Management of LV Thrombus After Primary PCI for STEMI

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Case 1.

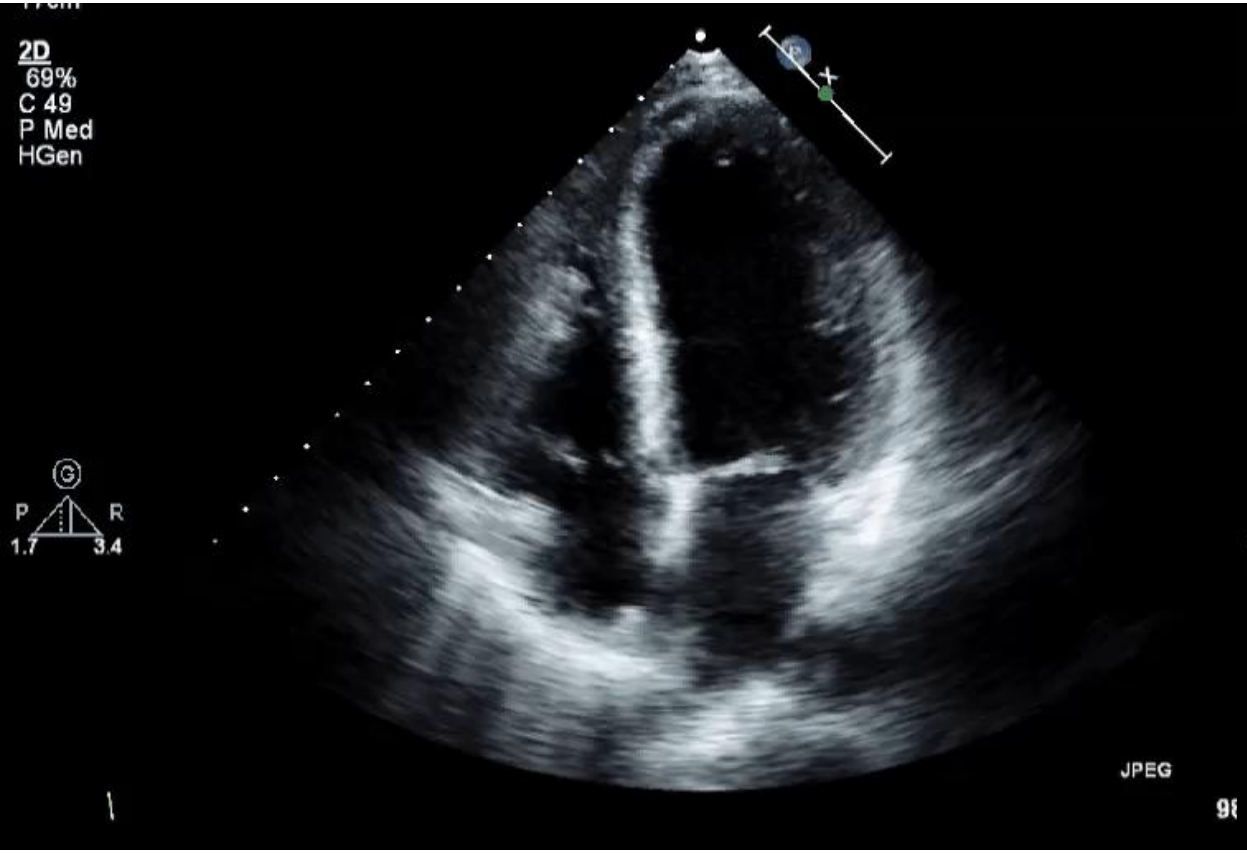
