.
- Les 2 mécanismes augmentent le recyclage des LDL-R et leur expression à la surface des hépatocytes, ce qui augmente l'absorption du LDL-C et diminue le taux de LDL-C sanguin.
- Circulating levels of PCSK9 are upregulated in the presence of statins, suggesting that inhibiting the PCSK9 pathway may complement the LDL-C lowering effect of statins

PCSK9 pathway and effect of PCSK9 antibody on LDL-R



LDL-R: low density lipoprotein cholesterol receptor.

PCSK9 INHIBITING DRUGS

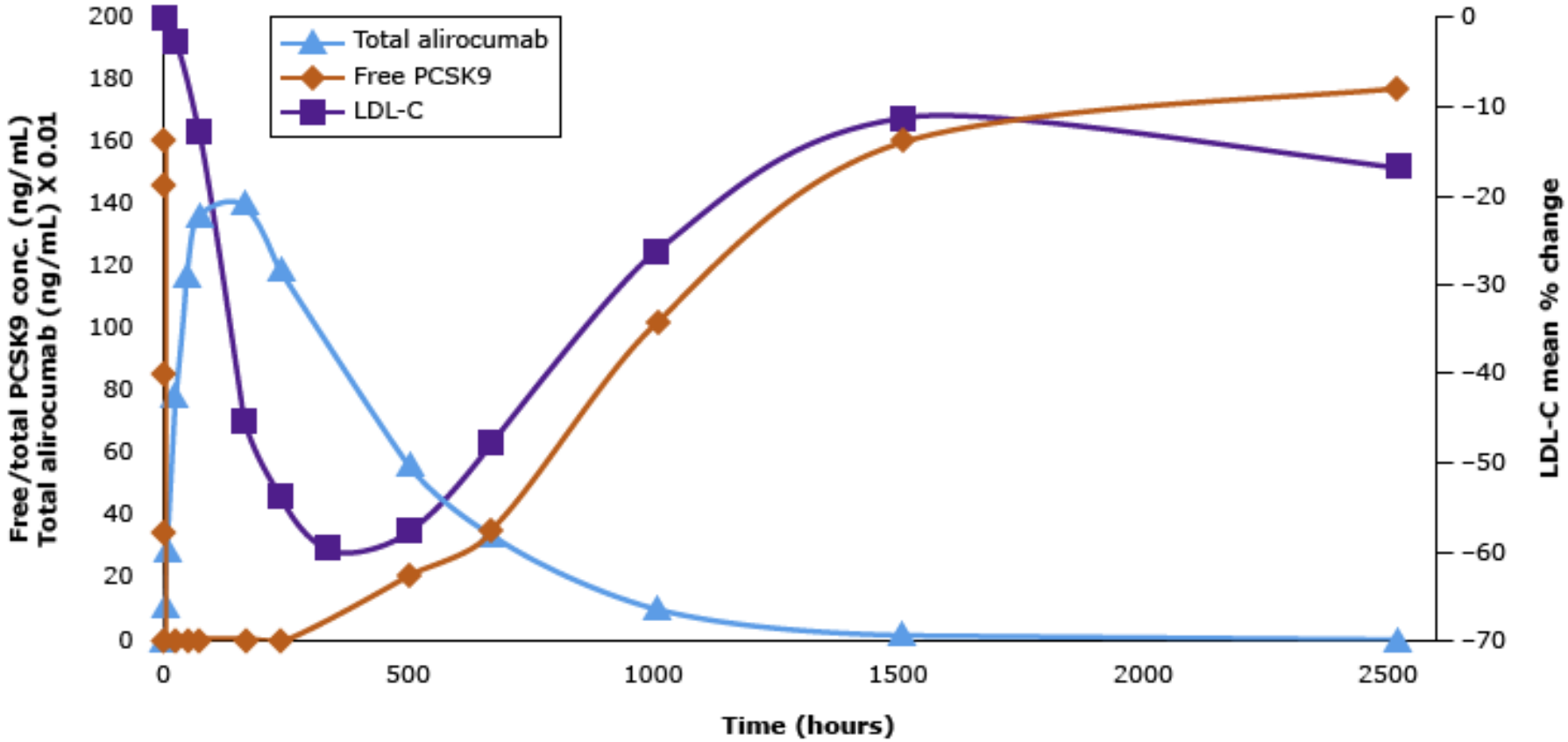


https://www.straighthealthcare.com/pcsk9-inhibitor-moa.html

PCSK9-Inhibitors - Posologies

- Alirocumab – Praluent
  - 75 - 150 mg sc toutes les 2 semaines ou 300 mg 1x/mois
- Evolocumab – Repatha
  - 140 mg sc toutes les 2 semaines ou 420 mg 1x/mois
- Inclisiran – Leqvio (small interfering RNA)
  - 284 mg sc à 0, 3 mois, puis tous les 6 mois

Effect of PCSK9 antibody on free PCSK9 concentration



Reproduced from: Stein EA, Raal FJ. New therapies for reducing low-density lipoprotein cholesterol. Endocrinol Metab Clin North Am 2014; 43:1007. Illustration used with the permission of Elsevier Inc. All rights reserved.

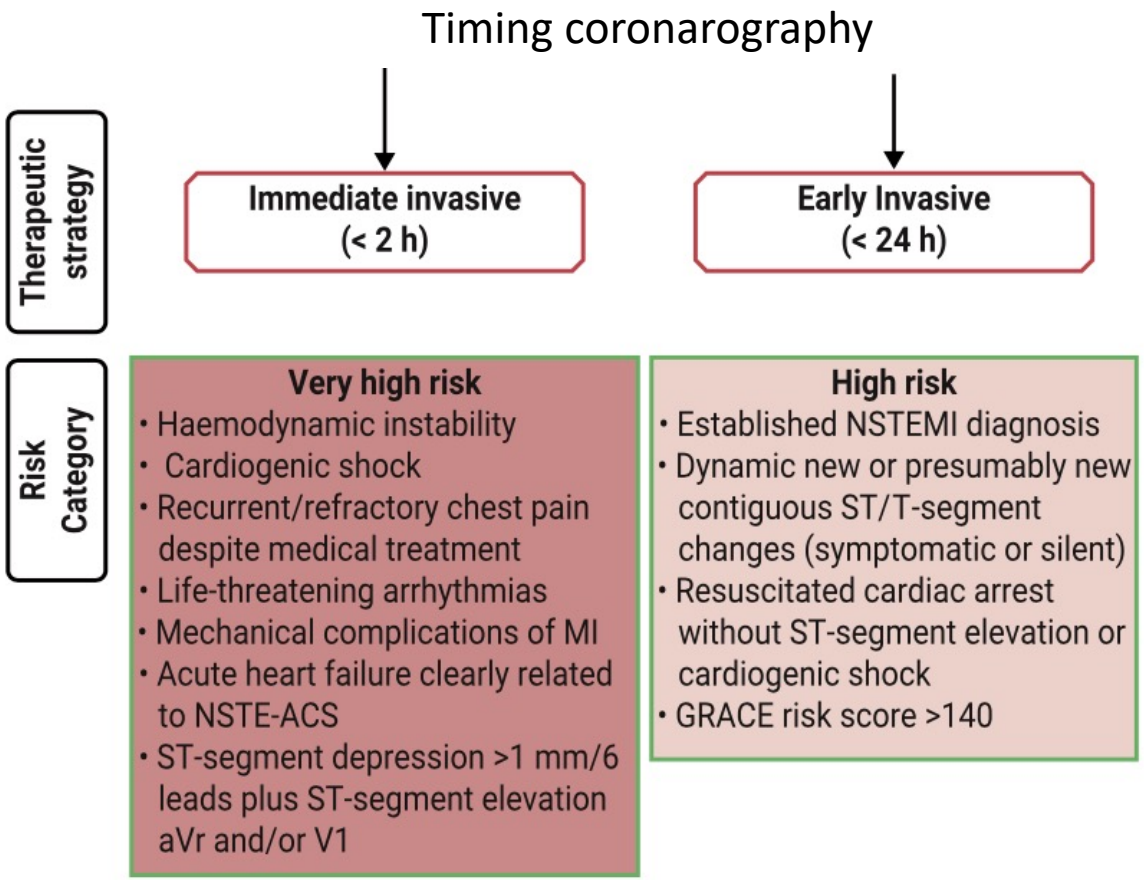
PCSK9-Inhibitors

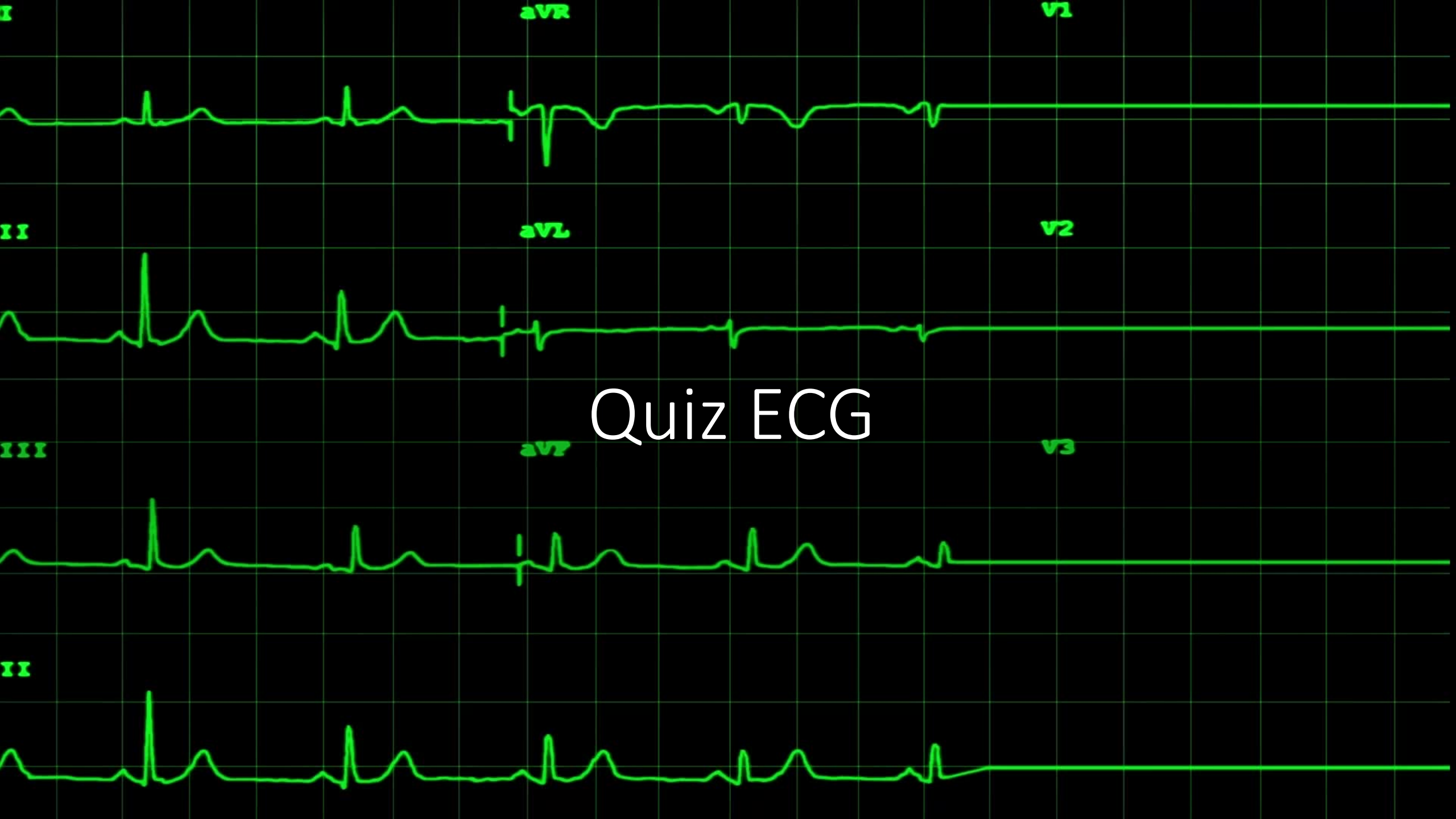
- Indications:
  - En cas de cible LDL-C non atteinte
  - En association avec et/ou en cas d'intolérance aux statines/ezetimibe
  - Hypercholestérolémie familiale (homo- et hétérozygote)
  - Prévention cardiovasculaire secondaire
  - (Prévention cardiovasculaire primaire chez les patients à très haut risque (IIb, C))
- Effets:
  - LDL-C : réduction de 60%, indépendamment de la prise ou non de statine
  - Lp(a): réduction de 18-36%
  - Mortalité CV et risque d'infarctus: réduction jusqu'à 50% (!)
- Peu/pas d'effet secondaire
- Inconvénient : prix très élevés …

ODYSSEY Trial - Alirocumab vs Placebo for Secondary Prevention of CVD, NEJM (2018)
FOURIER Trial - Evolocumab vs Placebo for Secondary Prevention of CVD, NEJM (2017)
ORION-10 and ORION-11 Trials - Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol, NEJM (2020)
Efficacy and safety of evolocumab in reducing lipids and cardiovascular events. NEJM (2015)

NSTEMI – quelques précisions

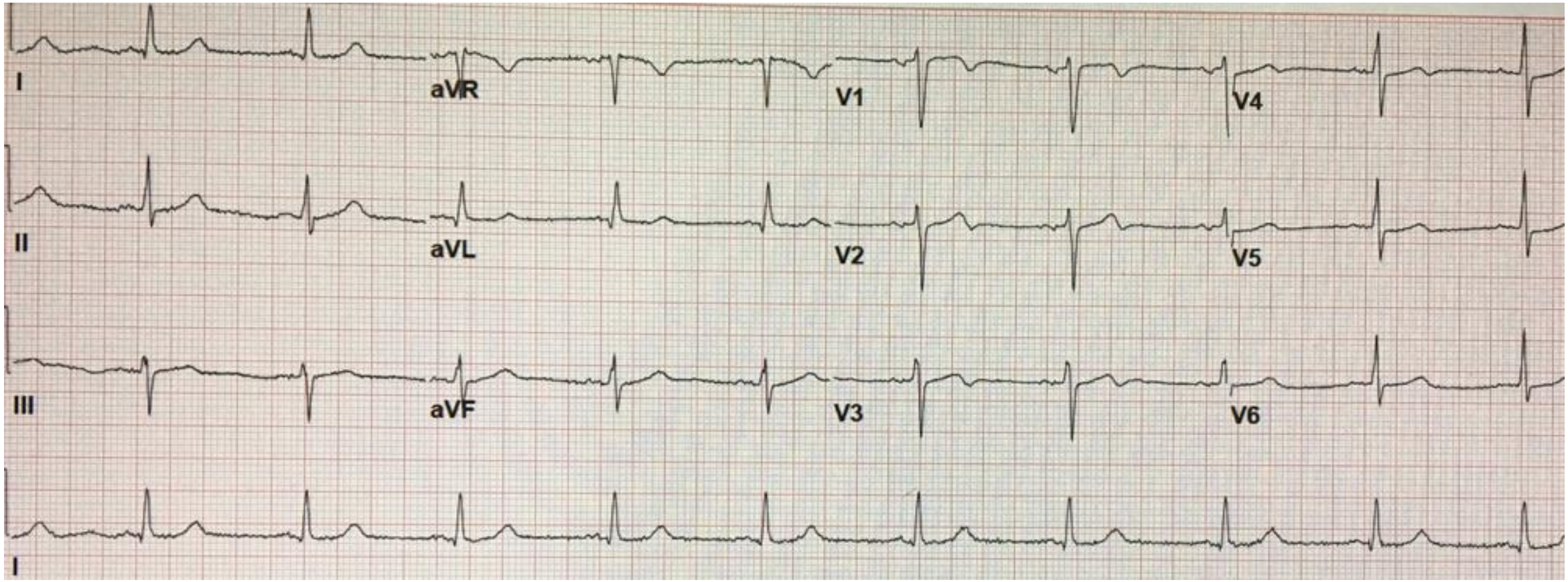
Pas de pré-traitement par $P2Y_{12}$-Inhib (Efient, Brilique, Plavix), avant la coronarographie et de connaitre l'anatomie coronarienne.





