Incidence, diagnostic methods and evolution of left-ventricular thrombus for patients with anterior myocardial infarction and low left-ventricular ejection fraction: a prospective multicenter study.

P Meurin[1], V Brandao Carreira[2], R Dumaine[1], A Shqueir[3], O Milleron[4], B Safar[4], S Perna[5], C Smadja[6], M Genest[7], J Garot[8], B Carette[9],L Payot[10] and JY Tabet[1]

For the Collège National de Cardiologues Français and the Collège National des Cardiologues des Hôpitaux Français.

(1) Centre de Réadaptation cardiaque de la Brie Les Grands Prés, Villeneuve Saint Denis, France.
(2)Hôpital de Marne La Vallée,, Jossigny, France.
(3) College National des Cardiologues Français and cabinet médical, Esbly 77450 France.
(4) Hôpital Le Raincy-Montfermeil Montfermeil, France.
(5) Hôpital de Meaux l, France.
(6) Clinique de Tournan ,Tournan en Brie, France.
(7)Hôpital Léon Binet ,Provins, France.
(8) Hôpital privé Jacques Cartier,Massy, France
(9) CliniqueCourlancy, Reims, France.
(10) Centre Hospitalier Inter communal André Grégoire, Montreuil sous bois, France.

Question n°1 :What is **Today** the incidence of Left Ventricular (LV) thrombus after Anterior-MI complicated with LV systolic dysfunction ?

- Before reperfusion techniques generalization for acute MI :
  - 25-40% of patients after Ant-MI
- Nowadays:
  - 7-10% of patients after unselected Ant-MI

But what is the incidence of LV thrombus after Ant-MI complicated with LV systolic dysfunction inspite of a modern treatment ?

-angioplasty

-dual antiplatelet therapy

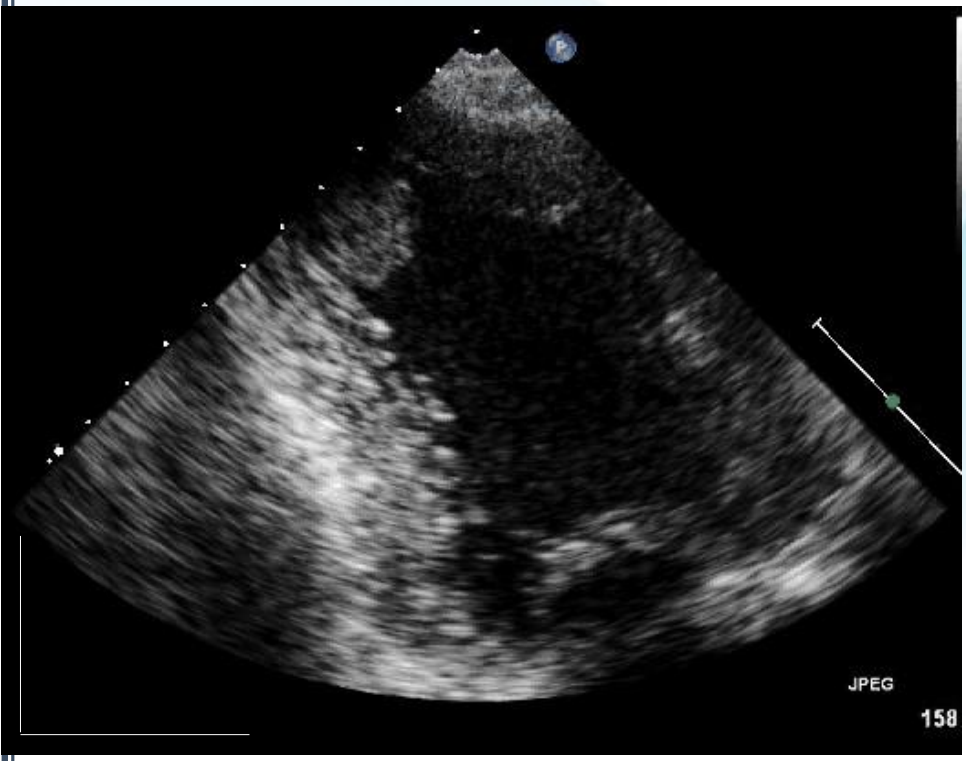
Question n°2: Is Transthoracic Echocardiography (TTE) a Good Exam to Detect These LV Thrombi… Or should all these patients undergo a cardiac magnetic resonance imaging (CMR-DE) ?

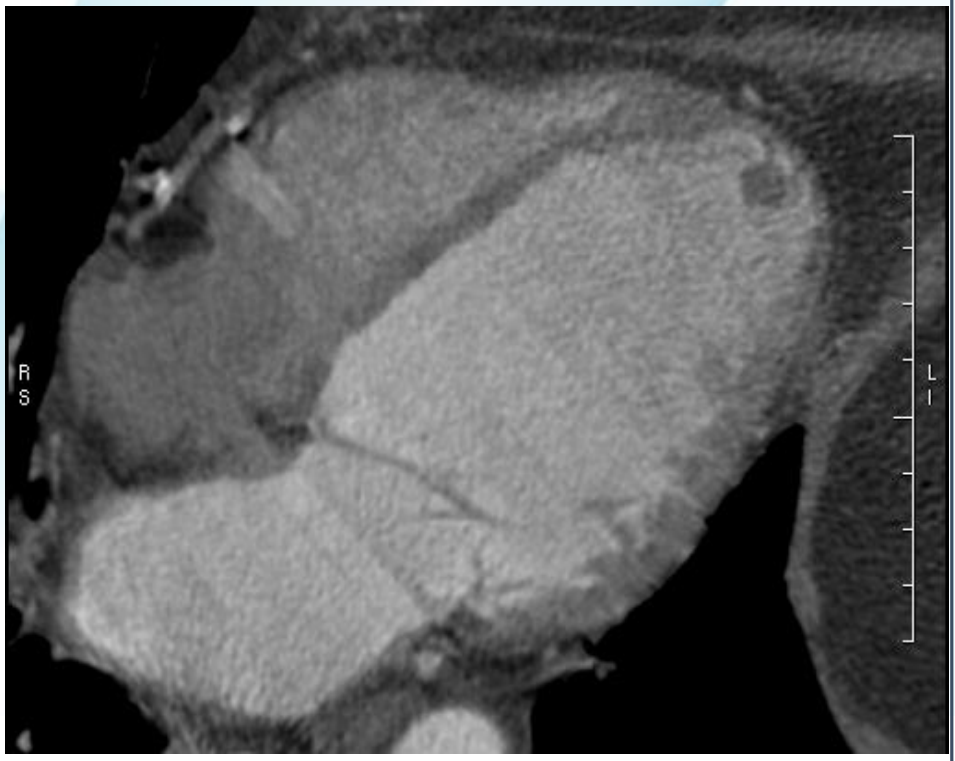
- ✓ Only 2 prospective studies compared the 2 techniques, in 41 LV thrombi[1,2], but they had flaws:
  - -Substudies[1]
  - -No prespecification of LV thrombus search on the echographic prescription[1,2]

Their Results Suggest a very Low Sensibility for TTE: 20-25 %

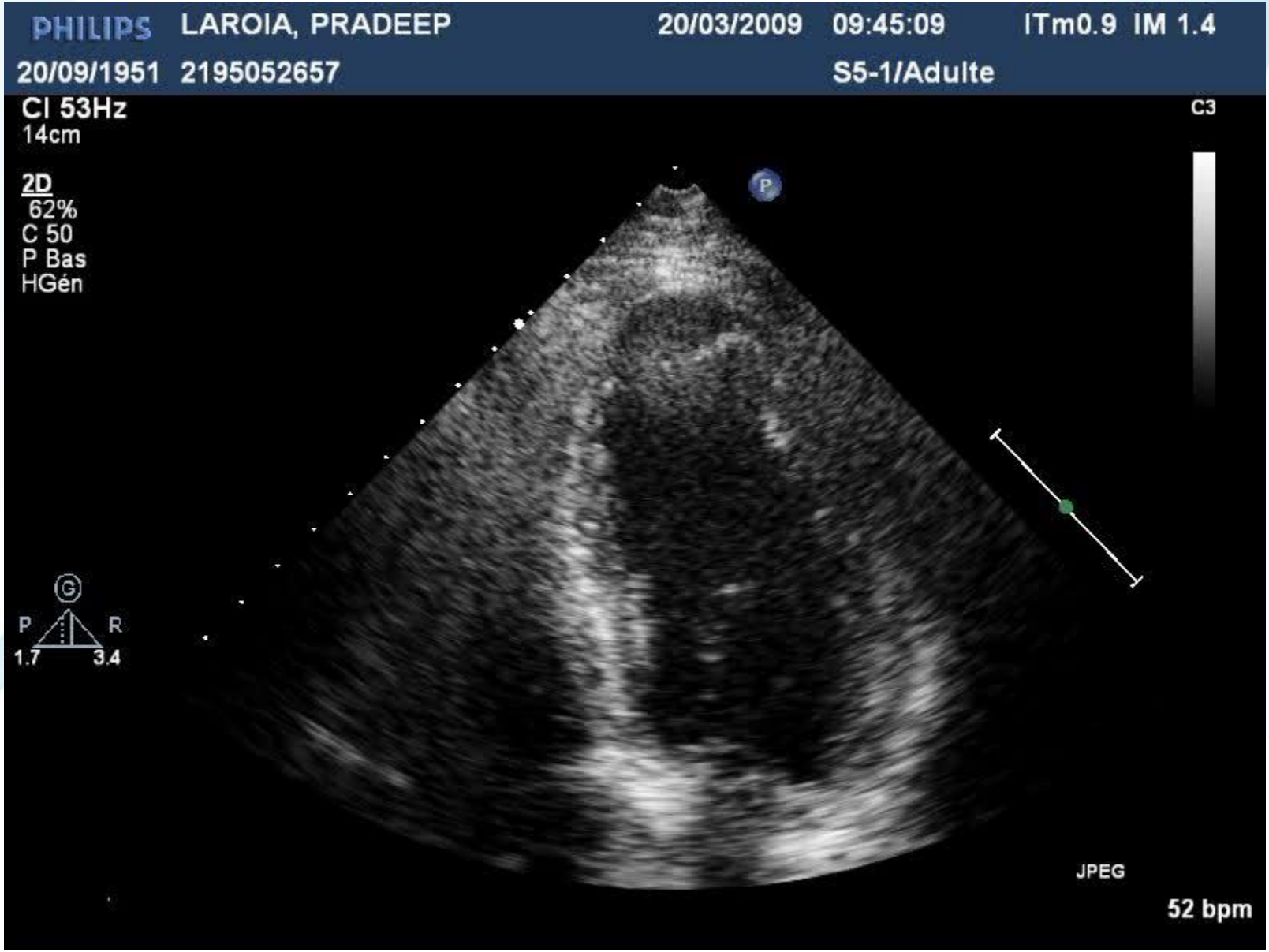
(1) Delewi R et al. Eur J Radiol. 2012 ; 81:3900-4. (2) Mollet NR, et al.Circulation. 2002;106:2873-6.