M/44

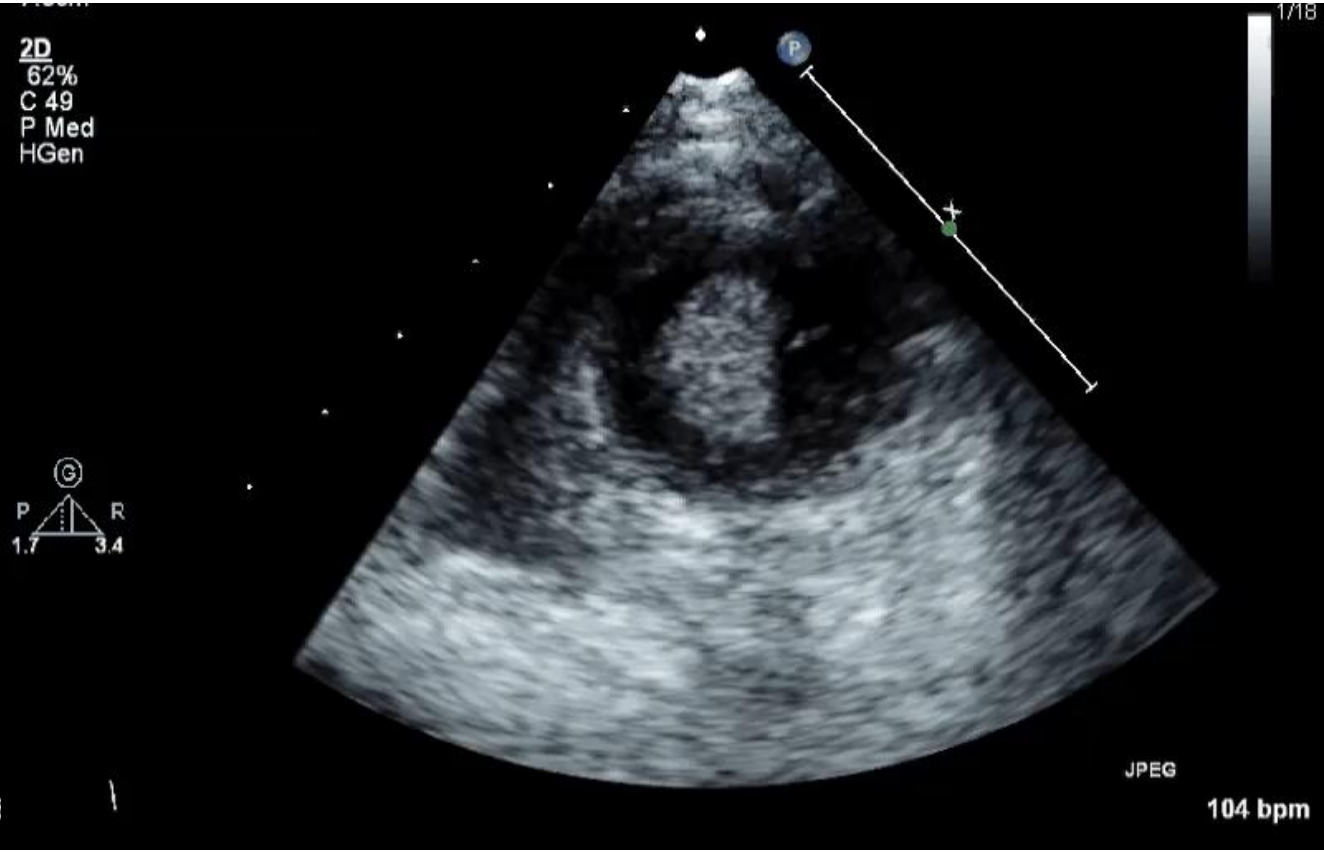
Anterior STEMI (Primary PCI at LAD)

Risk factor: Diabetes /Hypertension/Hyperlipidemia/Smoking (-/+/-/-)