Quiz ECG

F, 42 ans, HTA
Douleurs thoraciques intermittentes depuis qq jours.
N'a plus de douleurs actuellement

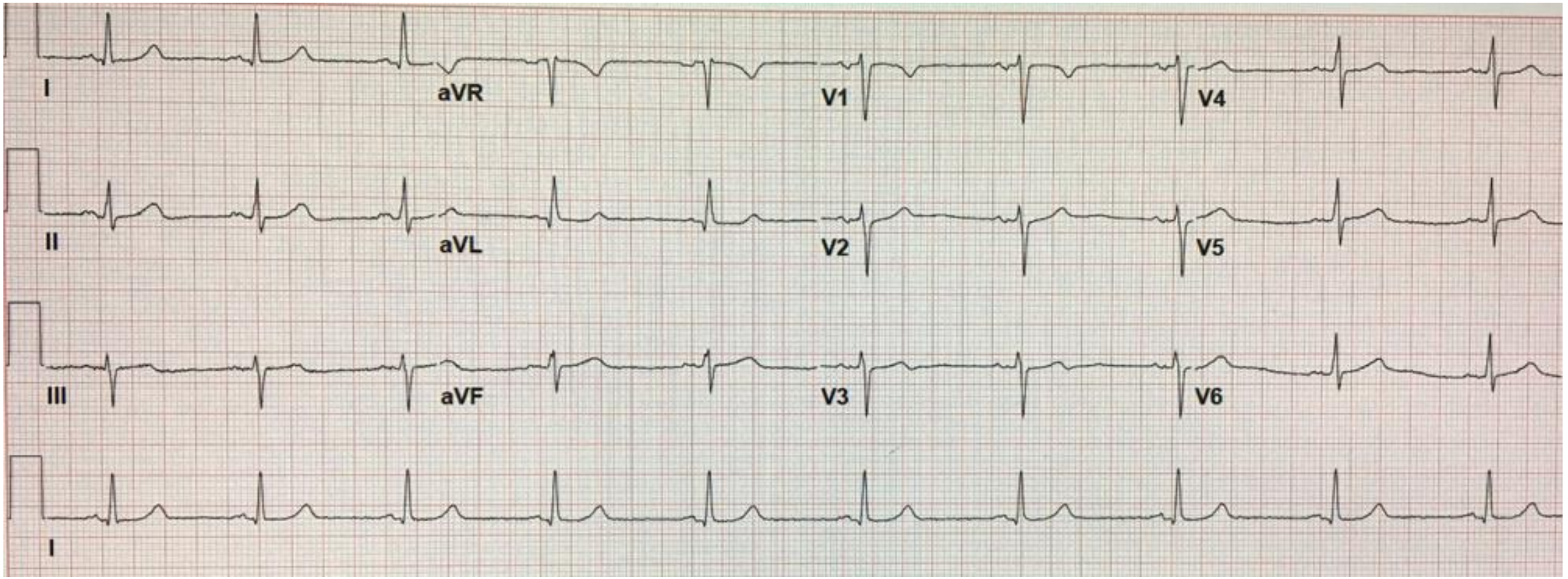


Status: sp

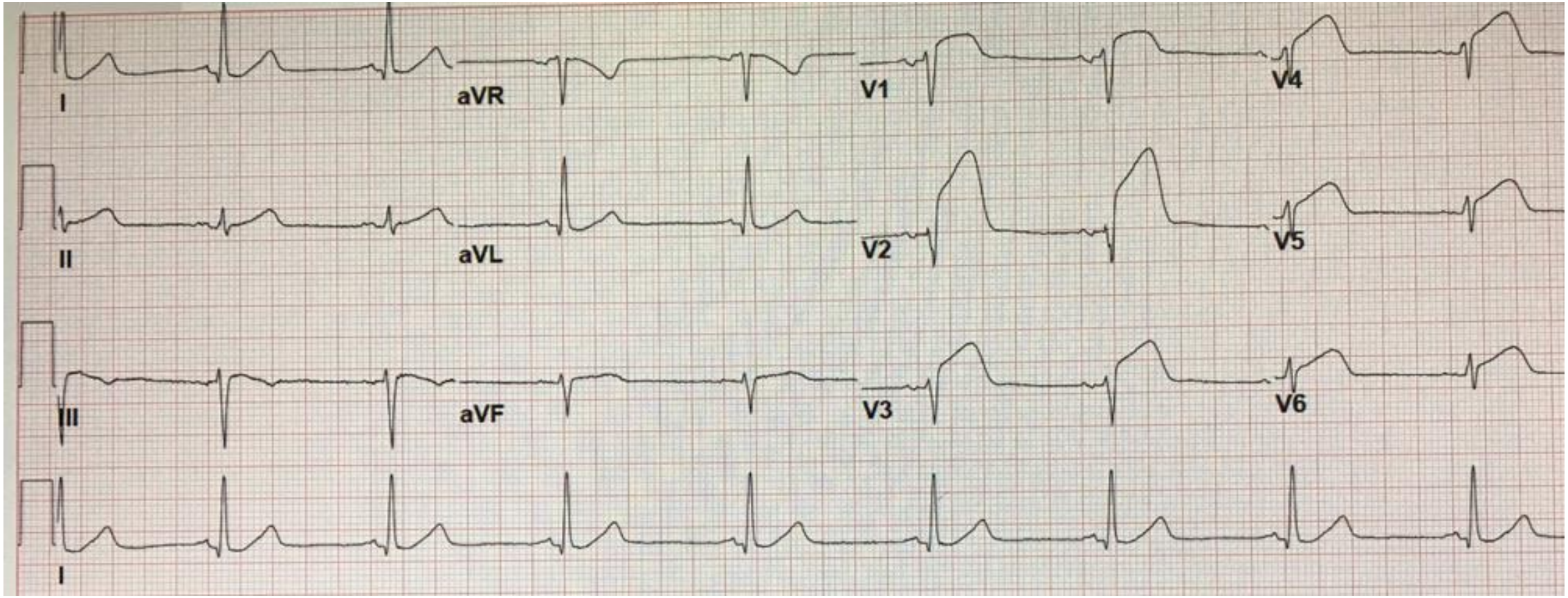
Labo: Troponine-I HS : négative

http://hqmeded-ecg.blogspot.com/2017/03/subtle-dynamic-t-waves-followed-by-lad.html

T 1.5h – toujours asymptomatique



T 3.5h – DRS reviennent…



Troponine T3 : à peine positive

Juste après, développe FV

ROSC difficilement obtenu

IVA moyenne: occlusion 100%

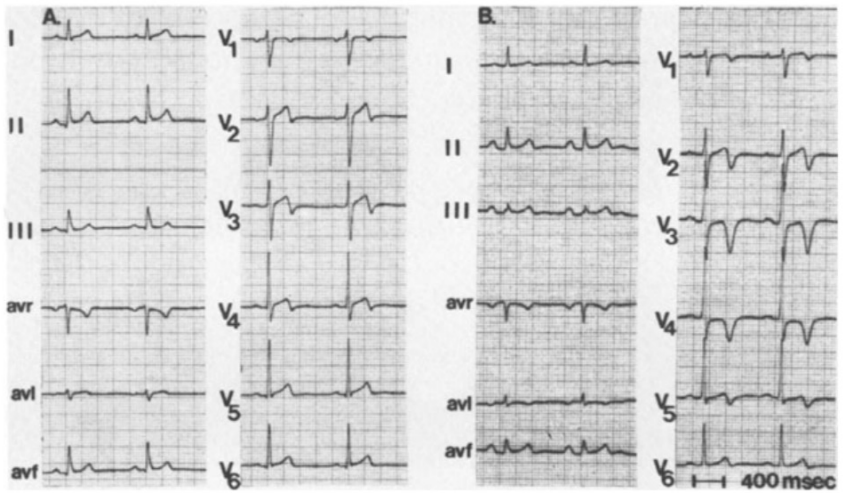
Evolution favorable

Diagnostic ? Wellens' syndrome

Am Heart J 103: 730–735, 1982

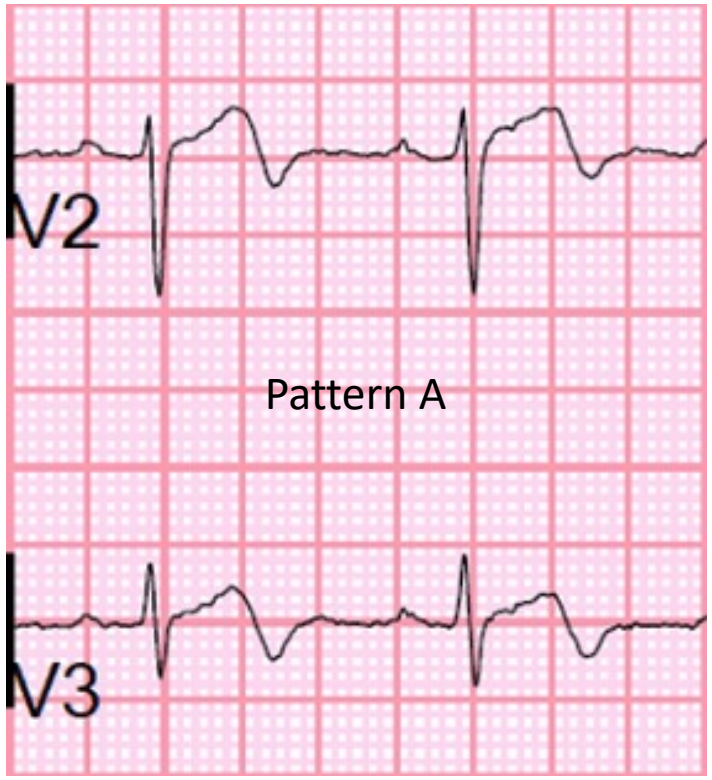
Characteristic electrocardiographic pattern indicating a critical stenosis high in left anterior descending coronary artery in patients admitted because of impending myocardial infarction

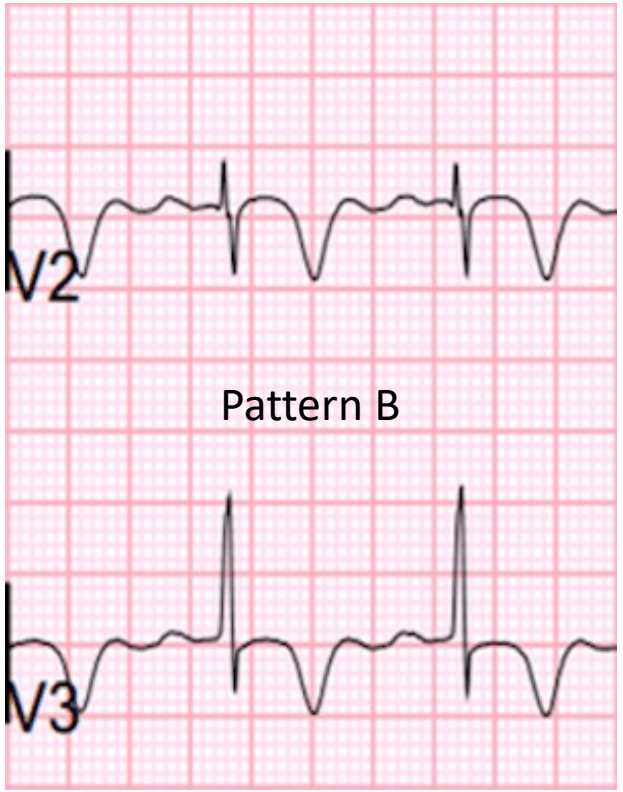
CHRIS DE ZWAAN, FRITS W.H.M. BÄR, and HEIN J.J. WELLENS
Department of Cardiology, University of Limburg, Annadal Hospital, Maastricht, The Netherlands