It is not always so easy…





PHILIPS
ELOTHMANI ABDELKADER
10/12/2008
11:56:11
ITm0.9 IM 1.4
01/01/1941
43501120081210
S5-1/Adulte
CI 58Hz
12cm
2D
67%
C 50
P Bas
HGén
C3
P
R
1.7
3.4
JPEG
158 bpm


PHILIPS
LAROIA, PRADEEP
20/03/2009
09:45:09
ITm0.9 IM 1.4
20/09/1951
2195052657
S5-1/Adulte
CI 53Hz
14cm
2D
62%
C 50
P Bas
HGén
C3
P
G
P
R
1.7
3.4
JPEG
52 bpm

Question n°3: Quel traitement anti-thrombotique administrer à ces patients ?

- Etude pensée avant les résultats de l'étude WOEST donc:
  - Arrêt prasugrel ou ticagrélor remplacés par plavix sans dose de charge
  - Lovenox 100ui/kg/bid jusqu'à INR ≥ 2
  - AVK au moins 6 mois
  - Aspirine 75 mg
- Que ferions nous aujourd'hui ?
  - NACO ?
  - Arrêt de l'aspirine ?

The WOEST Trial: First randomised trial comparing two regimens with and without aspirin in patients on oral anticoagulant therapy undergoing coronary stenting

Willem Dewilde, Tom Oirbans, Freek Verheugt, Johannes Kelder, Bart De Smet, Jean-Paul Herrman, Tom Adriaenssens, Mathias Vrolix, Antonius Heestermans, Marije Vis, Saman Rasoul, Kaioum Sheikjoesoef, Tom Vandendriessche, Carlos Van Mieghem, Kristoff Cornelis, Jeroen Vos, Guus Brueren, Nicolien Breet and Jurriën ten Berg

The WOEST Trial= **W**hat is the **O**ptimal antiplat**E**let and anticoagulant therapy in patients with oral anticoagulation and coronary **S**ten**T**ing (clinicaltrials.gov NCT00769938)

Lancet 2013; 381: 1107-15|

WOEST

Aim of the study

To test the hypothesis that in patients on OAC undergoing PCI, *clopidogrel alone* is superior to the combination *aspirin and clopidogrel* with respect to bleeding but is not increasing thrombotic risk in a multicentre two-country study (The Netherlands and Belgium)

WOEST

Study Design-1

Inclusion criteria:

1/ Indication for OAC for at least 1 year

2/ One coronary lesion eligible for PCI

3/ Age over 18

Exclusion criteria:

1/ History of intracranial bleeding

2/ Cardiogenic shock during hospitalisation

3/ Peptic ulcer in the previous 6 months

4/ TIMI major bleeding in the previous year

5/ Contra-indication for aspirin or clopidogrel

6/ Thrombocytopenia (platelet count less than 50,000 per ml)

7/ Pregnancy

8/ Age >80

WOEST

Study Design-2

1:1 Randomisation:

Double therapy group:	Triple therapy group
OAC + 75mg Clopidogrel	OAC + 75mg Clopidogrel + 80mg Aspirin
1 month minimum after BMS 1 year after DES	1 month minimum after BMS 1 year after DES

Follow up: **1 year**

Primary Endpoint: **The occurence of all bleeding events (TIMI criteria)**

Secondary Endpoints:

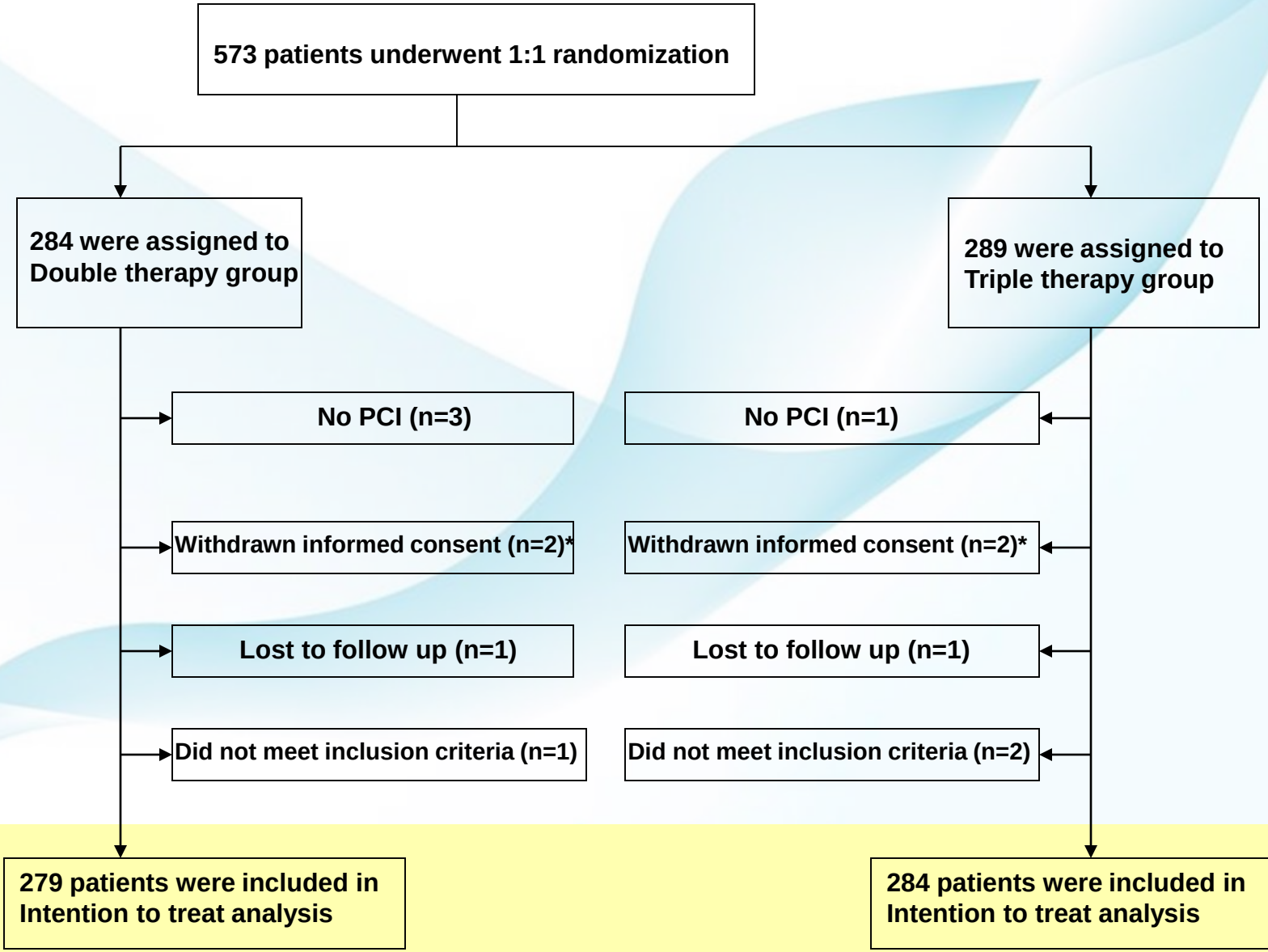
- **Combination of stroke, death, myocardial infarction, stent thrombosis and target vessel revascularisation**
- **All individual components of primary and secondary endpoints**

Study Design-3

- Power calculation was based on the largest retrospective study by Karjalainen[1] addressing this issue.
- We anticipated a 12% bleeding rate in the triple therapy group and a 5% bleeding rate in the double therapy group
- Power was chosen to be 80% and α level 5%. The total patient number is estimated at n = 496
- The study is designed as a superiority trial
- All events were adjudicated by a committee blinded to treatment allocation

