IC à FE préservée: de la physiopathologie au traitement

Insuffisance cardiaque à FE préservée en pratique clinique

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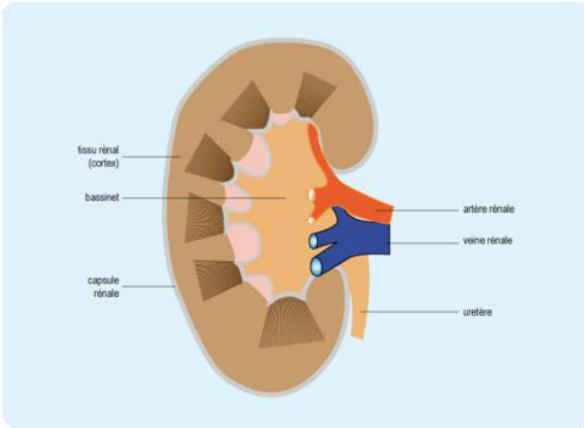
Déclaration de conflits d'intérêts

Pas de conflit d'intérêt

Plusieurs phénotypes….

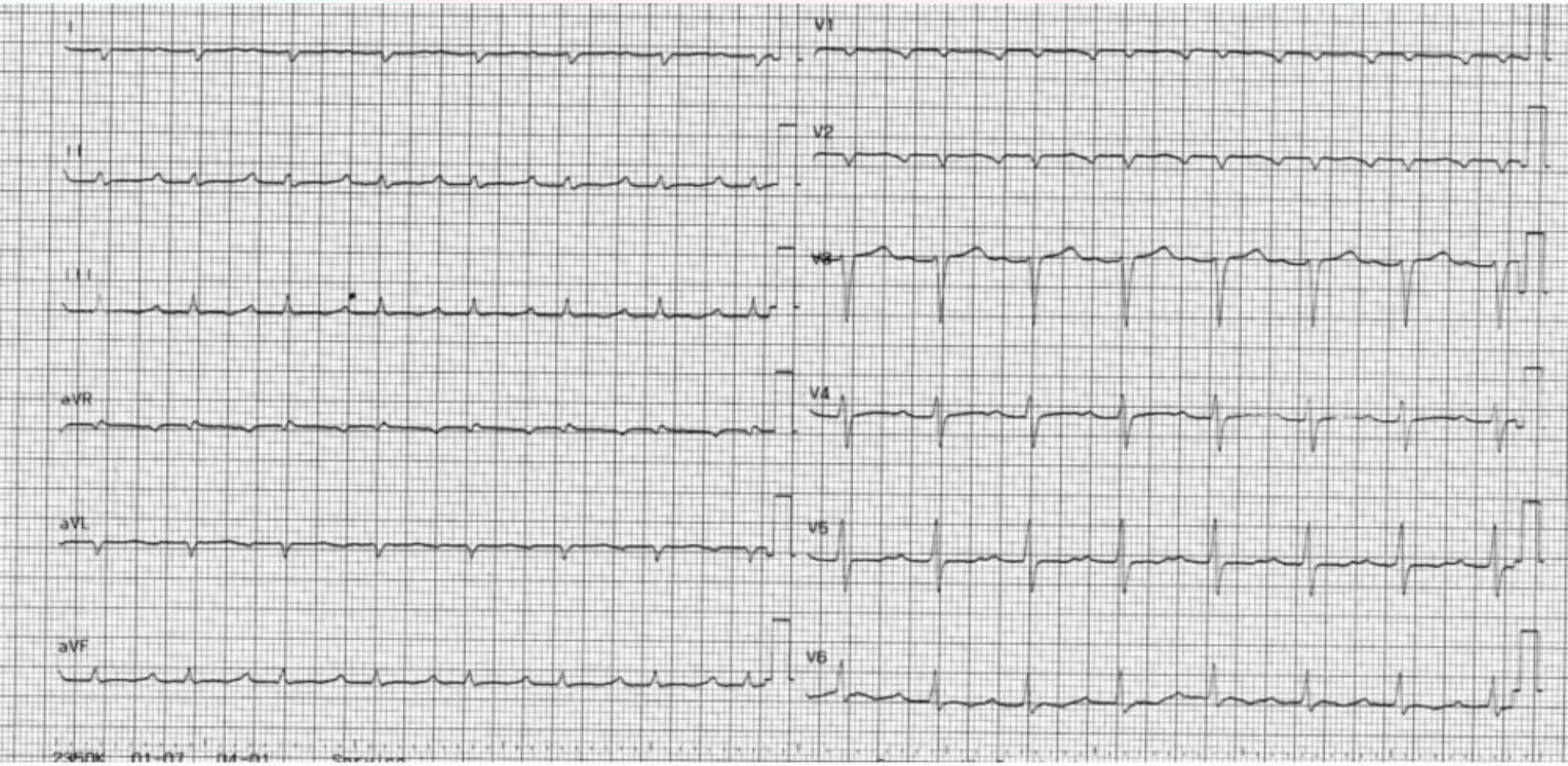
Patients with HFpEF are a heterogeneous group with various underlying aetiologies and pathophysiological abnormalities. Based on specific suspected causes, additional tests can be performed (*Web Table 4.4*).[71,88–94] However, they can only be recommended if the results might affect management.



Cas Clinique

- 46 ans
- FDRCV: HTA sous périndopril 5 mg/j
- Hypothyroïdie sous Levothyrox
- Dyspnée d'effort III NYHHA
- Douleur thoracique atypique
- Examen physique: normal à part PA=100/70 mmHg

ECG



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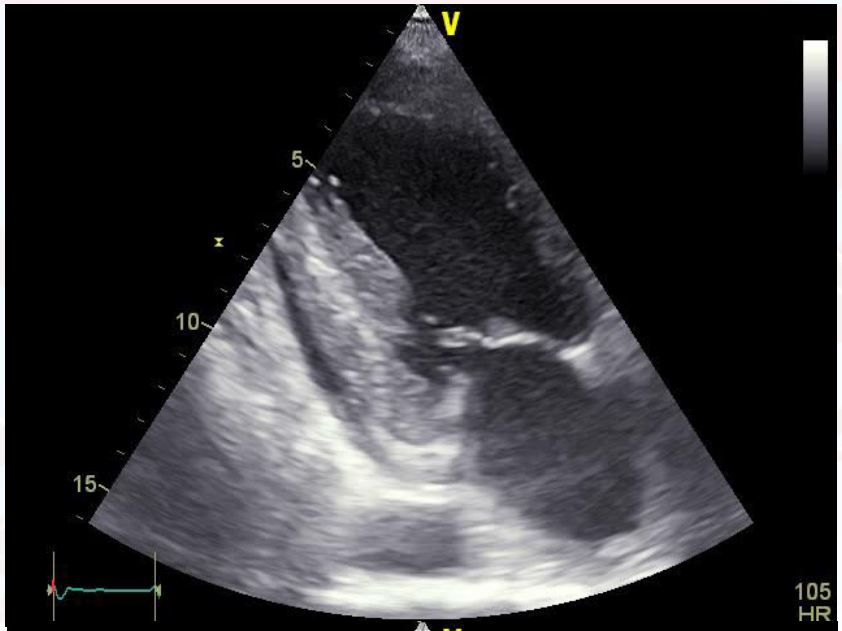
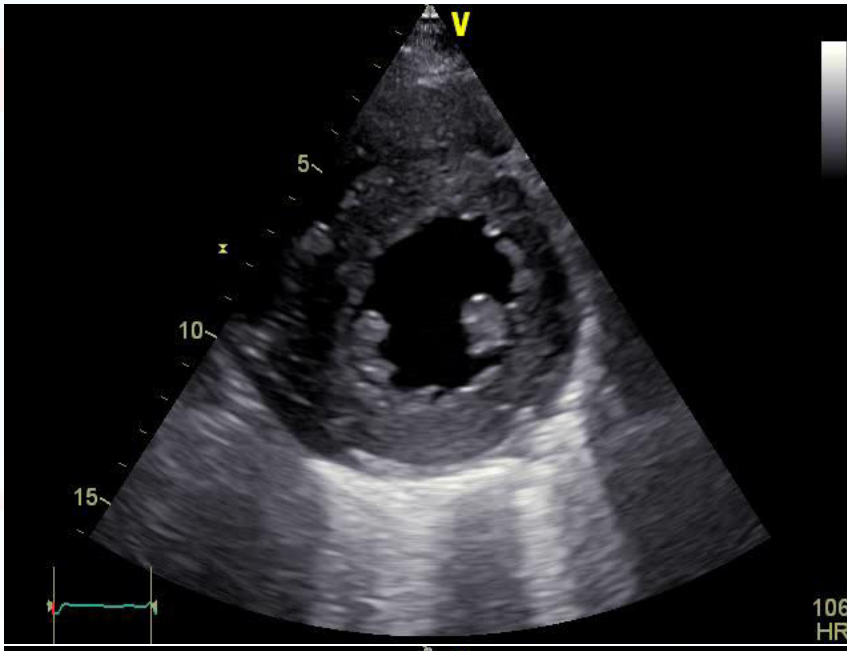
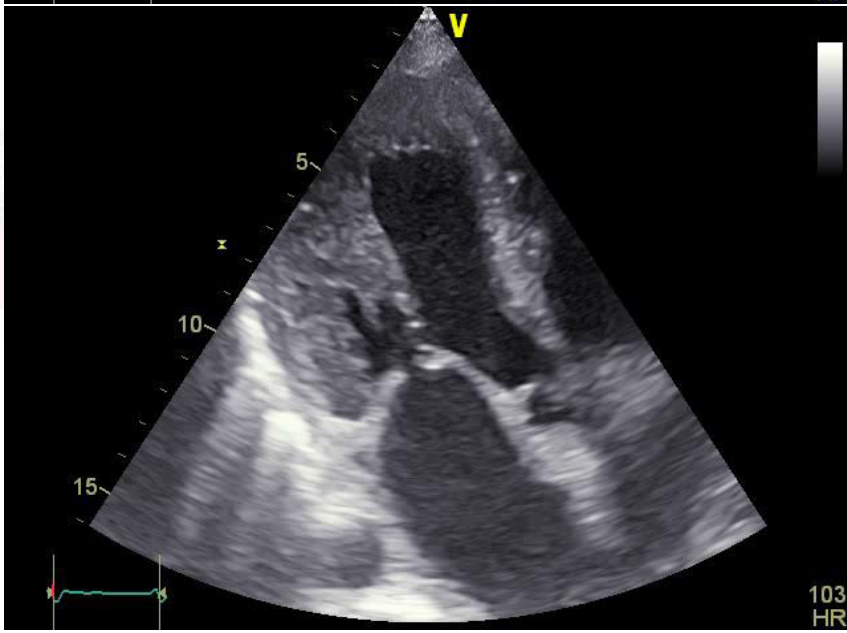
Biologie

- NFS: Hb=10,2 g/dl
- Créatinine: 92 umol/l
- Bilan thyroïdien normal
- Troponine= 0,06 ug/l
- Pro-BNP= 8211pg/l

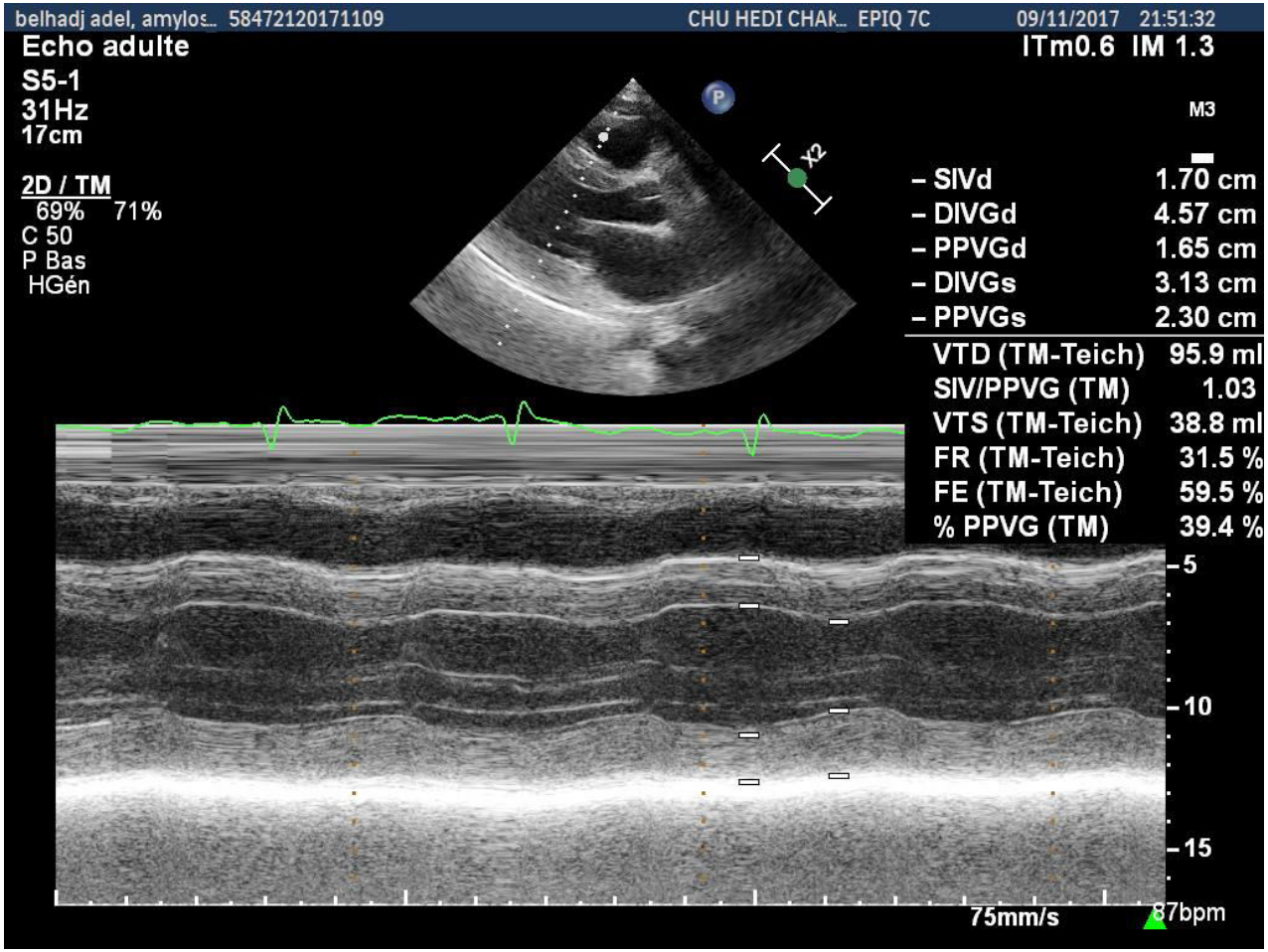
Echo-coeur Transthoracique





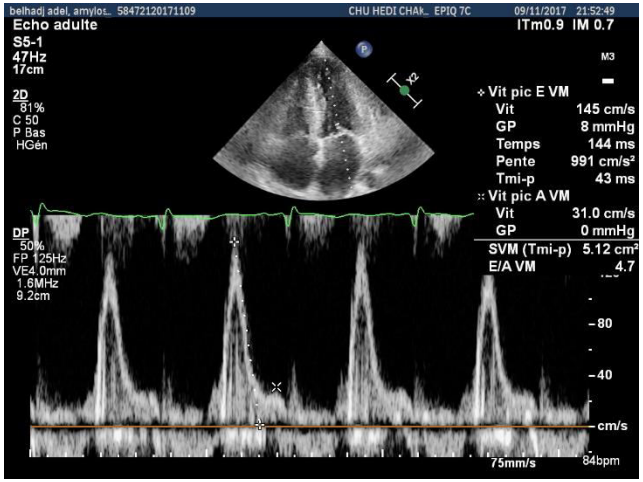


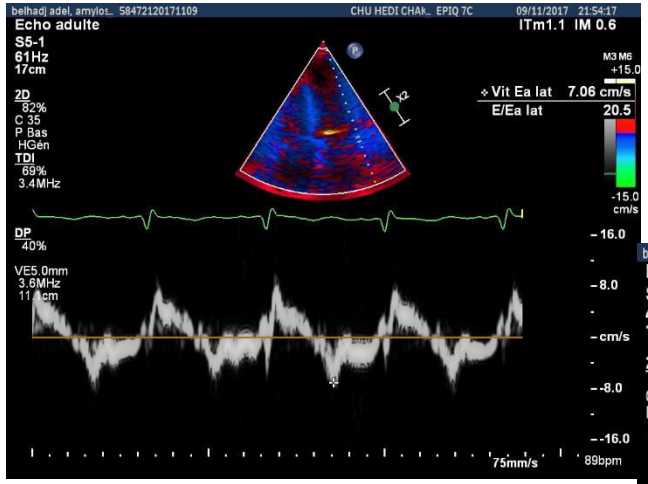
Echo-coeur Transthoracique

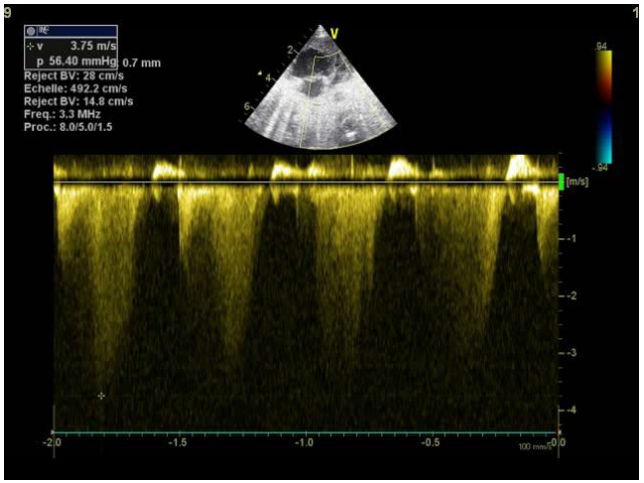


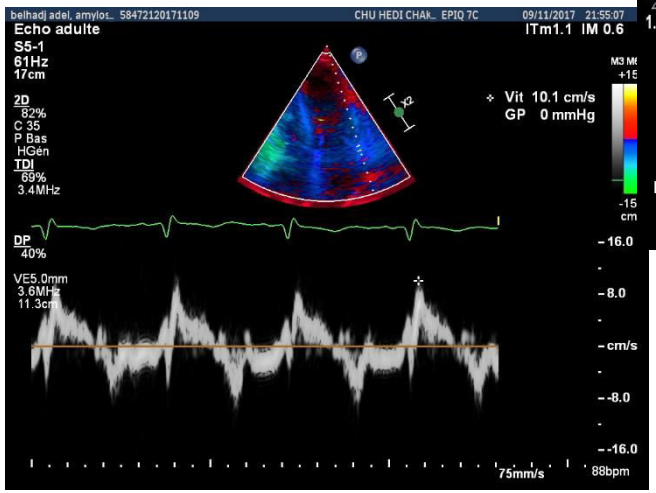
Masse VG= 180 g/m²

Etude de la fonction diastolique







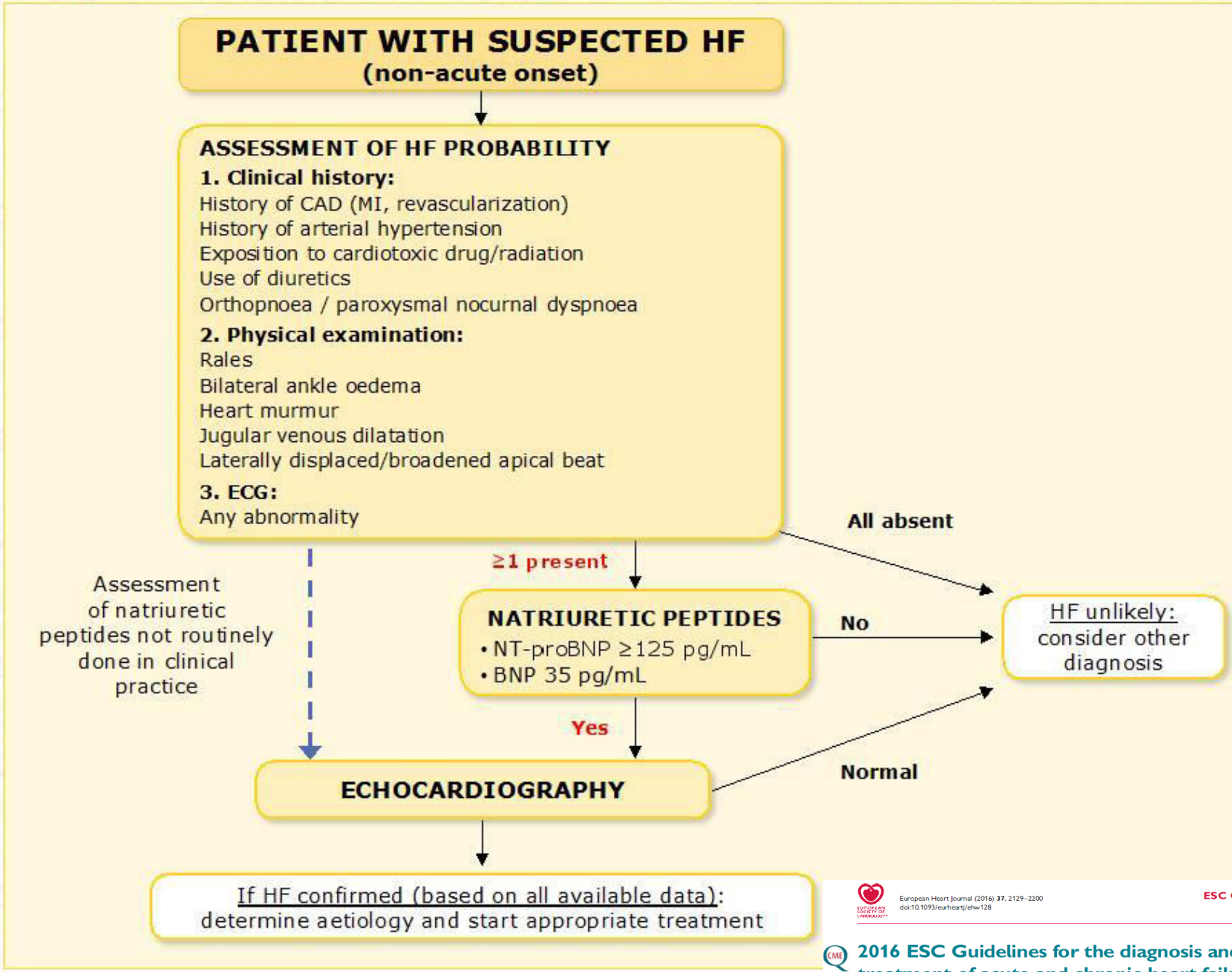


Volume OG 41 ml/m2

Résumé des données cliniques, biologiques et échocardiographiques….

- Dyspnée d'effort III
- ECG: Microvoltage
- FEVG=5O%
- Pro-BNP très élevé
- Anomalies structurelles: HVG, dilatation OG
- Anomalies fonctionnelles: Dysfonction diastolique

Diagnostic algorithm for a diagnosis of heart failure of non-acute onset



European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

Une nouvelle classification

Heart failure with preserved, mid-range and reduced EF

Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.
[b]BNP >35 pg/ml and/or NT-proBNP >125 pg/mL.

www.escardio.org/guidelines

European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

IC à FEVG Préservée

Diagnosis of HFpEF/HFmrEF

Signs (± symptoms) of HF

+

HFpEF: EF≥50%
HFmrEF: EF 40-49%

+

Structural abnormalities

LAVI
>34ml/m²

LVMI
>115g/m² (m)
>95 g/m² (f)

Functional abnormalities

E/e'$_{avg}$ ≥ 13

e' average (lateral-septal) < 9 cm/s

- Limited data (Unmet Need!)
- Cut-offs arbitrary
- More criteria; greater certainty of diagnosis
- Diastolic stress test?
- Invasive hemodynamic measurements?