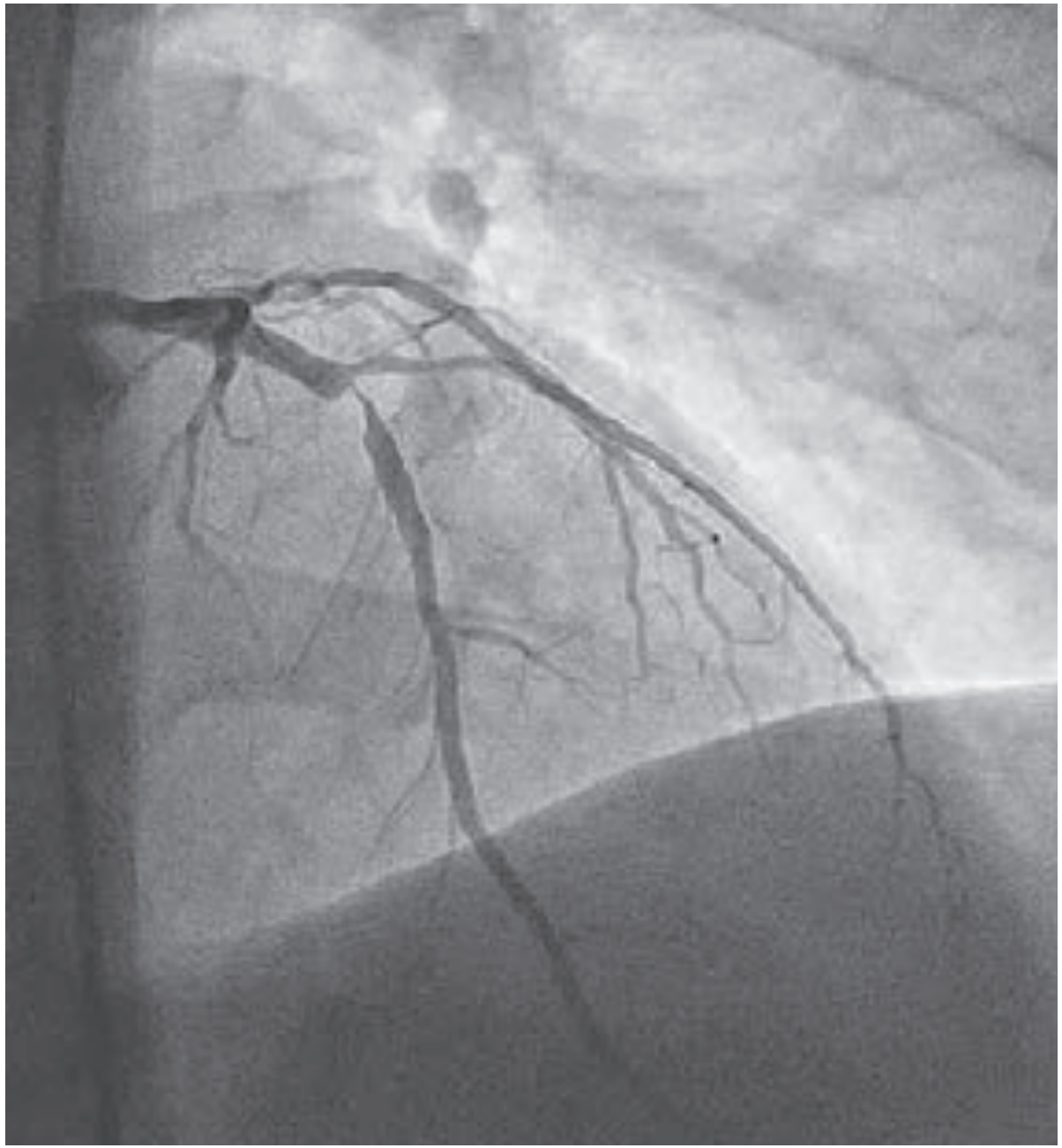


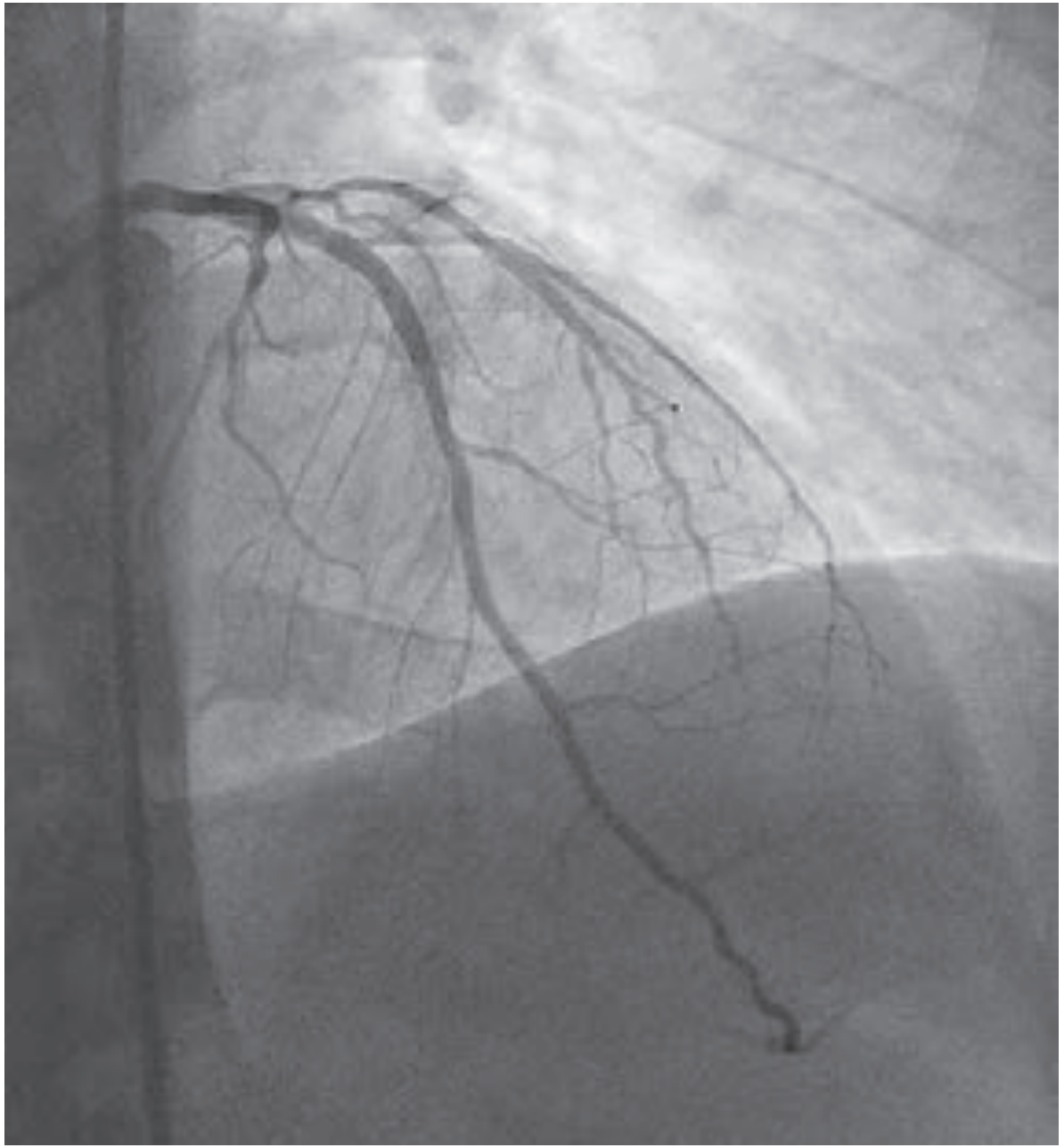
Wellens' syndrome

- Très suspect de sténose critique de l'IVA (ou d'une autre coronaire)
- Les patients n'ont plus de douleur ! (reperfusion spontanée après une période d'ischémie critique)
- Pas/peu d'enzymes cardiaques
- Lésion très instable, très haut risque de ré-occlusion
- Signe ECG également rencontré après PCI ou lors de spasme coronarien = signe de reperfusion
- Attention à la pseudo-normalisation des ondes T = ré-occlusion !!!