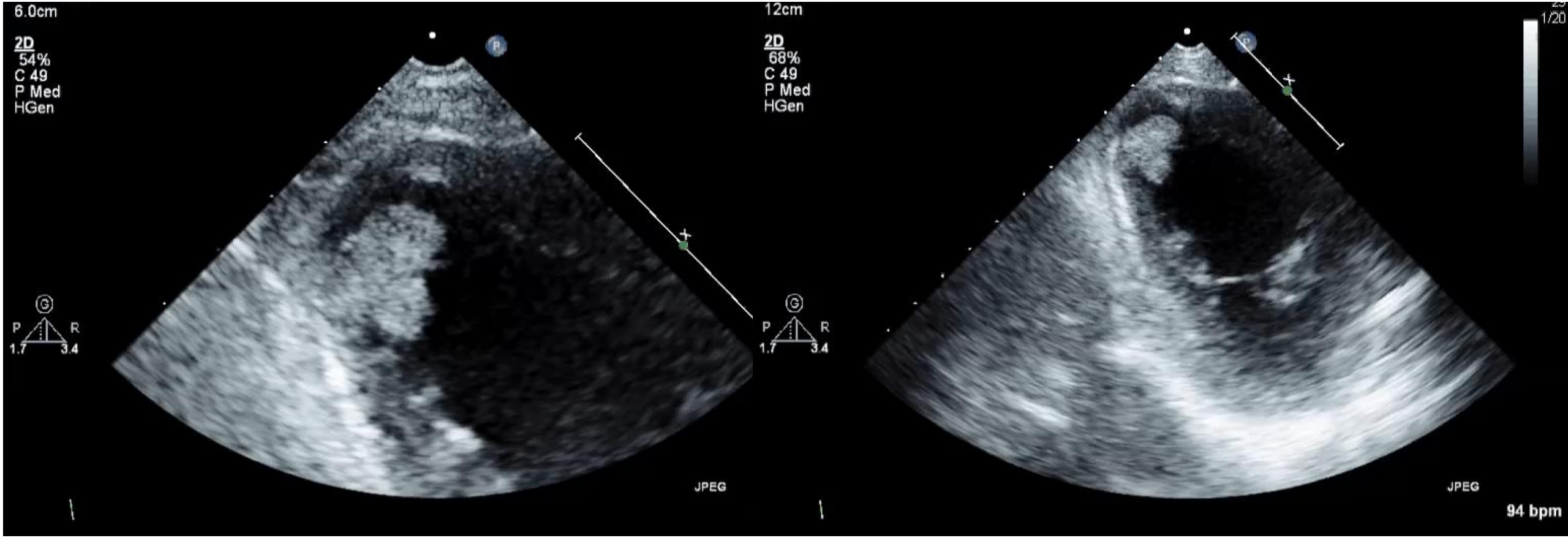
Cardiac echocardiography was done at admission 3 day.

Echocardiography 3 days after PPCI





Echocardiography 3 days after PPCI



Proper management of LVT in this patient ?

- Aspirin 100mg + Clopidogrel 75mg + OAC
- Follow up Echocardiography at 3 month
- Consider OAC cessation

Case 2.