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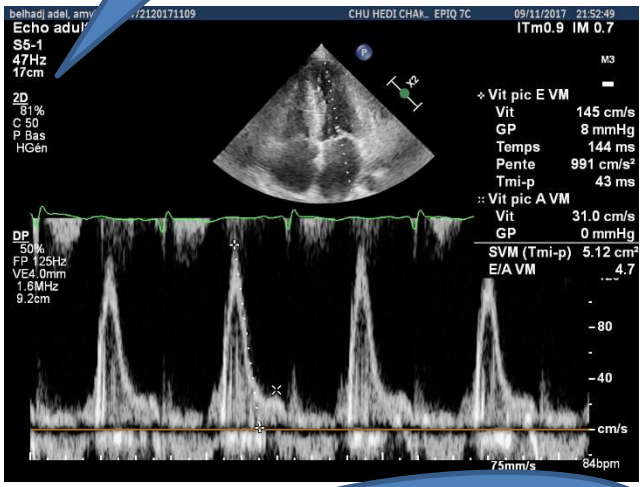
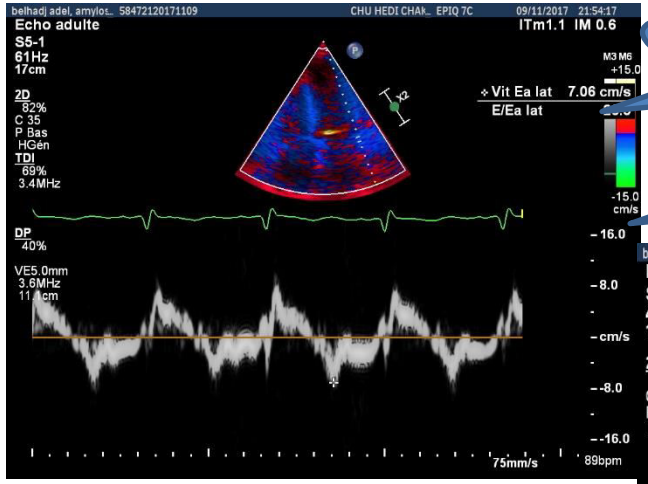
EUROPEAN SOCIETY OF CARDIOLOGY

Fonction diastolique: Au Total

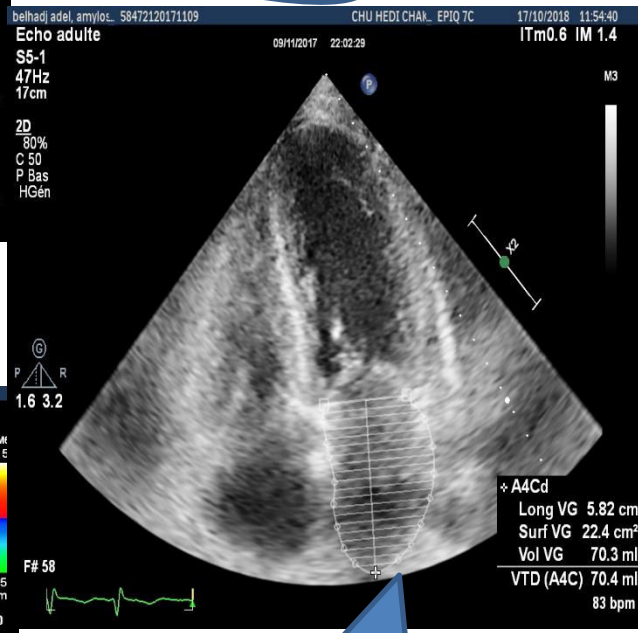
Profil Restrictif



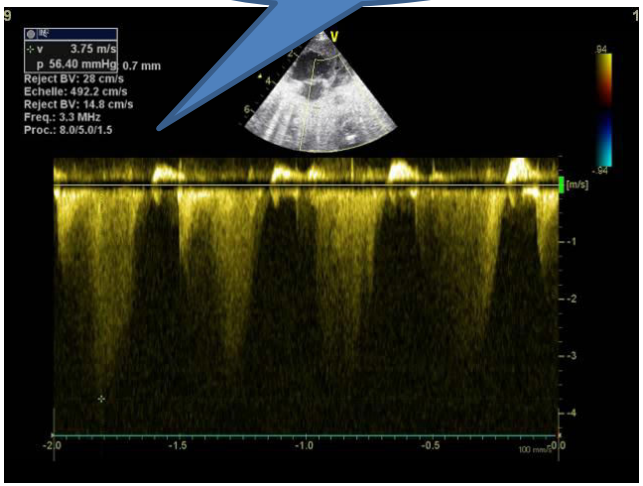


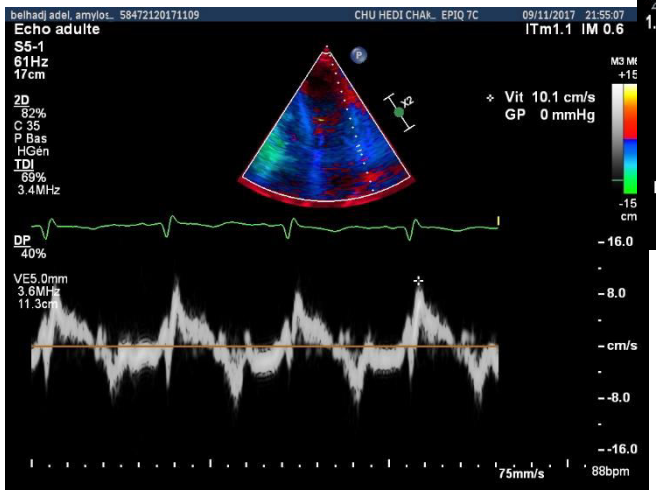
E'=7

E/E'13



Vmax IT=3,75 m/s





Volume OG>34 ml/m²

Étude de la fonction diastolique

European Heart Journal – Cardiovascular Imaging
doi:10.1093/ehjci/jew082

Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

Sherif F. Nagueh, Chair, MD, FASE[a1], Otto A. Smiseth, Co-Chair, MD, PhD[b2], Christopher P. Appleton, MD[c1], Benjamin F. Byrd III, MD, FASE[d1], Hisham Dokainish, MD, FASE[e1], Thor Edvardsen, MD, PhD[b2], Frank A. Flachskampf, MD, PhD, FESC[f2], Thierry C. Gillebert, MD, PhD, FESC[g2], Allan L. Klein, MD, FASE[h1], Patrizio Lancellotti, MD, PhD, FESC[i2], Paolo Marino, MD, FESC[j2], Jae K. Oh, MD[k1],

(J Am Soc Echocardiogr 2016;29:277-314.)

Keywords: Diastole, Echocardiography, Doppler, Heart failure

e’ septal < 7 cm/s

e’ latéral < 10 cm/s

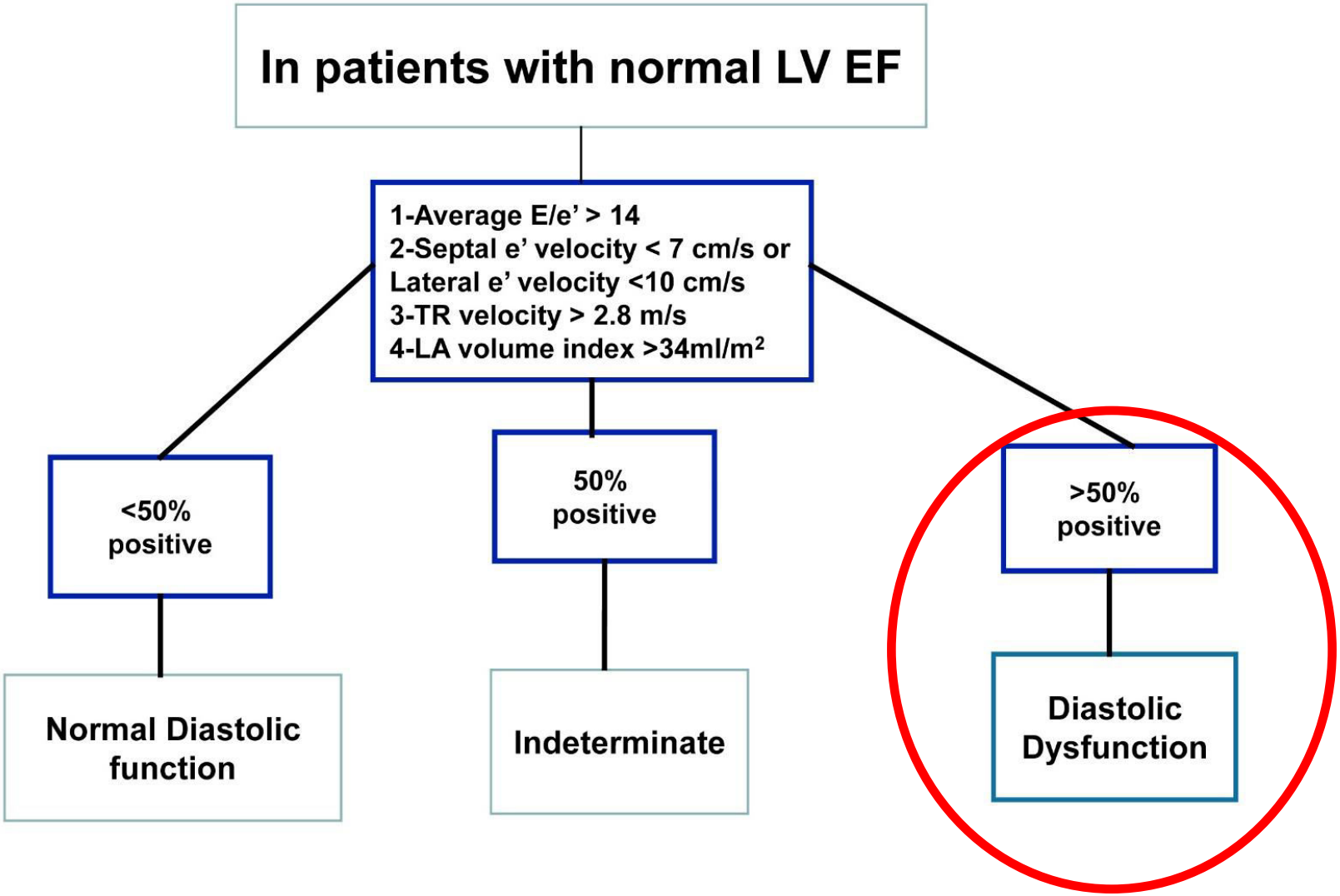
Average E/e’ > 14

LA vol > 34ml/m²

TR > 2.8 m/s

Key Points

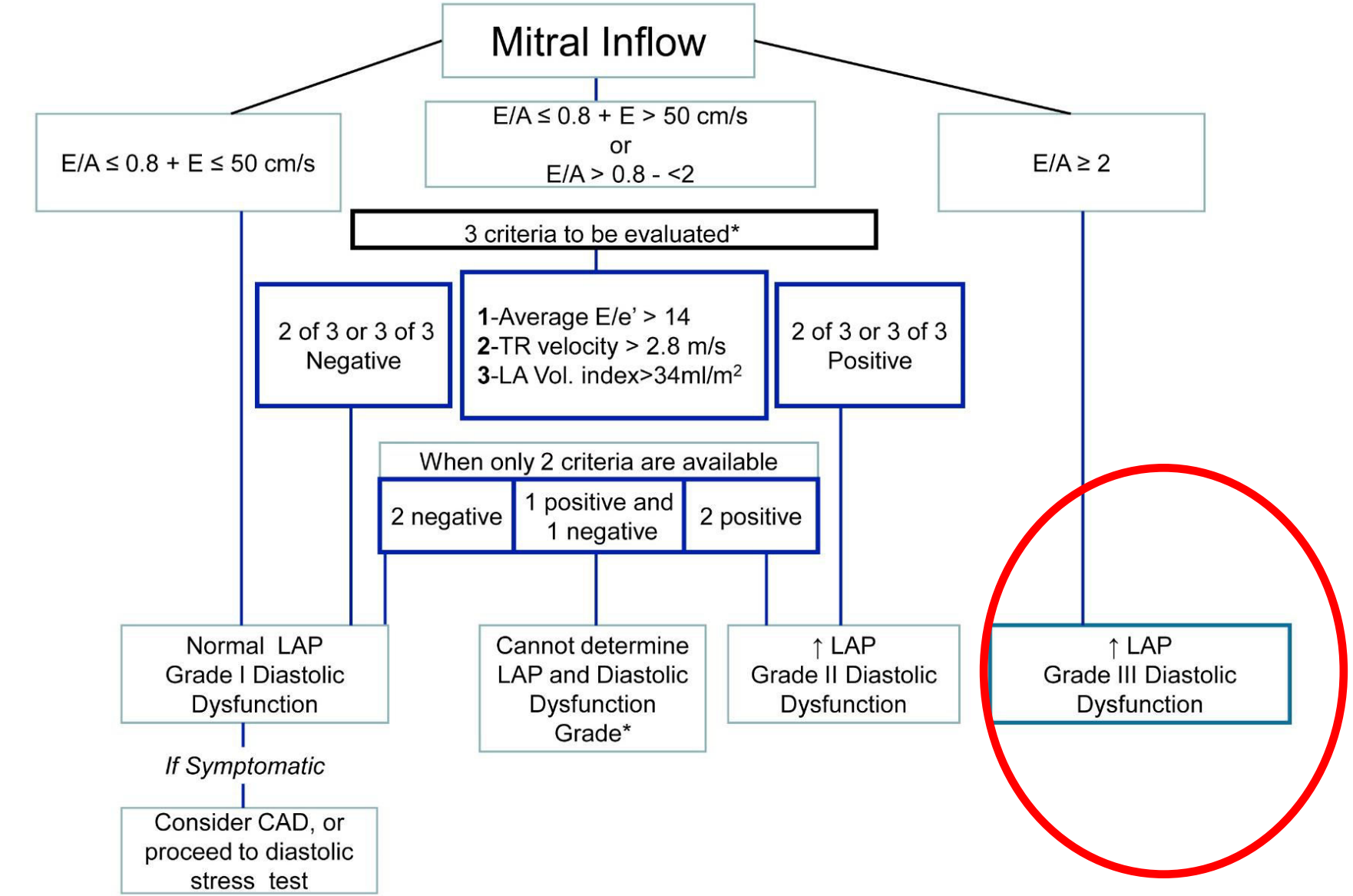
1. The four recommended variables for identifying diastolic dysfunction and their abnormal cutoff values are annular e′ velocity: septal e′ < 7 cm/sec, lateral e′ < 10 cm/sec, average E/e′ ratio > 14, LA volume index > 34 mL/m^2, and peak TR velocity > 2.8 m/sec.
2. LV diastolic function is normal if more than half of the available variables do not meet the cutoff values for identifying abnormal function. LV diastolic dysfunction is present if more than half of the available parameters meet these cutoff values. The study is inconclusive if half of the parameters do not meet the cutoff values.



Dysfonction diastolique

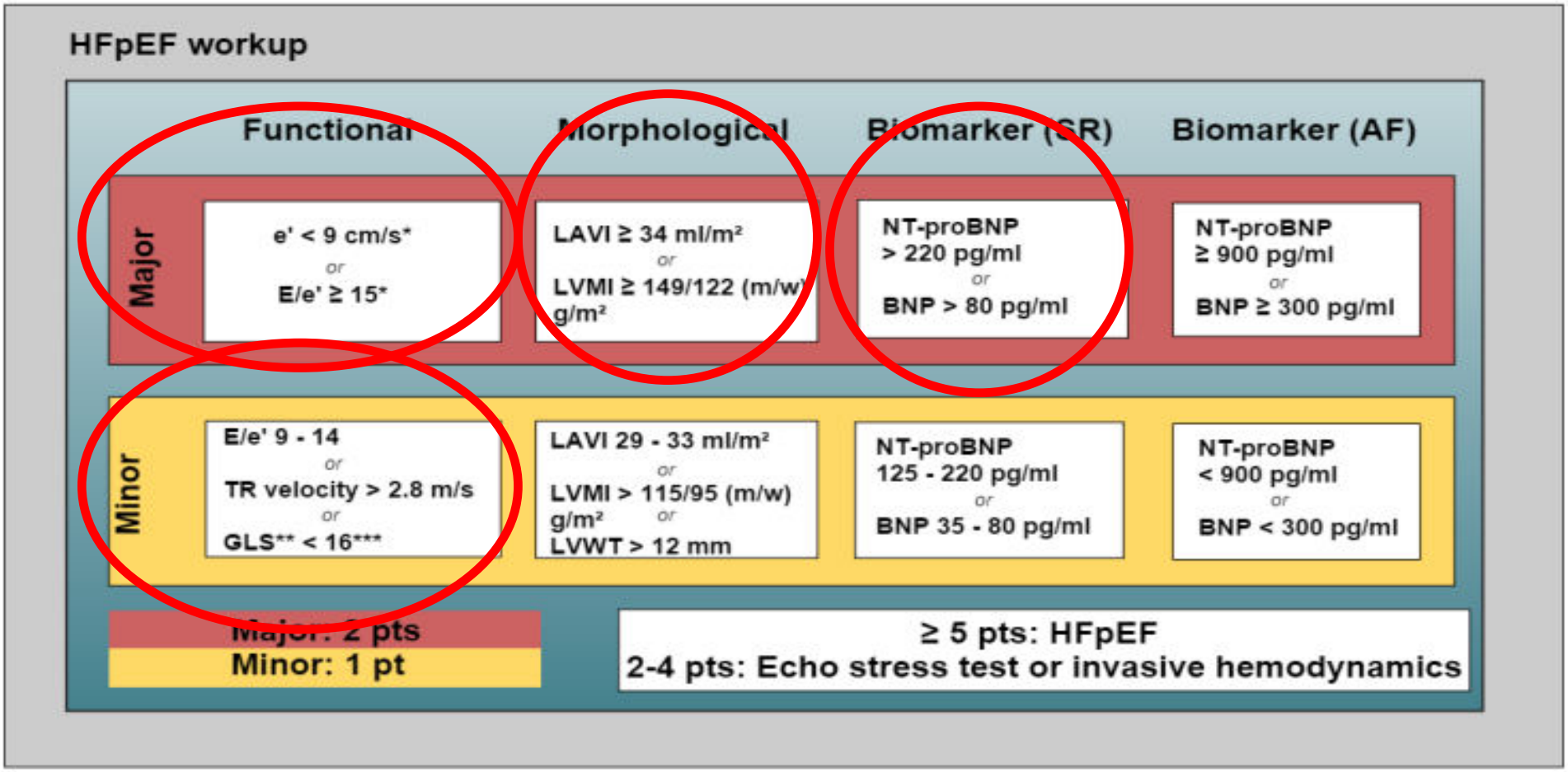
Nagueh et al J Am Soc Echocardiogr 2016 29, 277-314

Algorithme d'Evaluation des PRVG: FEVG réduite ou Maladie du myocarde avec FEVG préservée



(* : LAP indeterminate if only 1 of 3 parameters available. Pulmonary vein S/D ratio <1 applicable to conclude elevated LAP in patients with depressed LV EF)

Nagueh et al J Am Soc Echocardiogr 2016 29, 277-314



* average from septal and lateral e'
** LV global longitudinal strain
*** depending on software package

Score ≥ 5: IC à FE préservée

E Donal

Etiologie???

Diverse aetiology of hypertrophic cardiomyopathy

MYL3
TPM1
TNN13
TNNT3
MYH7
MYBPC3

Sarcomeric protein gene mutation 40-60%

Unknown ~ 25-30%

~ 5-10%

The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes.

Other genetic and non-genetic causes

- **Inborn errors of metabolism**
  Glycogen storage diseases:
  - Pompe
  - Danon
- **AMP-Kinase (PRKAG2)**
- **Carnitine disorders**
- **Lysosomal storage diseases**
  - Anderson-Fabry
- **Neuromuscular diseases**
  - Friedreich's ataxia
  - FHL1
- **Mitochondrial diseases**
  - MELAS
  - MERFF
- **Malformation Syndromes**
  - Noonan
  - LEOPARD
  - Costello
  - CFC
- **Amyloidosis**
  - Familial ATTR
  - Wild type TTR (senile)
  - AL amyloidosis
- **Newborn of diabetic mother**
- **Drug-induced**
  - Tacrolimus
  - Hydroxychloroquine
  - Steroids

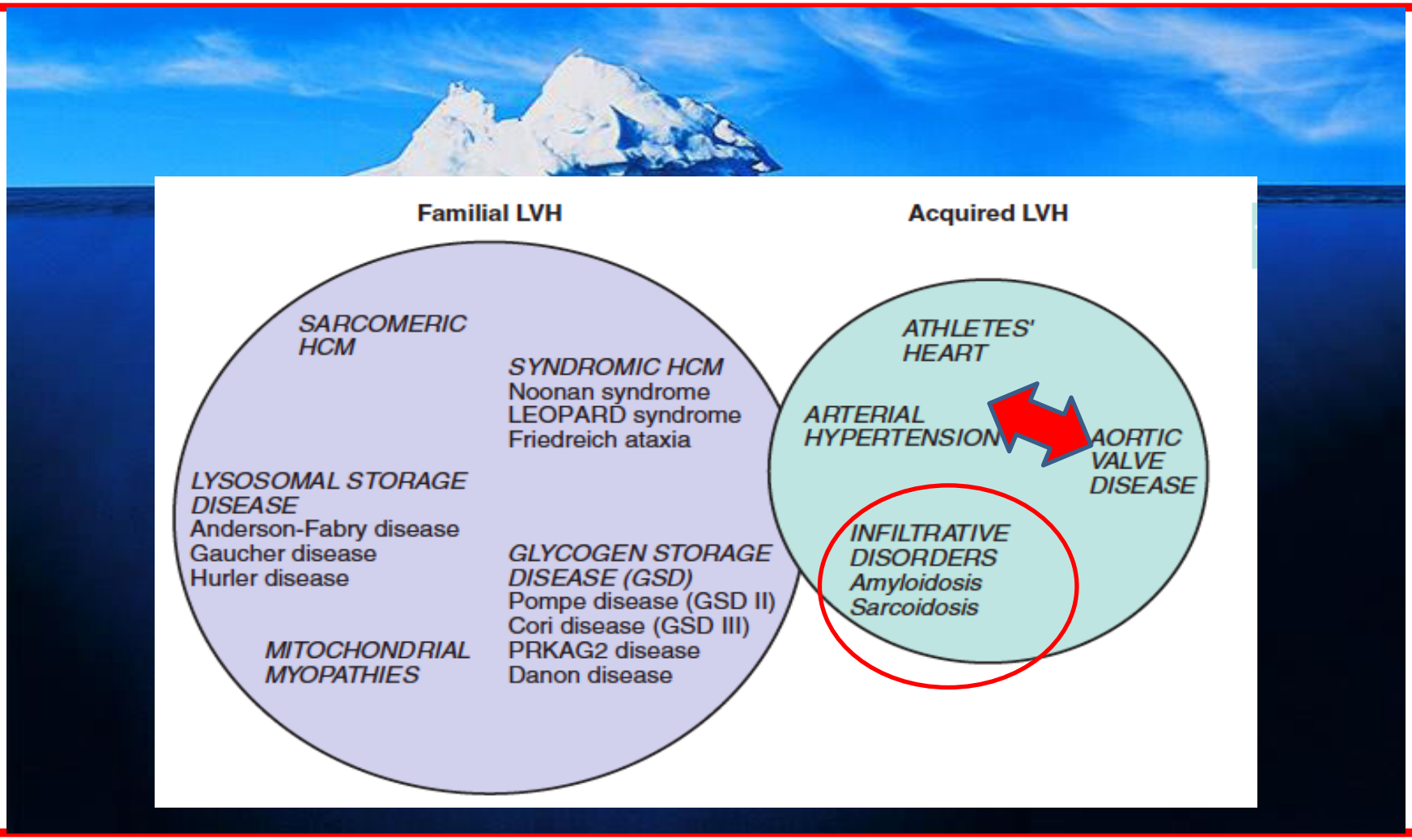
European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Echocardiographie

Pas de signes échocardiographiques spécifiques de la CMH sarcomérique

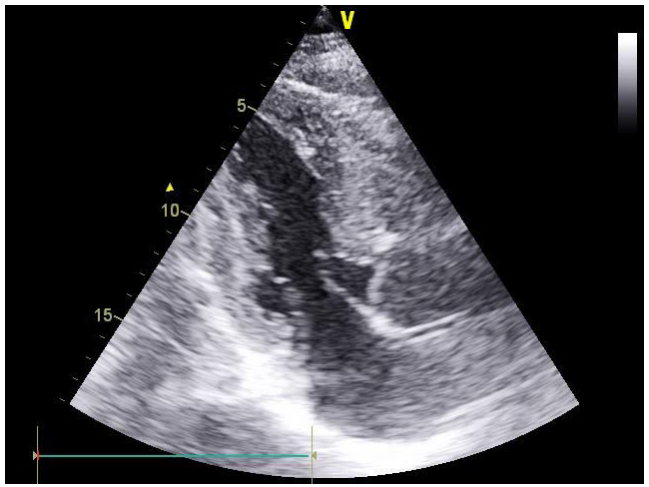
Pas de signes échocardiographiques spécifiques de la CMH non sarcomérique

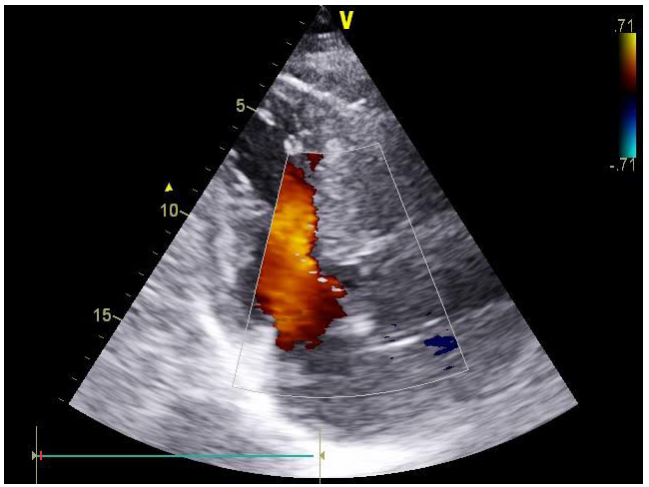
Plusieurs pathologies miment la CMH



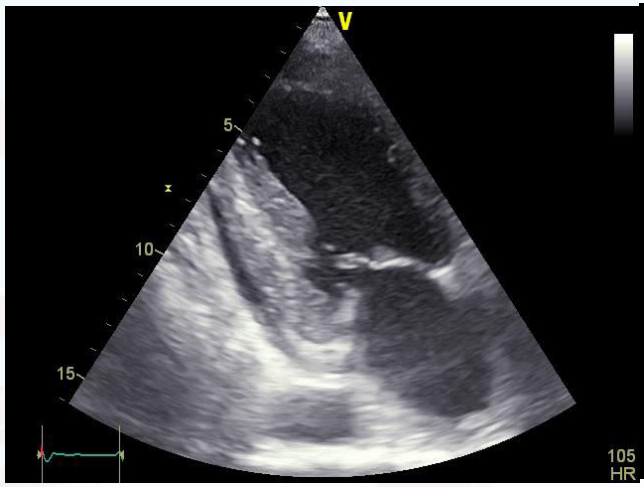
ASE comprehensive' text book

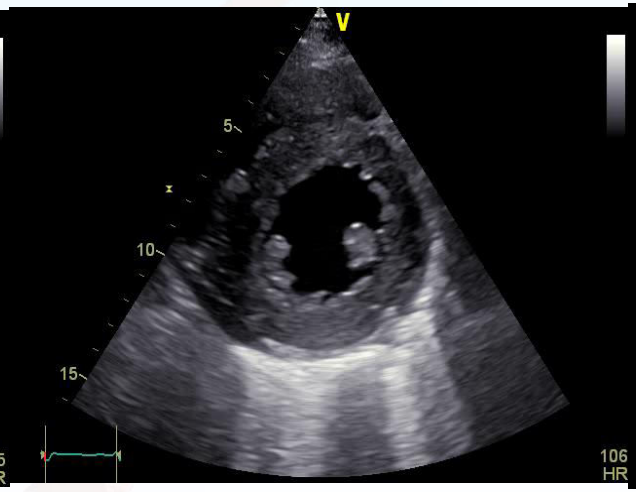
HVG asymétrique +++ (+) obstruction VG et anomalies valvulaires mitrales sont suggestives de CMH primitive sarcomérique

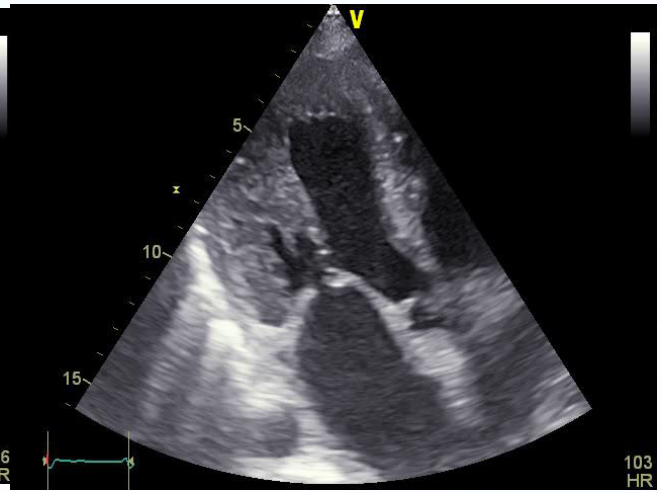


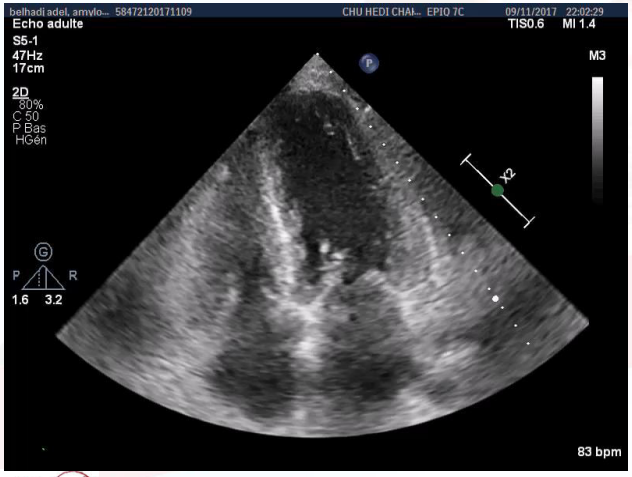


Echo-coeur Transthoracique









- Cardiomyopathie concentrique homogène
- Tout petit peu d'épanchement péricardique

→ **Maladie de surcharge**

1er lieu Amylose

(Altération modérée de la FeVG, Hypertrophie VD, Dilatation biauriculaire, profil restrictif)

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Société Tunisienne de Cardiologie & de Chirurgie Cardio-Vasculaire

AMYLOSE : “TRIADE”

- Hypertrophie bi-ventriculaire
- Profil restrictif: E/A>2
- Epanchement péricardique

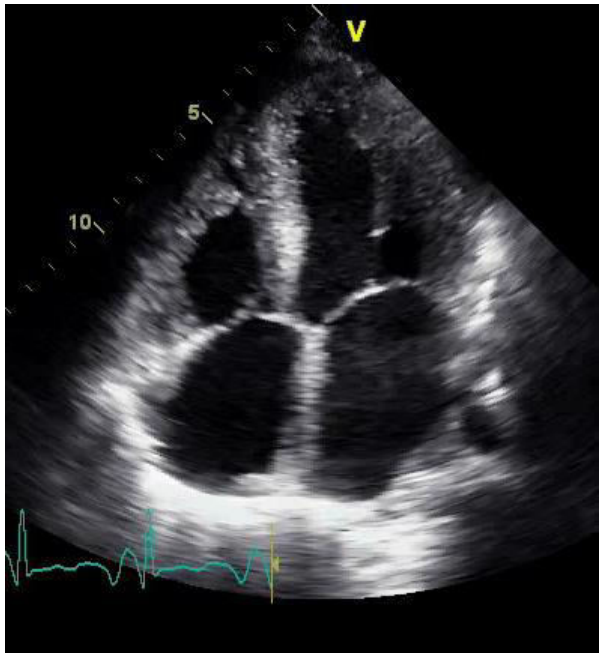
TOO LATE…

Amylose cardiaque: Echo-morphologie

Thickened LV walls ≥12mm

Thickened, aortic, mitral and tricuspid valves

Normal/small ventricular cavity sizes



Thickened RV free wall ≥ 5 mm

Thickened interatria septum

Atria dilation

Pericardial effusion

Mohty D, *Arch CardioVas Dis 2013 Oct;106(10):528-40*

Amylose: il faut y penser !!!