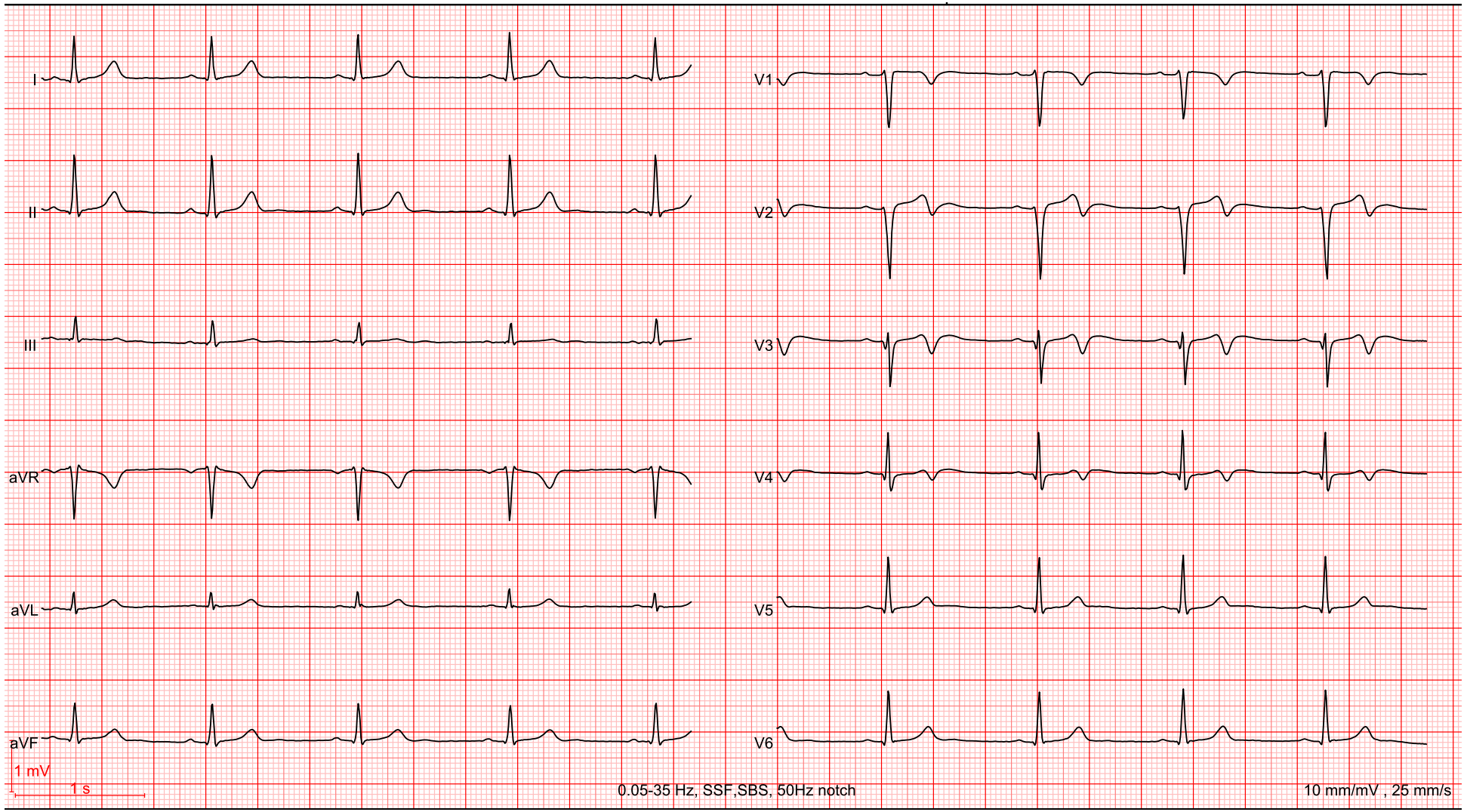


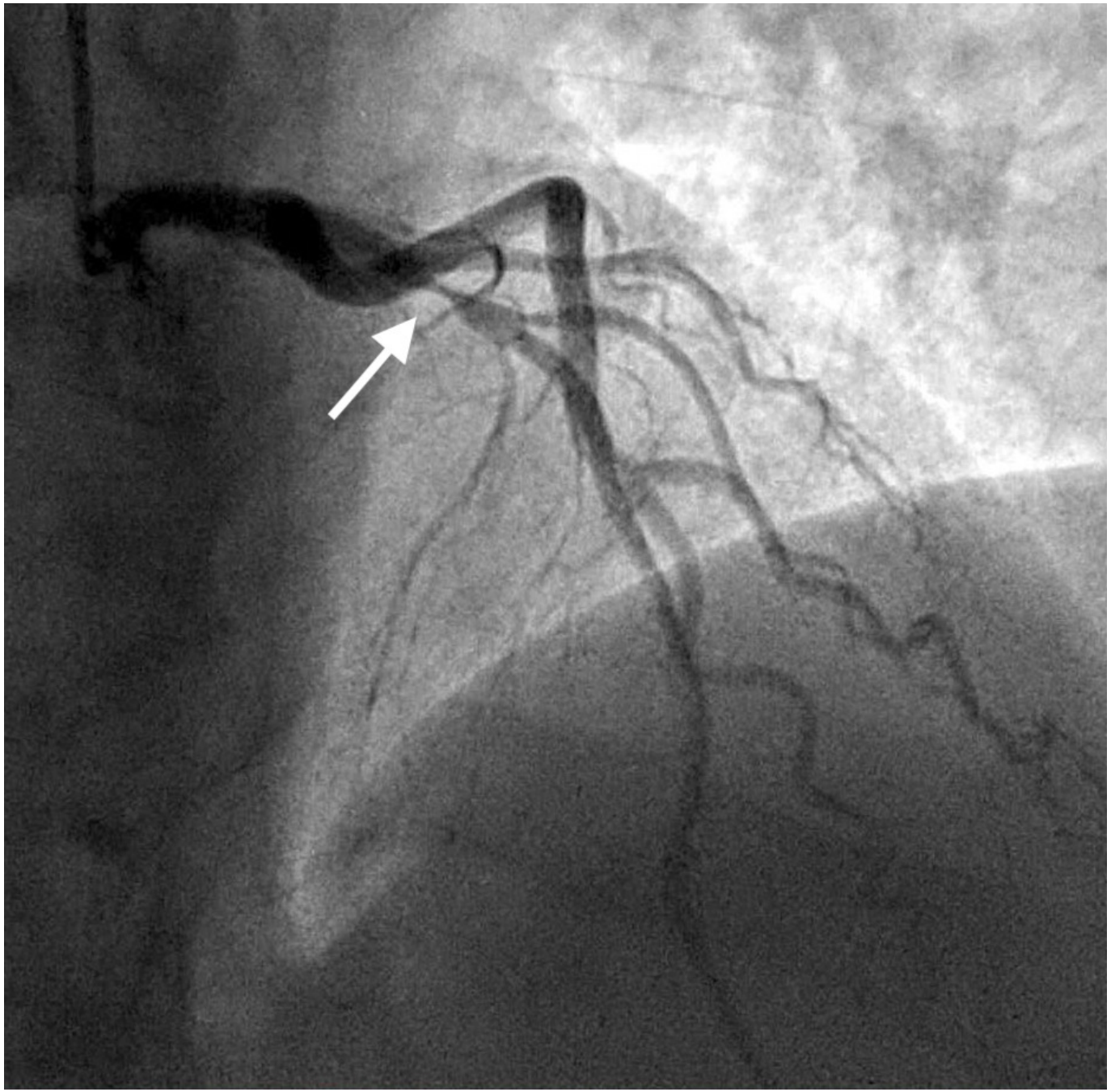


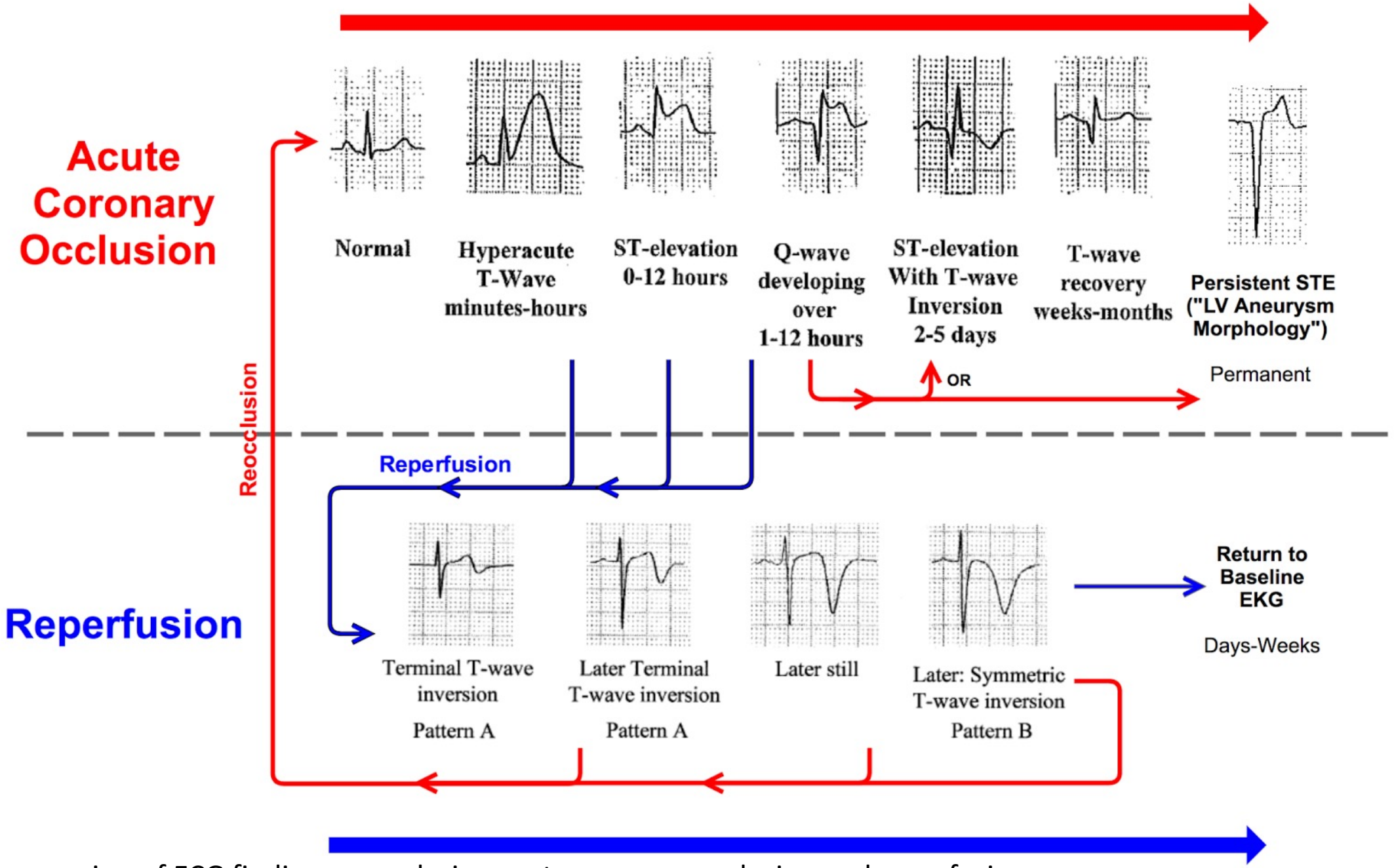


Lindsey R. Baden, M.D., Editor Wellens' Syndrome. DOI: 10.1056/NEJMicm1400946

Wellens’, autre exemple

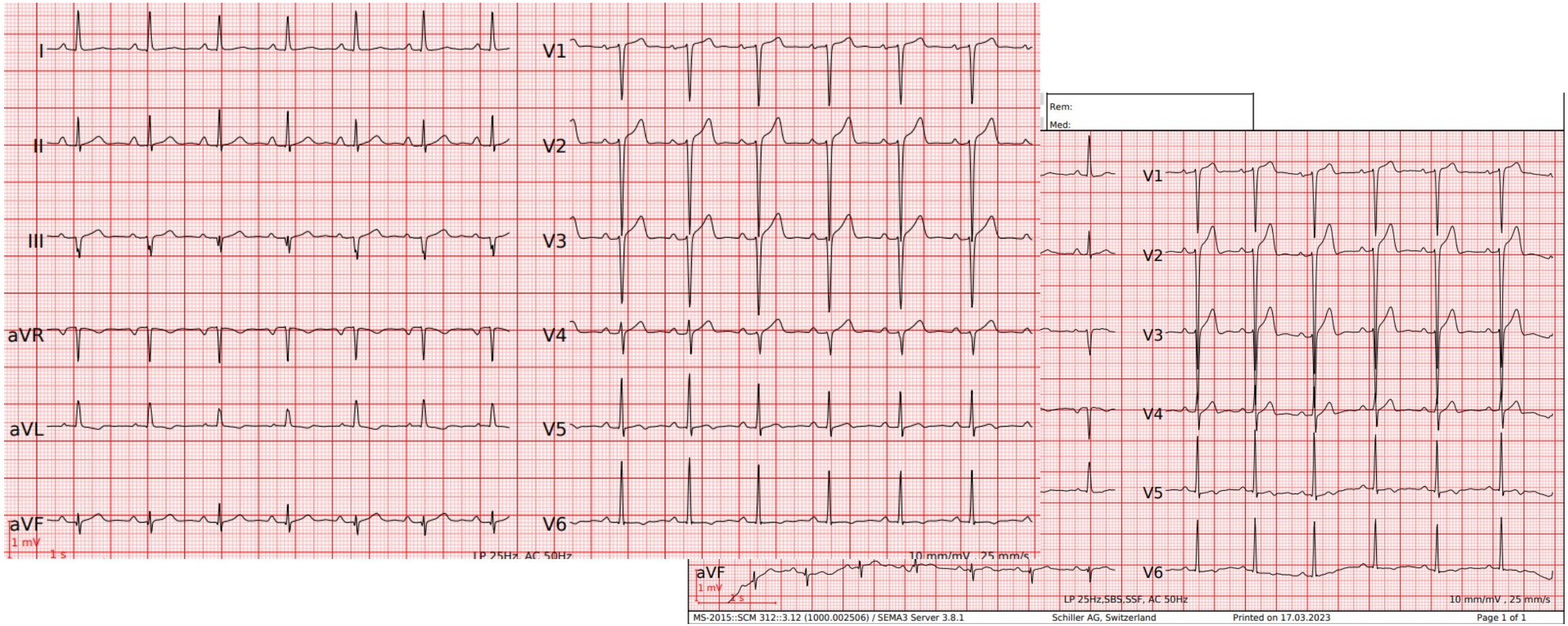




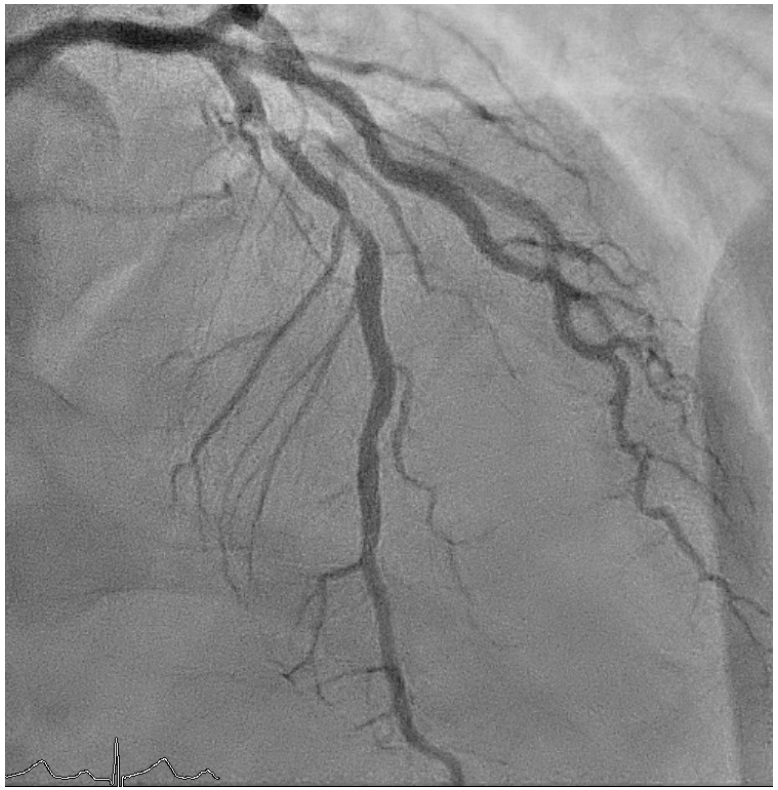


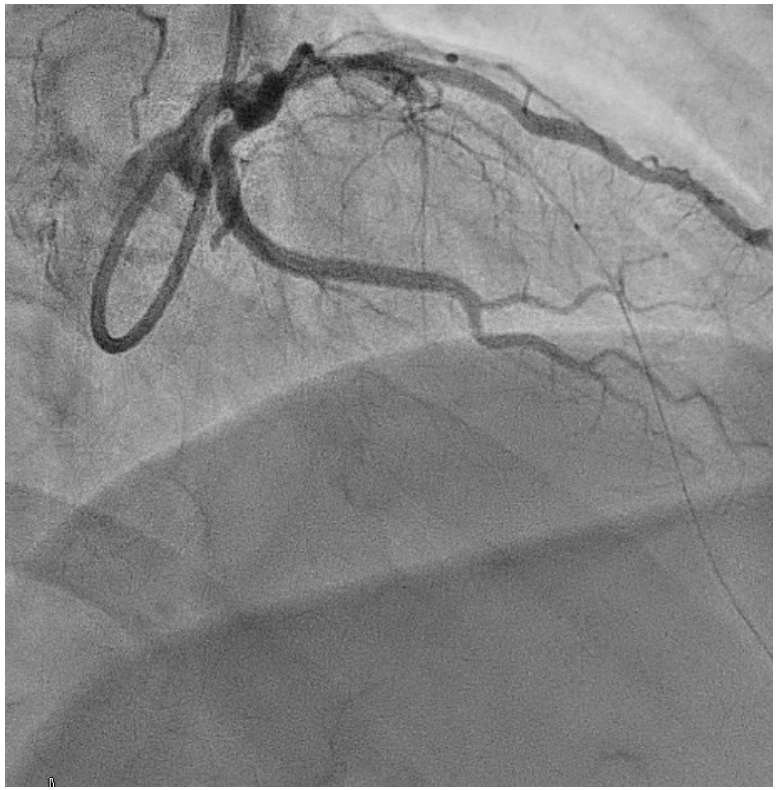
The progression of ECG findings seen during acute coronary occlusion and reperfusion.
Pendell, M., et al. (2018). "The OMI Manifesto." Dr. Smith's ECG Blog.

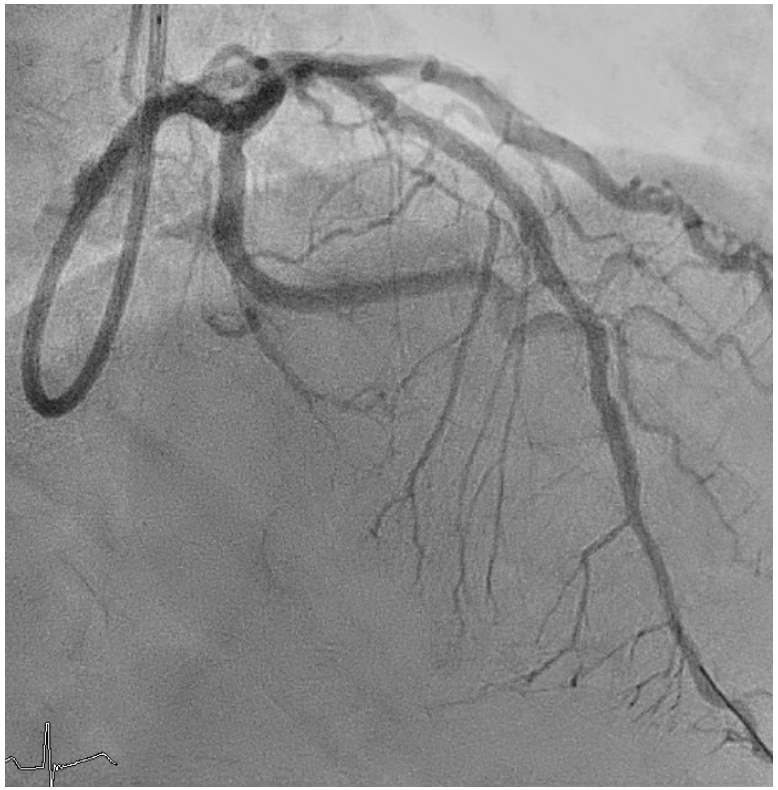
H, 43 ans, HTA, fortes douleurs thoraciques la veille, actuellement asymptomatique



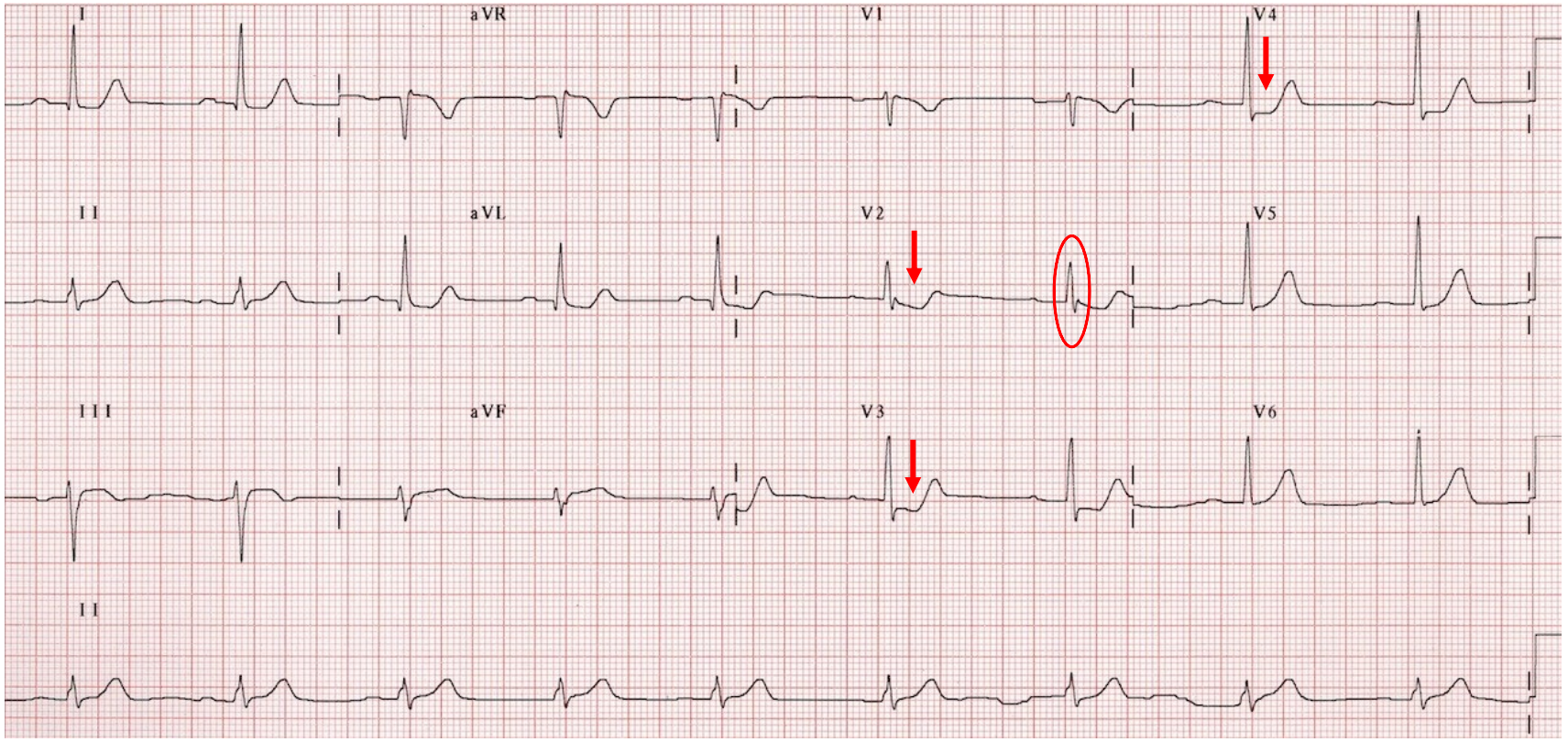
ETT: FEVG 65%, pas de trouble de la cinétique segmentaire
Troponin T hs: 60 ng/L, sans cinétique