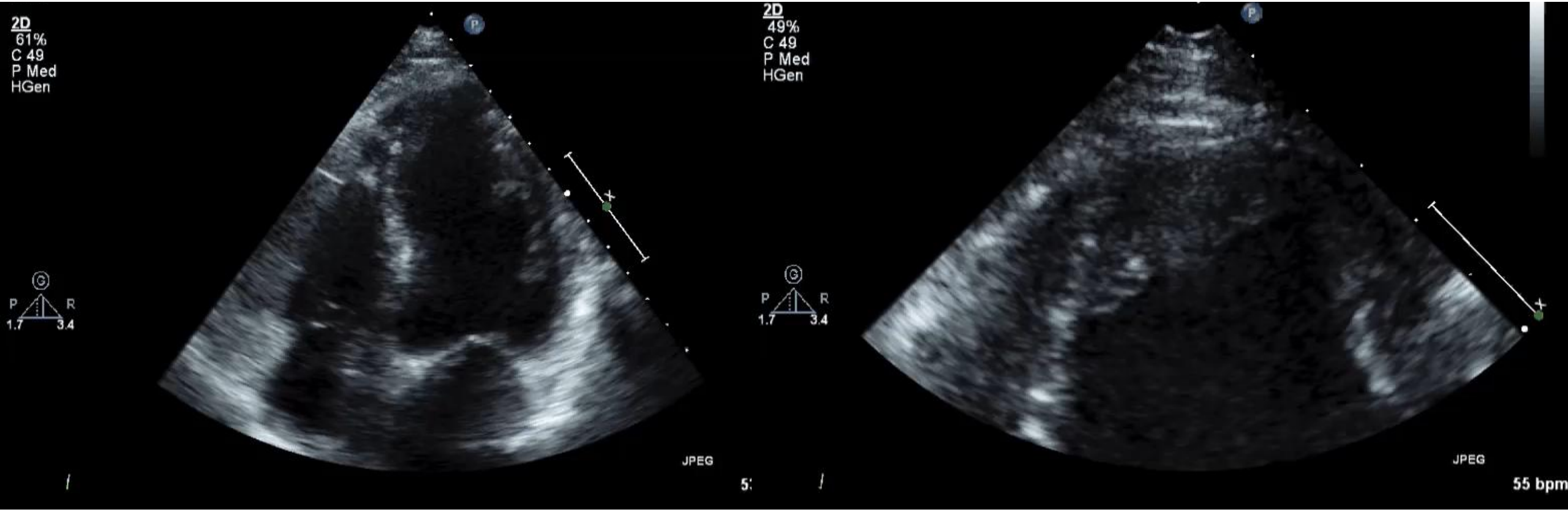
M/70

Anterior STEMI (Primary PCI at LAD)

Past medical Hx.: CVA (2 years ago)
Gastric Ulcer
DM with CKD (Creatinine: 3.5 dl/mg)

Risk factor : Diabetes / Hypertension / Hyperlipidemia / Smoking (+/+/-/-)

Echocardiography 3 days after PPCI

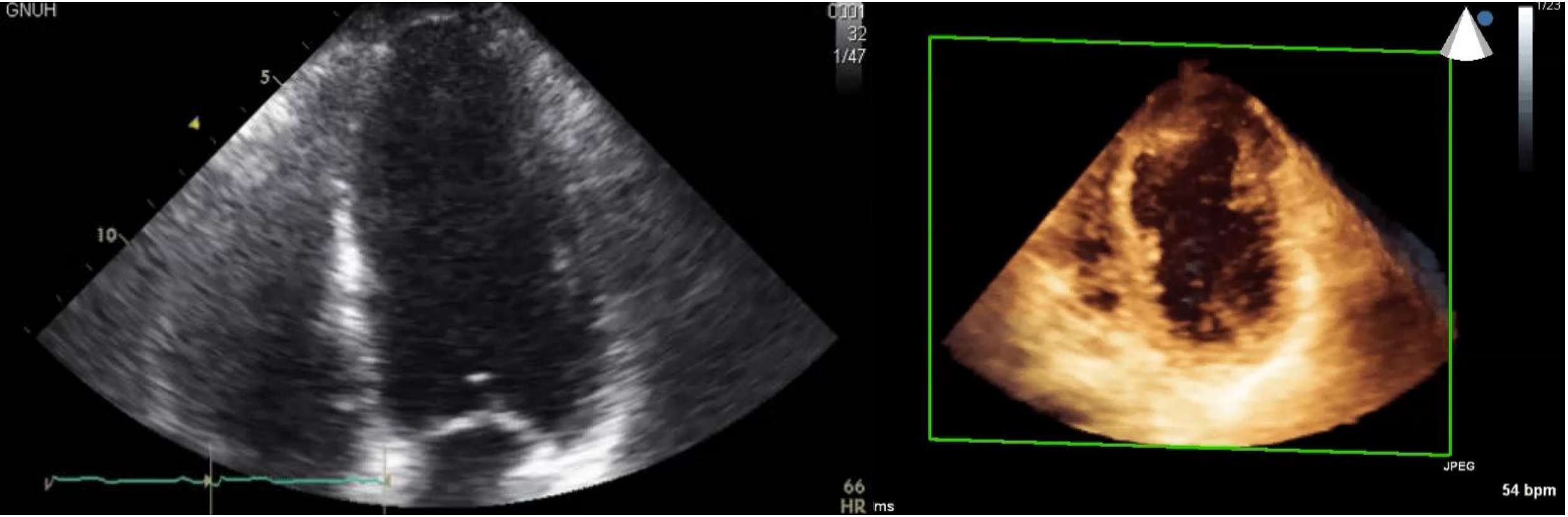


Management of LVT in this patient ?