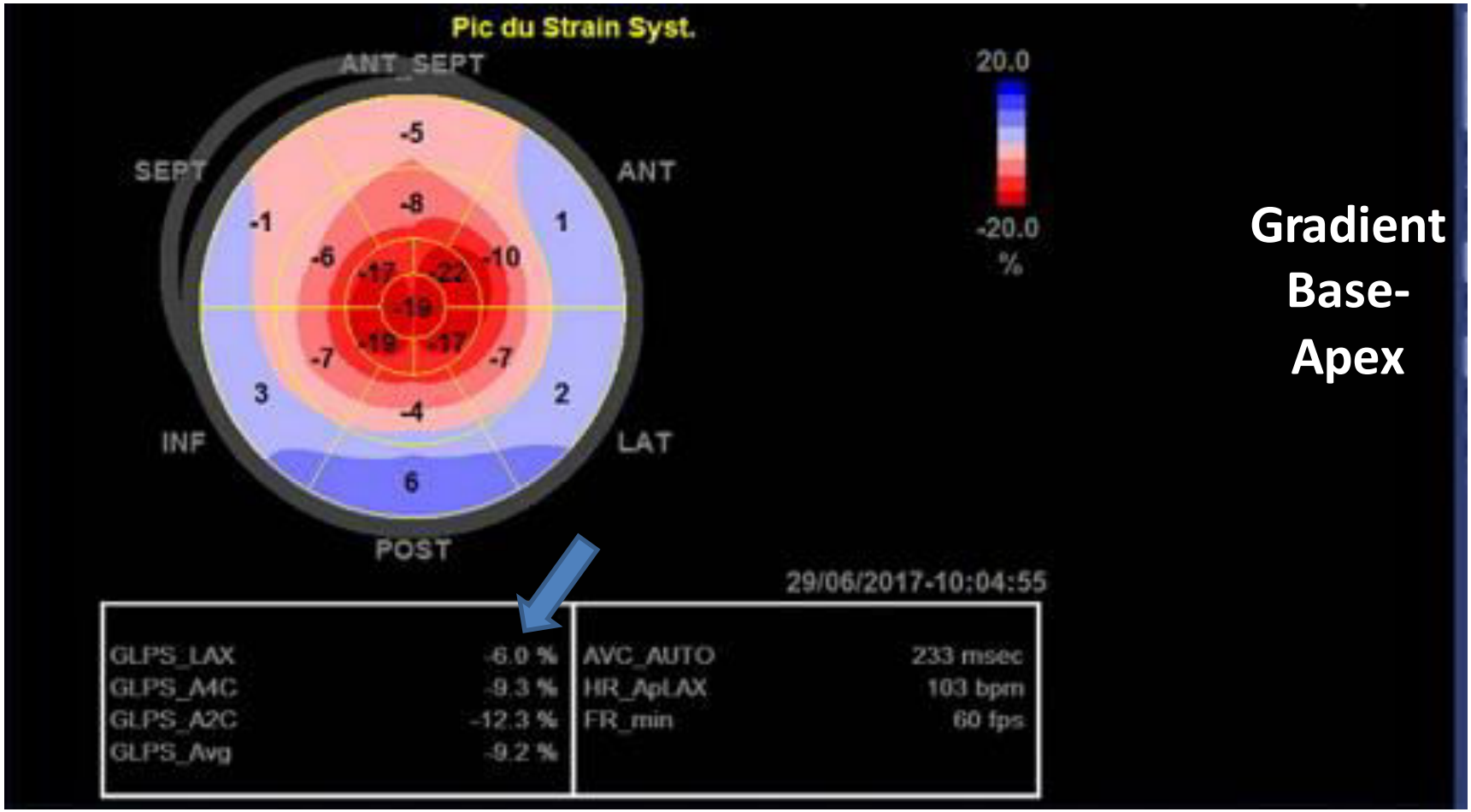
Echocardiographic features that suggest specific aetiologies

Finding	Specific diseases to be considered
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion.	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2-D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

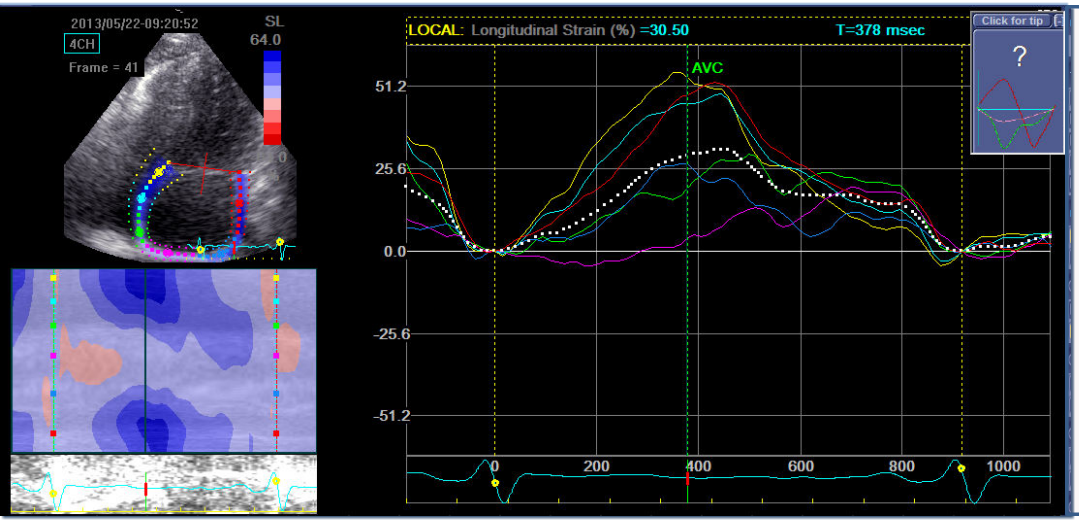
PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase;

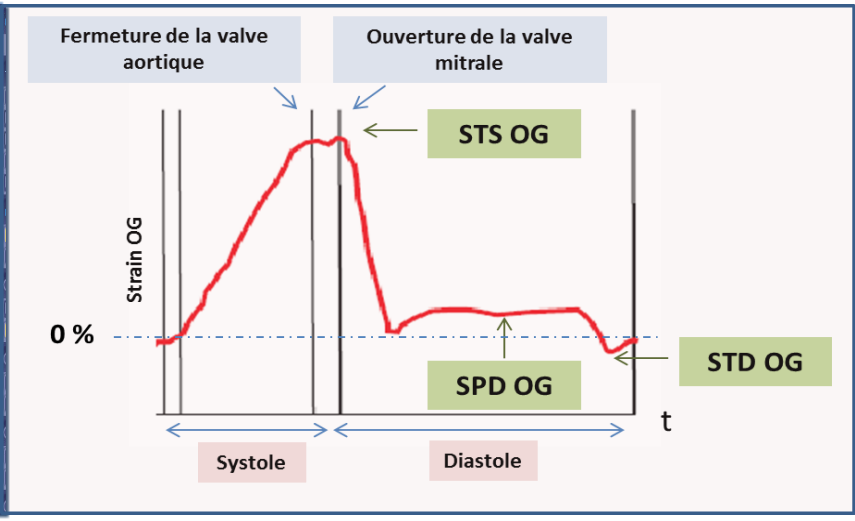
European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Strain longitudinal altéré
Suspect d'amylose cardiaque



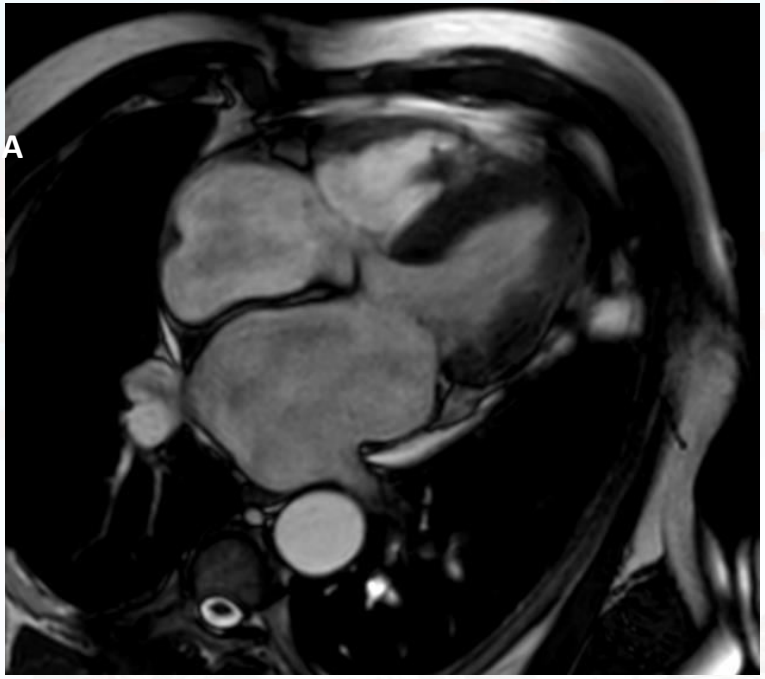
Dysfonction diastolique (Strain OG)

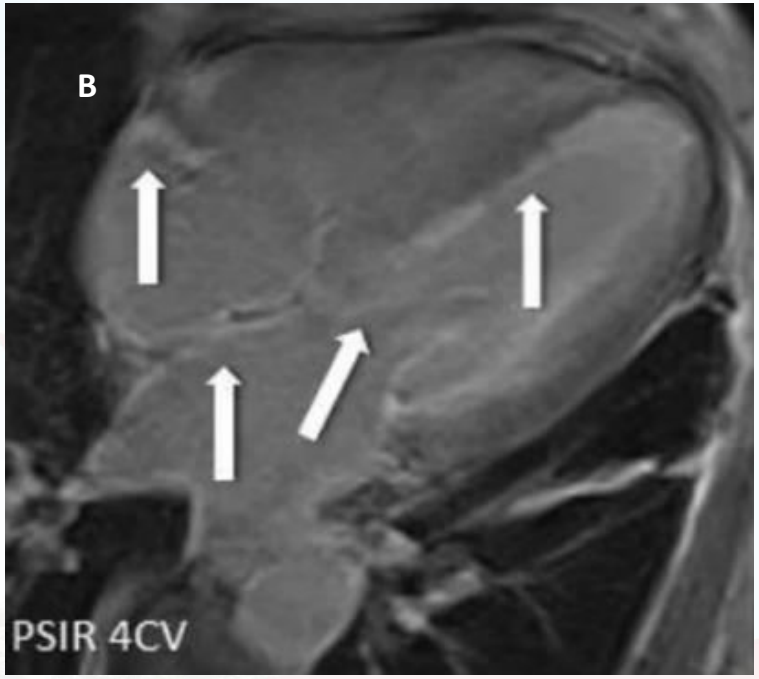




STS OG (%)	**42.2** ±6.1
SPD OG (%)	**23.2** ±6.7
STD OG (%)	**-14.6** ±3.5

IRM Cardiaque



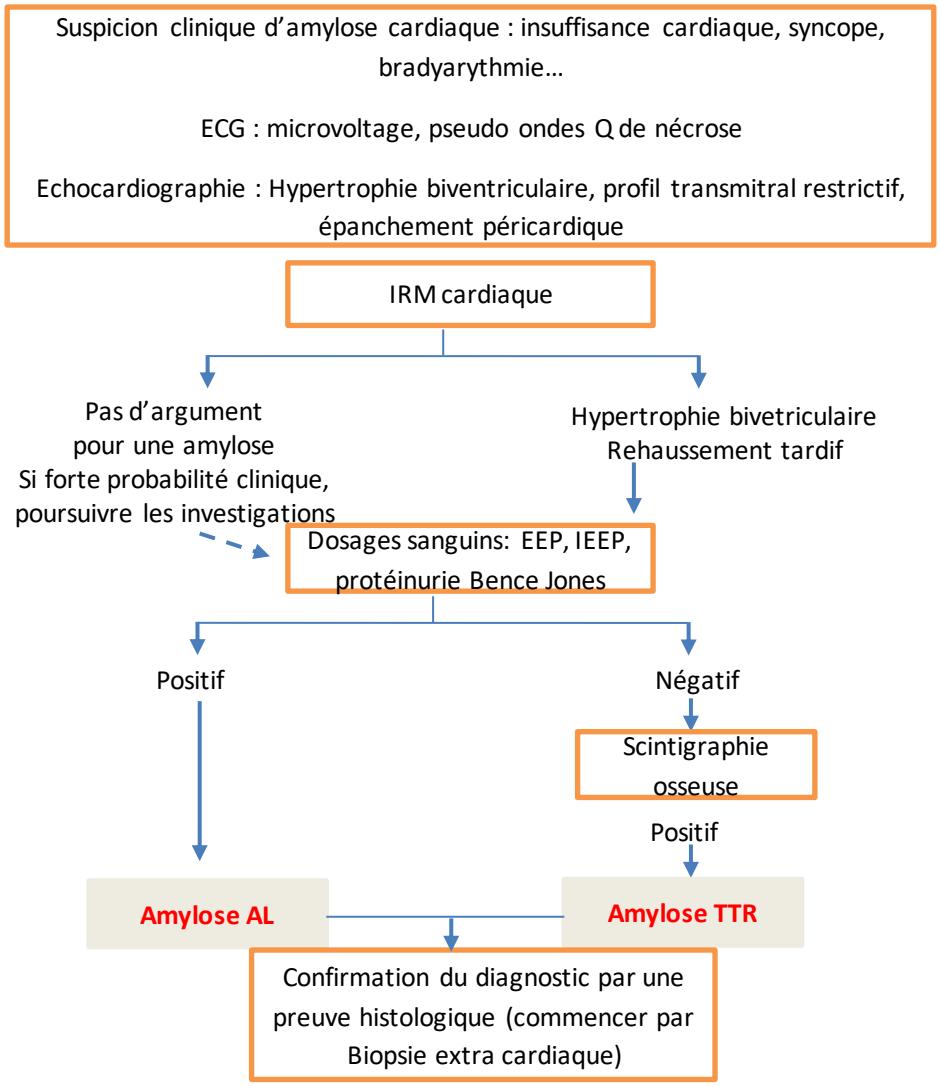


A. Pseudo égalisation en volume des oreillettes et des ventricules dans l'amylose avec hypertrophie concentrique du VG sur une séquence T2 en coupe 4 cavités. B. Rehaussement tardif de type sous endocardique circonférentiel intéressant les parois ventriculaires et atriales et les valves dans l'amylose sur une séquence PSIR en coupe 4 cavités

IRM: Amylose cardiaque

Biopsie labiale

- Amylose labiale



Algorithme d'orientation diagnostique devant une CMH avec signes évocateurs d'amylose

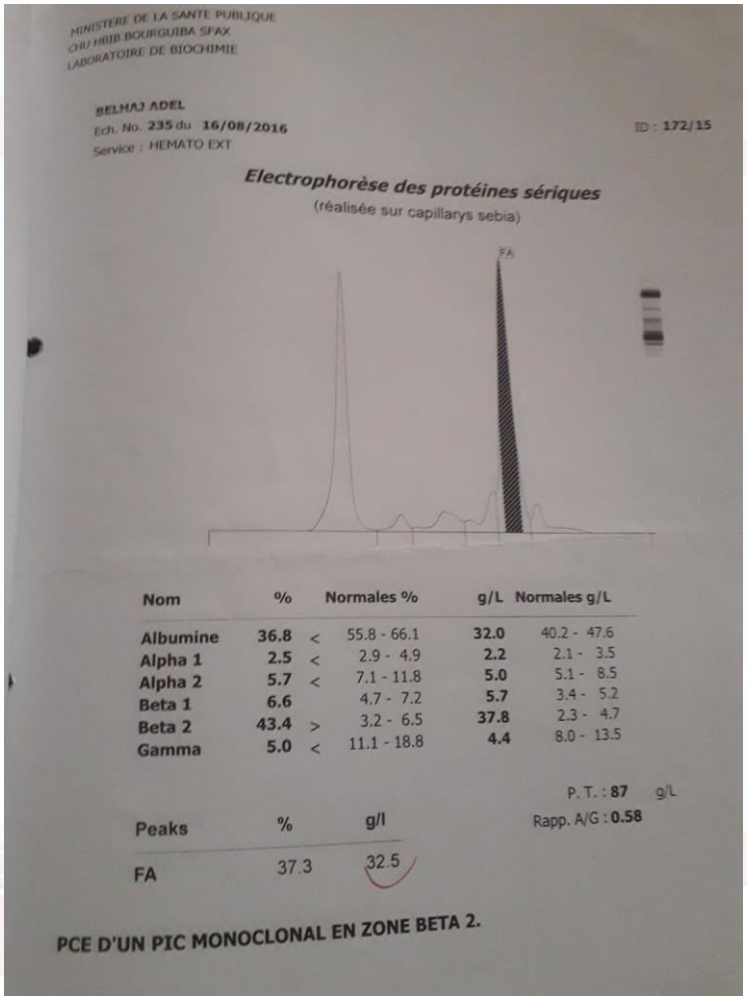
Biologie

- EPP: PT= 89g/l
- Alb=33,9 g/l

-Chaines légères: S lamda= 367 mg/l

U lamda= 275 mg/l

- Pic Monoclonal en zone Beta2



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Electrophorèse des protéines sériques
(réalisée sur capillarys sebia)

FA

Nom	%		Normales %	g/L	Normales g/L
Albumine	36.8	<	55.8 - 66.1	32.0	40.2 - 47.6
Alpha 1	2.5	<	2.9 - 4.9	2.2	2.1 - 3.5
Alpha 2	5.7	<	7.1 - 11.8	5.0	5.1 - 8.5
Beta 1	6.6		4.7 - 7.2	5.7	3.4 - 5.2
Beta 2	43.4	>	3.2 - 6.5	37.8	2.3 - 4.7
Gamma	5.0	<	11.1 - 18.8	4.4	8.0 - 13.5

P. T. : 87 g/L
Rapp. A/G : 0.58

Peaks	%	g/l
FA	37.3	32.5

PCE D'UN PIC MONOCLONAL EN ZONE BETA 2.

Diagnostic

- **Myélome Multiple à Ig A chaines légères Lamda**

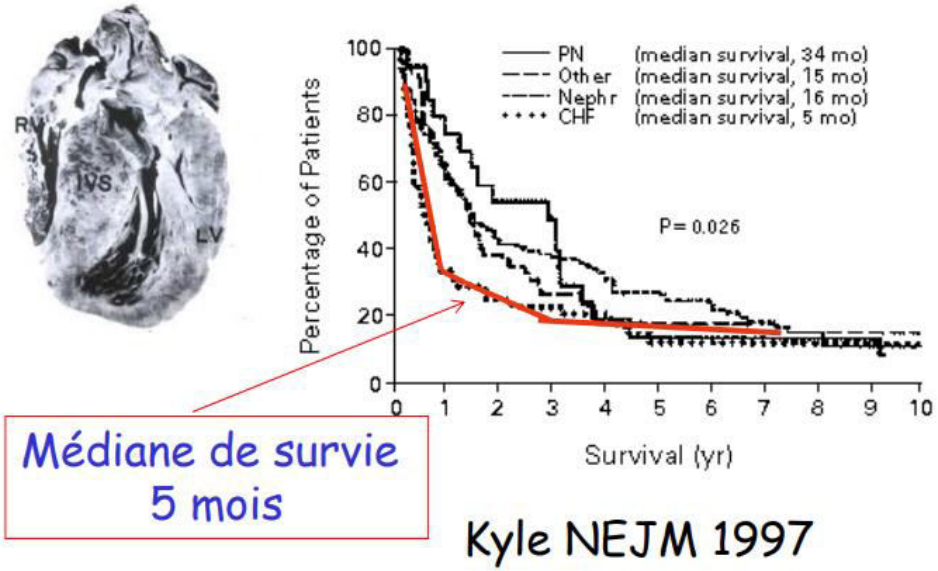
avec **amylose cardiaque AL**

Classée stage III A selon class de Mayo clinic

→ Traitement protocole cures VCD (velcade, endoxan, dexa)

Amylose AL et coeur

- Atteinte cardiaque: 50% des patients au diagnostic
- Facteur majeur pour le pronostic



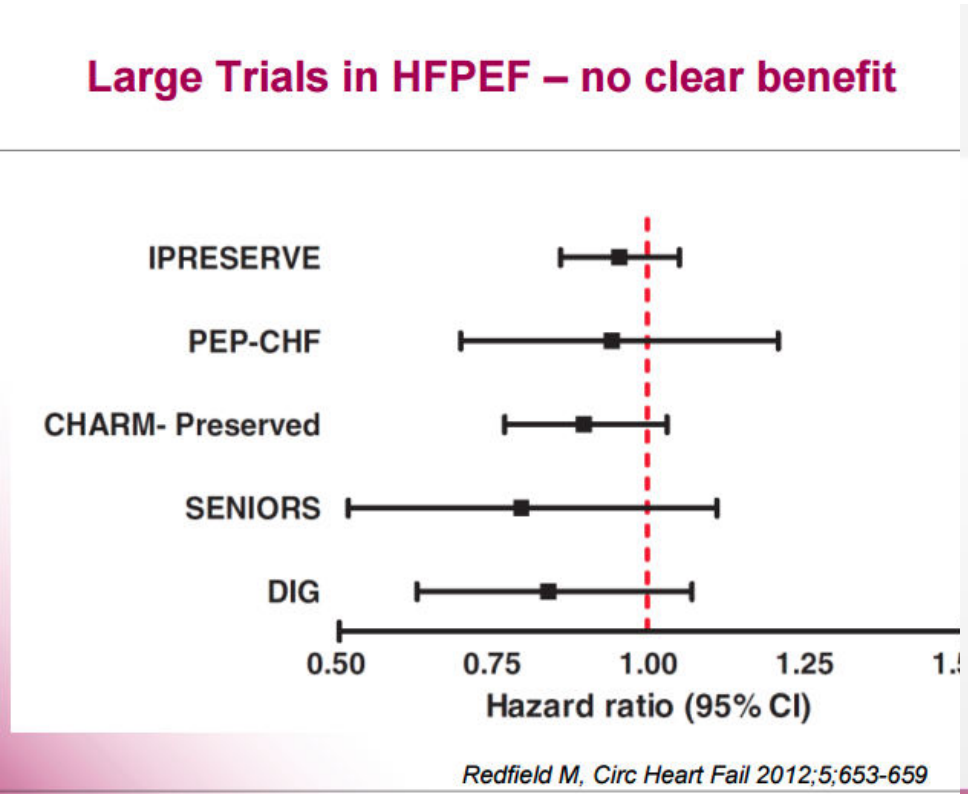
Majorité des décès par trouble de rythme ou de conduction

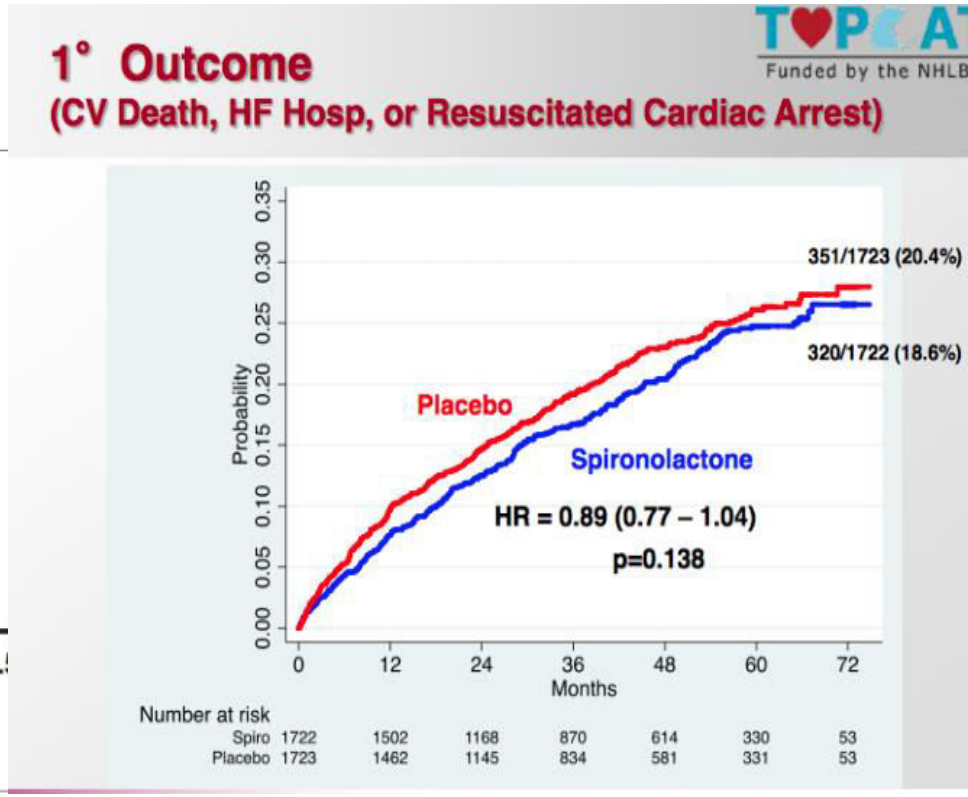
Traitement de l'IC FEVG préservée

- Lasilix: 40 mg/j
- Levothyrox 100 1c/j
- Nébivolol 5 mg 1c/j
- Périndopril 5 mg 1c/j

Que Pensez-vous?