[1] Eur Heart J 2007;28:726-32

WOEST



* withdrawn informed consent; in double group 2 patients and triple group 1 patient were included in intention to treat analysis until the day of withdrawal

Baseline Characteristics

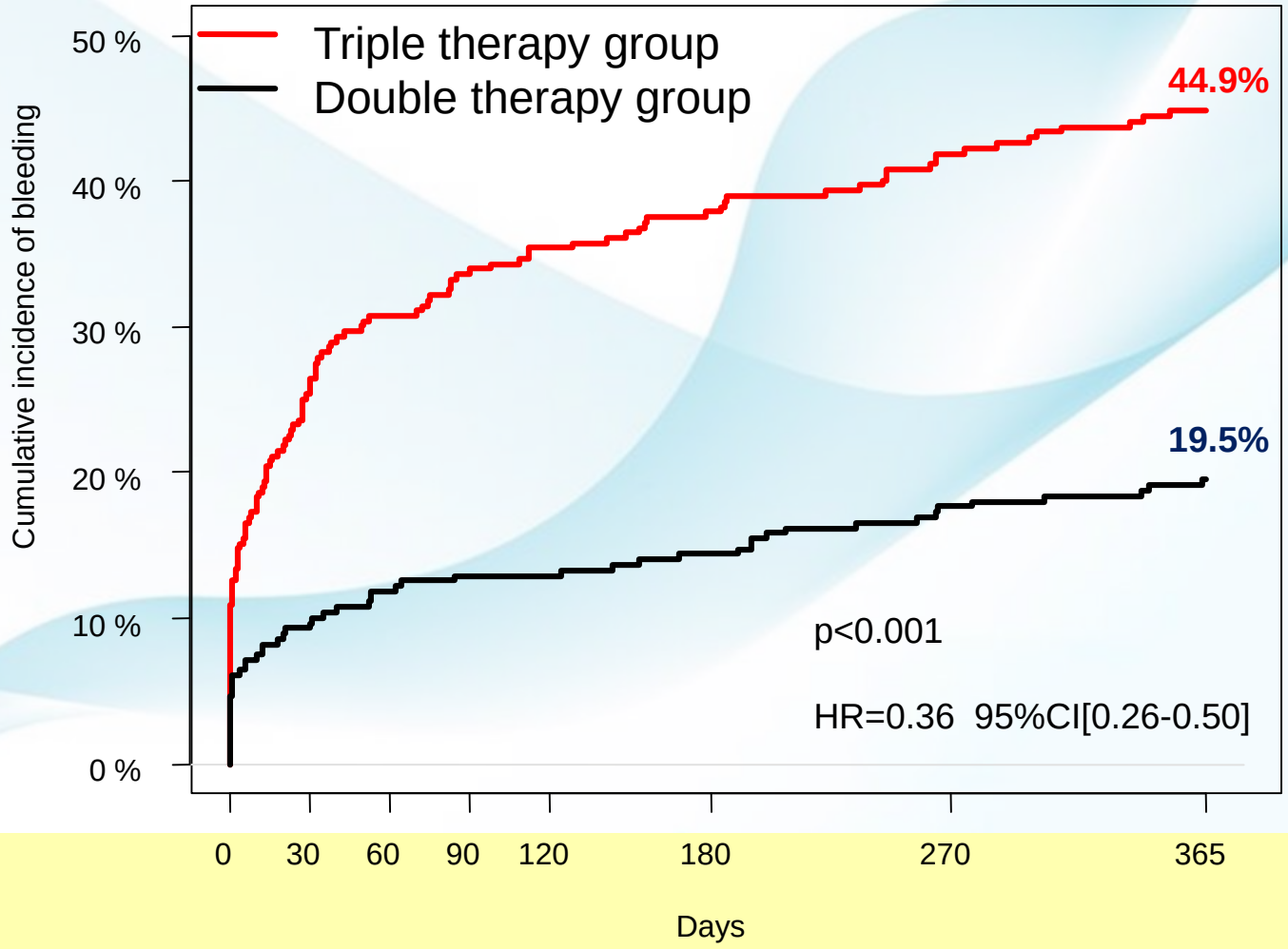
	Double therapy n=279 (%)	Triple therapy n=284 (%)
Age	70.3 (±7.3)	69.5(±8.0)
Male gender	214 (76.7%)	234 (82.4%)
BMI (kg/m2)	27.5 (±4.3)	27.9 (±4.2)
Current Smoker	60 (21.5%)	42 (14.8%)
Diabetes	68 (24.4%)	72 (25.4%)
Hypertension	193 (69.2%)	193 (68.0%)
Hypercholesterolemia	191 (68.5%)	205 (72.2%)
History of MI	96 (34.4%)	100 (35.2%)
History of Heart Failure	71 (25.4%)	70 (24.6%)
History of Stroke	49 (17.6%)	50 (17.6%)
History of PCI	86 (30.8%)	101 (35.6%)
History of CABG	56 (20.1%)	74 (26.1%)
History of GI bleeding	14 (5.0%)	14 (4.9%)
Indication for OAC		
AF/Aflutter	164 (69.5%)	162 (69.2%)
Mechanical valve	24 (10.2%)	25 (10.7%)
Other (pulmonary embolus,	48 (20.3%)	47 (20.1%)
EF<30%, Apical thrombus...)		
ACS at baseline	69 (25.0%)	86 (30.6%)

Procedural Characteristics

	Double therapy n=279 (%)	Triple therapy n=284 (%)
PCI vessel		
LAD	111(39.9%)	118 (41.8%)
RCX	59 (21.2%)	76 (27.0%)
RCA	92 (33.1%)	72 (25.5%)
Arterial/Venous Graft	16 (5.7%)	16 (5.6%)
INR on the day of PCI	1.86 (±0.9)	1.94 (±1.1)
LVEF <=30%	40 (21.1%)	37 (18.1%)
Stent type		
No	5 (1.8%)	4 (1.4%)
BMS	89 (32.0%)	86 (30.3%)
DES	181 (65.1%)	183 (64.4%)
BMS + DES	3 (1.0%)	11 (3.8%)
Femoral access	204 (73.4%)	208 (74.6%)
Radial access	74 (26.6%)	71 (25.4%)
Angioseal	166 (59.5%)	167 (59.4%)
Other closure device	43 (15.4%)	29 (10.3%)
Peri-produral OAC continuation	128 (45.9%)	113 (39.8%)
Peri-procedural LMWH	66 (23.7%)	68 (23.9%)
Peri-Procedural GPIIbIIIa	25 (8.9%)	26 (9.1%)
Peri-Procedural Fondaparinux	3 (1.0%)	2 (0.7%)