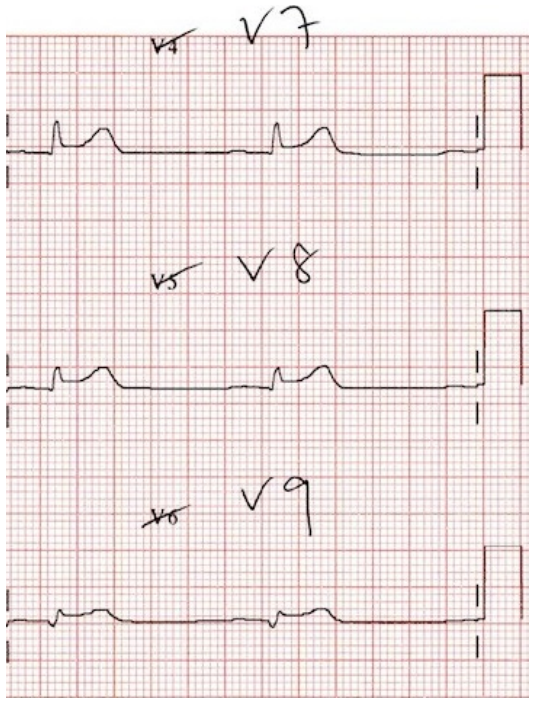






Homme 56 ans, DRS



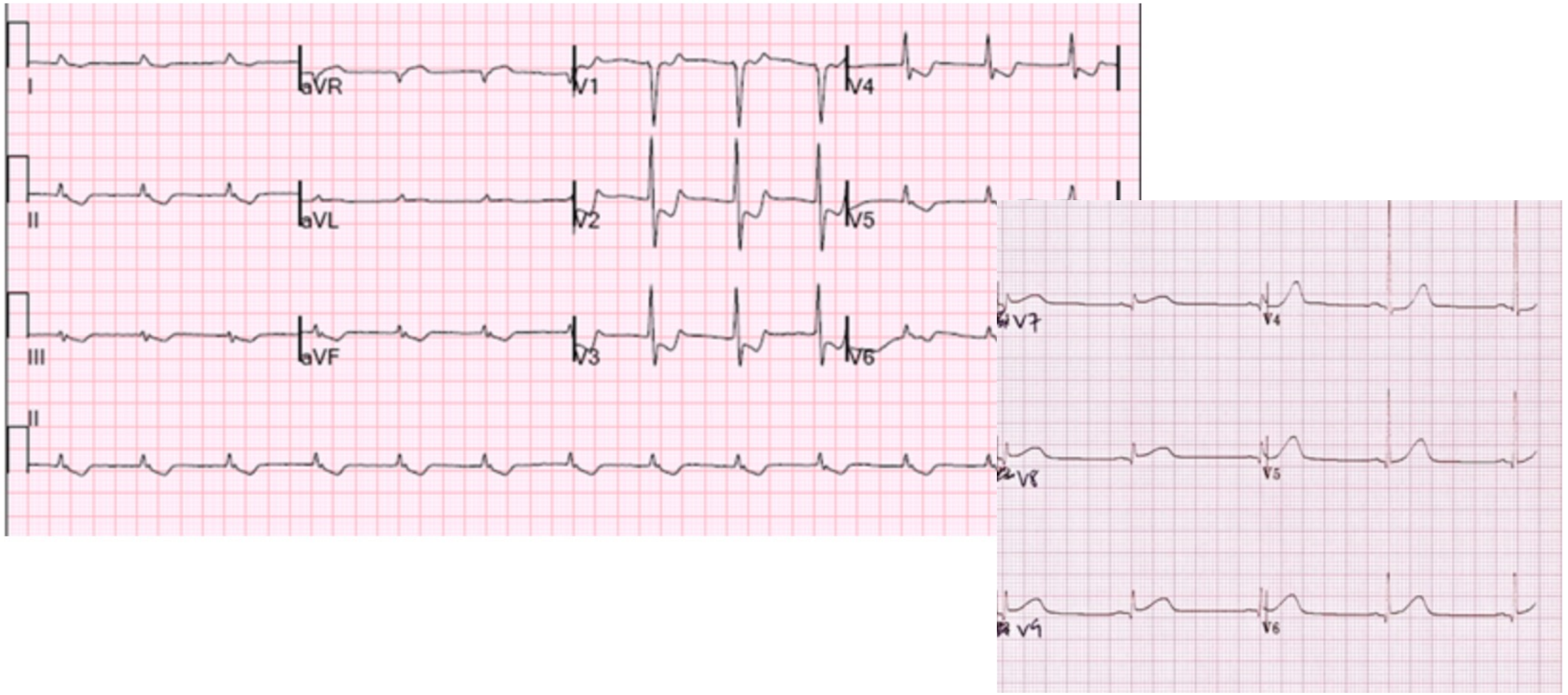


STEMI postérieur

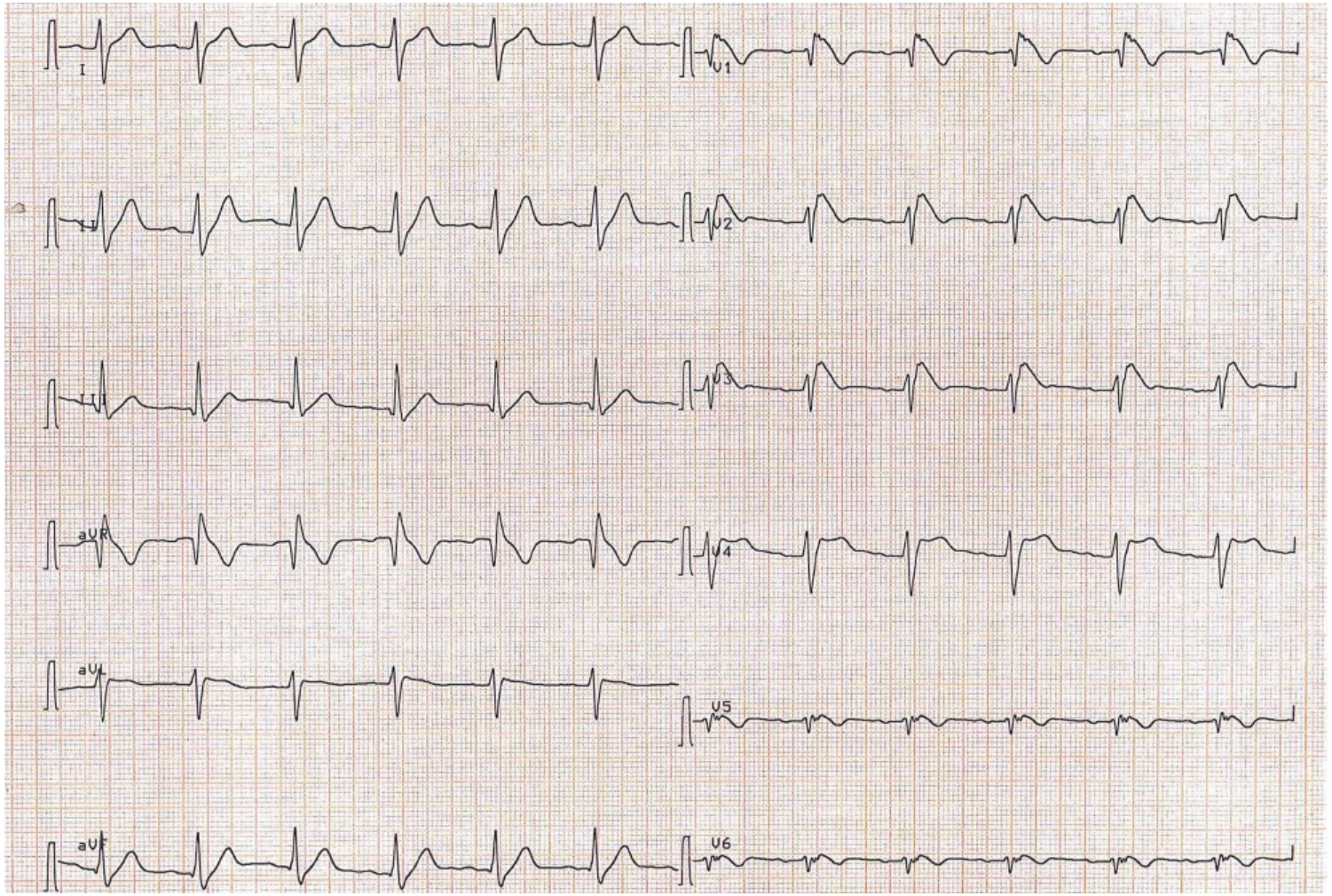
Territoire électriquement silencieux
3-8% des infarctus touchent uniquement la paroi postérieure
Diagnostic souvent manqué
CAVE: Sous décalage en V2-V3 jamais normal
Transition R très précoce

Oraii, S., et al., J Electrocardiol, 1999
O'Keefe, J.H., et al., Am J Cardiol, 1995
https://litfl.com/posterior-myocardial-infarction-ecg-library/