Traitement de l'ICFEp





Traitement de l'insuffisance cardiaque à FEVG préservée

Absence de preuve pour le traitement de l'IC à FE préservée.

There is no guidance on how to treat HFpEF...

8. Pharmacological treatment of heart failure with 'preserved' ejection fraction (diastolic heart failure)

No treatment has yet been shown, convincingly, to reduce morbidity and mortality in patients with HF-PEF. Diuretics are used to control sodium and water retention and relieve breathlessness and oedema as in HF-REF. Adequate treatment of hypertension and myocardial ischaemia is also considered to be important, as is control of the ventricular rate in patients with AF (see Section

GUIDELINES

McMurray JJV, *et al. Eur Heart J* 2012; 33, 1787–1847.

CME

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Traitement de l'amylose AL cardiaque

Lasilix?, Nébivolol ?, Périndopril?

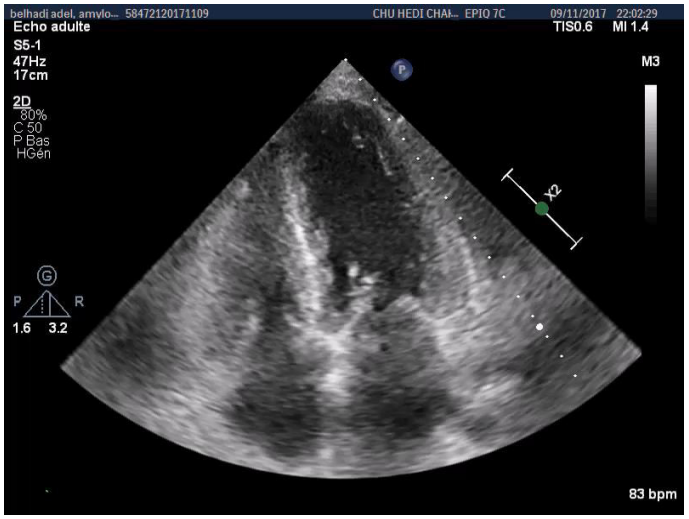
- Eviter Bêta-Bloquant, IC -, IEC
- Diurétiques: Lasilix de 40 mg/j à 500 mg/j
- Anticoagulation si FA

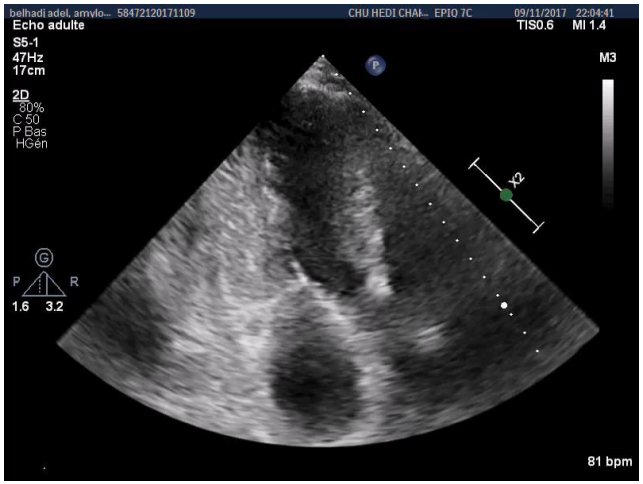
- Transplantation cardiaque

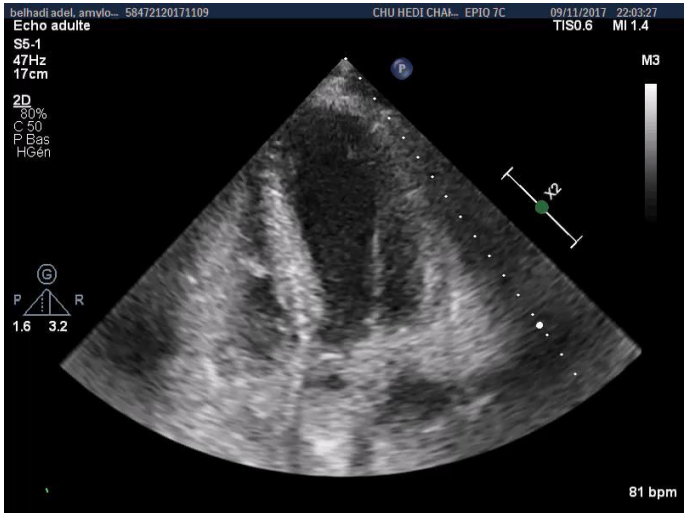
Evolution sous traitement (7 cures) Aout 2017

- Dyspnée +/- (lasilix 40 mg/j)
- Protéinurie : 30 mg/24h
- Hb=12 g/dl
- Créatinine: 70 umol/l
- Troponine 0,07, Ca2+:2,26 mmol/l
- Nt proBNP:1818 pg/l
- Pas de pic, lamda=1,09 g/l
- ETT: FEVG=60%, PAPS à 38 mmHg

ETT à un an du traitement







Traitement amylose AL

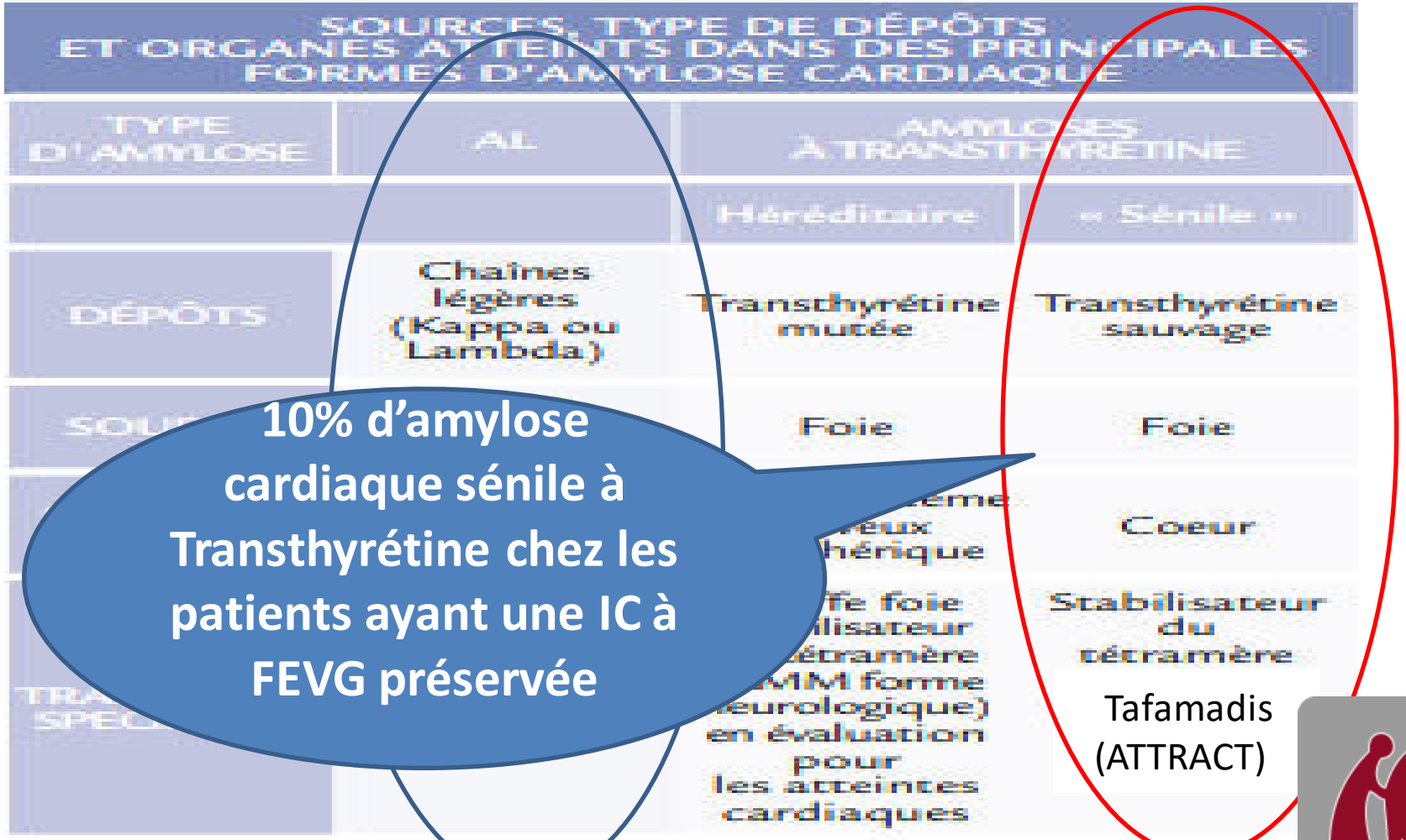
- Si Protéines baissent, les atteintes cliniques vont s'améliorer, très lentement et de façon différente suivant les organes:

Foie> rein> cœur> macroglossie

- Cœur: amélioration rapide clinique (et NT-proBNP) si les chaînes légères baissent de façon importante
- Rein: baisse parfois rapide de la proteinurie + Svt plus lente après 6 mois
- La réponse clinique peut être très retardé (> 1 An)

⇒ le traitement ne peut donc pas être monitoré sur l'efficacité clinique beaucoup trop lente à apparaître

Les différents types d'amylose



STCCCV
Société Tunisienne de Cardiologie
& de Chirurgie Cardio-Vasculaire

Registre Tunisien: Nature-HF

Groupe de travail d'insuffisance Cardiaque STCCCV

ICFEp: 42,6%

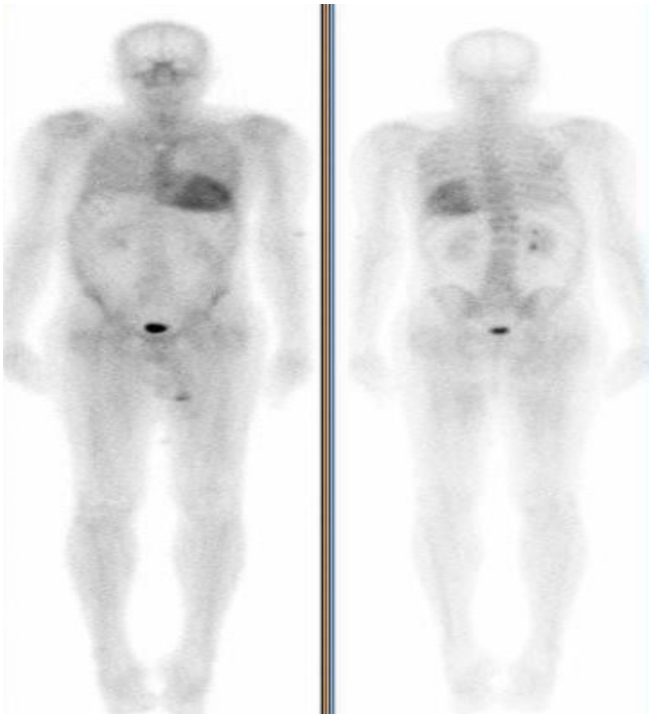
Diagnostic Amylose

- Évoqué devant toute « CMH », IC à FEVG préservée avec hypertrophie….stt + signes IC
- Signes cliniques extra-cardiaques: Syndrome du canal carpien, Macroglossie, échymoses périorbitaires, neuropathie….
- ECG: Micro-voltage, pseudo-onde Q

Diagnostic Amylose

- Bilan Biologique: EPP, Immunofixation, Dosage des chaines légères libres, NT-proBNP et troponine
- IRM cardiaque (rehaussement tardif au gadolinium)
- Scintigraphie fixation cardiaque
- Diagnostic anatomopathologique: biopsies les moins invasives (1ère intention), sinon cardiaque

Scintigraphie osseuse

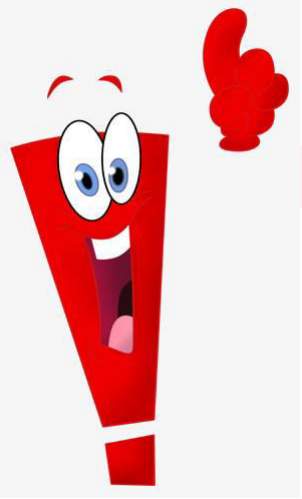


Take Home Message
Ce qu'il ne faudrait pas faire…

Consultation Cardio pour **dyspnée d'effort**/ fatigabilité musculaire

- **Echo-coeur**: Fonction systolique VG normale: IC FEVG préservée !!!!!

« Vous avez un cœur un peu gros parce que vous êtes: sportif, Hypertendu….. »



- **Coronarographie normale**

« Le problème n'est pas cardiaque ???»

CoSAC
Le congrès des Sociétés Africaines de Cardiologie

STCCCV
Société Tunisienne de Cardiologie & de Chirurgie Cardio-Vasculaire


Merci pour
votre
attention
CoSAC
Le congrès des
Sociétés Africaines
de Cardiologie
STCCCV
Société Tunisienne
de Cardiologie & de Chirurgie
Cardio-Vasculaire

ACTION Study Group
Institute of Cardiology
Pitié-Salpêtrière Hospital
Paris - France

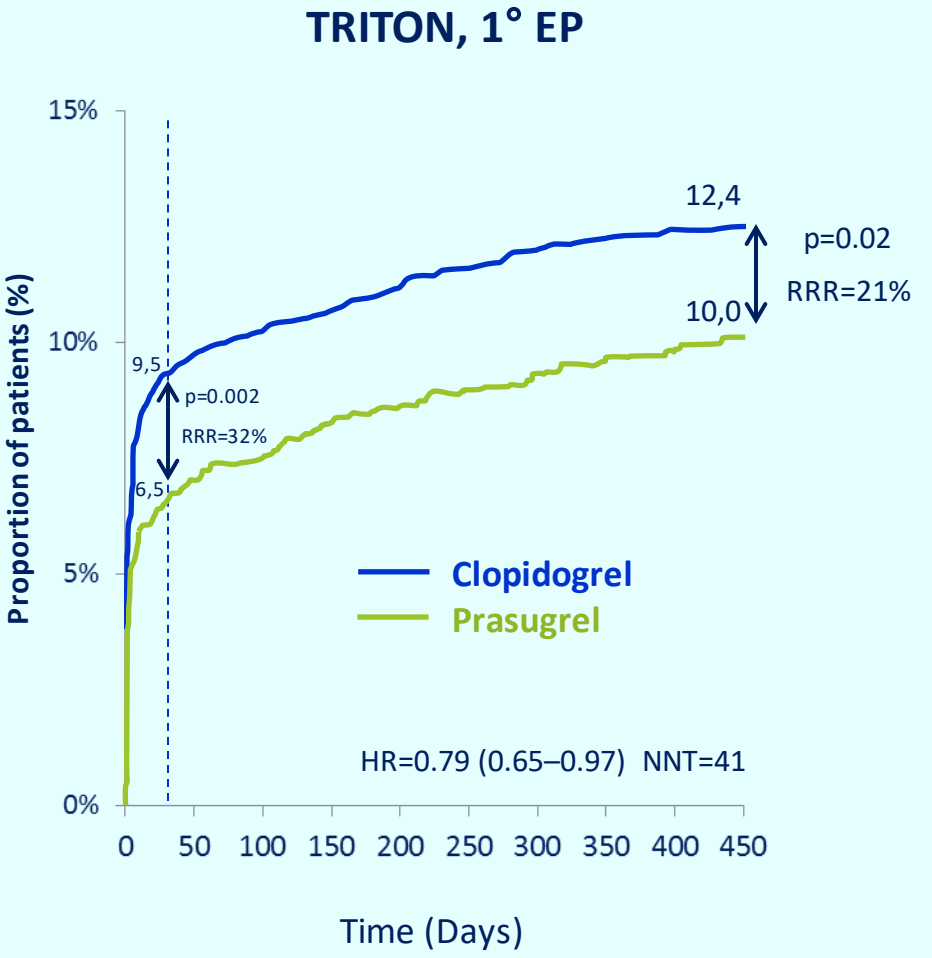
Individualisation du traitement Anti Agrégeant Plaquettaire dans la PEC des Syndromes coronaires aigus

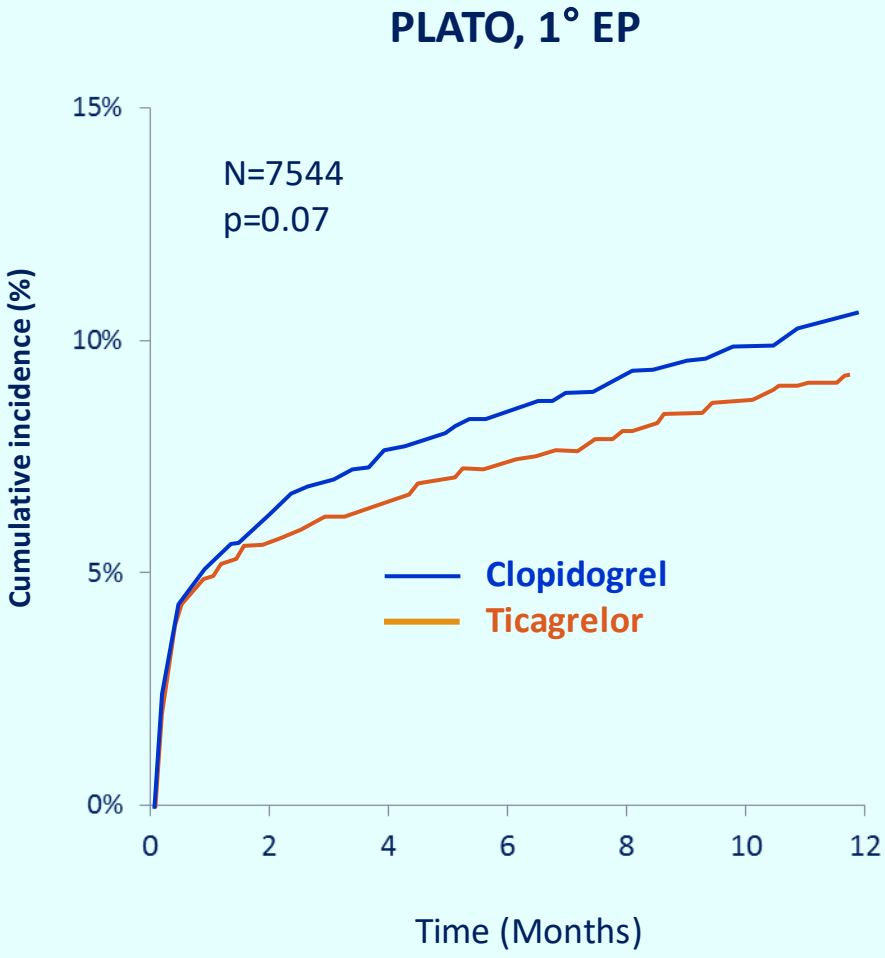
G. Montalescot

Dr. Montalescot reports research Grants to the Institution or Consulting/Lecture fees which are published at www.action-coeur.org

Giving new P2Y12 RA earlier in STEMI

New P2Y12 antagonists in STEMI



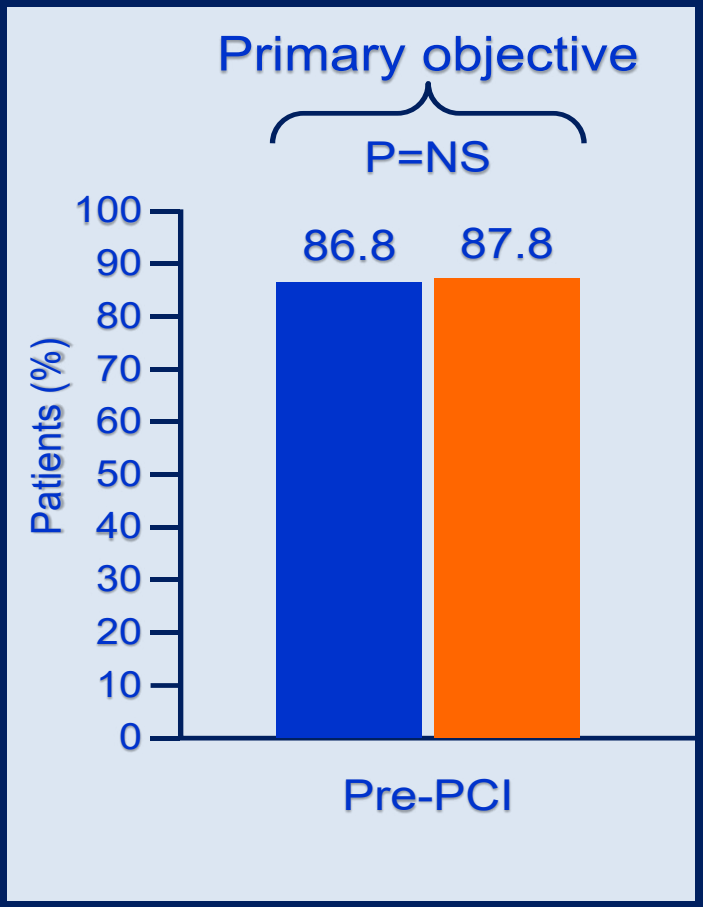


Montalescot G, et al. Lancet 2009;373:723–31

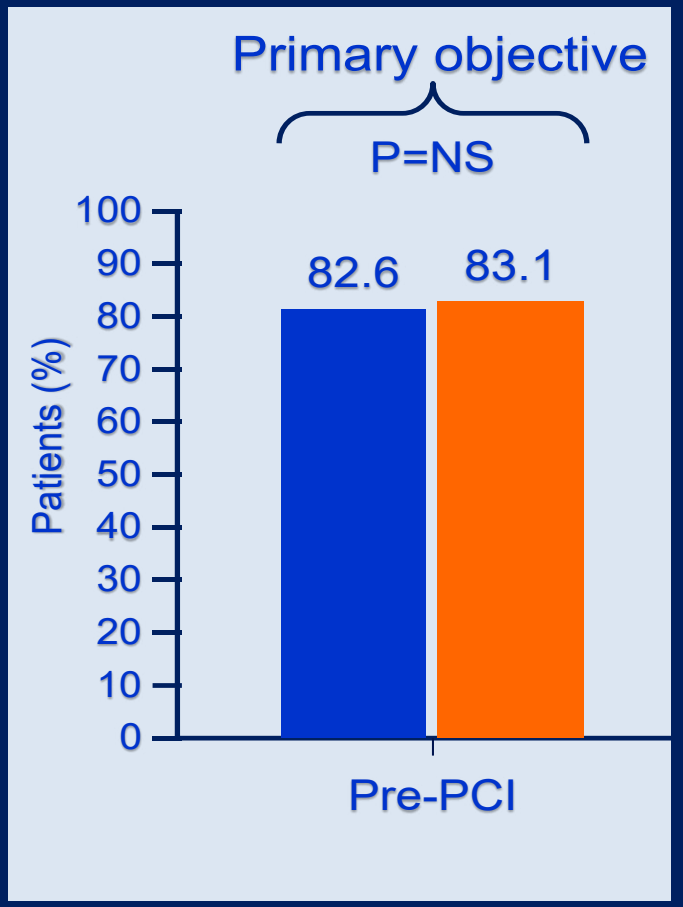
Steg PG, et al. Circulation. 2010;122:2131-41

ATLANTIC: *reperfusion criteria*

1st Co-primary endpoint
No ST-segment resolution (≥70%)