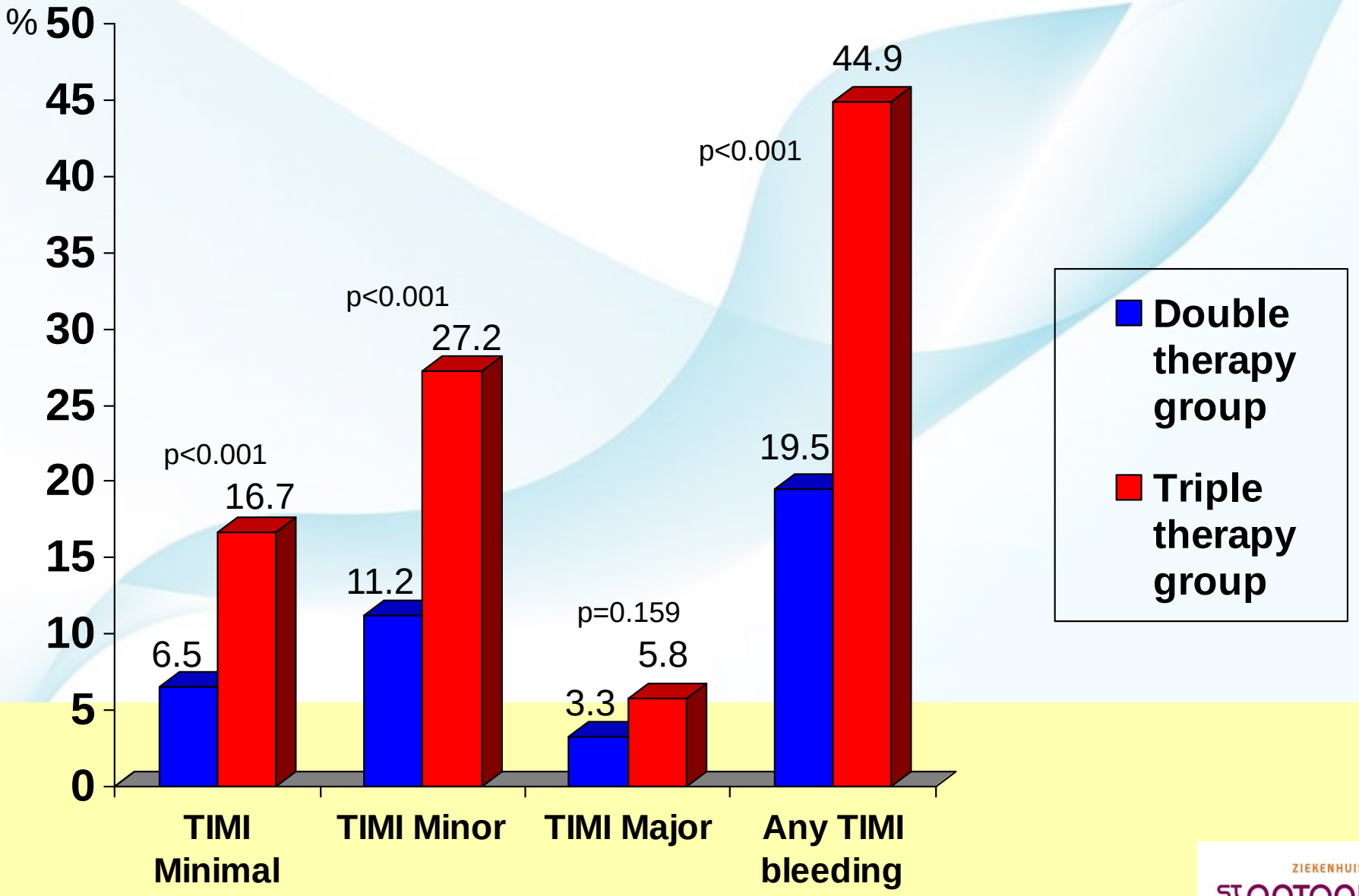
WOEST: Results

Primary Endpoint: Total number of TIMI bleeding events

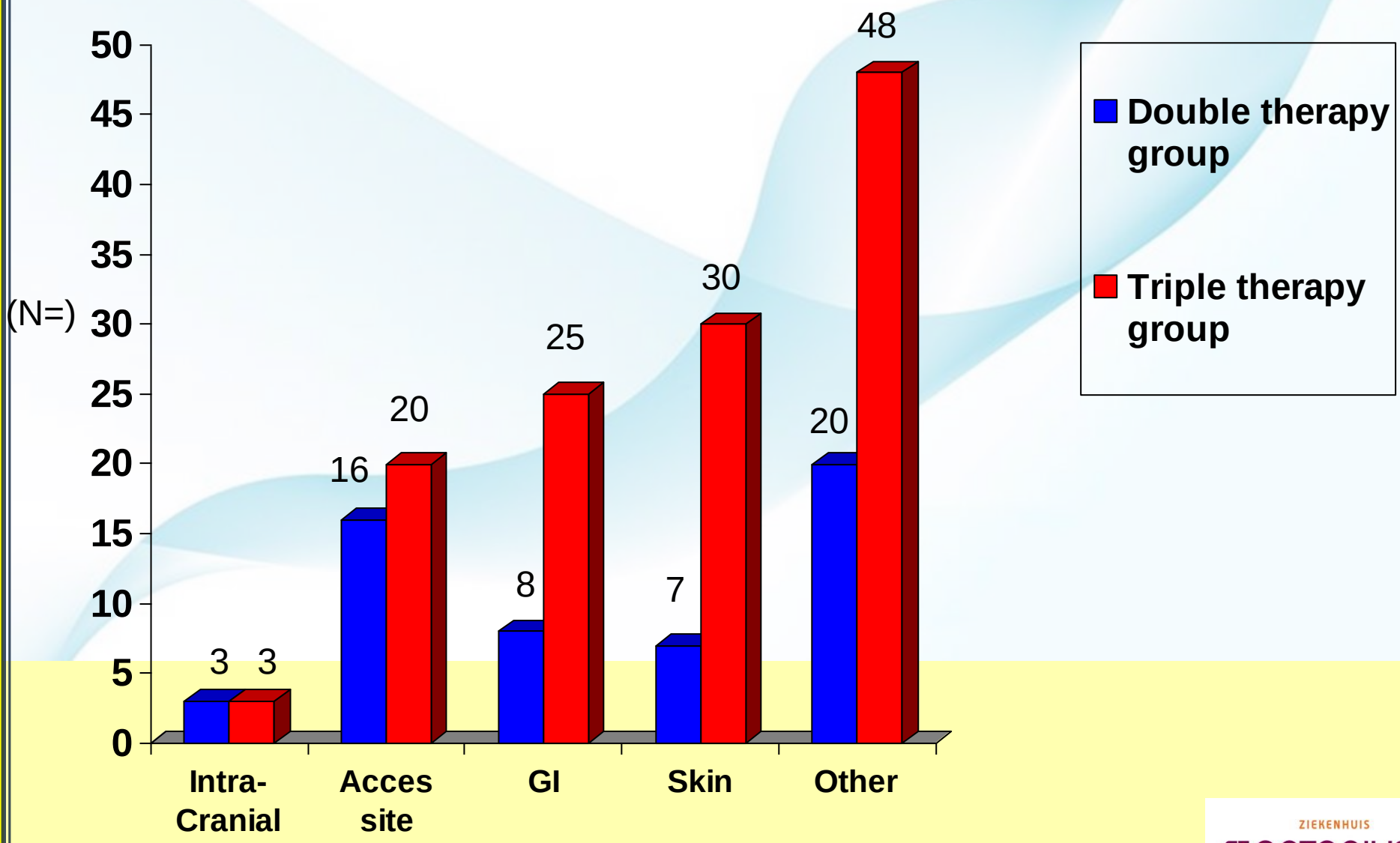


n at risk:	284	210	194	186	181	173	159	140
	279	253	244	241	241	236	226	208

Primary Endpoint: Bleeding events TIMI classification



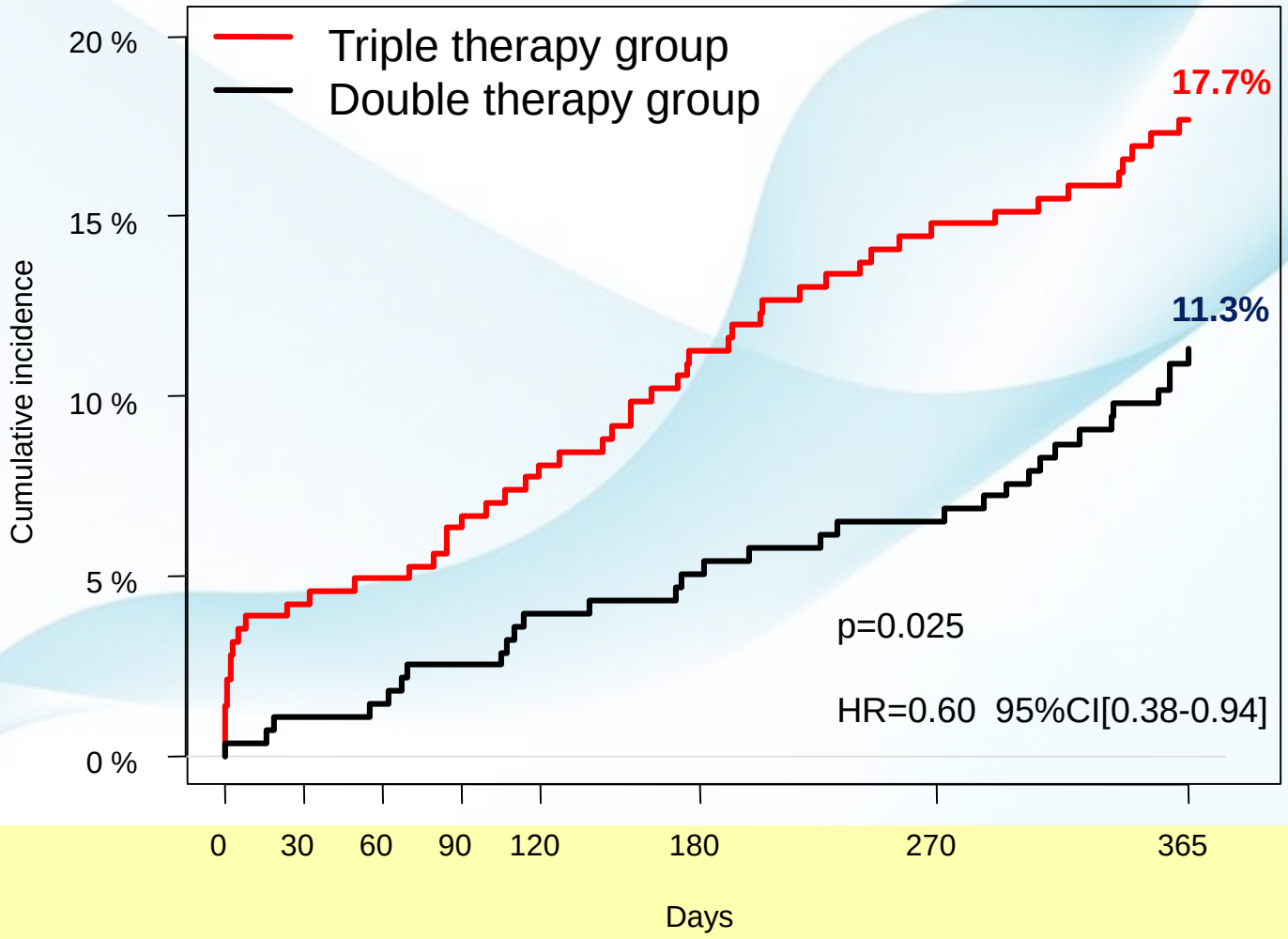
Locations of TIMI bleeding: Worst bleeding per patient



GI=gastro intestinal; Other bleeding consists of eye, urogenital, respiratory tract, retroperitoneal, mouth, PMpocket bleeding