- aspirin 100mg + clopidogrel 75 mg + OAC + pantoprazole 20mg
- Follow up echocardiography at 3 month

Echocardiography 3 months after PPCI

aspirin 100mg + clopidogrel 75 mg + OAC + pantoprazole 20mg



Echocardiography 12 months after PPCI

Continue aspirin 100mg + clopidogrel 75 mg + OAC+ pantoprazole 20mg

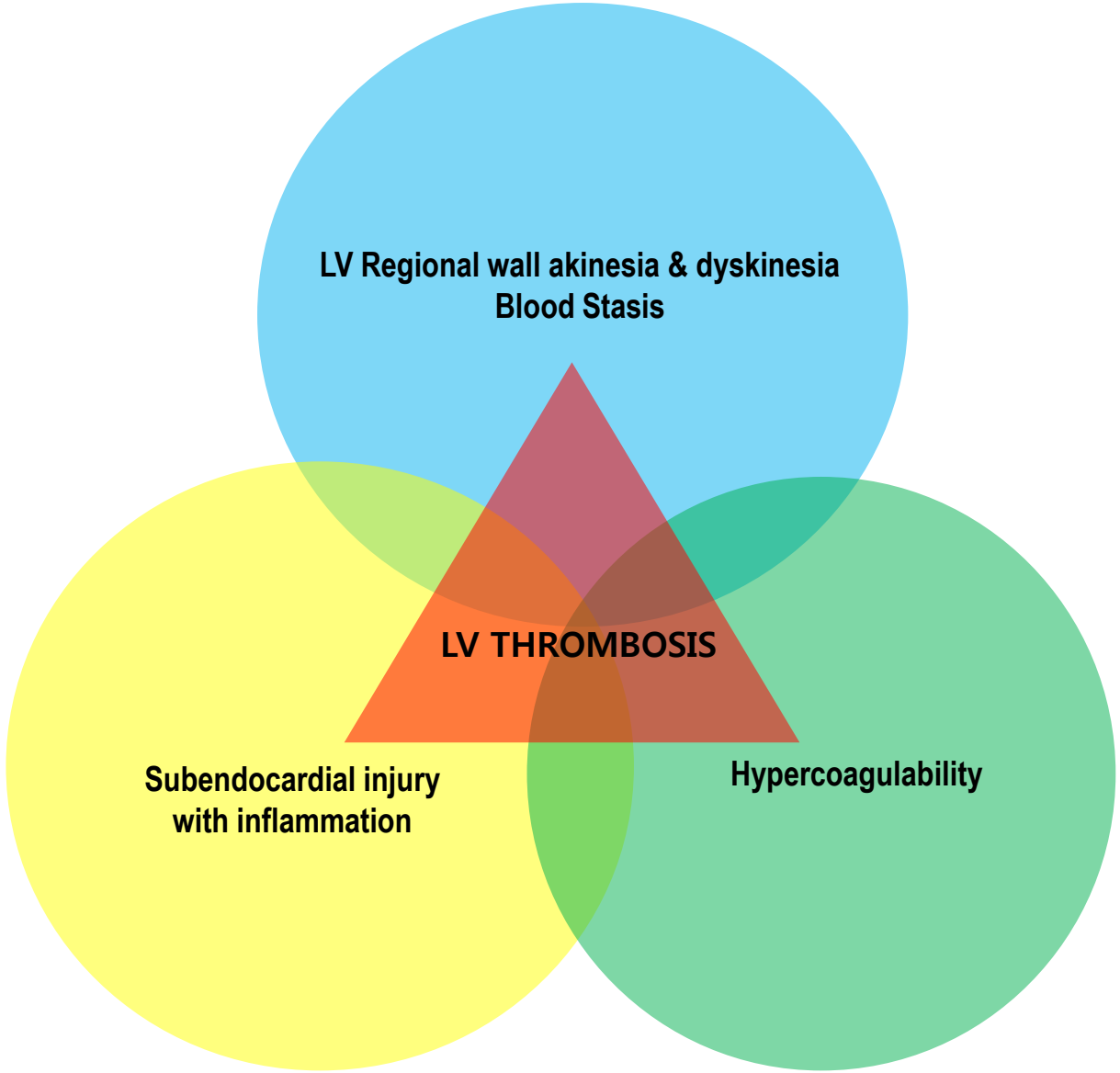
ICH occurred 17 months after PPCI

Aspirin 100mg + clopidogrel 75 mg + OAC (INR :2.2)

Proper management in this patient ?

- Is it necessary to triple antithrombotic therapy ?
- Dual therapy ? (Aspirin + Clopidogrel, Clopidogrel + OAC , Aspirin + OAC…)
- Monotherapy ?
- Hybrid therapy ? - How long ?

Pathogenesis of Left Ventricular thrombus (LVT) in AMI



Heart 2012;98 1743

Natural history of LVT in AMI

- LV thrombus can occur within 24 hours after AMI.

- 90% of LV thrombus are formed within maximum 2 weeks after the Index event.

- New LV thrombus can occur after discharge in worsening LV systolic function, ventricular aneurysm or dyskinesia.

LVT contributing condition

- Anterior STEMI
- Low LV systolic function (EF < 35%)
- Apical aneurysm formation

Incidence of LVT in AMI: Thrombolytic era

A GISSI-2 Connected Study

The overall incidence of left ventricular thrombi in this population treated with thrombolytic agents was 26%.

	heparin		No heparin		Total	
	n	%	*n*	%	*n*	%
First examination: LV thrombi presence						
SK	6/49	12	6/39	15	12/88	14
rt-PA	9/45	20	13/47	28	22/92	24