Posterior STEMI

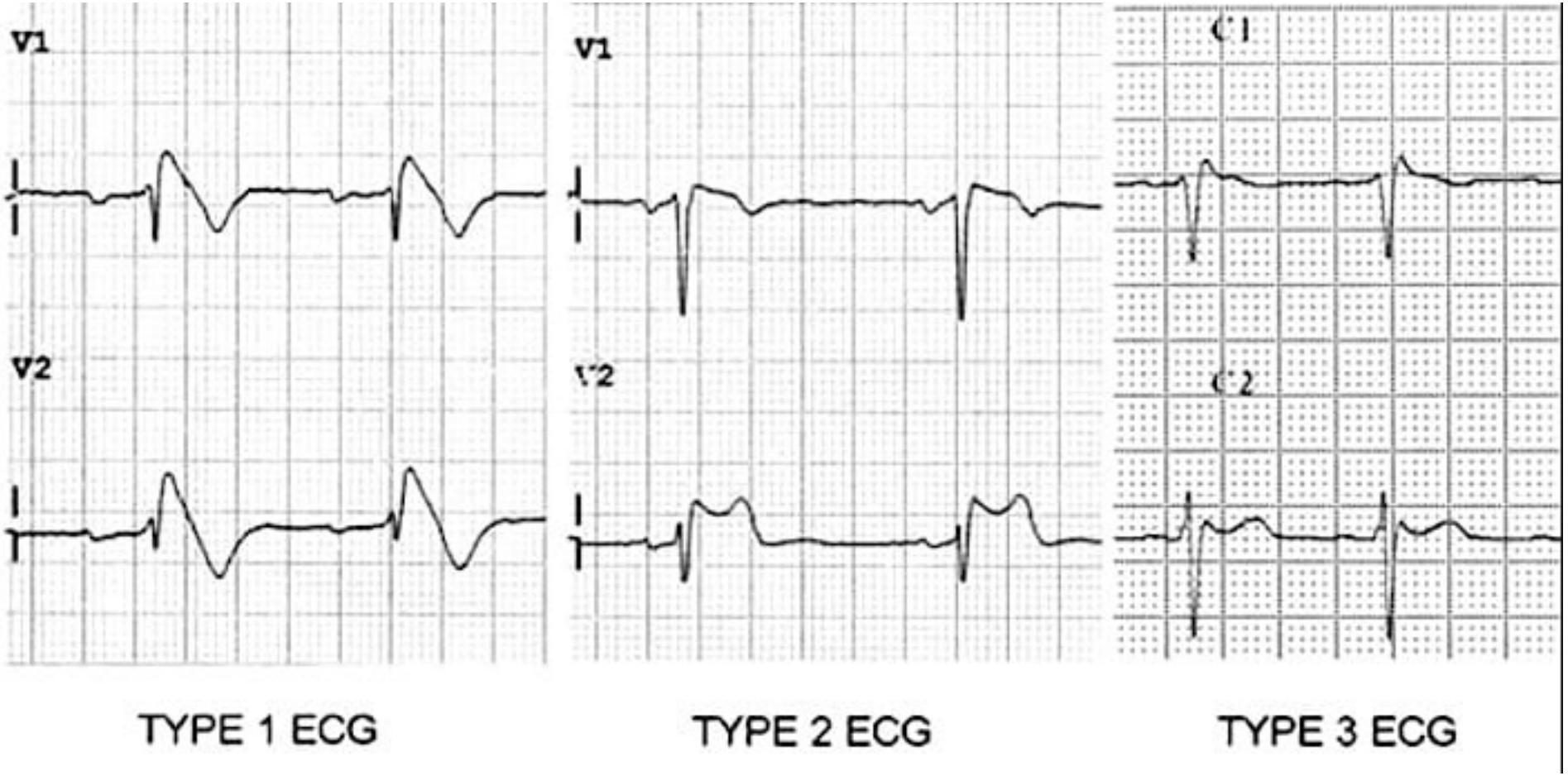


H, 20 ans, syncope en jouant au foot
Mort subite du père à 42 ans, il y a 3 mois



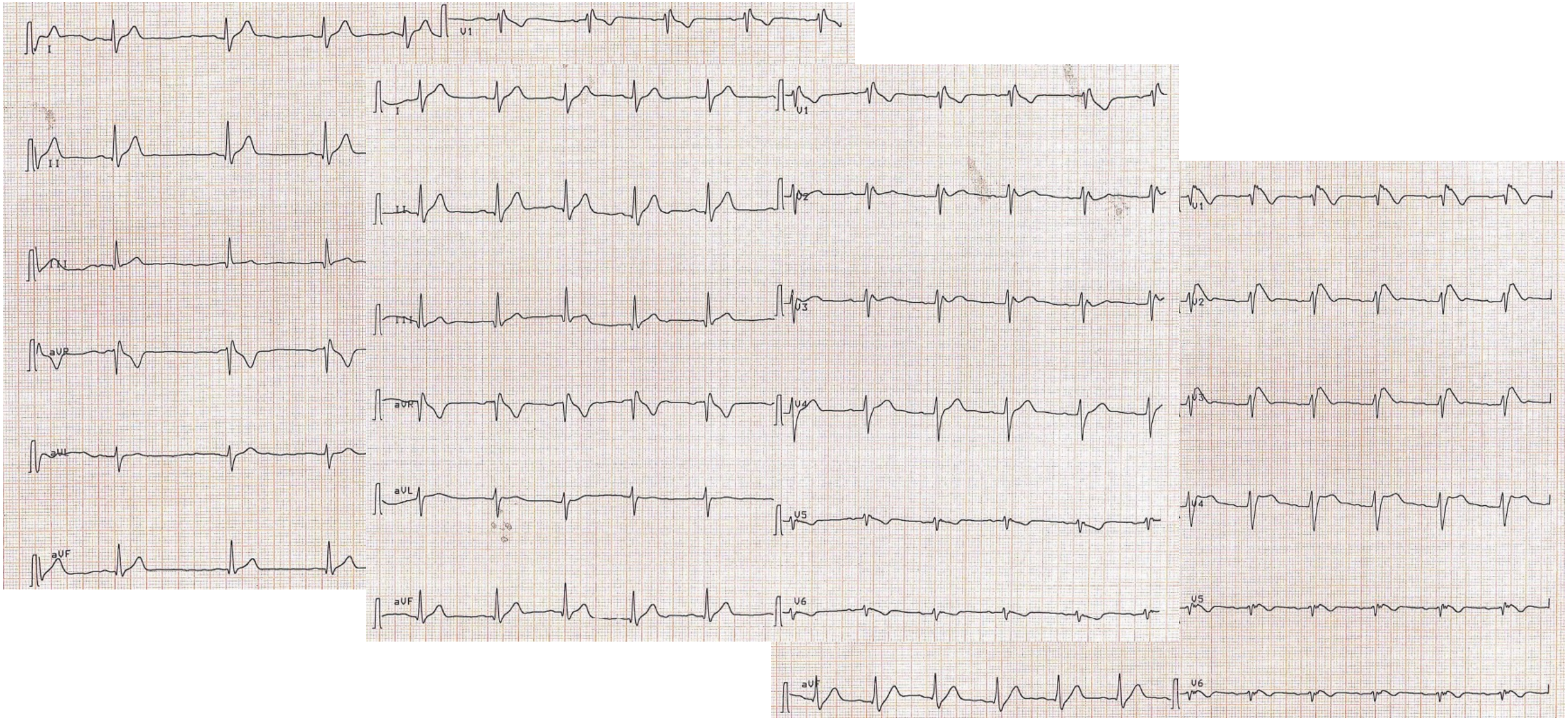
Diagnostic ?

Brugada syndrom

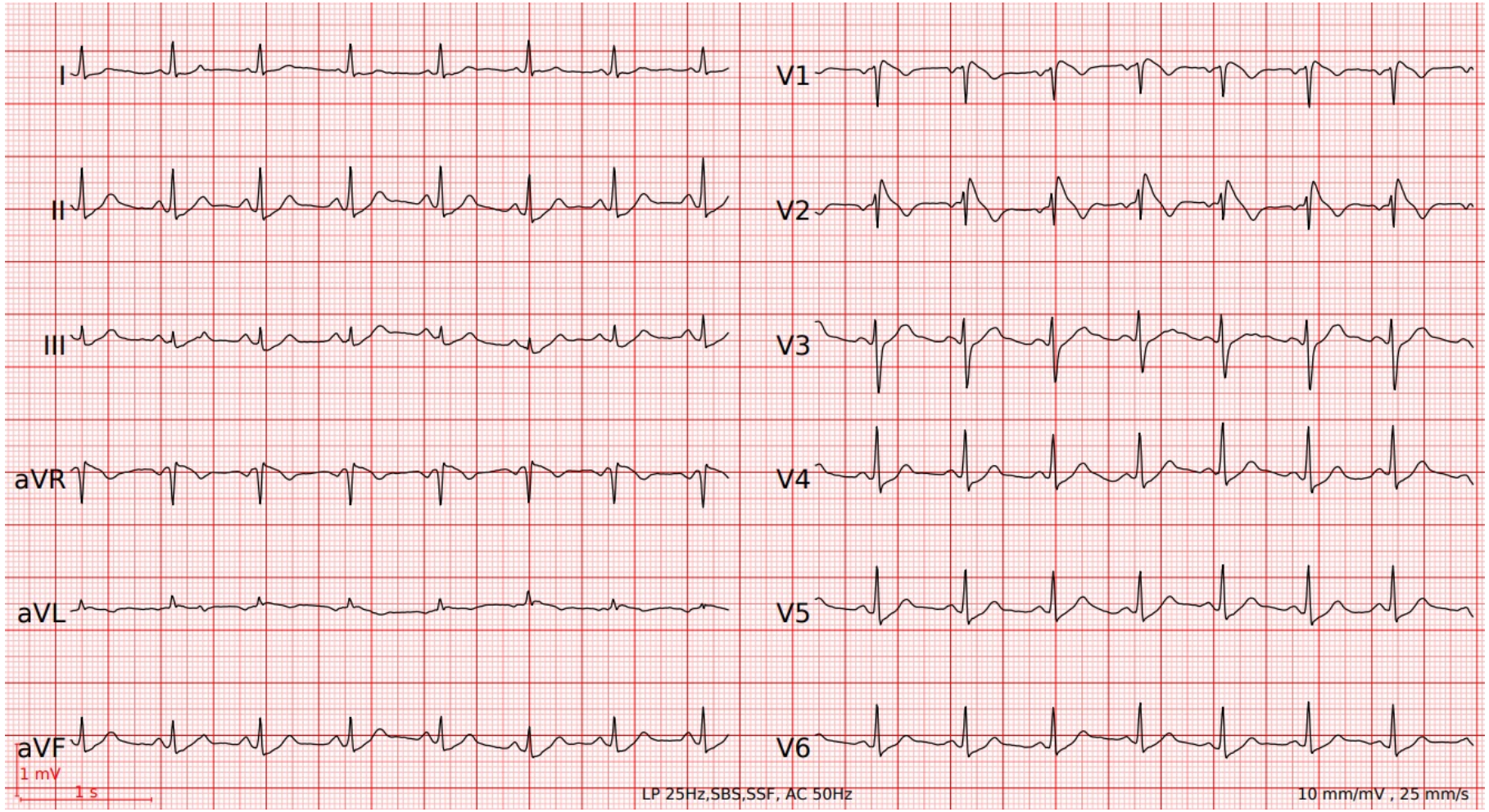


https://litfl.com/brugada-syndrome-ecg-library/

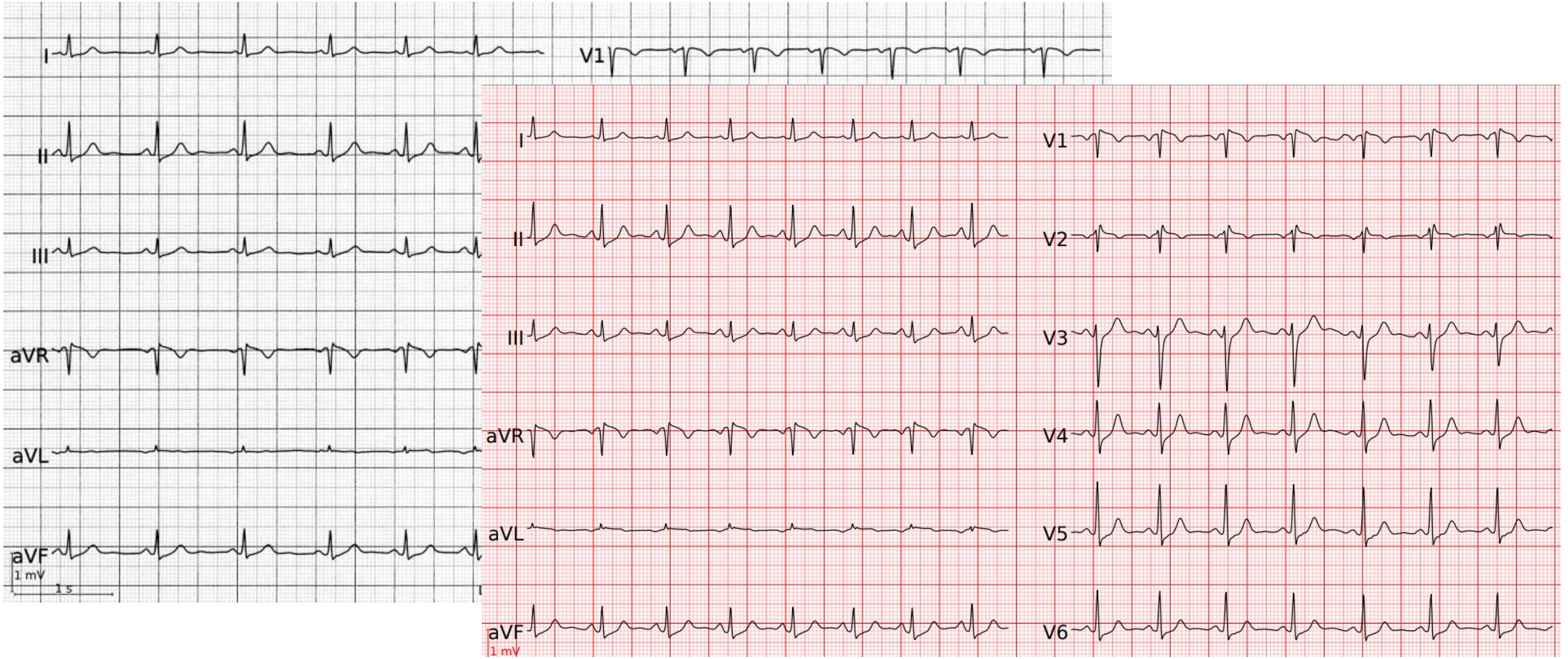
Test à l’ajmaline



Autre exemple, F 24 ans, T 39°



ECG de base



V1-V2 positionnés dans le 2è espace intercostale

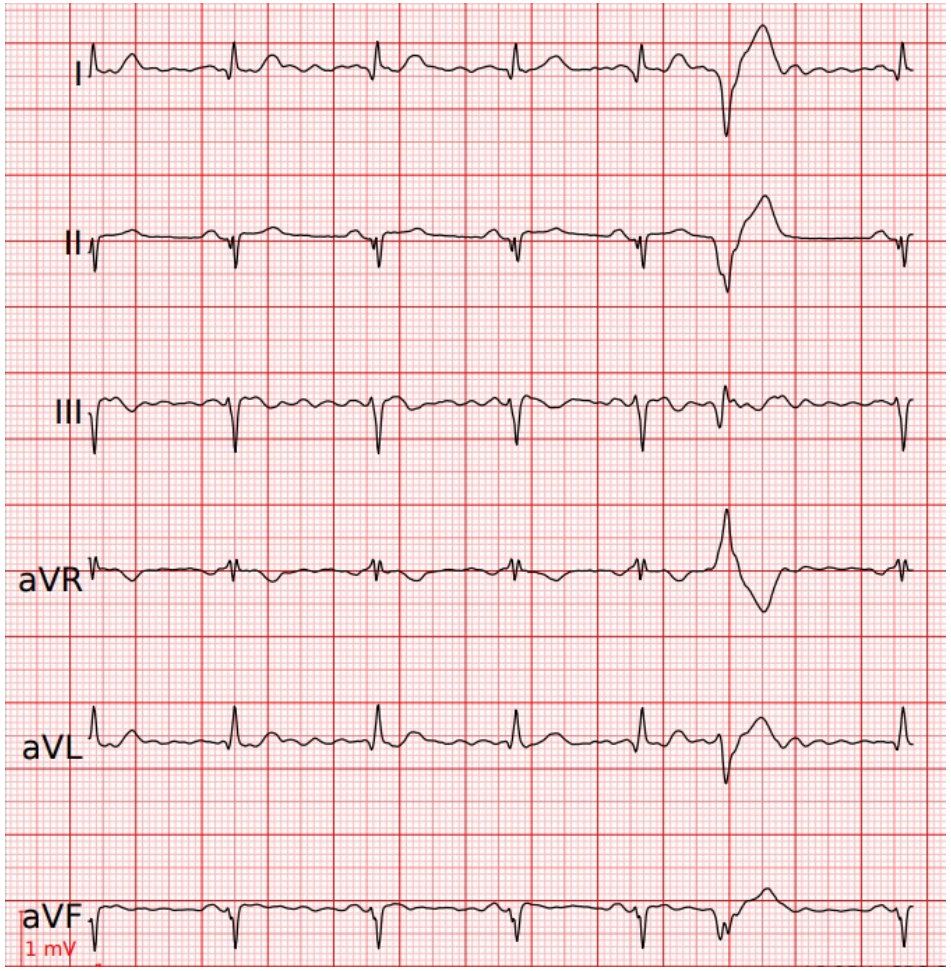
Brugada syndrom vs. pattern

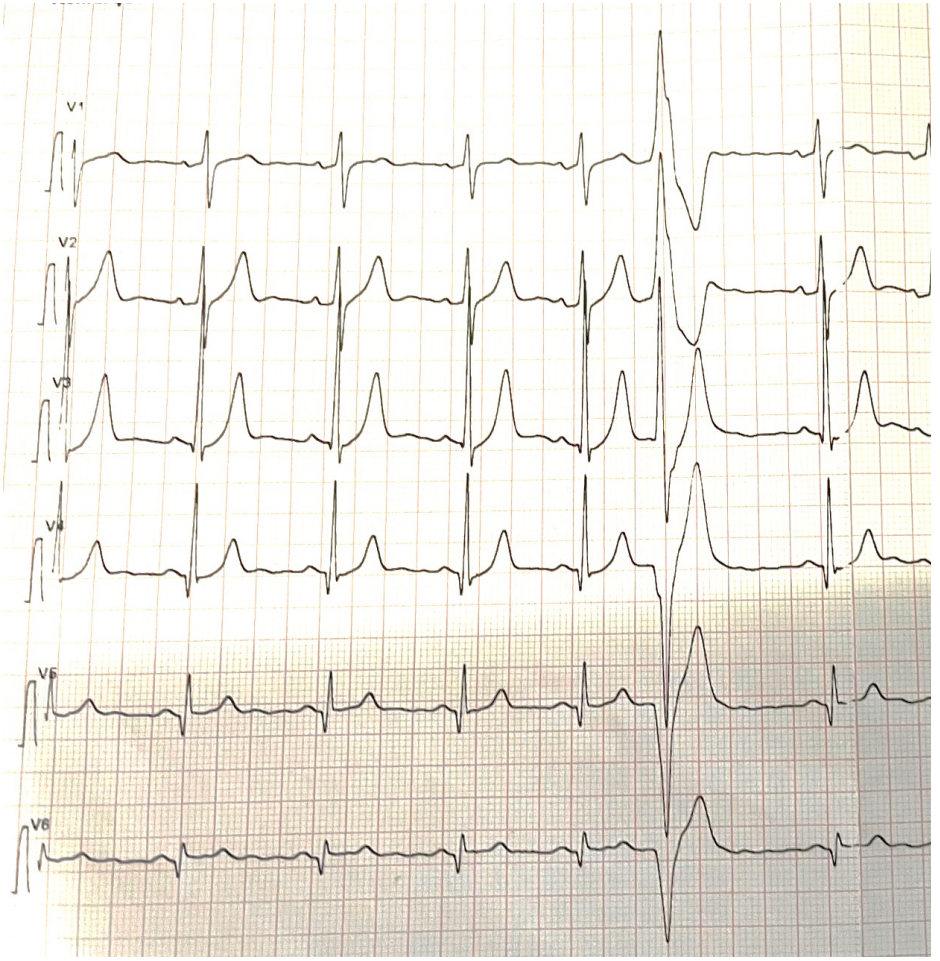
This ECG abnormality ***must*** be associated with one of the following ***clinical criteria*** to make the diagnosis:

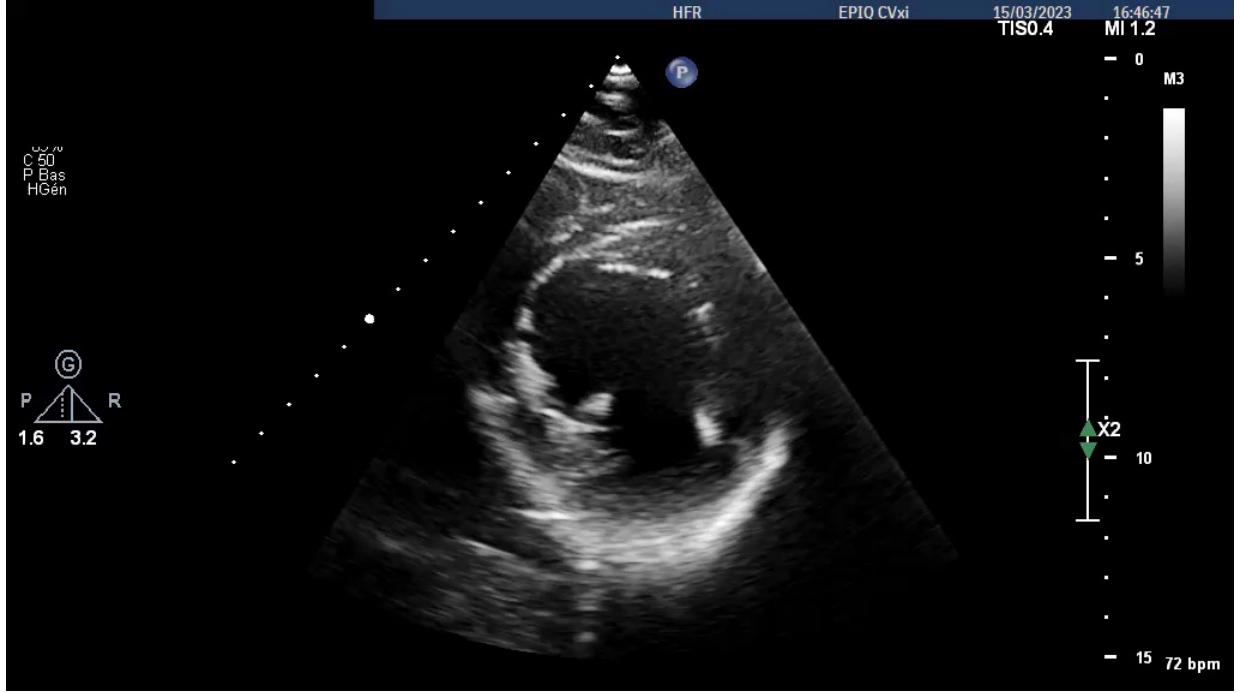
- Documented ventricular fibrillation (VF) or polymorphic ventricular tachycardia (VT).
- Family history of sudden cardiac death at <45 years old .
- Coved-type ECGs in family members.
- Inducibility of VT with programmed electrical stimulation .
- Syncope.
- Nocturnal agonal respiration.

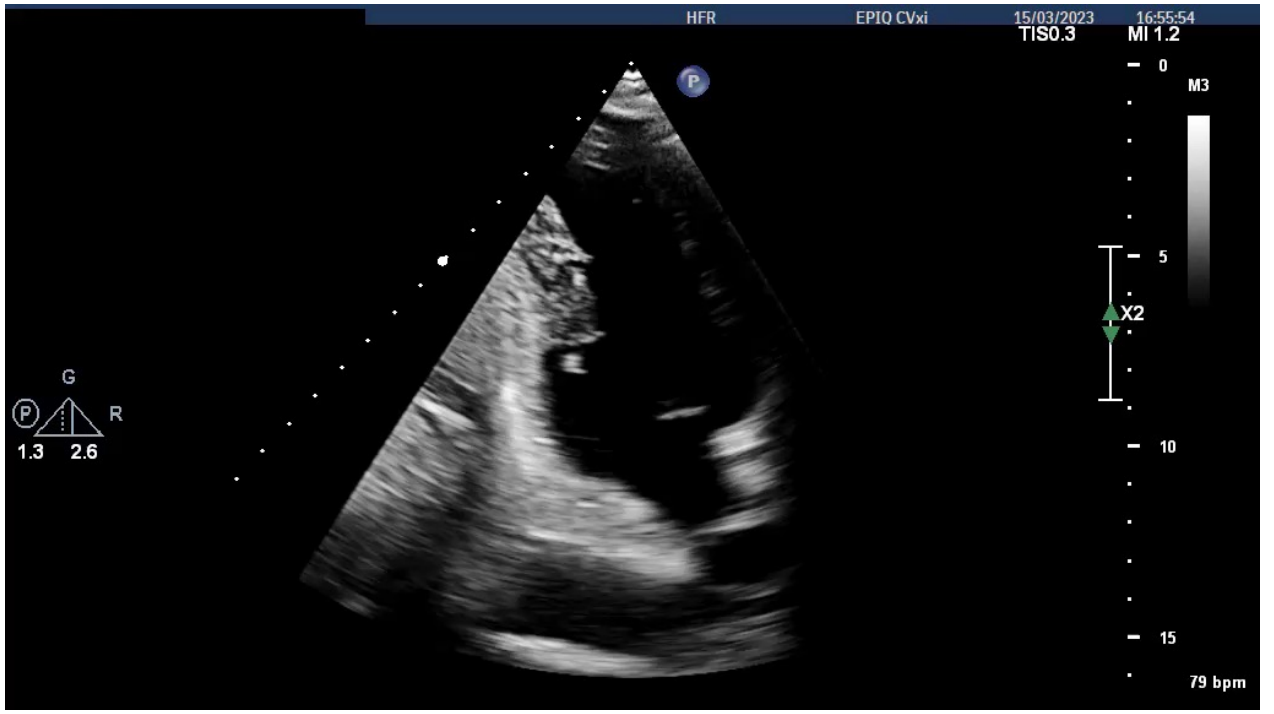
https://litfl.com/brugada-syndrome-ecg-library/

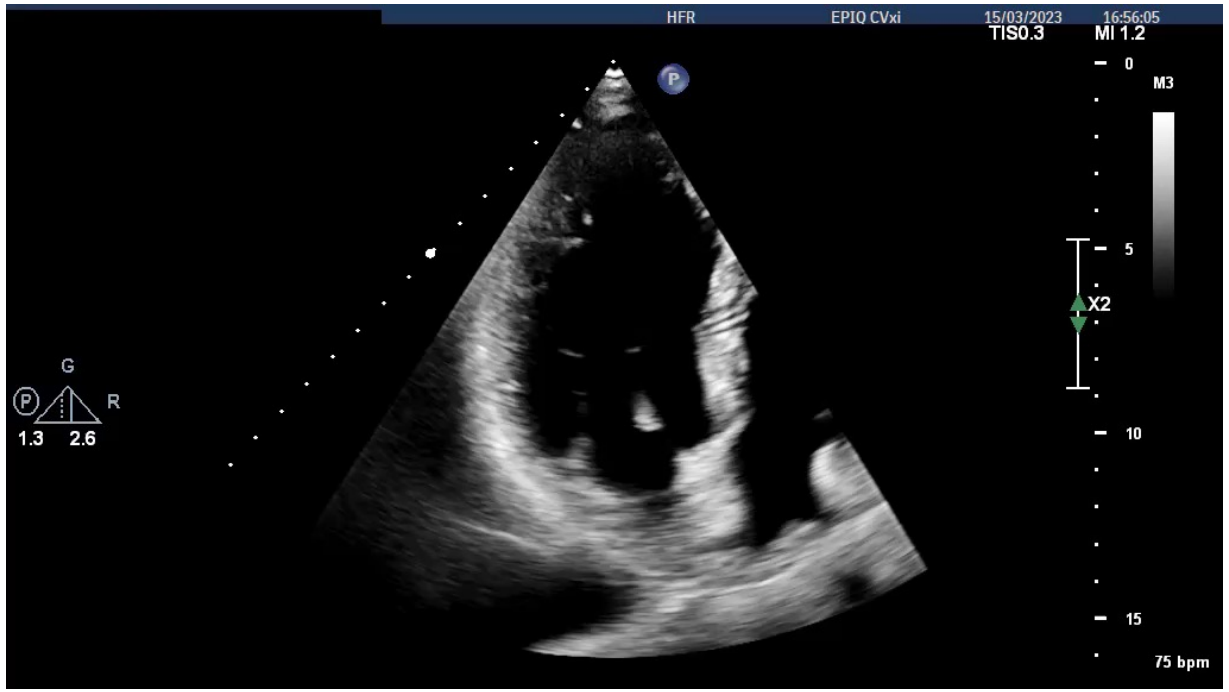
H, 50 ans, épigastralgies depuis 7 jours, vomissements ++






HFR
EPIQ CVxi
15/03/2023
16:46:47
TIS0.4
MI 1.2
M3
C 50
P Bas
HGén
G
P
R
1.6
3.2
X2
72 bpm