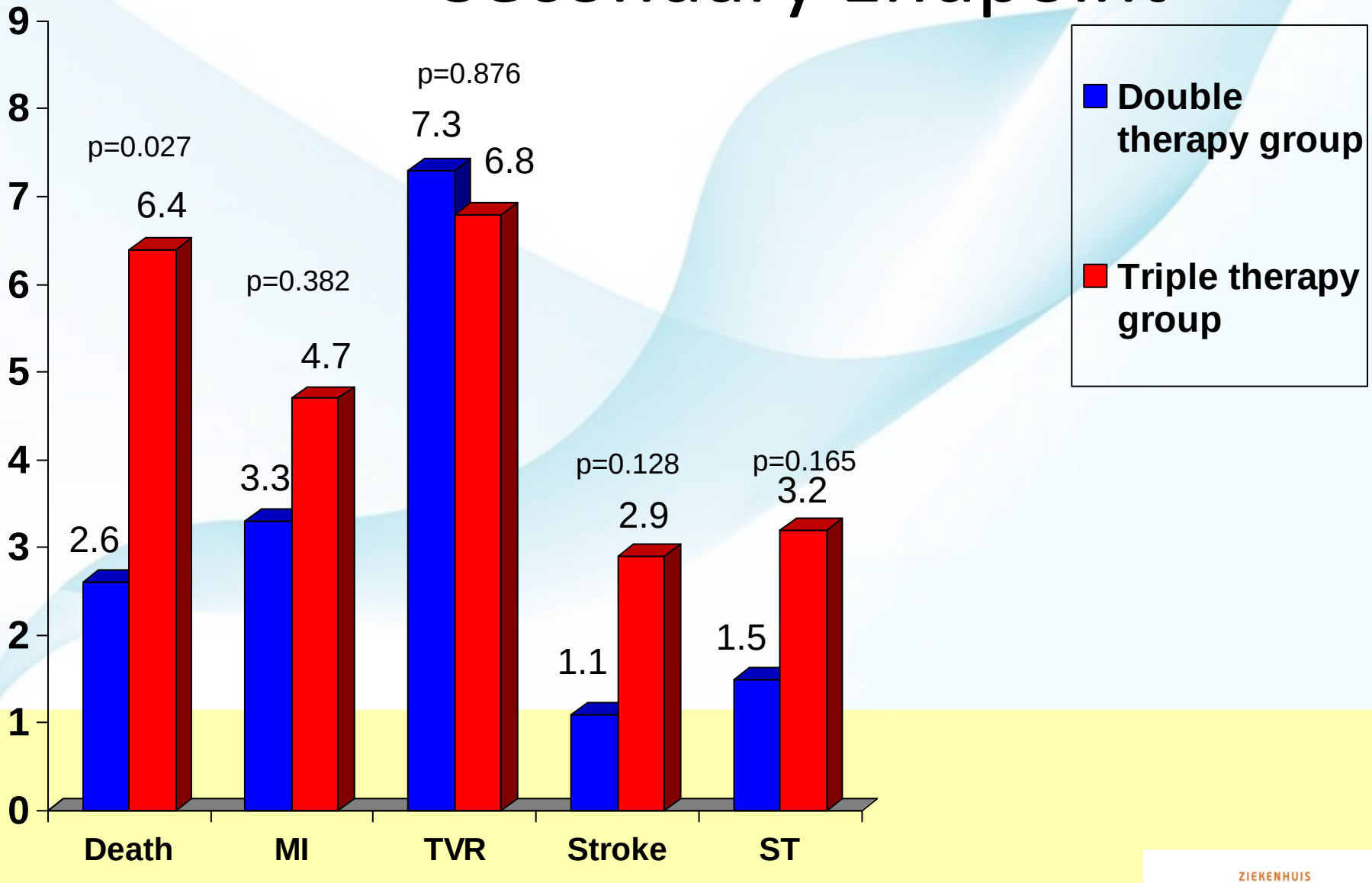
WOEST

Secondary Endpoint (Death, MI,TVR, Stroke, ST)



n at risk:								
	284	272	270	266	261	252	242	223
	279	276	273	270	266	263	258	234

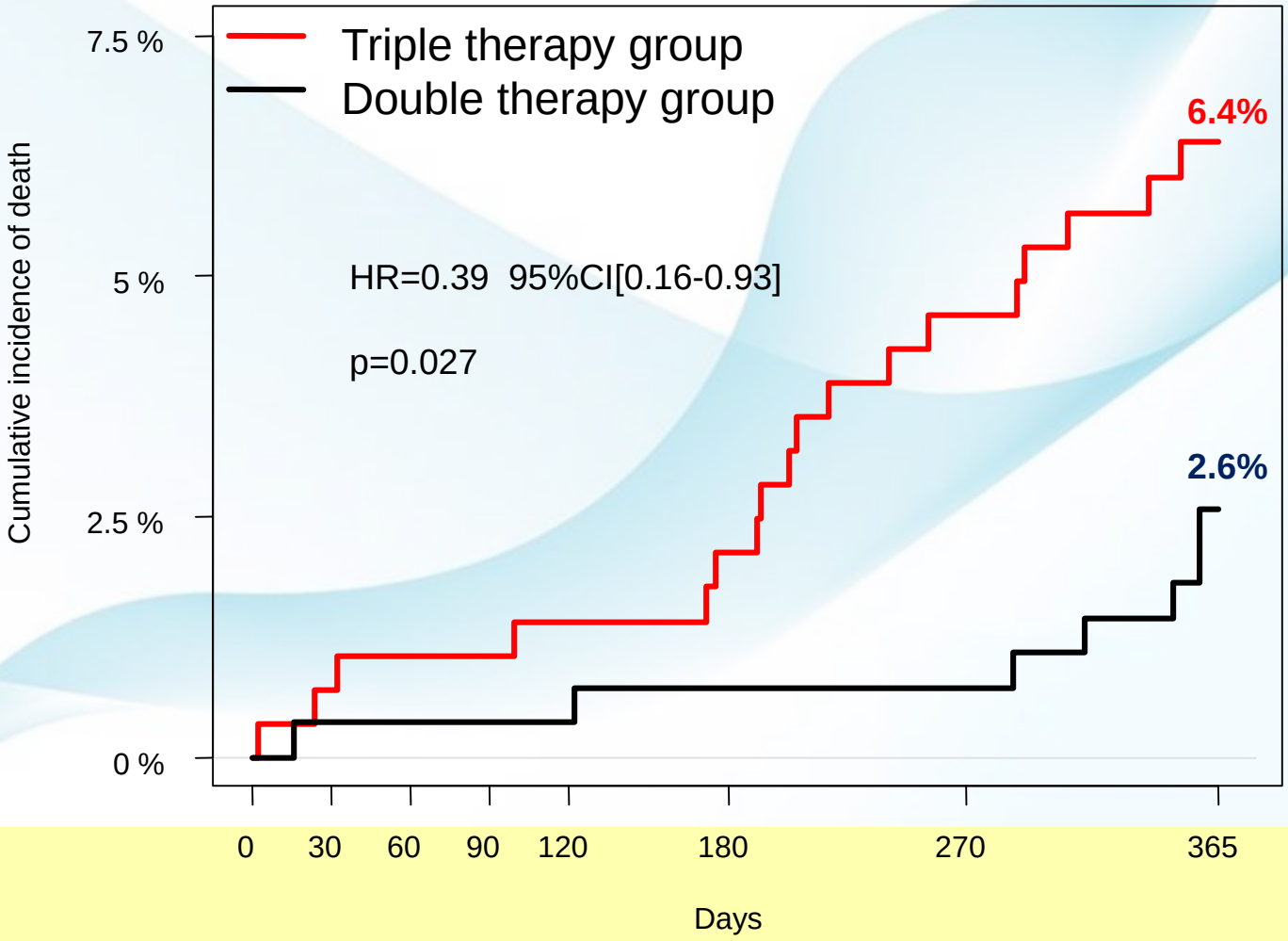
Secondary Endpoint



MI=any myocardial infarction; TVR= target vessel revascularisation (PCI + CABG); ST= stent thrombosis

WOEST

All-Cause Mortality



n at risk:								
	284	281	280	280	279	277	270	252
	279	278	276	276	276	275	274	256

Limitations

- The study was powered to show superiority on the primary bleeding endpoint, but not to show non-inferiority on the secondary endpoint

- Open label trial design with its inherent bias

- Classification of smaller bleeding, although well defined and blindly adjudicated, may be subjective

WOEST

Conclusions

1. First randomized trial to address the optimal antiplatelet therapy in patients on OAC undergoing coronary stenting

2. In this study which was specifically designed to detect bleeding events, the bleeding rate was higher than expected

3. Primary endpoint was met: OAC plus clopidogrel causes less bleeding than triple antithrombotic therapy, but now shown in a randomized way

4. Secondary endpoint was met: with double therapy there is no excess of thrombotic/thromboembolic events: stroke, stent thrombosis, target vessel revascularisation, myocardial infarction or death

5. Less all-cause mortality with double therapy

WOEST

Implications

We propose that a strategy of oral anticoagulants plus clopidogrel, but without aspirin could be applied in this group of high-risk patients on OAC when undergoing PCI

Conséquences de WOEST

- Modifications des Guidelines dans la FA:
  - In pts with ACS and AF at high risk of bleeding (HAS-BLED ≥ 3), the initial use of triple therapy consisting of OAC (NOAC or VKA), aspirin and clopidogrel should be considerred for for 4 weeks following PCI irrespective of stent type. This should be followed by long term therapy (up to 12 months)with OAC and a single antiplatelet therapy drug (preferably clopidogrel 75 mg or as an alternative, aspirin 75-100mg) (IIaC)