Total	15/94	16	19/86	22	34/180	19
Second examination: LV thrombi presence						
SK	10/48	21	9/35	26	19/83	23
rt-PA	10/41	24	15/44	34	25/85	29
Total	20/89	22%	24/79	30%	44/168*	26%

*12 patients died.
H, heparin; LV, left ventricular; SK, streptokinase; rt-PA, recombinant tissue-type plasminogen activator (alteplase).

Circulation 1991;84:512-519
2016 Annual Spring Scientific Conference of the KSC

LVT in STEMI treated with PPCI

Incidece of of 4 % LVT in 1059 patients treated with primary PCI (2009 to 2012)

	Thrombus				Total		p Value
	No		Yes				
	(n = 1,017)		(n = 42)		(n = 1,059)		
	Mean	SD	Mean	SD	Mean	SD	
Age (yrs)	62	13	62	14	62	13	0.984
Ejection fraction	47	10	35	8	46	10	<0.001
	Median	IQR	Median	IQR	Median	IQR	p Value
Symptoms-to-balloon time	198.5	144–290	200	145–290	198	144–290	0.110

AJC. 2014 Apr

Recent data of LVT in STEMI patients

Incidece of of 4 % LVT in 1059 patients treated with primary PCI (2009 to 2012)

Multivariate analysis of potential predictors of left ventricular thrombus

Multivariate Analysis	OR	p Value	95% CI	
Men	1.9	0.250	0.63	6.06
Family history	0.4	0.069	0.17	1.07
Diabetes	0.5	0.344	0.11	2.19
Previous coronary angioplasty/stent	0.3	0.327	0.03	3.06
EF*	0.9	<0.001	0.87	0.95
Symptoms-to-balloon time*	1.002	0.055	1.00	1.01
Anterior site of myocardial infarction	10.9	<0.001	3.07	38.75
Glycoprotein IIb/IIIa inhibitors	3.3	0.008	1.36	8.16
TIMI flow postangioplasty/stenting	0.6	0.468	0.19	2.16