HFR
EPIQ CVxi
15/03/2023
16:55:54
TIS0.3
MI 1.2
M3
G
P
R
1.3
2.6
X2
79 bpm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EPIQ CVxi
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16:56:05
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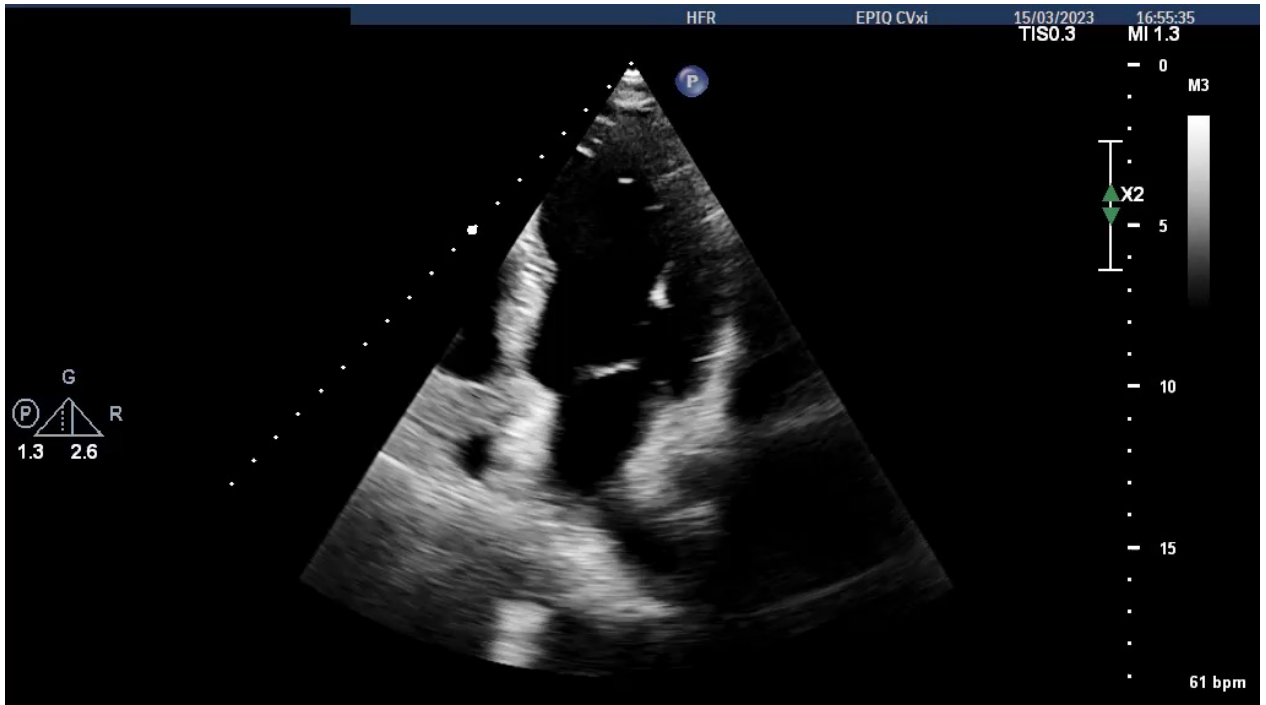
MI 1.2
M3
G
P
R
1.3
2.6
X2
75 bpm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EPIQ CVxi
15/03/2023
16:55:35
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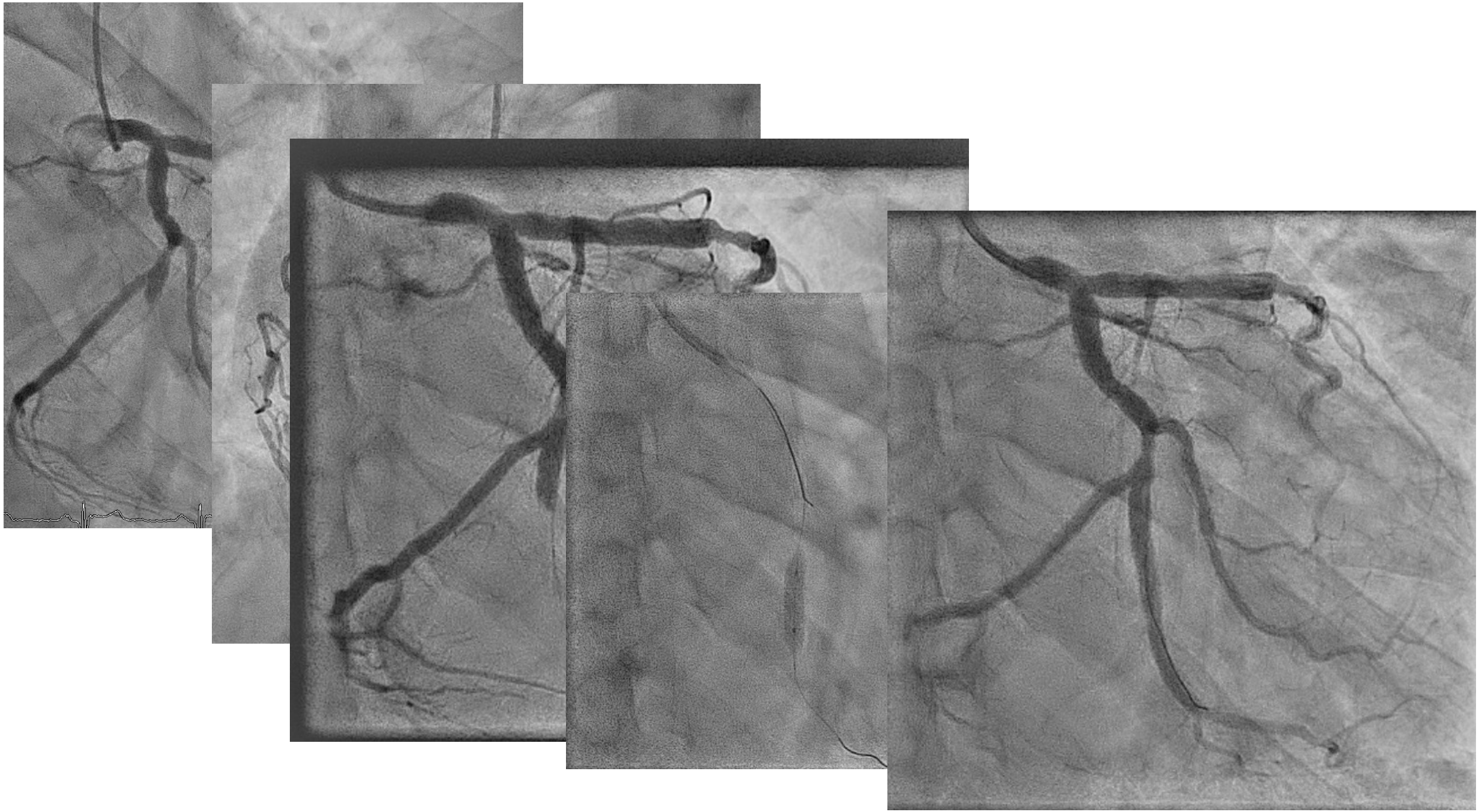
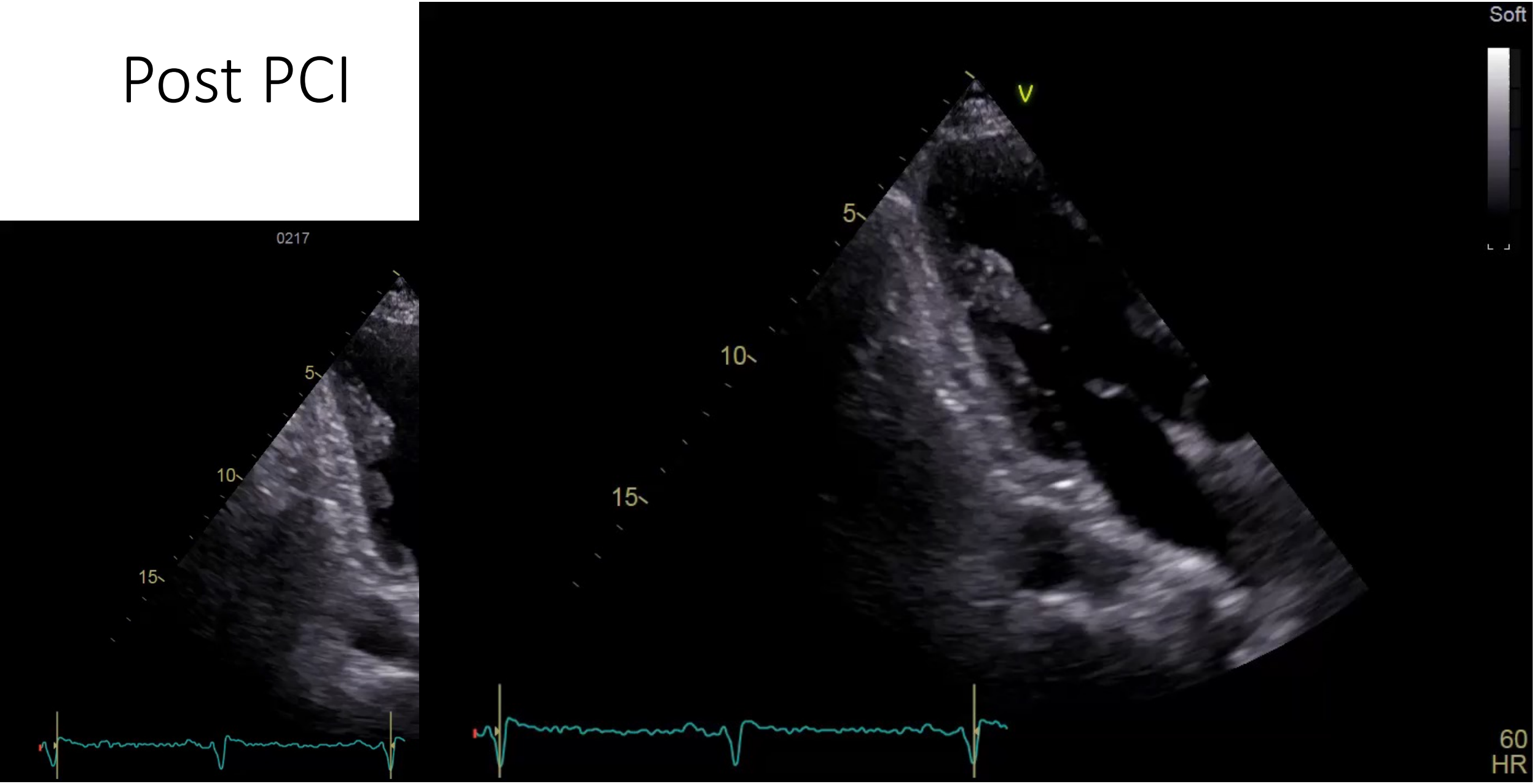
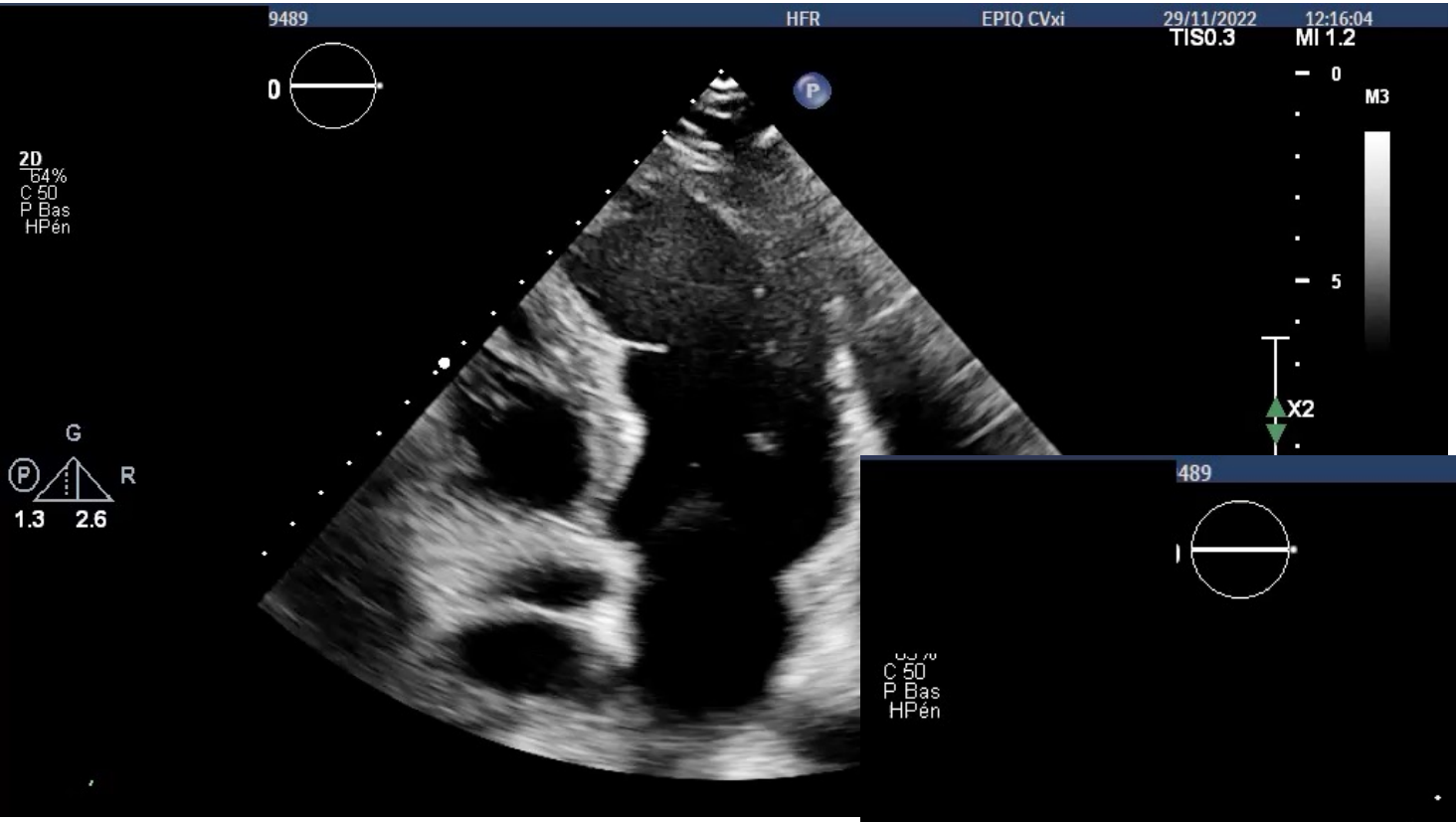
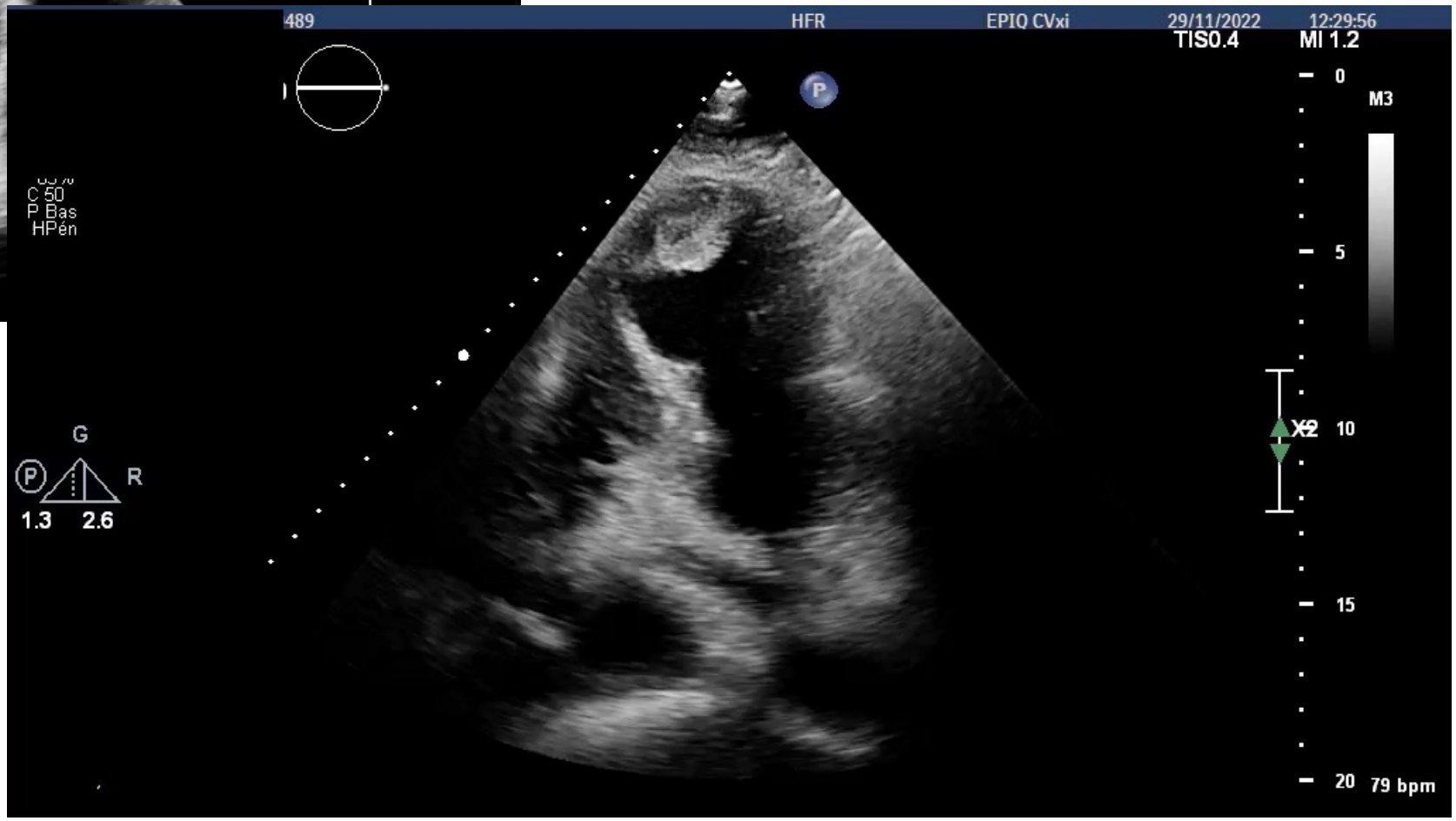
MI 1.3
M3
G
P
R
1.3
2.6
X2
61 bpm



Post PCI







Apical LV Thrombus after anterior MI