- Etudes en coursdans la FA
  - ISAER triple, MUSICA 2, LASER registry
  - REDUAL

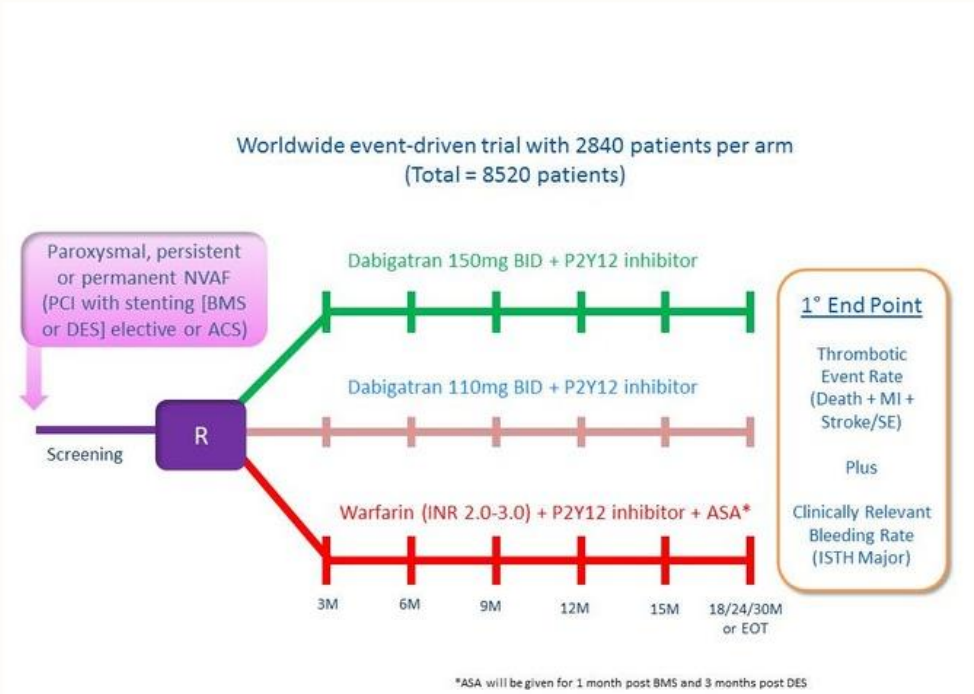
Management of antithrombotic therapy in atrial fibrillation patients presenting with SCA or undergoing PCI: joint consensus document of the ESC working group on thrombosis, EHRA, EAPCI…
Eur Heart J 2014

REDUAL-PCI: utiliser un NACO ? (dabigatran)

Primary Endpoints:

- Time to death or first thrombotic event (DTE) (all death, myocardial infarction (MI), stroke/systemic embolism (SE))
- Time to first International Society of Thrombosis and Haemostasis Major Bleeding Event (MBE)

Study Design Note: Dr. Cannon's presentation entitled " Patients with Atrial Fibrillation and PCI or ACS Need Triple Therapy - Practical Guidance" with additional detail on the REDUAL-PCI study design can also be viewed here.



Pourrons nous ensuite faire l’analogie FA / TIG ?

Question n°1 :What is **Today** the incidence of Left Ventricular (LV) thrombus after Anterior-MI complicated with LV systolic dysfunction ?

What is the incidence of LV thrombus after Ant-MI complicated with LV systolic dysfunction inspite of a modern treatment ?

- **-angioplasty**
- **-dual antiplatelet therapy**

Question n°2: Is Transthoracic Echocardiography (TTE) a Good Exam to Detect These LV Thrombi… Or should all these patients undergo a cardiac magnetic resonance imaging (CMR-DE) ?

Previous biased studiesSuggest a very Low Sensibility for TTE: 20-25 %

(1) Delewi R et al. Eur J Radiol. 2012 ; 81:3900-4. (2) Mollet NR, et al.Circulation. 2002;106:2873-6.

Methods

- in 7 Centers,Inclusion of 100 consecutive Patients :
  - With LVEF < 45 % within 7 days After Ant-MI
  - Without CMR contra indication at baseline

- LV thrombus incidence and evolution
  - At least 3 mandatory assessments including TTE and clinical evaluation
    - TTE_1: inclusion
    - TTE_2: 30 days after MI
    - TTE_3: 6 to 12 months after MI

- Comparison TTE and CMR-DE
  - At day 30 after MI: TTE_2 and CMR-DE performed the same day and blindly evaluated
    - CMR not performed in case of excellent LV recovery (LVEF > 50%) observed between TTE_1 and TTE_2.

Results

TTE_1: 100 patients with LVEF < 45% 6.0 days (median) after Ant-MI

-LV thrombus: n = 7

CMR-DE not performed, n = 22

- No need (LVEF at day 30 ≥ 50%), n= 9
- New CMR contra-indication (CRT), n = 13

Second assessment 30.0 days after Ant-MI2 including TTE_2 *and* CMR-DE, n = 78

-Persisting LV thrombus (existing at TTE_1), n = 3

-New LV thrombus, n = 16

-Dissolution of the former thrombus, n = 2

Second assessment 30.0 days after Ant-MI including TTE_2 *but* no CMR-DE, n = 22

-Persisting LV thrombus (existing at TTE_1), n = 1

-New LV thrombus, n = 2

-Dissolution of the former thrombus, n = 1

Patients not continuing (n=5): 3 deaths; 2 cardiac transplantation

Third assessment 270 days TTE_3 after Ant-MI, n = 95

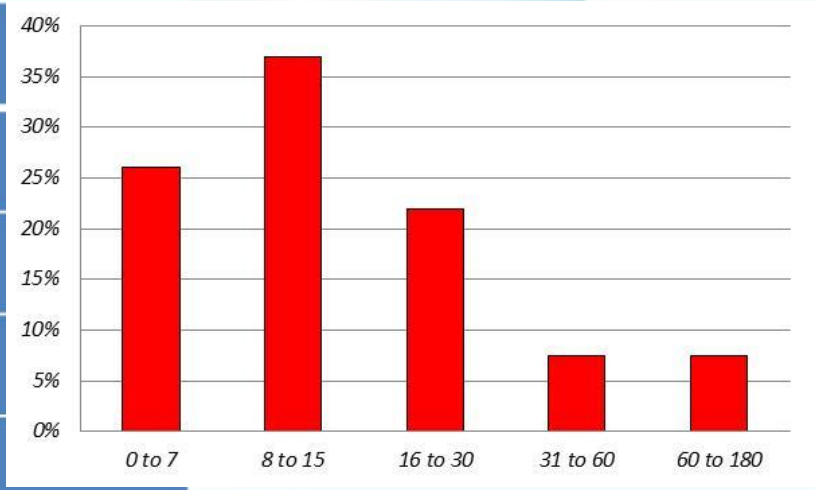
-Persisting LV thrombus (existing at TTE_2), n = 1

-New LV thrombus, n = 1

-Dissolution of the former thrombus, n = 17

LV Thrombi Characteristics (n = 26)

Post MI first discovery, days, mean ± SD	12 days IQR_{25-75}: 7.2-28.7
Thrombus maximal area, cm^2, mean ± SD	2.1 ± 1.7
Mobile thrombi, n(%)	4 (15)
Protruding thrombi, n(%)	17 (65)
Thrombus resolution, n (%) duration, days, mean ± SD	24 (92.3) 12 days IQR_{25-75}: 11.0-60.2
Thromboembolic event, n(%)	1 (3.8)