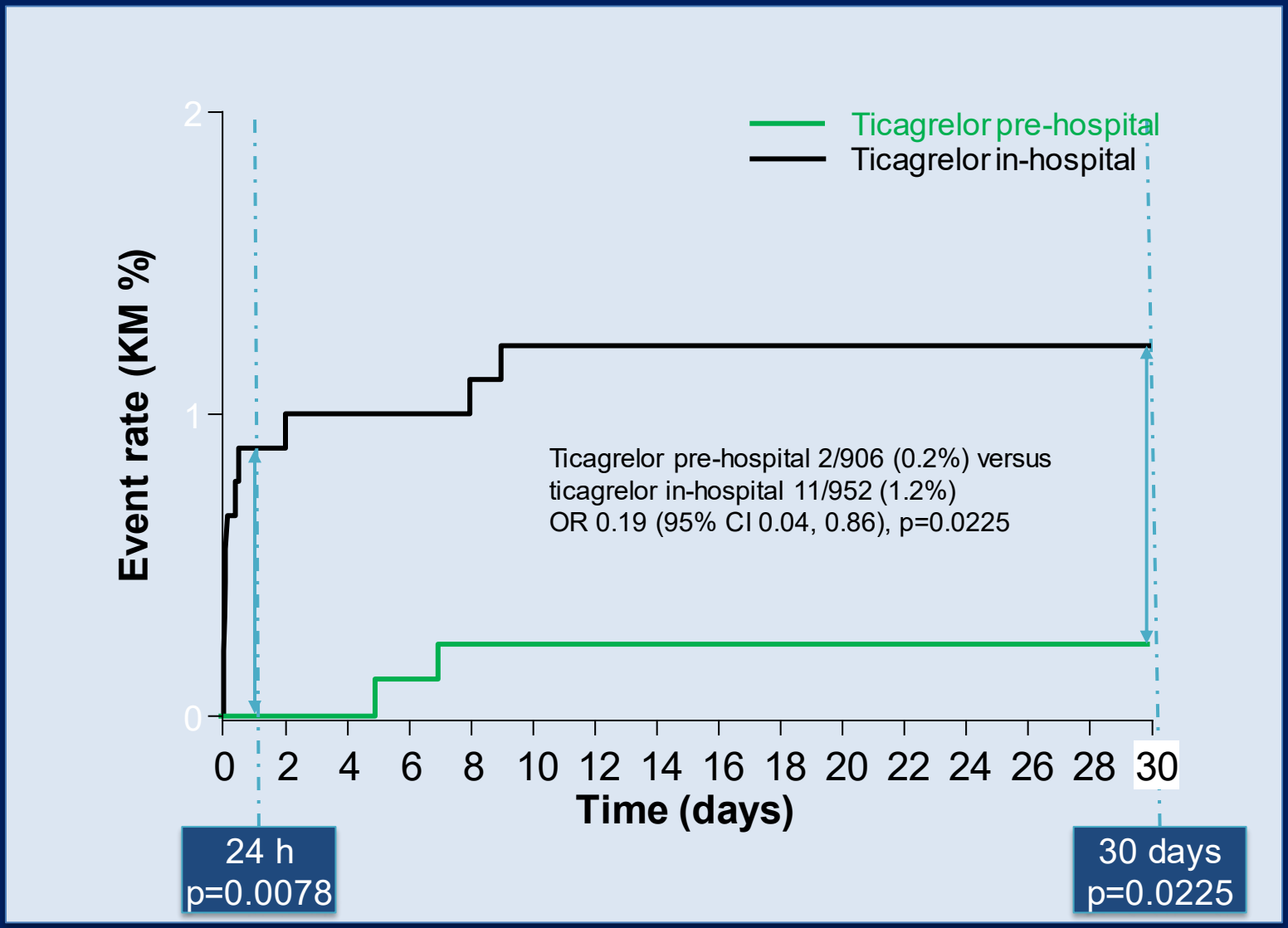
2nd Co-primary endpoint
No TIMI 3 flow in infarct-related artery



Pre-hospital In-hospital

Montalescot G, et al. NEJM 2014

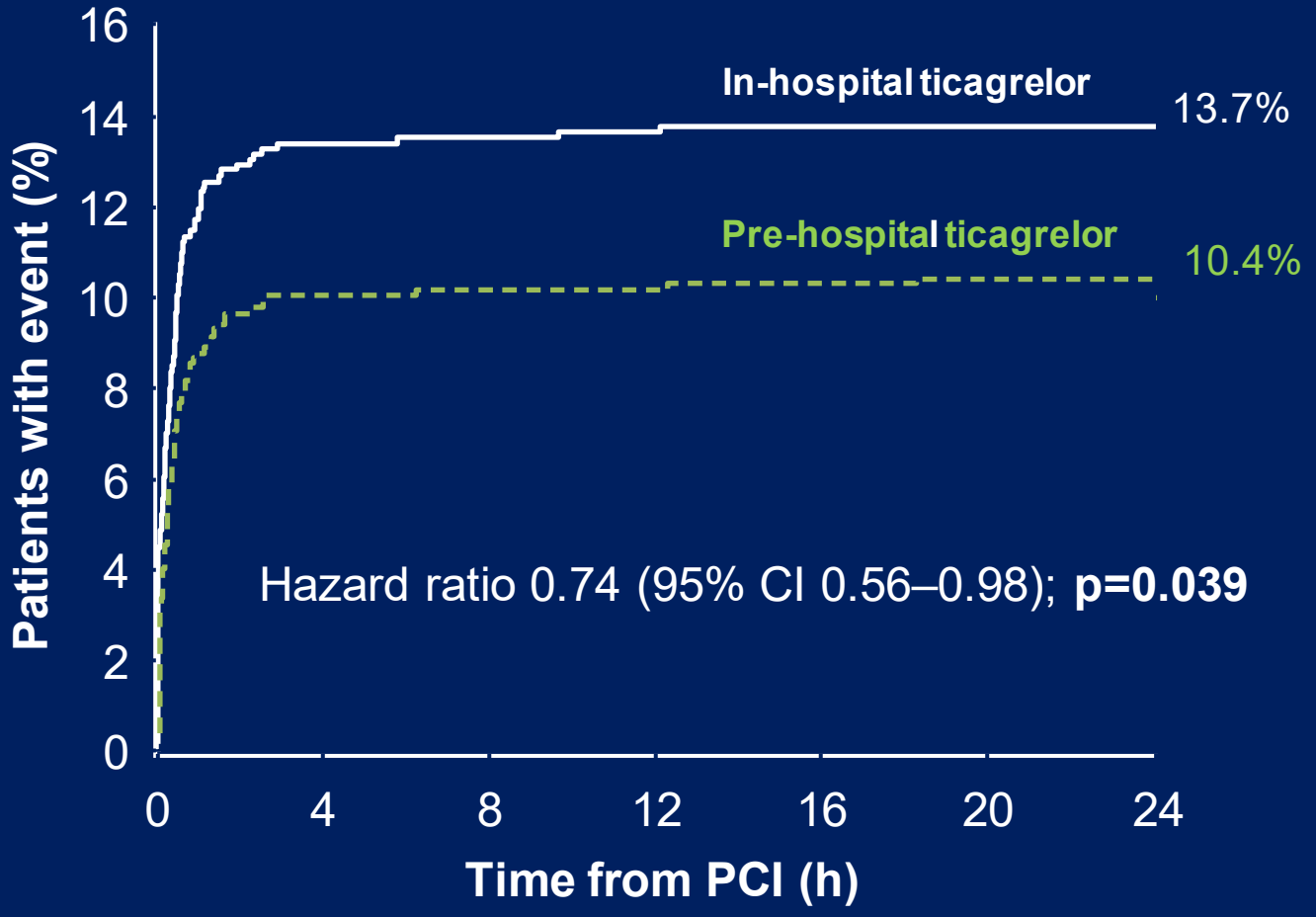
ATLANTIC *Stent thrombosis*



Montalescot G, et al. NEJM 2014

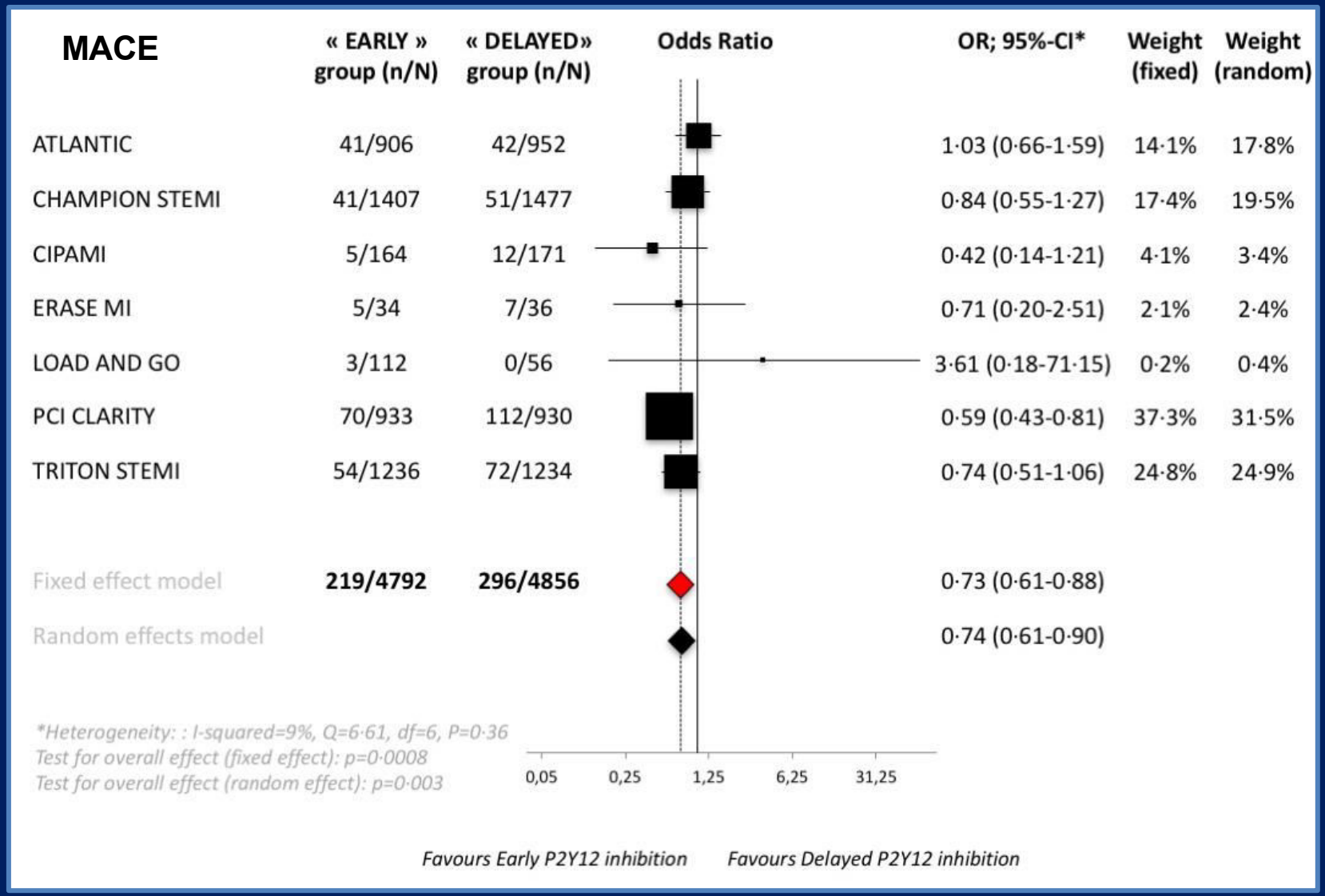
ATLANTIC-H24

Composite ischaemic endpoint: death, MI, urgent revasc, definite stent thrombosis or bail-out GP IIb/IIIa inhibitor use



Montalescot G et al. JACC CVI 2016

Early administration of P2Y12 inhibitors in STEMI



Bellemain-Appaix A. et al. EuroIntervention. 2018 Feb 20. pii: EIJ-D-17-00852. doi: 10.4244/EIJ-D-17-00852

Giving new P2Y12 RA later in NSTEMI

Definition of Pre-treatment

ER-CCU

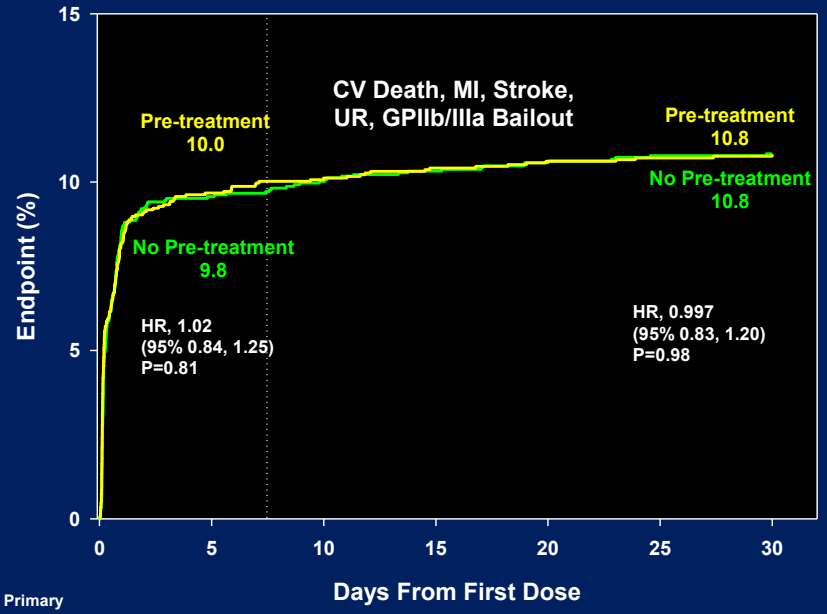
- **Working diagnosis of ACS**
- **Invasive strategy decided**
- **On aspirin + anticoagulation**

→ $P2Y_{12}$ antagonist given before coronary visualization

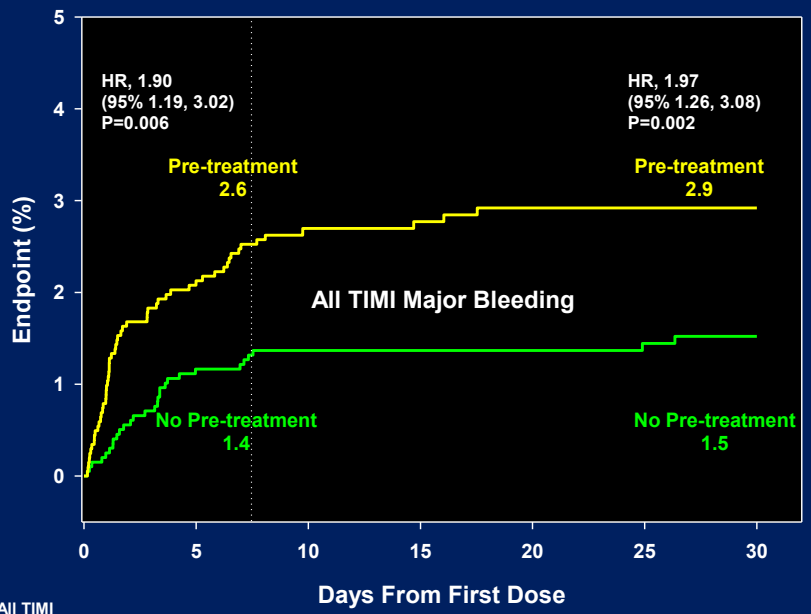
Cath Lab

- **PCI → benefit expected**
- Medical treatment → **?**
- CABG → **no benefit expected**
- Other diagnosis (pericarditis, aortic dissection, heart failure, LVH, pulmonary embolism, GI ulcer, pancreatitis...) → **harm expected**

ACCOAST: 1° Efficacy and Safety Endpoints



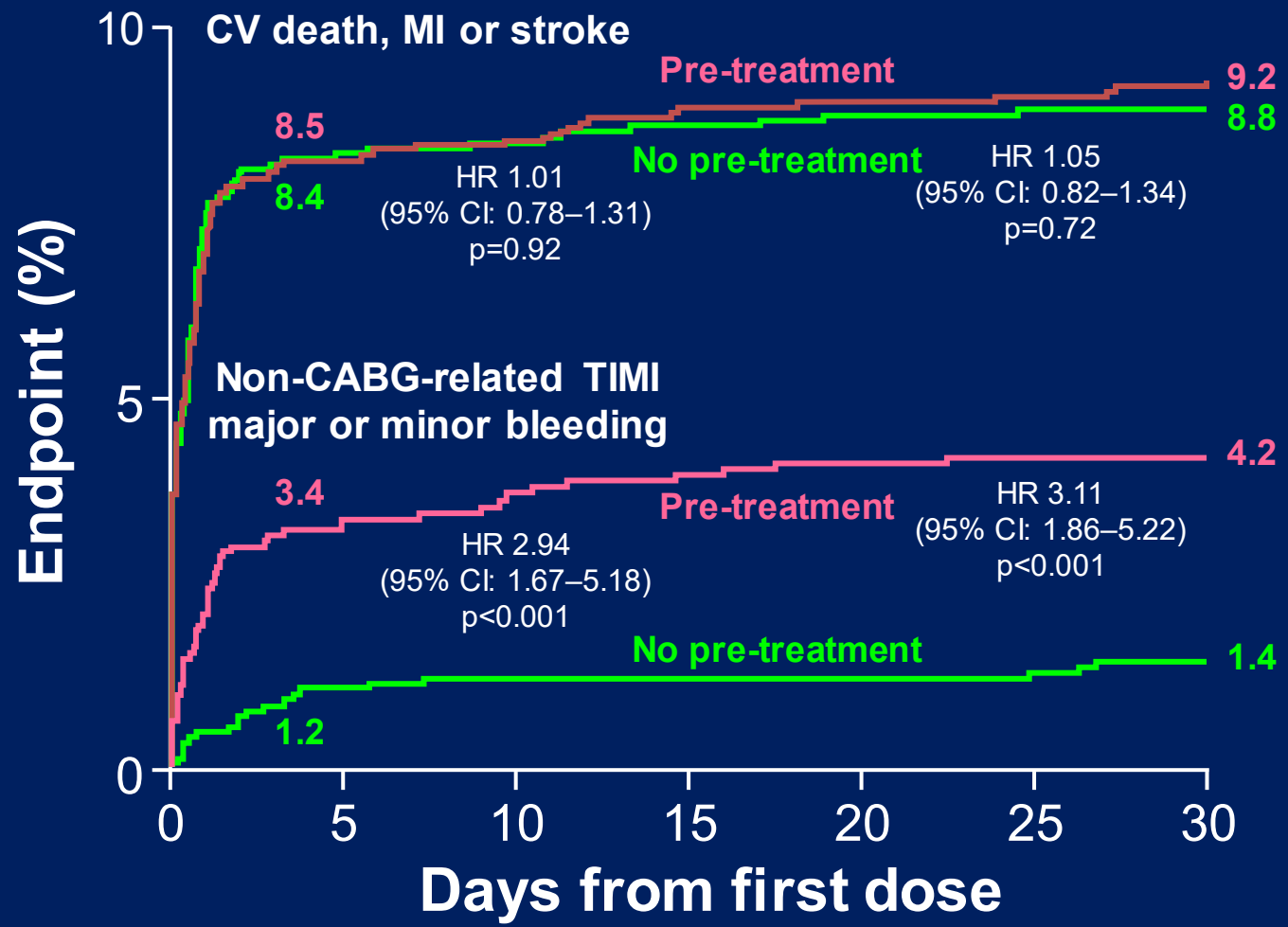
No. at Risk, Primary Efficacy End Point:							
No pre-treatment	1996	1788	1775	1769	1762	1752	1621
Pre-treatment	2037	1821	1809	1802	1797	1791	1616



No. at Risk, All TIMI Major Bleeding:							
No pre-treatment	1996	1947	1328	1297	1288	1284	1263
Pre-treatment	2037	1972	1339	1310	1299	1297	1280

Montalescot G et al. N Engl J Med.2013;369(11):999-1010

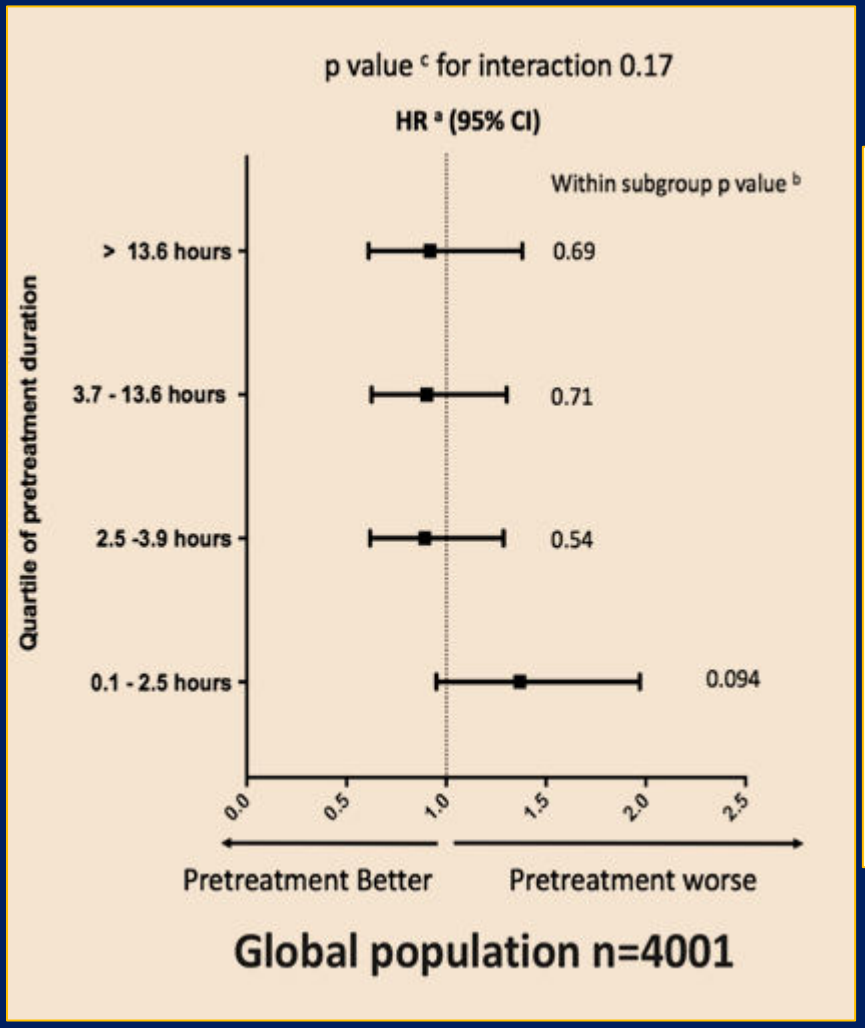
ACCOAST: PCI patients

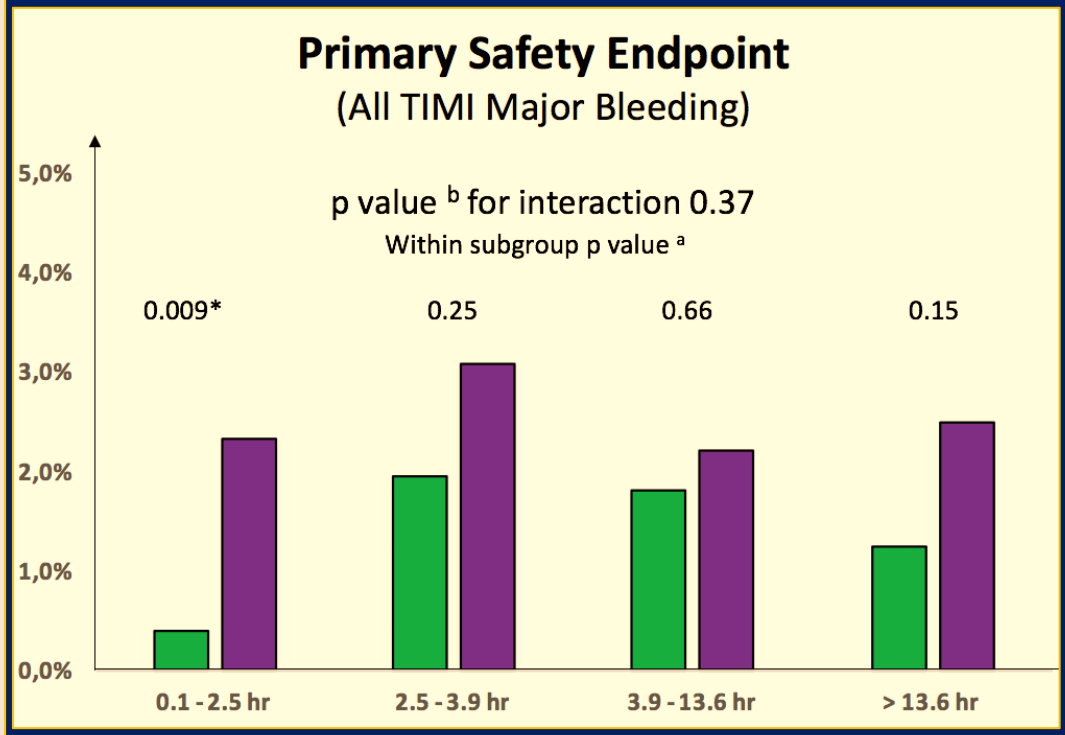


Montalescot et al. *J Am Coll Cardiol* 2014;64:2563–71

Duration of pretreatment

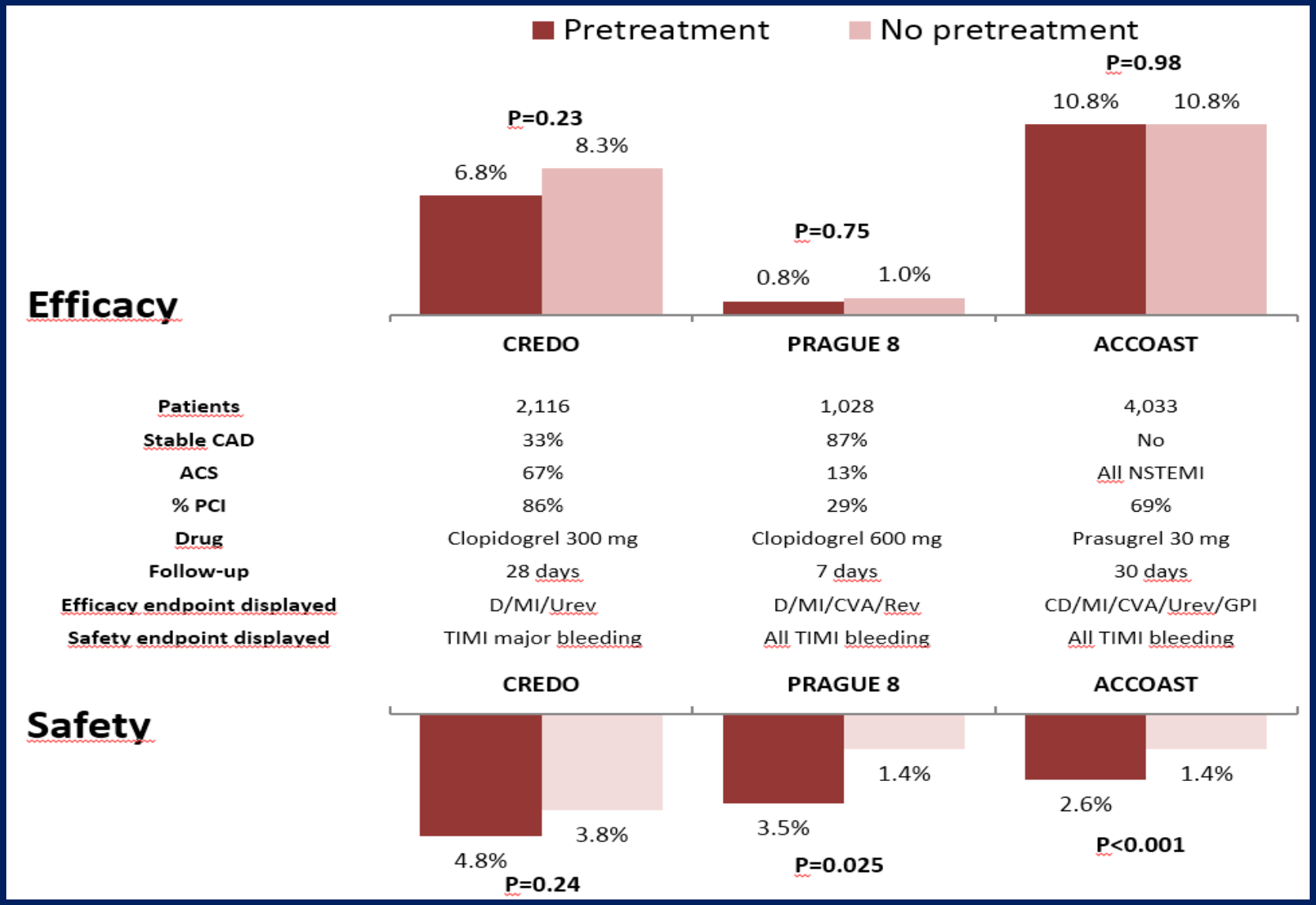
Primary efficacy EP





Silvain et al. JACC 2018 in press

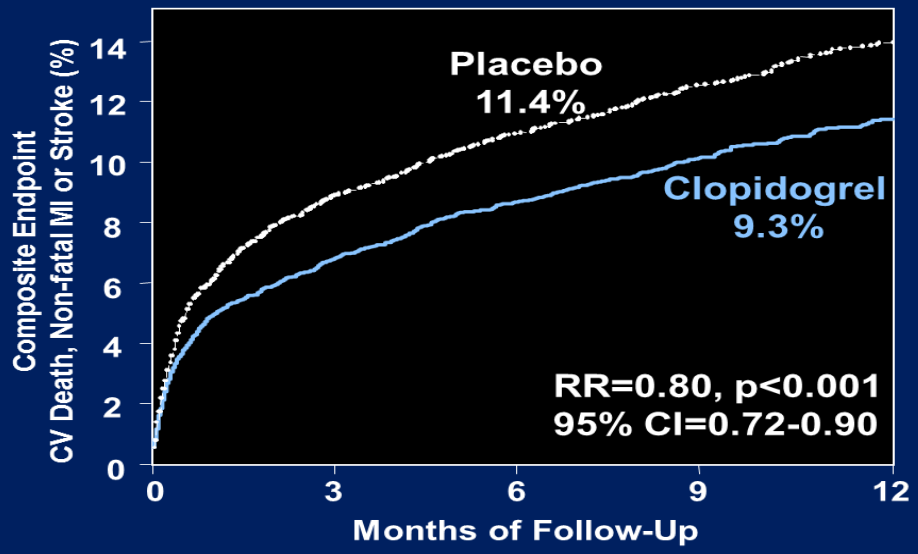
Studies of pretreatment with $P2Y_{12}$ receptor inhibitors in patients with stable CAD and NSTE-ACS