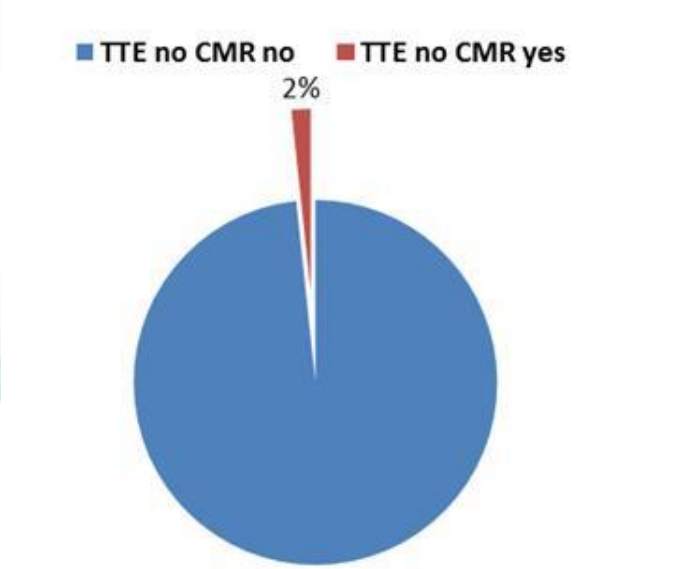


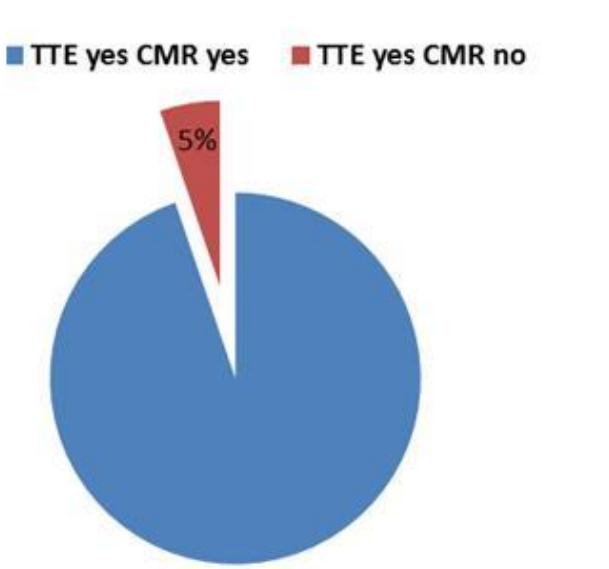
	Thrombus (n = 26)	No thrombus (n = 74)	P value
Age, years, mean±SD	57.4 ± 12.7	59.7 ± 11.9	0.40
Male gender	20 (76.1)	52 (70.3)	0.78
Coronary angiography	25 (96.2)	74 (100)	0.10
Primary PCI	20 (77.0)	68 (92.0)	0.04
LAD PCI	18 (69.2)	66 (89.2)	0.02
Left main PCI	1 (3.8)	4 (5.5)	0.75
LVEF, %, mean±SD			
at TTE_1 (day 6)	32.3 ± 4.6	34.0 ±6.4	0.22
at TTE_2 (day 30)	34.1± 6.6	39.0 ± 9.2	0.01
at TTE_3 (day 270)	37.0 ± 10.4	43.6 ± 9.9	0.006
Drug therapy at TTE_1			
Aspirin	26 (100)	74 (100)	1
Clopidogrel	15 (57.7)	38 (51.4)	0.58
Prasugrel	8 (30.8)	29 (39.1)	0.47
Ticagrelor	2 (7.7)	3 (4.1)	0.50
Beta-blocker	26 (100)	74 (100)	1
Ivabradine	1 (3.8)	1 (1.4)	0.45
ACE-I	26 (100)	73 (95.9)	0.29
Statin	25 (96.2)	74 (100)	0.10
MRA inhibitor	16 (61.5)	43 (58.3)	0.77

Accuracy of LV Thrombus Detection by TTE as Compared to CMR-DE

	CMR-DE	
TTE	No Thrombus	Thrombus
No Thrombus	58	1
Thrombus	1	18

Sensitivity: 94,7%; Spécificity: 98,5%





TTE Negative Predictive Value: 98%

TTE Positive Predictive Value: 95%

Clinical Follow-up

Patients receiving a Triple Anti-Thrombotic Therapy (VKA + Clopidogrel + Aspirin):

N = 26: 25 LV Thrombi and 1 pt with AF

- 2 severe Haemorragias:7,7%
  - Rectorragias (unknown cancer)
  - Post traumatic intracerebral haematoma
- 1 Arterial inferior Limb Embolism at Day 6
  - Patient with a 9 cm^2 Thrombus receiving VKA + Clopidogrel + Aspirin + Lovenox

Patient receiving a Dual Anti-Platelet Therapy [(Prasugrel or Clopidogrel or Ticagrelor) + aspirin]: N = 74

- 3 severe haemorragias: 4%
  - Rectorragia
  - Psoas Haematoma
  - Lethal Recurrent Subdural Haematoma

Other Events

-3 Deaths:

- ✓ **1 Sudden Death Day 60, 1 Subdural Haematoma Day 52,1 after CABG Day 44**

-2 Cardiac Tansplant

-15 DAI and/or CRT

- 7 Hospitalizations for Acute Heart Failure

Conclusion (1)

1-LV Thrombus Still Occur in a Substantial Number of Patients

after Major Ant-MI: 26 % of Patients

2-Contrarily to Routine TTE,

Focused TTE has a high Accuracy for LV Thrombus Detection

Sensitivity: 94,7%; Spécificity: 98,5%
Negative Predictive Value: 98%
Positive Predictive Value: 95%

Conclusion (2)

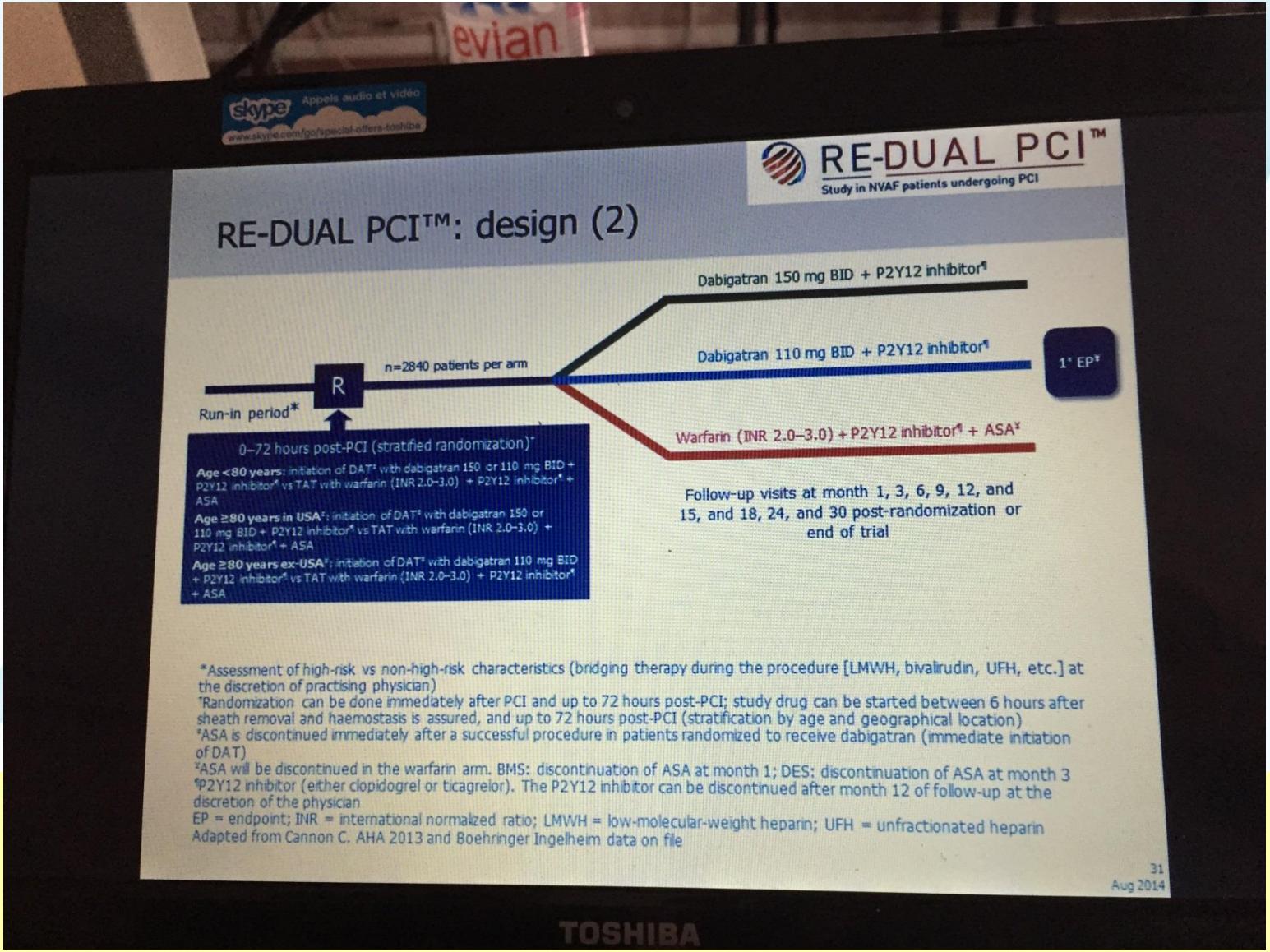
3- Pas d'argument pour IRM systématique si la pointe est bien vue