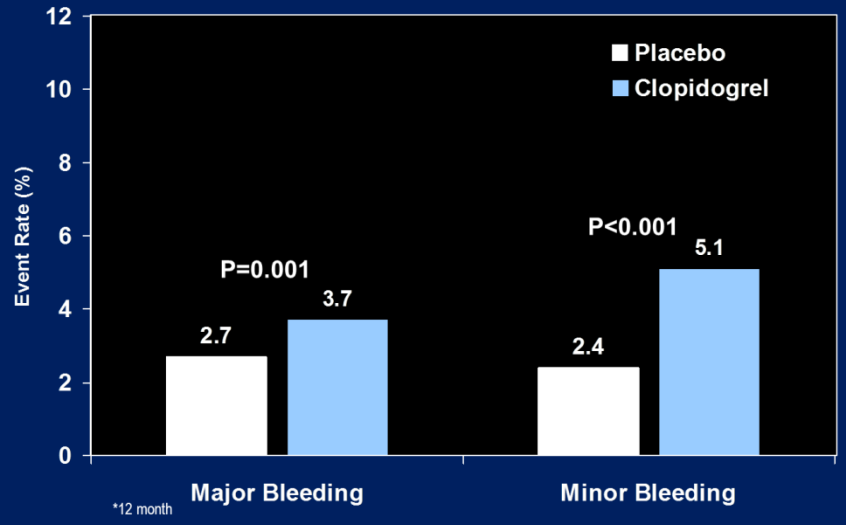
Capodanno D & Angiolillo DJ. Circ Cardiovasc Interv 2015

ACS

CURE Efficacy



CURE Safety*



57% no cath…

20% PCI

Yusuf S, et al. *N Engl J Med* 2001;345:494-502

DAPT Guidelines

In patients with SCAD **pre-treatment with clopidogrel** may be considered if the **probability of PCI is high.**	IIb	C
Pre-treatment with a P2Y12 inhibitor is generally recommended in patients in whom **coronary anatomy is known** and the decision to proceed to PCI is made as well as in **patients with STEMI**	I	A
In NSTE-ACS patients undergoing invasive management, ticagrelor or clopidogrel if ticagrelor is not an option, should be considered **as soon as the diagnosis is established.**	IIa	C
In NSTE-ACS patients İt is not recommended to administer **prasugrel** in patients in whom coronary anatomy is not known.	III	B

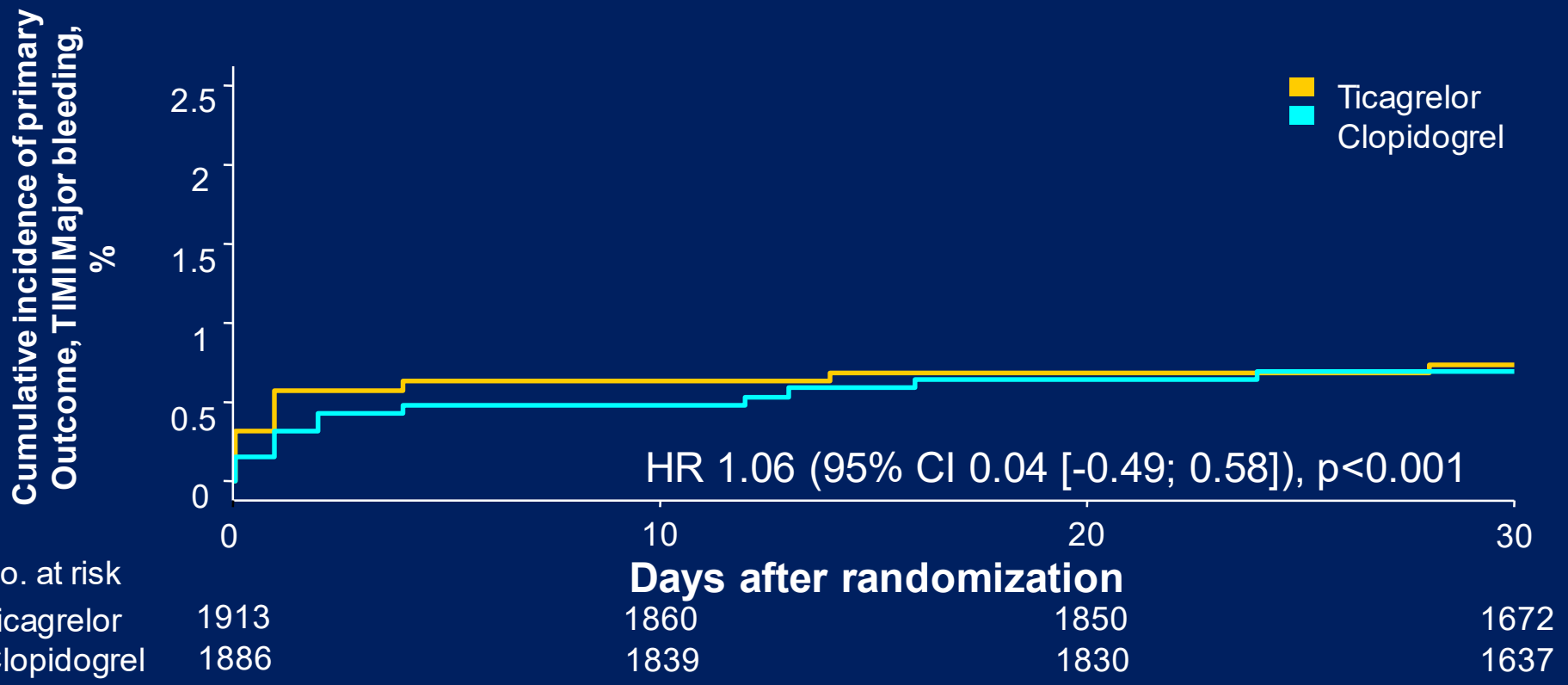
2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

$P2Y_{12}$ inhibitors				
• Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin	75 mg	I	B	(291)
• $P2Y_{12}$ inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy: – Clopidogrel – Ticagrelor*	300-mg or 600-mg loading dose, then 75 mg/d 180-mg loading dose, then 90 mg BID	I	B	(289,292) (293,294)
• $P2Y_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post-PCI patients treated with coronary stents	N/A	I	B	(293,296,302, 330,331)
• Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy	N/A	IIa	B	(293,294)

P2Y12 RA with fibrinolysis

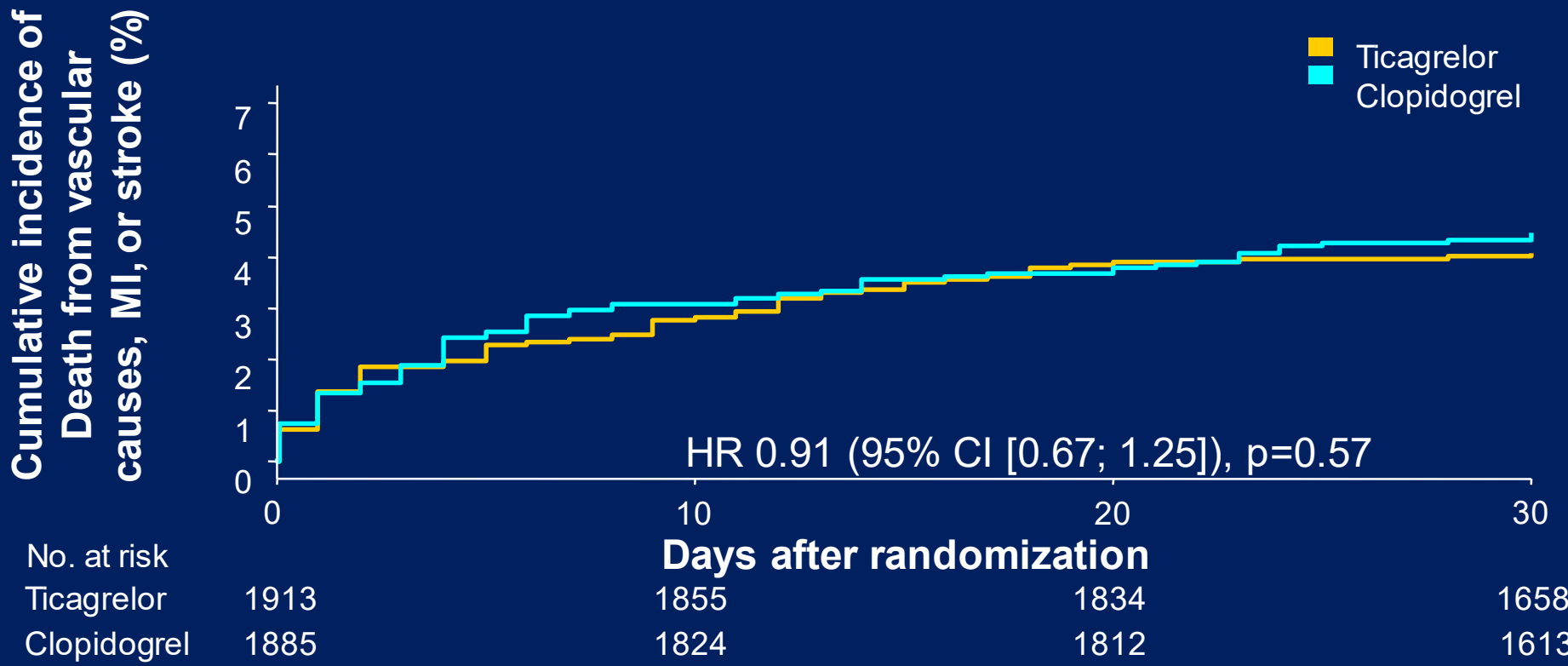
Time to major bleeding – primary safety event



Jama cardiol 2018

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

Secondary efficacy – outcomes over time



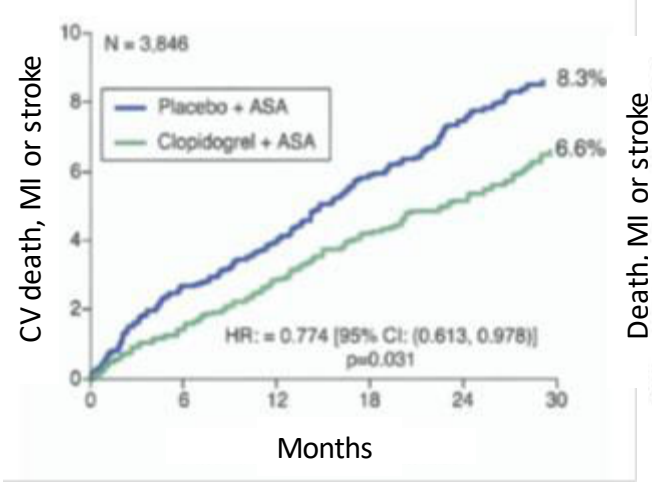
Jama cardiol 2018

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

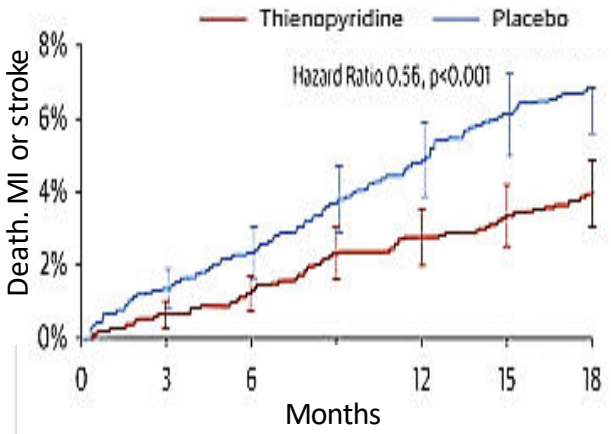
DAPT prolongation to improve post-ACS prevention

DAPT > 1year after Myocardial Infarction

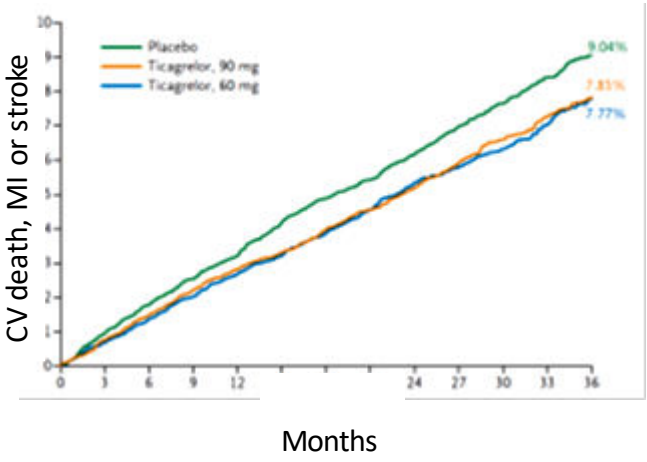
CHARISMA (prior MI subgroup)



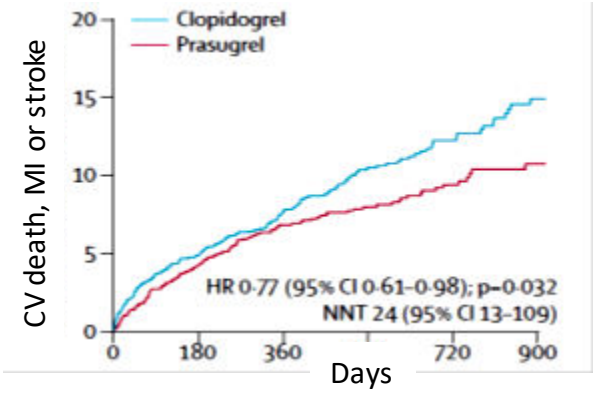
DAPT (prior MI subgroup)



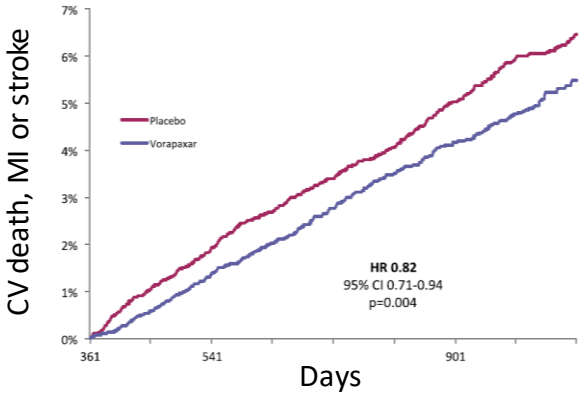
PEGASUS-TIMI 54 trial (prior MI)



TRILOGY (prior angiogram subgroup)

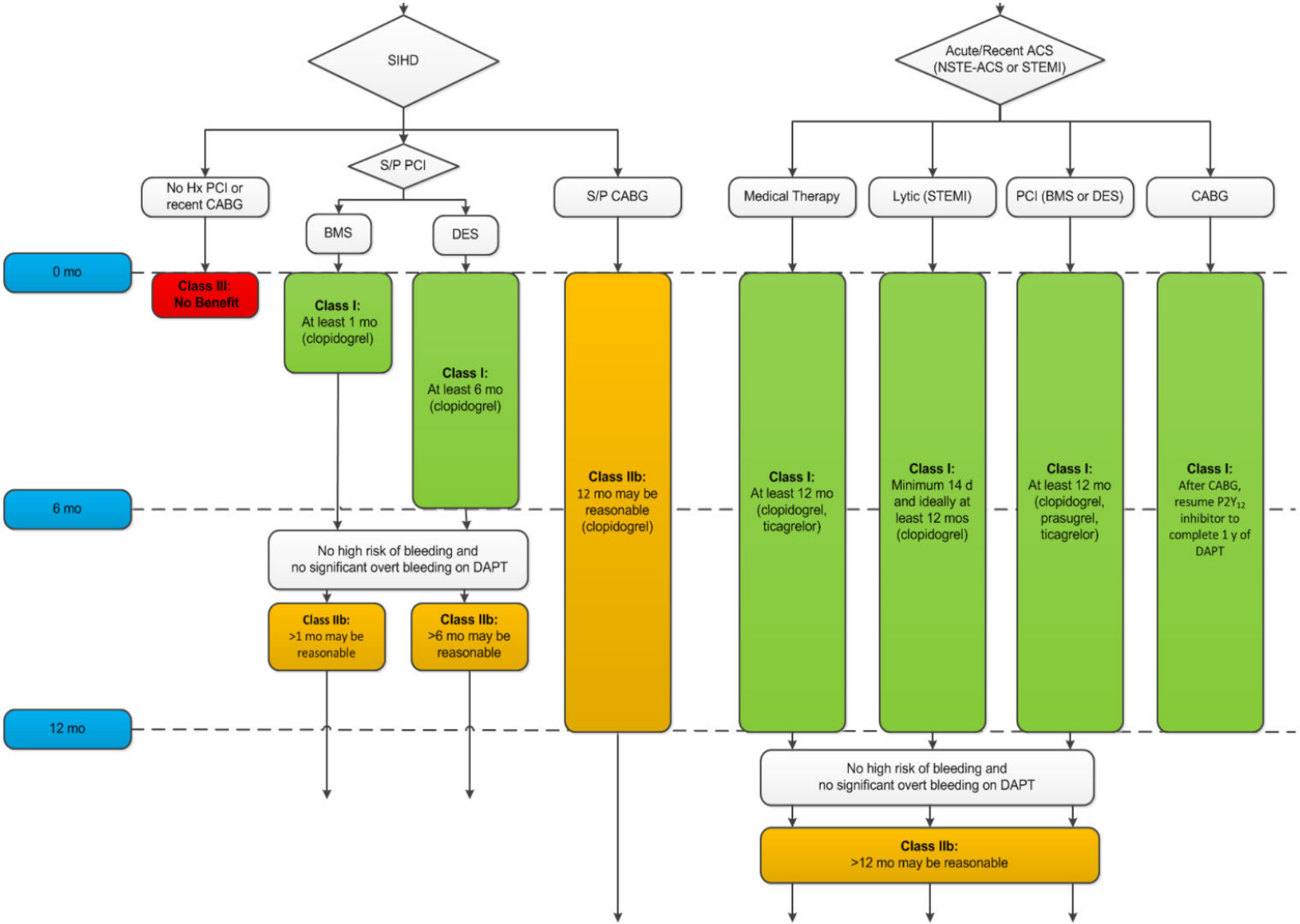


TRA-2P (prior MI subgroup)



Montalescot G and Sabatine M. EHJ 2015

Duration of DAPT in CAD



Oral dual antiplatelet therapy: what have we learnt from recent trials?

Gilles Montalescot[1]* and Marc S. Sabatine[2]

[1]ACTION Study Group, Institute of Cardiology, Pitié-Salpêtrière Hospital (AP-HP), Université Paris-6, Paris 75013, France; and [2]TIMI Study Group, Division of Cardiovascular Medicine, Brigham & Women's Hospital and Harvard Medical School, Boston, MA, USA

Duration of DAPT in ACS

SAPT only

- No Q-wave
- No prior stent
- No prior CABG
- No coronary angio
- No CT scan
- Negative troponin
- High bleeding risk

3-month DAPT

- Documented obstructive CAD
- Recent/prior bleeding
- Scheduled surgery
- Oral anticoagulation needed

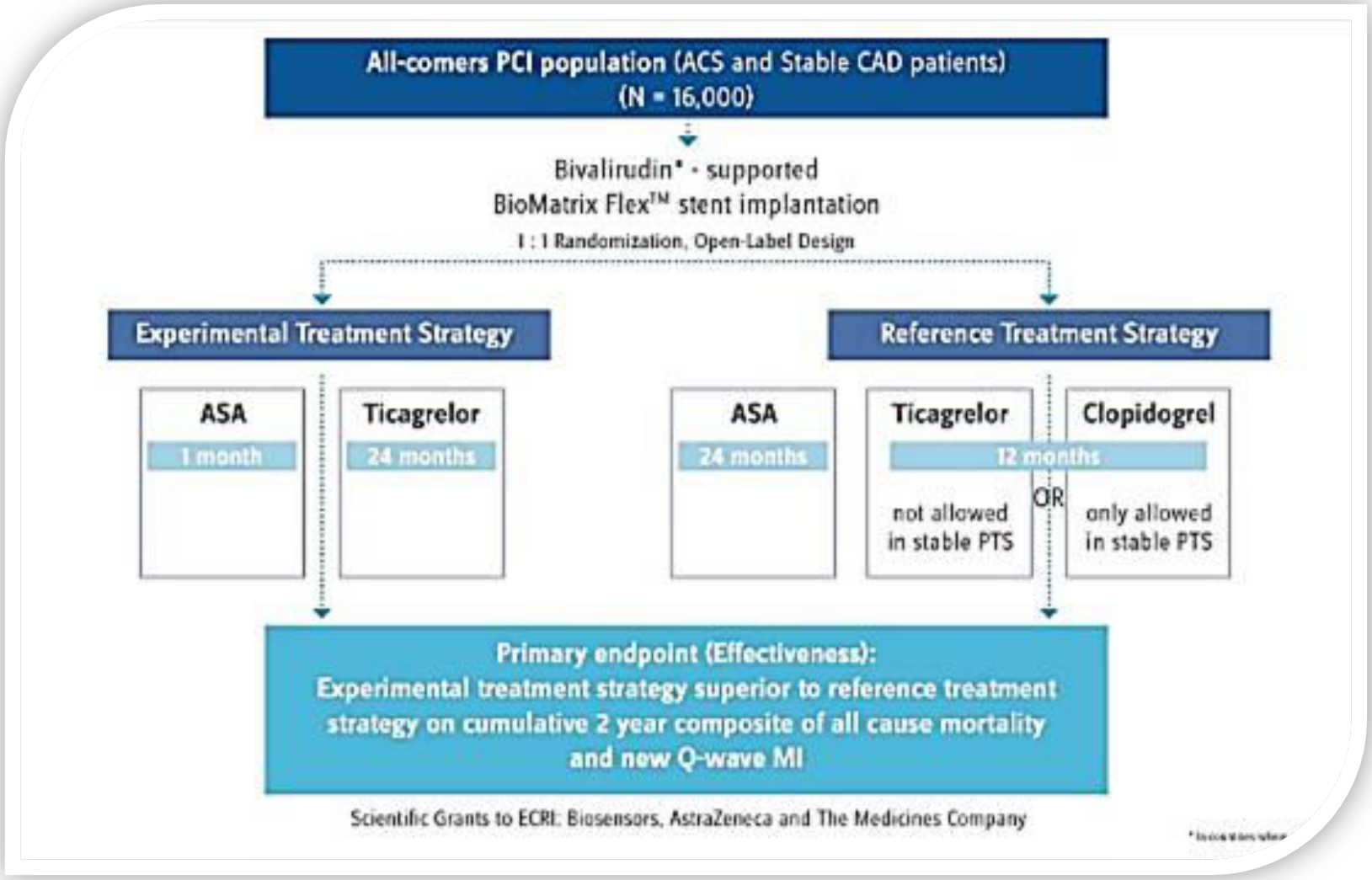
6–12 month DAPT

- Documented obstructive CAD
- Bleeding risk factors (age, gender, anaemia...)

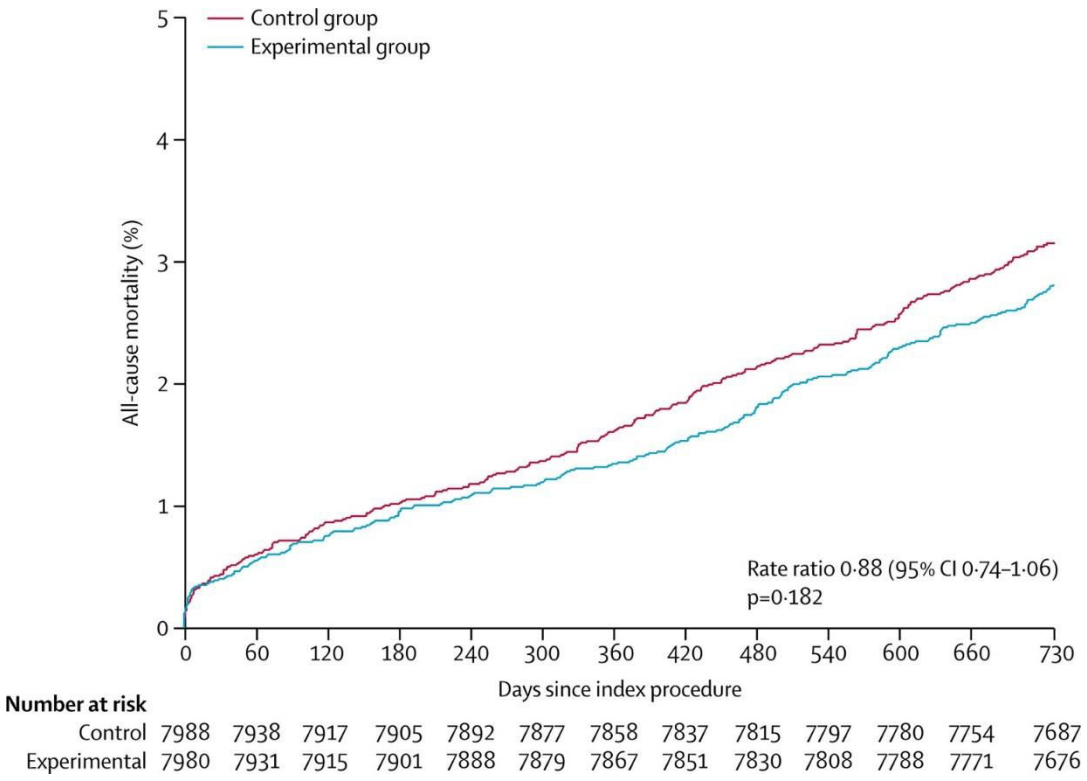
> 12-month DAPT

- Documented obstructive CAD
- No excess bleeding risk
- No bleeding event during 1st year of DAPT

Global-leaders



Global-leaders



	Experimental treatment group (N=7980)	Control group (N=7988)	Rate ratio (95% CI)	p value
All-cause mortality or new Q-wave myocardial infarction	304 (3·81%)	349 (4·37%)	0·87 (0·75–1·01)	0·073
All-cause mortality	224 (2·81%)	253 (3·17%)	0·88 (0·74–1·06)	0·182
New Q-wave myocardial infarction*	83 (1·04%)	103 (1·29%)	0·80 (0·60–1·07)	0·14
Composite of all-cause mortality, stroke, or new Q-wave myocardial infarction	362 (4·54%)	416 (5·21%)	0·87 (0·76–1·00)	0·056
Myocardial infarction	248 (3·11%)	250 (3·13%)	1·00 (0·84–1·19)	0·98
Stroke				
Overall	80 (1·00%)	82 (1·03%)	0·98 (0·72–1·33)	0·90
Ischaemic	63 (0·79%)	68 (0·85%)	0·93 (0·66–1·31)	0·68
Haemorrhagic	13 (0·16%)	9 (0·11%)	1·45 (0·62–3·39)	0·39
Undetermined	6 (0·08%)	5 (0·06%)	1·21 (0·37–3·95)	0·76
Revascularisation	739 (9·26%)	793 (9·93%)	0·93 (0·84–1·03)	0·17
Target vessel revascularisation	389 (4·87%)	442 (5·54%)	0·88 (0·77–1·01)	0·068
Definite stent thrombosis	64 (0·80%)	64 (0·80%)	1·00 (0·71–1·42)	0·98
BARC				
BARC 3 or 5 bleeding	163 (2·04%)	169 (2·12%)	0·97 (0·78–1·20)	0·77
BARC 5 bleeding				
Any	22 (0·28%)	24 (0·30%)	0·92 (0·52–1·64)	0·78
5b bleeding	15 (0·19%)	18 (0·23%)	0·84 (0·42–1·66)	0·61
5a bleeding	7 (0·09%)	6 (0·08%)	1·17 (0·39–3·49)	0·78
BARC 3 bleeding				
Any	150 (1·88%)	159 (1·99%)	0·95 (0·76–1·18)	0·63
3c bleeding	35 (0·44%)	25 (0·31%)	1·41 (0·84–2·35)	0·19
3b bleeding	53 (0·66%)	74 (0·93%)	0·72 (0·51–1·02)	0·065
3a bleeding	77 (0·96%)	70 (0·88%)	1·10 (0·80–1·53)	0·55

Shown are the first event per event type for each patient only. Multiple events of the same type within the same patient are disregarded. Data were censored 730 days after index percutaneous coronary intervention. BARC=Bleeding Academic Research Consortium.[13] *New Q-wave or equivalent left bundle branch block (n=3) as adjudicated by the core laboratory.

Table 3: Primary and prespecified secondary outcomes

Vranckx P et a. Lancet 2018

TWILIGHT

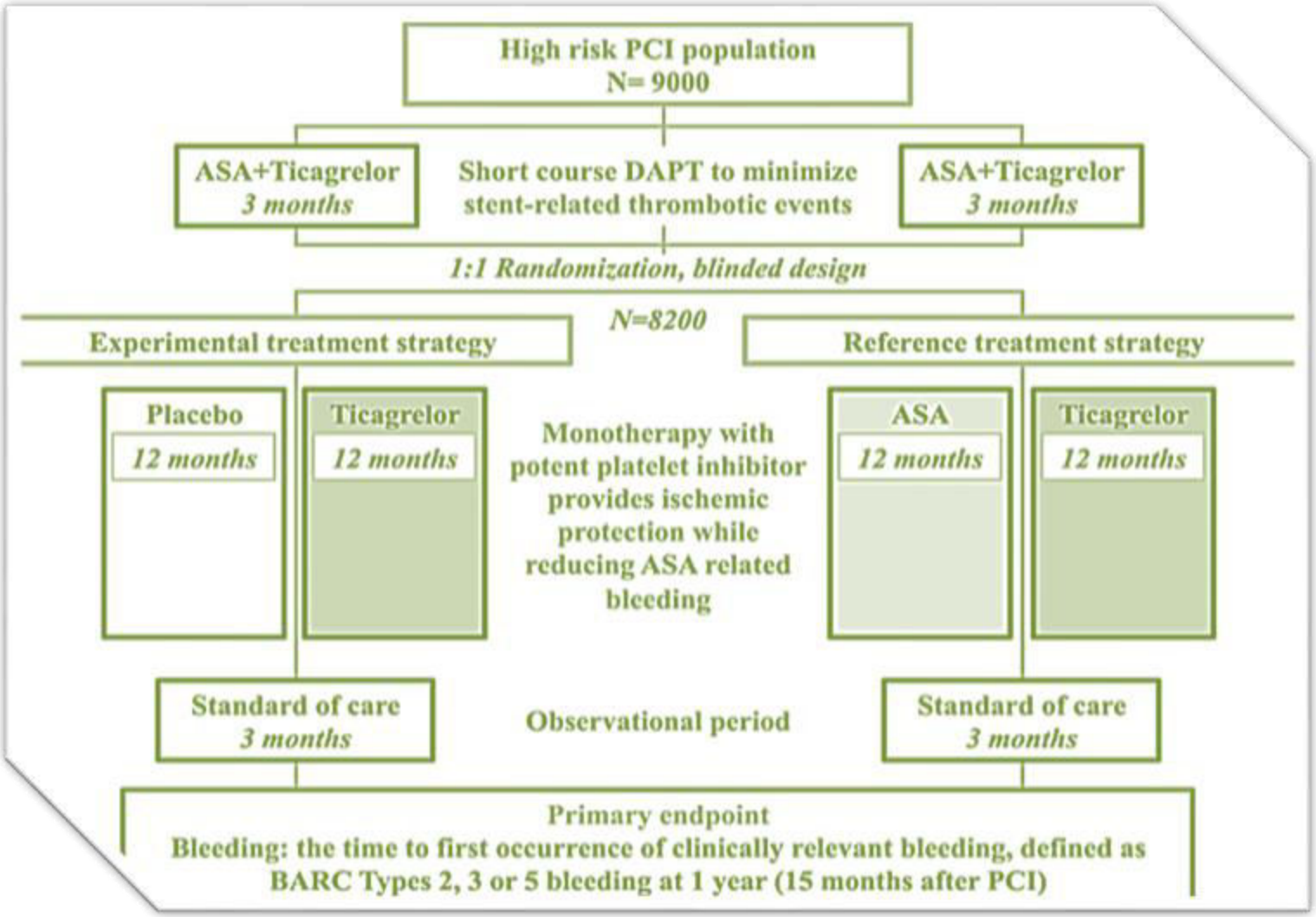
Elective

3 mths

Ticagrelor

1 year

Bleeding



Removing ASA after PCI

Study	n	Drug left	Efficacy	Safety
GLOBAL-LEADERS	16,000	ticagrelor	→	→
TWILIGHT	9,000	ticagrelor	?	?
TICO	3,056	ticagrelor	?	?
SMART-CHOICE	3,000	clopidogrel	?	?
STOPDAPT-2	3,045	clopidogrel	?	?

De-escalation if HBR

Scores (DAPT)

DAPT STUDY

LOGIN | Contact

About | For Patients | For Clinicians | For Media

DAPT Score Calculator

Patient Characteristics

Age: Between 65 and 74

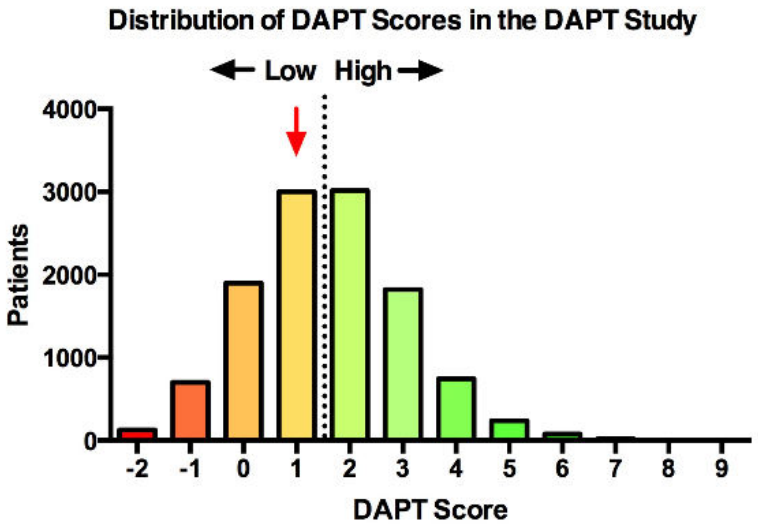
- Diabetes Mellitus ☑
- Cigarette Smoking Within Last Two Years ☐
- Prior Myocardial Infarction or Percutaneous Coronary Intervention ☑
- History of Congestive Heart Failure or Left Ventricular Ejection Fraction < 30% ☐

Index Procedure Characteristics

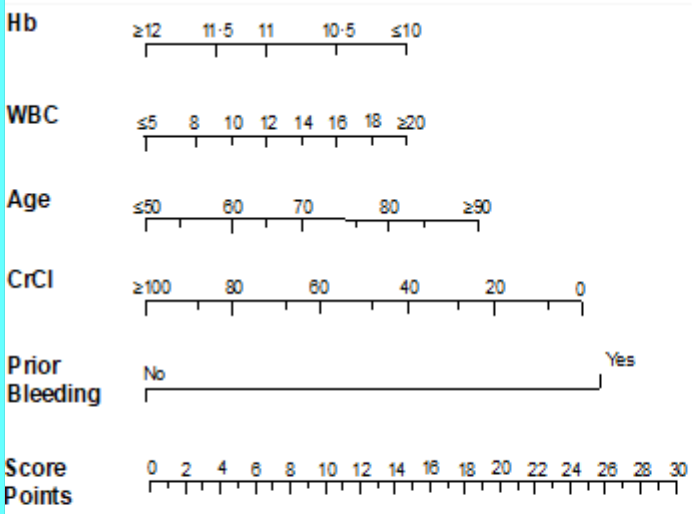
- Myocardial Infarction at Presentation ☐
- Stenting of Vein of Graft ☐
- Stent Diameter < 3mm ☐

DAPT Score = 1: LOW

Calculated DAPT Score Shown by Red Arrow



Scores to help decision

PRECISE DAPT score	DAPT score
At the time of coronary stenting	After 12 months of uneventful DAPT
Short DAPT (3-6 months) vs. Standard/Long DAPT (12-24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)
	Age ≥75 –2 pt 65 to <75 –1 pt <65 0 pt Cigarette smoking +1 pt Diabetes mellitus +1 pt MI at presentation +1 pt Prior PCI or prior MI +1 pt Paclitaxel-eluting stent +1 pt Stent diameter <3 mm +1 pt CHF or LVEF <30% +2 pt Vein graft stent +2 pt
0 to 100 points	-2 to 10 points
Score ≥25	Score ≥2
www.precisedaptscore.com	www.daptstudy.org

Costa F. et al. Lancet 2017

Yeh RW et al. JAMA 2016

Scores (Paris)

Risk score for Major bleeding

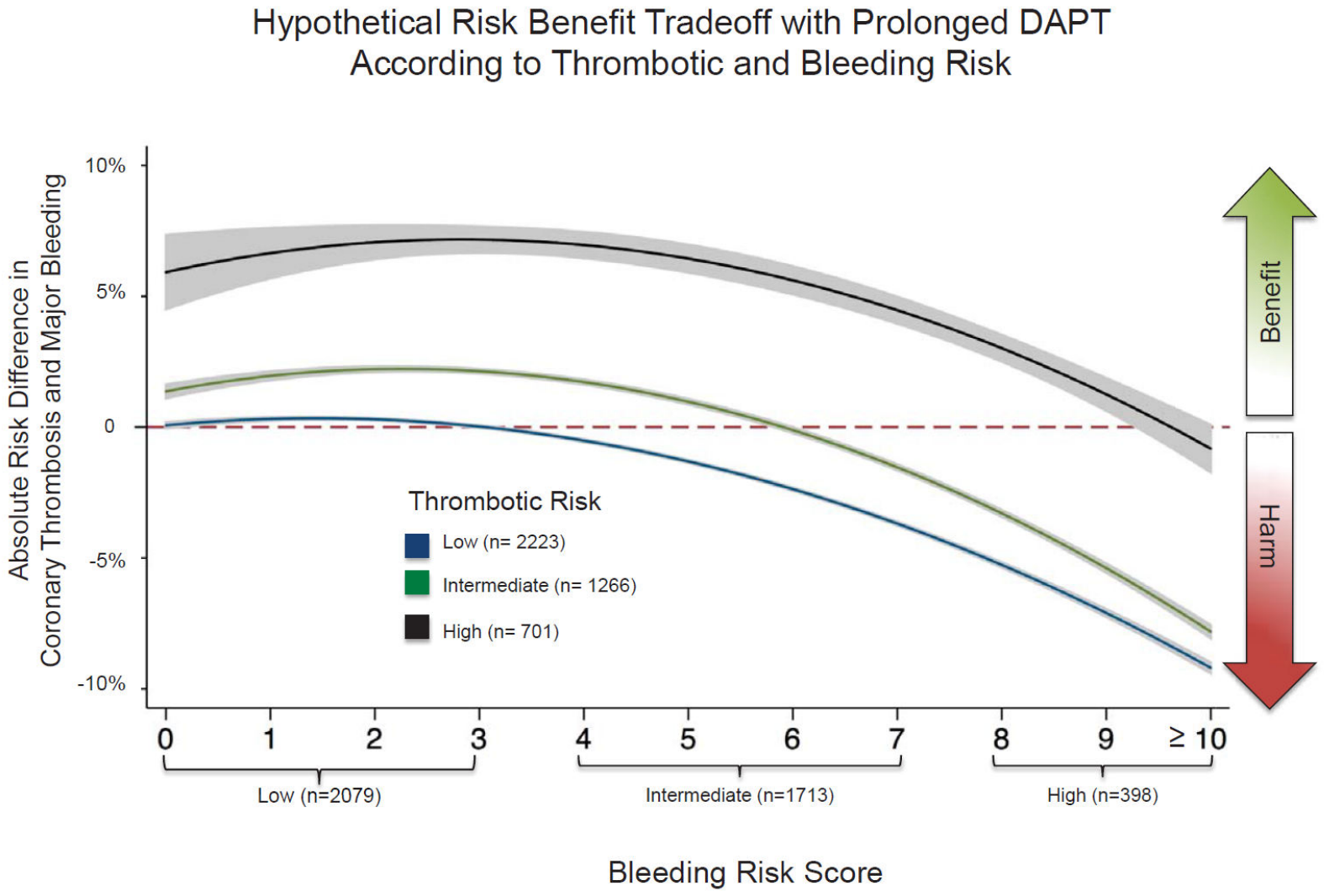
Age	0 → 4
BMI	0 → 2
Current smoking	0 → 2
Anemia	0 → 3
CrCl < 60	0 → 2
Triple therapy	0 → 2

Risk score for coronary event

Diabetes	0 → 4
ACS	0 → 2
Current smoking	0 → 2
Prior PCI	0 → 3
CrCl < 60	0 → 2
Prior CABG	0 → 2

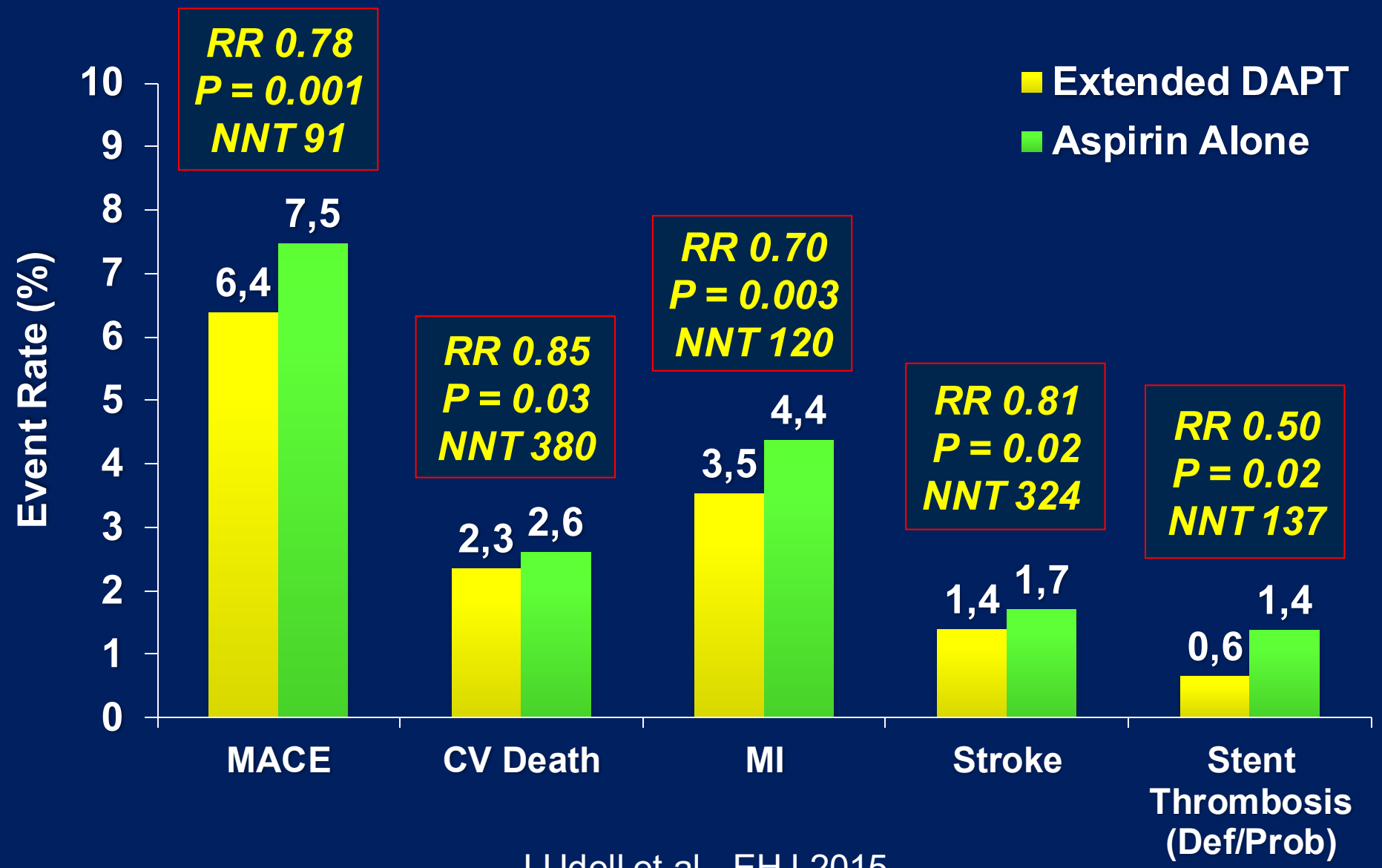
Baber U. et al. JACC 2016

Scores (Paris)



Baber U. et al. JACC 2016

Individual CV Endpoints



J Udell et al - EHJ 2015

Tradeoff between ischemic and bleeding risk

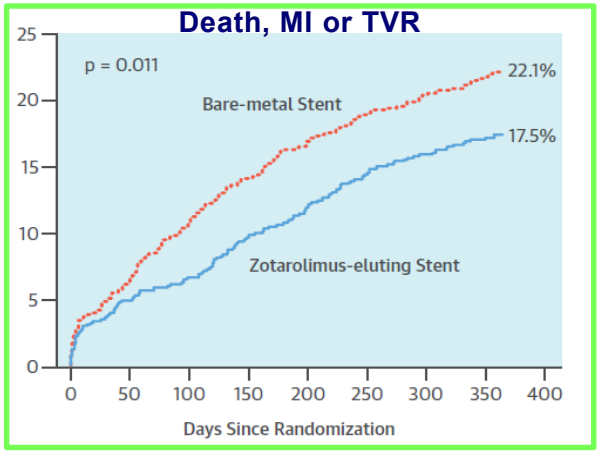
- Prolongation of DAPT for 18-36 months **in post-DES patients:**
  - ↘ ~1-2% of ST / MACE
  - ↗ ~1% of MB
  - Neutral on death

- Prolongation of DAPT for 18-36 months **in post-MI patients:**
  - ↘ ~1% of ST / MACE
  - ↗ ~1% of MB
  - ↘ ~0.3% CV death

Duration de-escalation

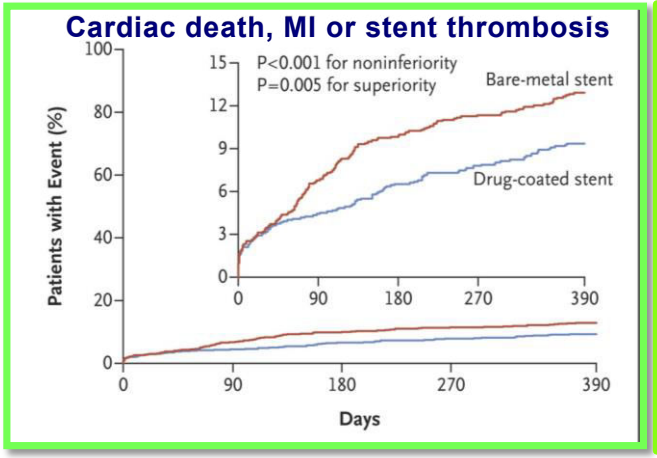
STENT in high bleeding risk

ZEUS study (n=1606)



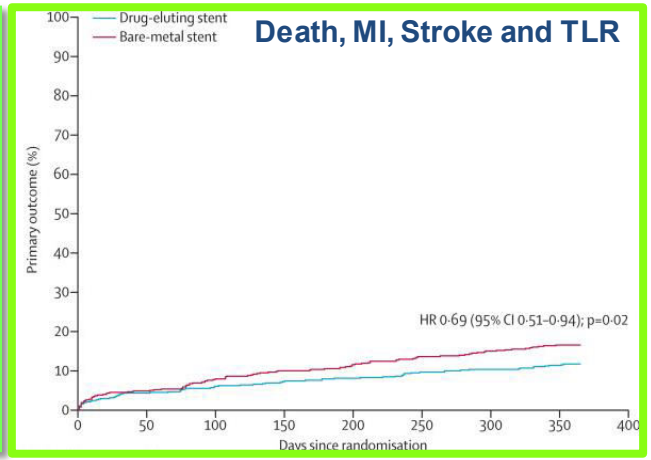
Valgimigli M et al. JACC 2015

LEADERS-FREE study (n=2466)



Urban P et al. NEJM 2015

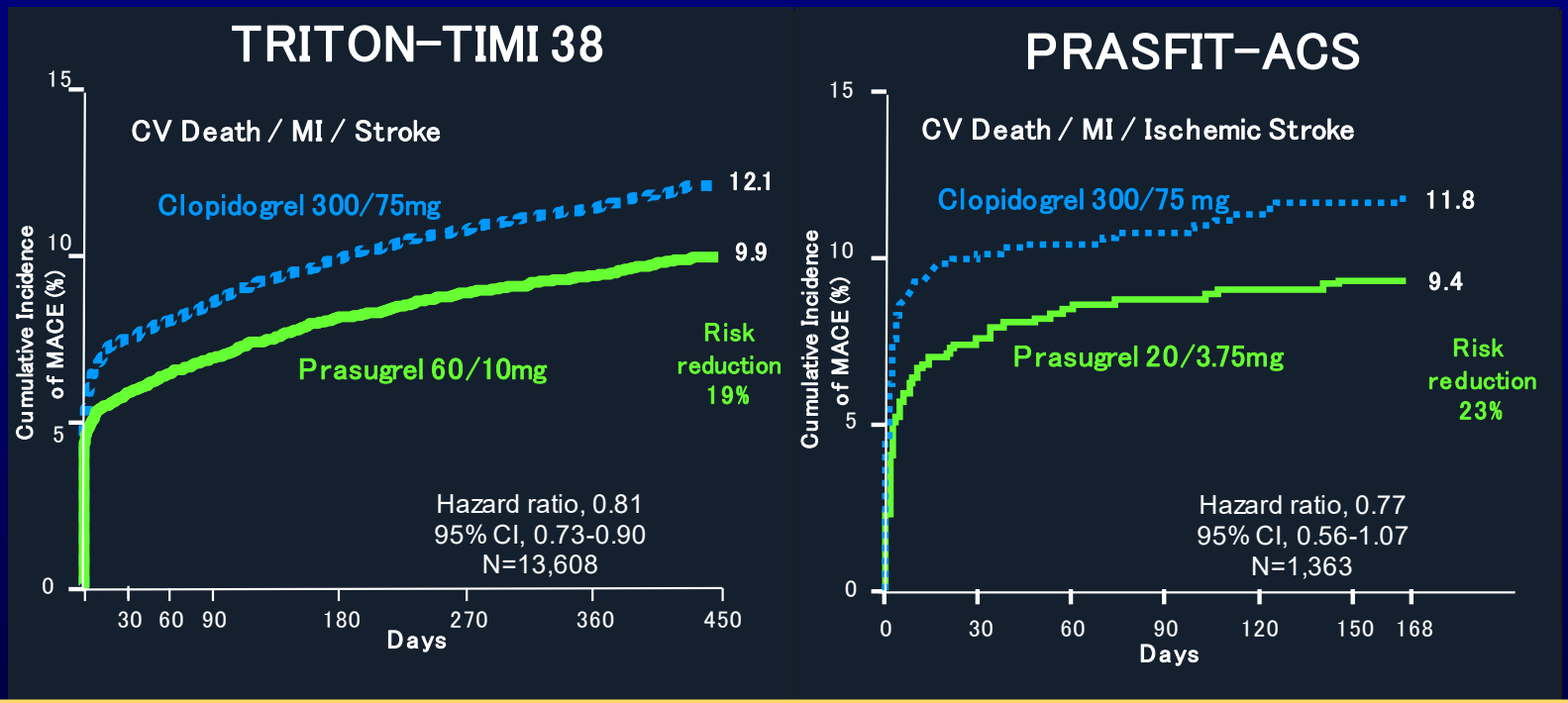
SENIOR study (n=1200)