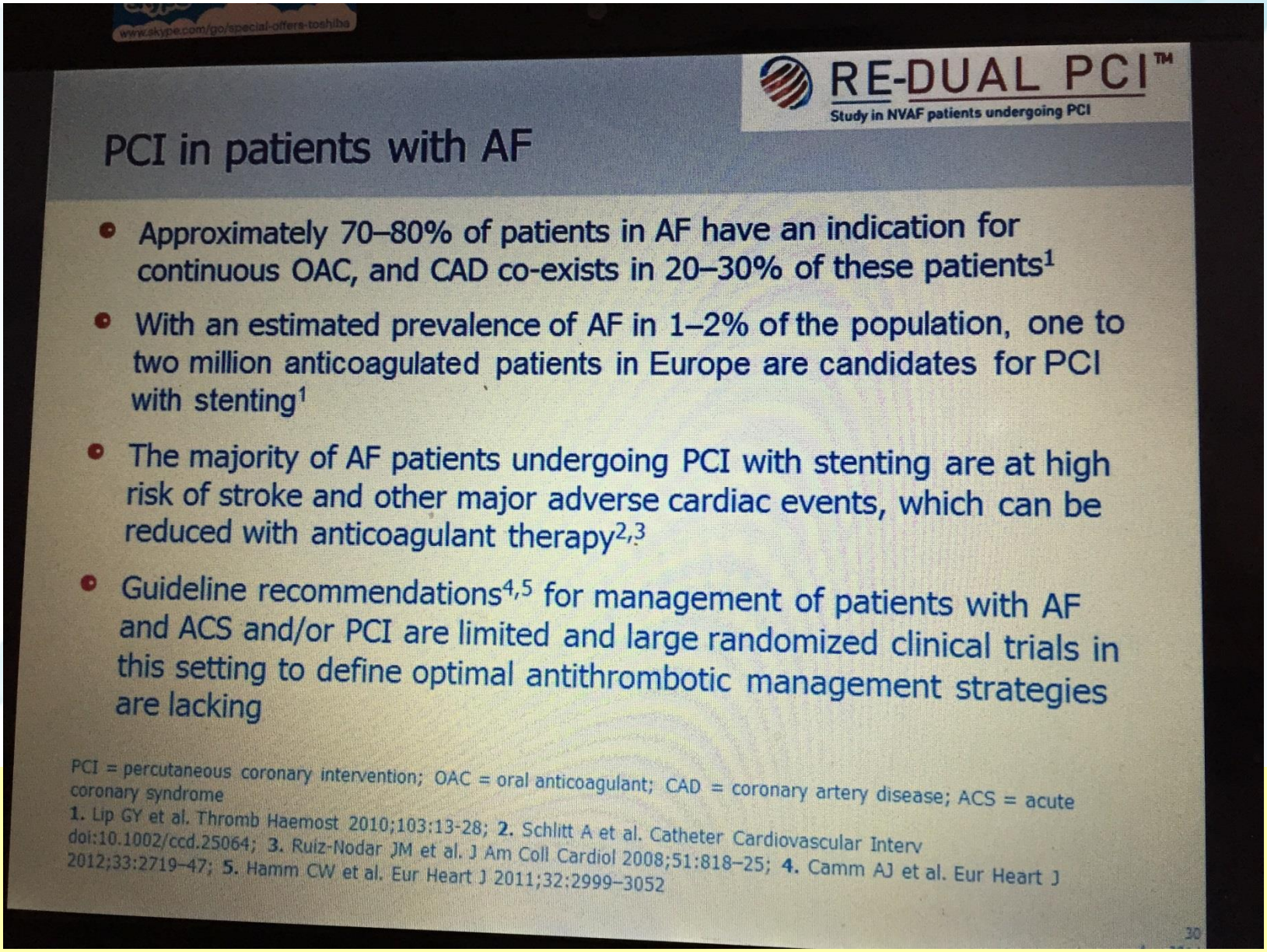
4-Quel cocktail antithrombotique proposer ?

-En prévention en cas de large séquelle apicale ?

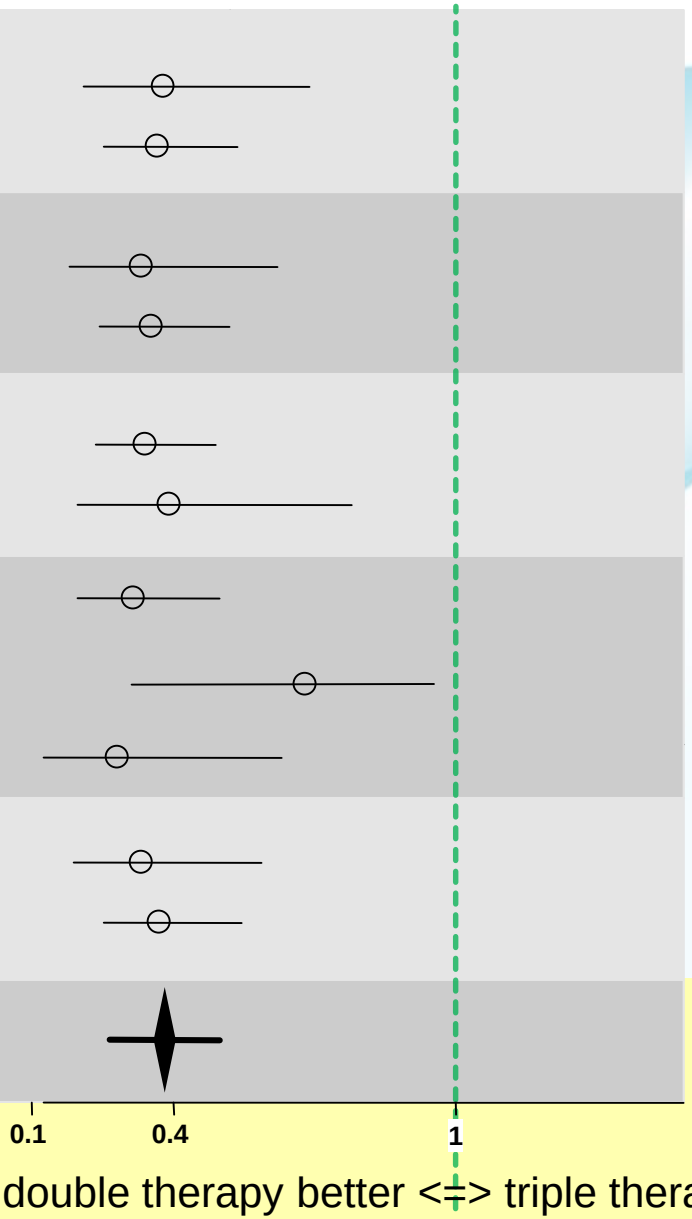
-En curatif

-places respectives des AVK et des NAOC, des nouveaux antiagrégants ?


evian
skype Appels audio et vidéo
RE-DUAL PCI™
Study in NVAF patients undergoing PCI
RE-DUAL PCI™: design (2)
Dabigatran 150 mg BID + P2Y12 inhibitor¶
Dabigatran 110 mg BID + P2Y12 inhibitor¶
Warfarin (INR 2.0–3.0) + P2Y12 inhibitor¶ + ASA¥
n=2840 patients per arm
R
Run-in period*
1° EP¥
0–72 hours post-PCI (stratified randomization)*
Age <80 years: initiation of DAT‡ with dabigatran 150 or 110 mg BID + P2Y12 inhibitor¶ vs TAT with warfarin (INR 2.0–3.0) + P2Y12 inhibitor¶ + ASA
Age ≥80 years in USA£: initiation of DAT‡ with dabigatran 150 or 110 mg BID + P2Y12 inhibitor¶ vs TAT with warfarin (INR 2.0–3.0) + P2Y12 inhibitor¶ + ASA
Age ≥80 years ex-USA£: initiation of DAT‡ with dabigatran 110 mg BID + P2Y12 inhibitor¶ vs TAT with warfarin (INR 2.0–3.0) + P2Y12 inhibitor¶ + ASA
Follow-up visits at month 1, 3, 6, 9, 12, and 15, and 18, 24, and 30 post-randomization or end of trial
*Assessment of high-risk vs non-high-risk characteristics (bridging therapy during the procedure [LMWH, bivalirudin, UFH, etc.] at the discretion of practising physician)
†Randomization can be done immediately after PCI and up to 72 hours post-PCI; study drug can be started between 6 hours after sheath removal and haemostasis is assured, and up to 72 hours post-PCI (stratification by age and geographical location)
‡ASA is discontinued immediately after a successful procedure in patients randomized to receive dabigatran (immediate initiation of DAT)
¥ASA will be discontinued in the warfarin arm. BMS: discontinuation of ASA at month 1; DES: discontinuation of ASA at month 3
¶P2Y12 inhibitor (either clopidogrel or ticagrelor). The P2Y12 inhibitor can be discontinued after month 12 of follow-up at the discretion of the physician
EP = endpoint; INR = international normalized ratio; LMWH = low-molecular-weight heparin; UFH = unfractionated heparin
Adapted from Cannon C. AHA 2013 and Boehringer Ingelheim data on file
31
Aug 2014
TOSHIBA


www.skype.com/go/special-offers-toshiba
RE-DUAL PCI™
Study in NVAF patients undergoing PCI
PCI in patients with AF
Approximately 70–80% of patients in AF have an indication for continuous OAC, and CAD co-exists in 20–30% of these patients[1]
With an estimated prevalence of AF in 1–2% of the population, one to two million anticoagulated patients in Europe are candidates for PCI with stenting[1]
The majority of AF patients undergoing PCI with stenting are at high risk of stroke and other major adverse cardiac events, which can be reduced with anticoagulant therapy[2,3]
Guideline recommendations[4,5] for management of patients with AF and ACS and/or PCI are limited and large randomized clinical trials in this setting to define optimal antithrombotic management strategies are lacking
PCI = percutaneous coronary intervention; OAC = oral anticoagulant; CAD = coronary artery disease; ACS = acute coronary syndrome
1. Lip GY et al. Thromb Haemost 2010;103:13-28; 2. Schlitt A et al. Catheter Cardiovascular Interv doi:10.1002/ccd.25064; 3. Ruiz-Nodar JM et al. J Am Coll Cardiol 2008;51:818–25; 4. Camm AJ et al. Eur Heart J 2012;33:2719–47; 5. Hamm CW et al. Eur Heart J 2011;32:2999–3052
30

WOEST

Forest plot of primary endpoint Hazard Ratios

Factor	Group	Triple	Double	P-value for interaction
age	<75 years	79	82	
	>75 years	200	194	0.9157
gender	female	50	65	
	male	234	214	0.8217
ACS	no	195	207	
	yes	86	69	0.7210
indication OAC	AF/AFlut	162	164	
	Mechanical valve	25	24	0.1116
	Other	47	48	0.7761
Stent type	BMS	90	94	
	DES	194	184	0.7894
Overall		**284**	**279**