Varenne O et al. Lancet 2017

Dose de-escalation

PRASFIT-ACS



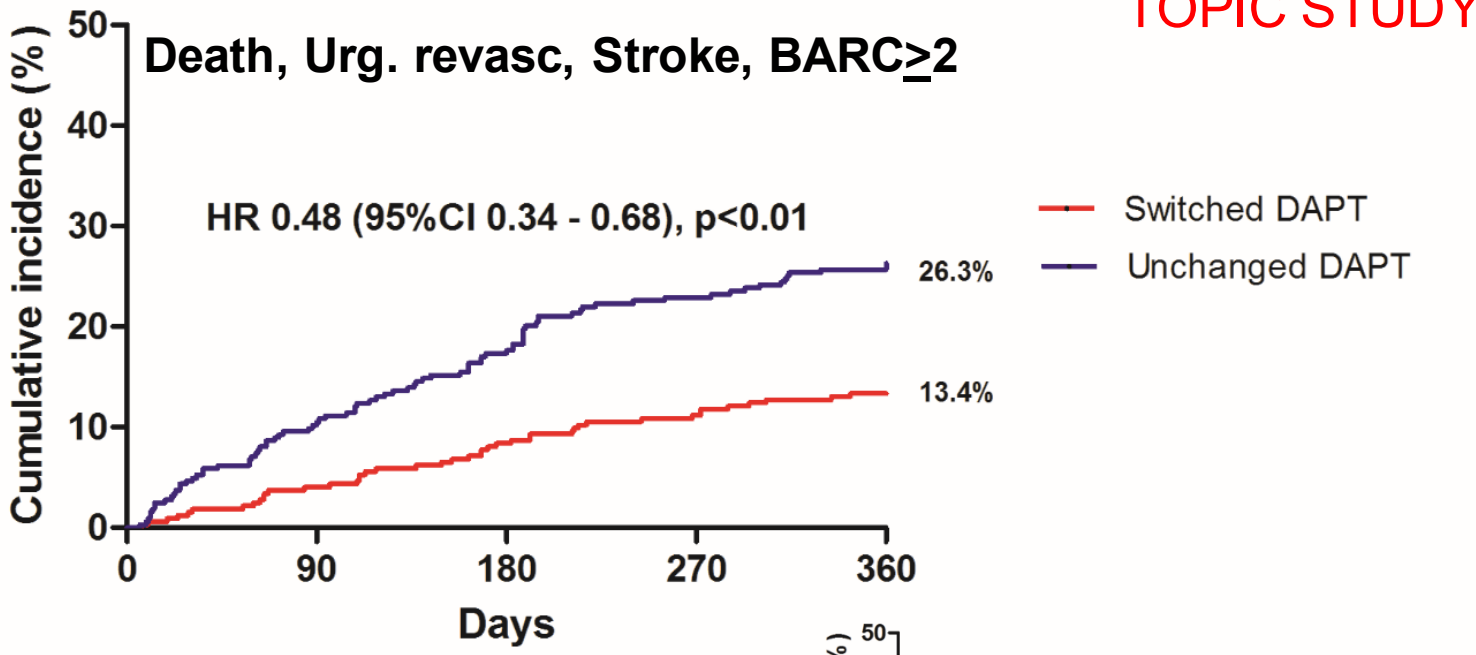
Major Bleed	2.2% prasu vs. 1.7% clopi	1.9 % prasu vs. 2.2% clopi

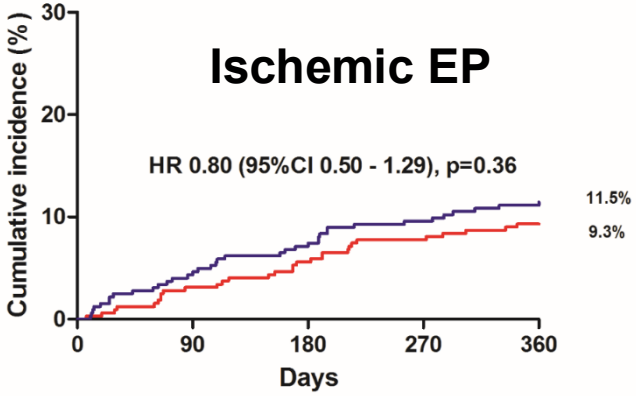
Wiviott S et al. NEJM 2007;357:2001–2015

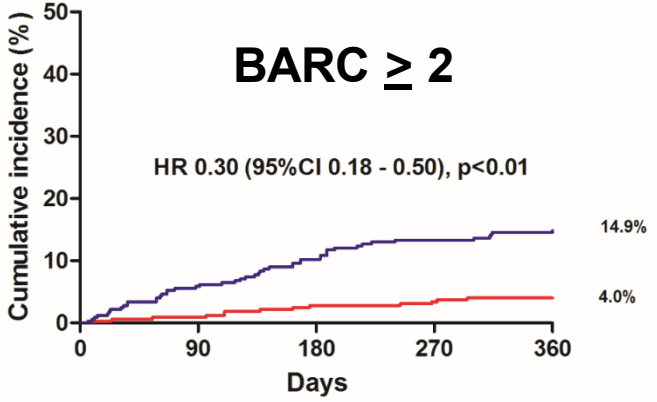
Saito S, et al. Circ J 2014; 78: 1684–92.

Time-related de-escalation

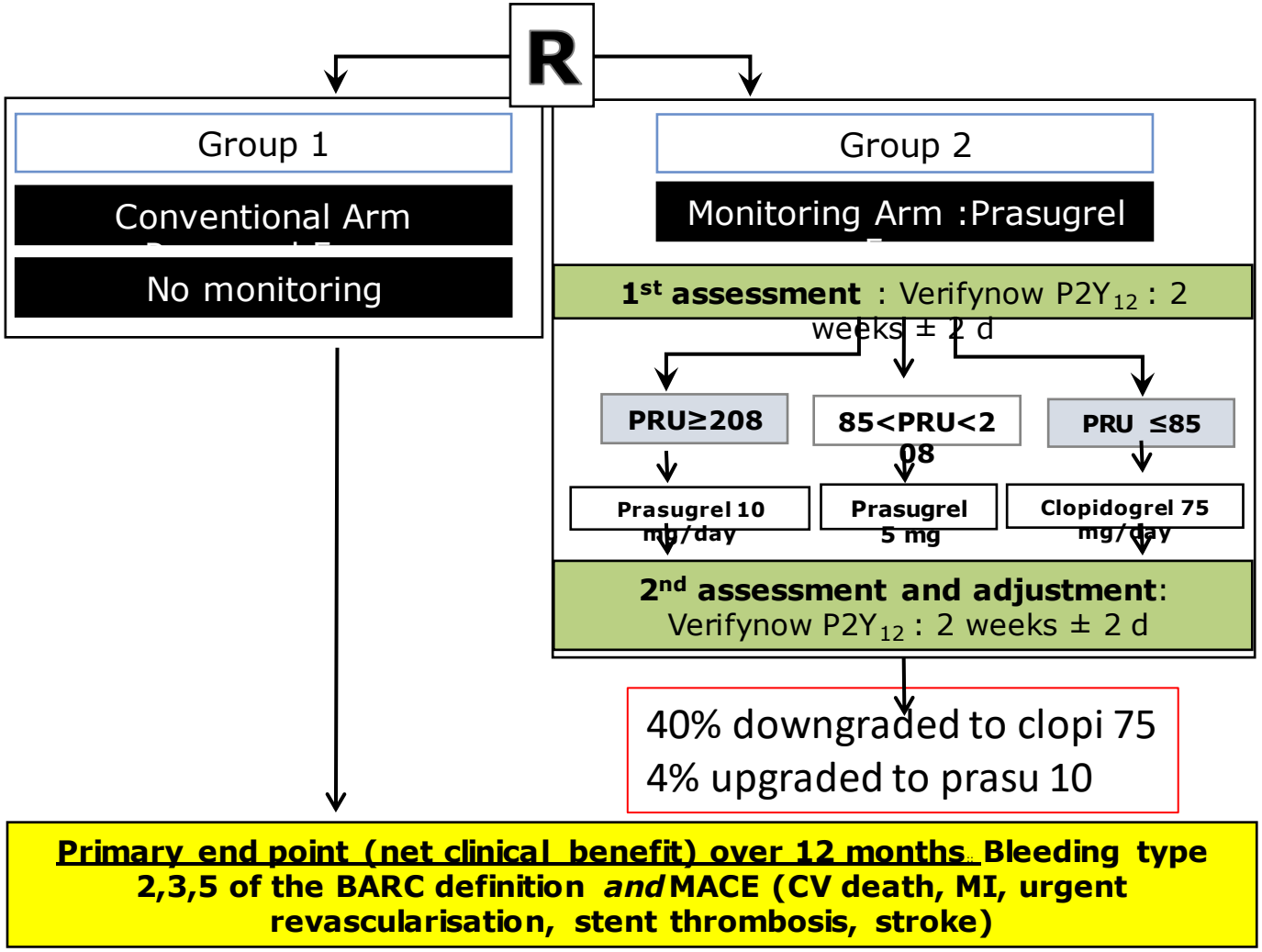
TOPIC STUDY







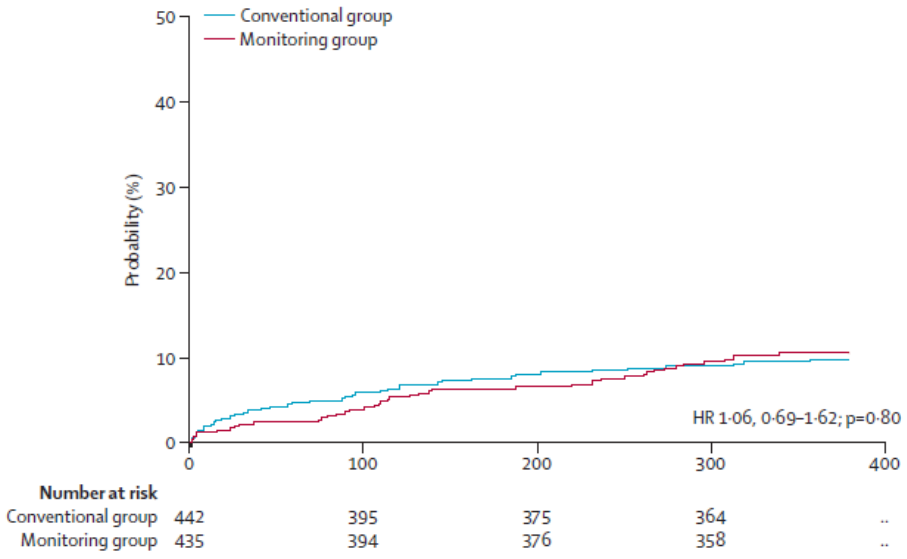
PFT-guided de-escalation: ANTARCTIC



PFT-guided de-escalation

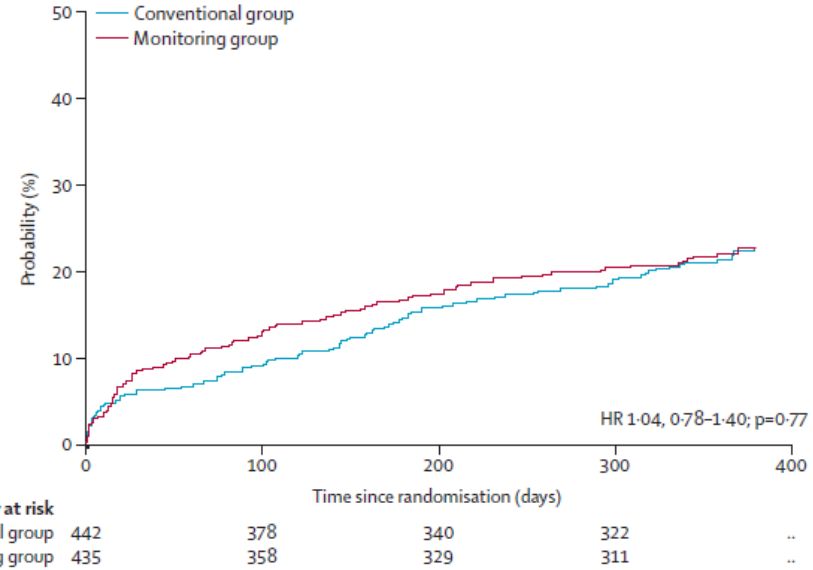
Ischemic Endpoint

CV death, MI, stent thrombosis, urgent revascularization



Bleeding Endpoint

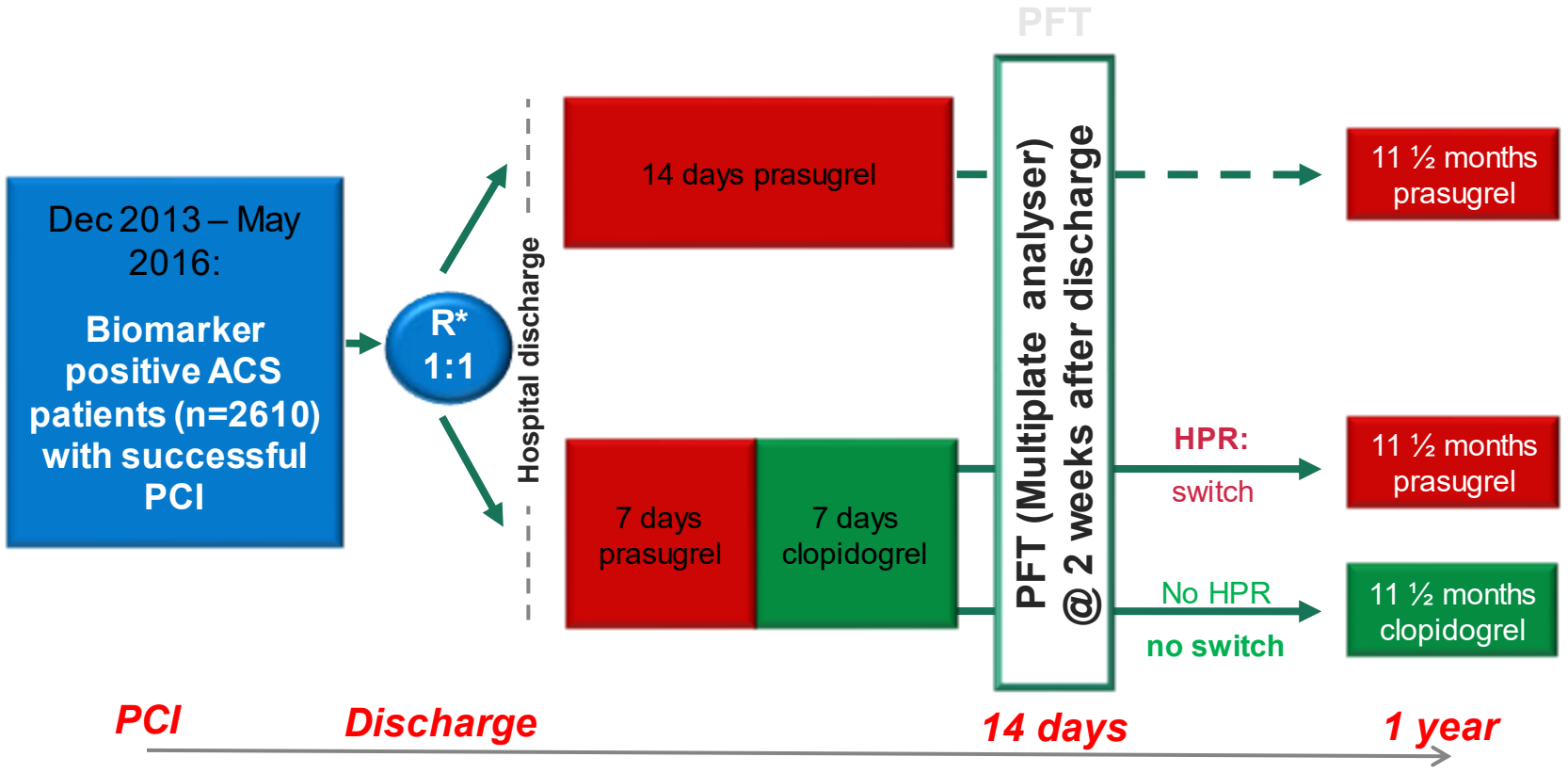
BARC 2,3,5



Cayla G. for the ANTARCTIC investigators. Lancet 2016

TROPICAL ACS

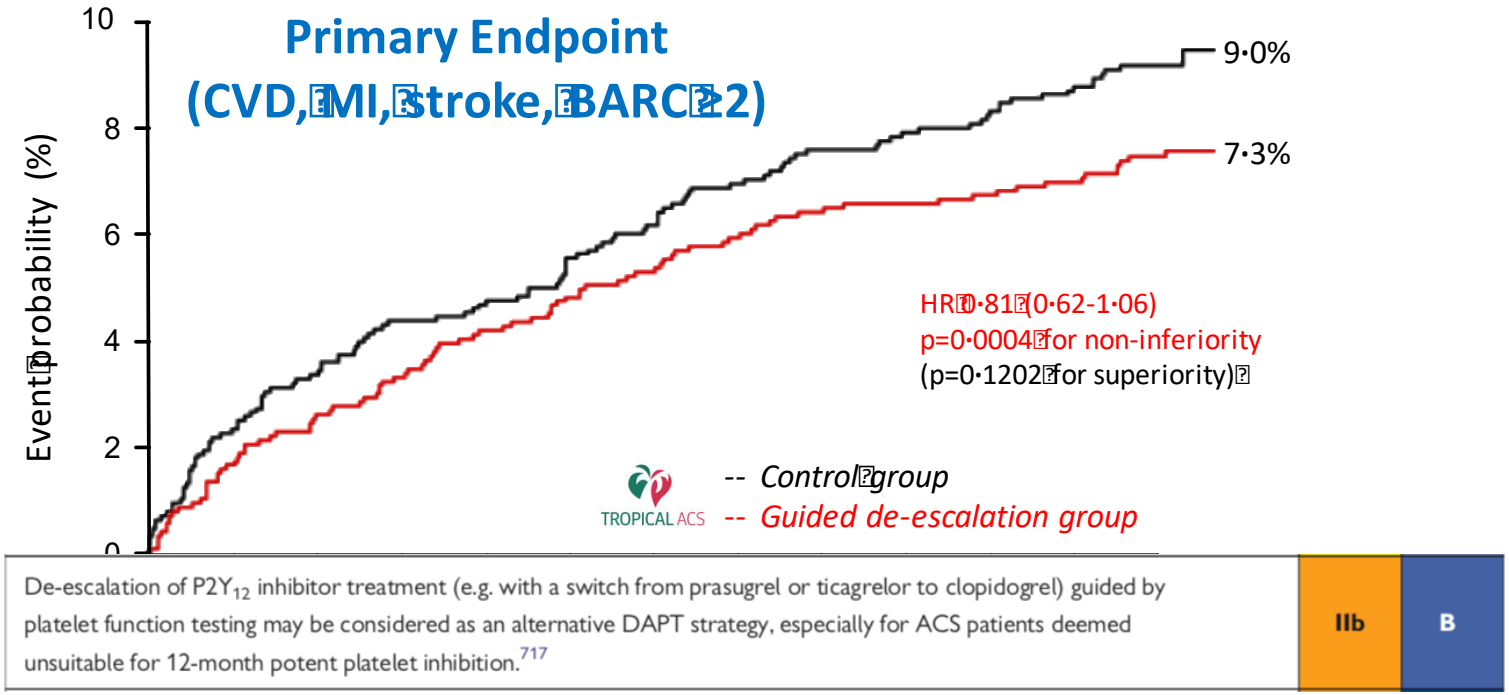
DE-ESCALATION



Sibbing, Aradi et al., Lancet 2017;390:1747-1757 .

TROPICAL ACS

DE-ESCALATION



De-escalation of $P2Y_{12}$ inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) guided by platelet function testing may be considered as an alternative DAPT strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition.[717]

IIb | B

Sibbing, Aradi et al., Lancet 2017;390:1747-1757 .
Neumann FJ et al. EHJ 2018;00,1–96.

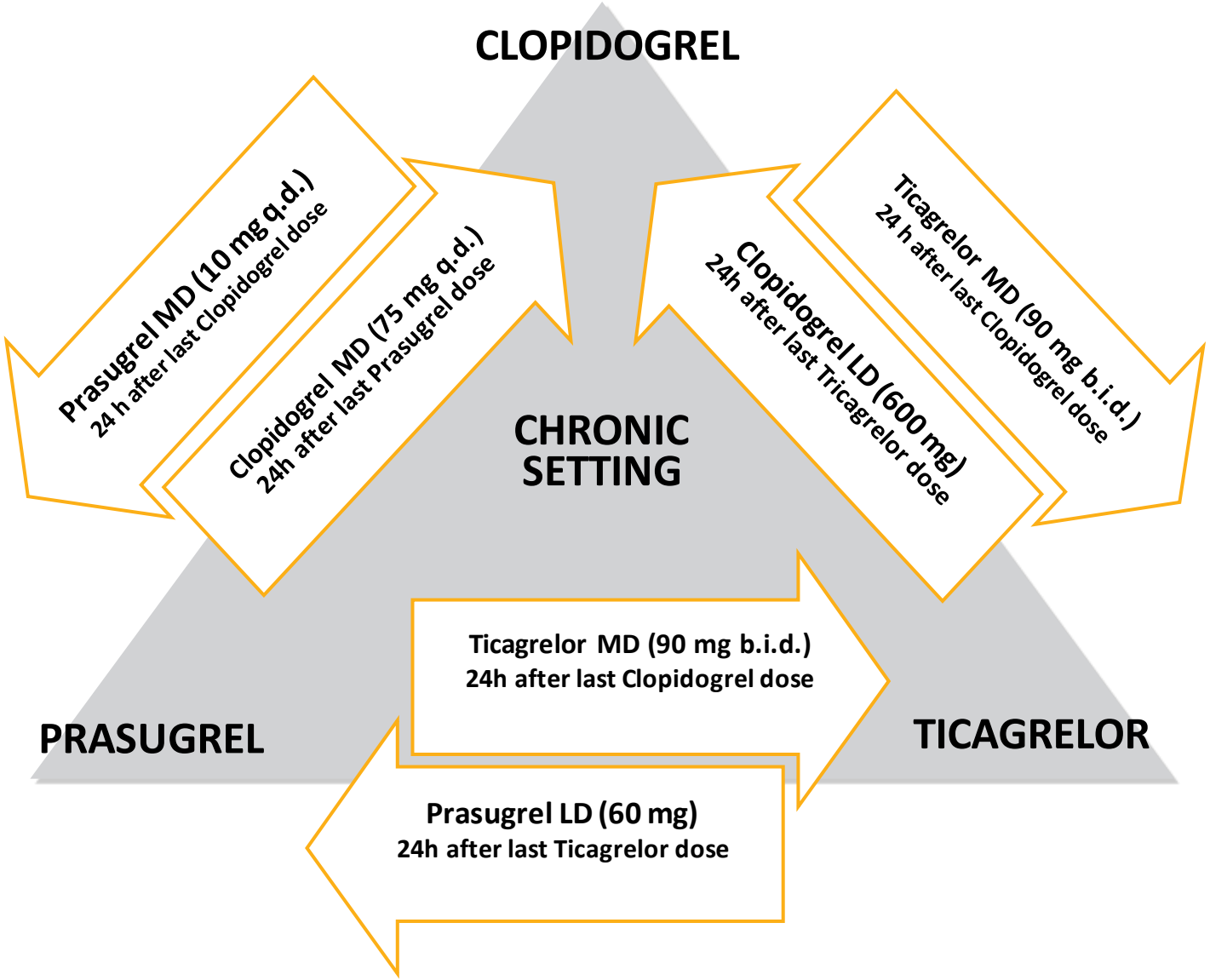
RESULTS: INDEPENDENT PREDICTORS OF BLEEDING

	Univariate analyses		Multivariate model	
	HR (95% CI)	**p**	**HR (95% CI)**	**P**
Age (years)	1.02 (1.01-1.04)	0.003	**1.02 (1.00-1.03)**	**0.04**
Female gender	1.47 (1.08-2.00)	0.015		-
BMI (kg/m^2)	0.96 (0.93-0.99)	0.014	**0.97 (0.93-0.99)**	**0.04**
STEMI vs. NSTEMI	0.69 (0.53-0.92)	0.010	**0.72 (0.54-0.95)**	**0.02**
LPR	1.71 (1.26-2.33)	0.001	**1.65 (1.21-2.26)**	**0.002**
Hemoglobin level (g/dl)	0.91 (0.85-0.97)	0.002	**0.92 (0.86-0.98)**	**0.008**
Prasugrel use **(both in control and guided groups)**	1.20 (0.88-1.65)	0.25		-
CKD 3-5	1.55 (0.95-2.51)	0.08		-

Risk factors of bleeding

- Short life expectancy
- Ongoing malignancy
- Poor expected adherence
- Poor mental status
- End stage renal failure
- Advanced age
- Prior major bleeding/prior haemorrhagic stroke
- Chronic alcohol abuse
- Anaemia
- Clinically significant bleeding on dual antithrombotic therapy

Algorithm for switching between oral $P2Y_{12}$ inhibitors in the chronic setting



Conclusions

1. STEMI: new P2Y12 tot, vite et fort
2. NSTEMI: P2Y12 qd diagnostic et PCI certains
3. CAD/PCI: clopidogrel
4. Switcher new P2Y12 vers clopidogrel quand haut risque hémorragique ou a distance de l'evenement
5. Prolonger ou interrompre P2Y12 ou ASA:

   → traitement individualisé (HBR)