AJC. 2014 Apr

Prognostic significance of LVT in AMI

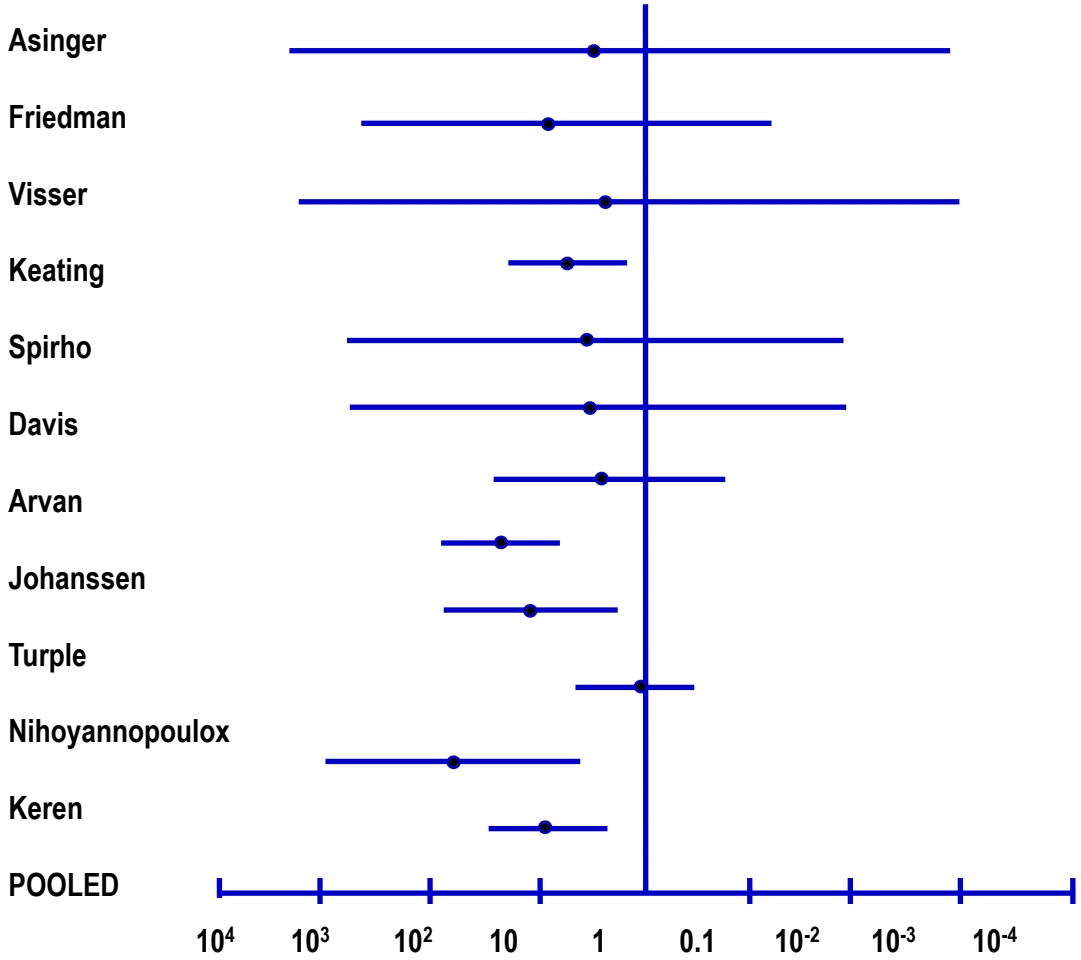
59 pts with anterior AMI with Two-dimensional echocardiograms 24 hr, 48 hr until day 15, and every month for a follow-up 12 months

	Killip class III or IV	Wall motion index	CVA	Mortality
Patients with LVT(n=24)	10 (42%)	0.67 $\pm$ 0.23	0	12 (50%)
Patients without LVT(n=34)	4 (12%)	0.35 $\pm$ 0.26	1 (3%)	4 (12%)

Circulation 72, No. 4, 774-780, 1985.

Embolic Risk of LVT complicating AMI : Meta-Analysis

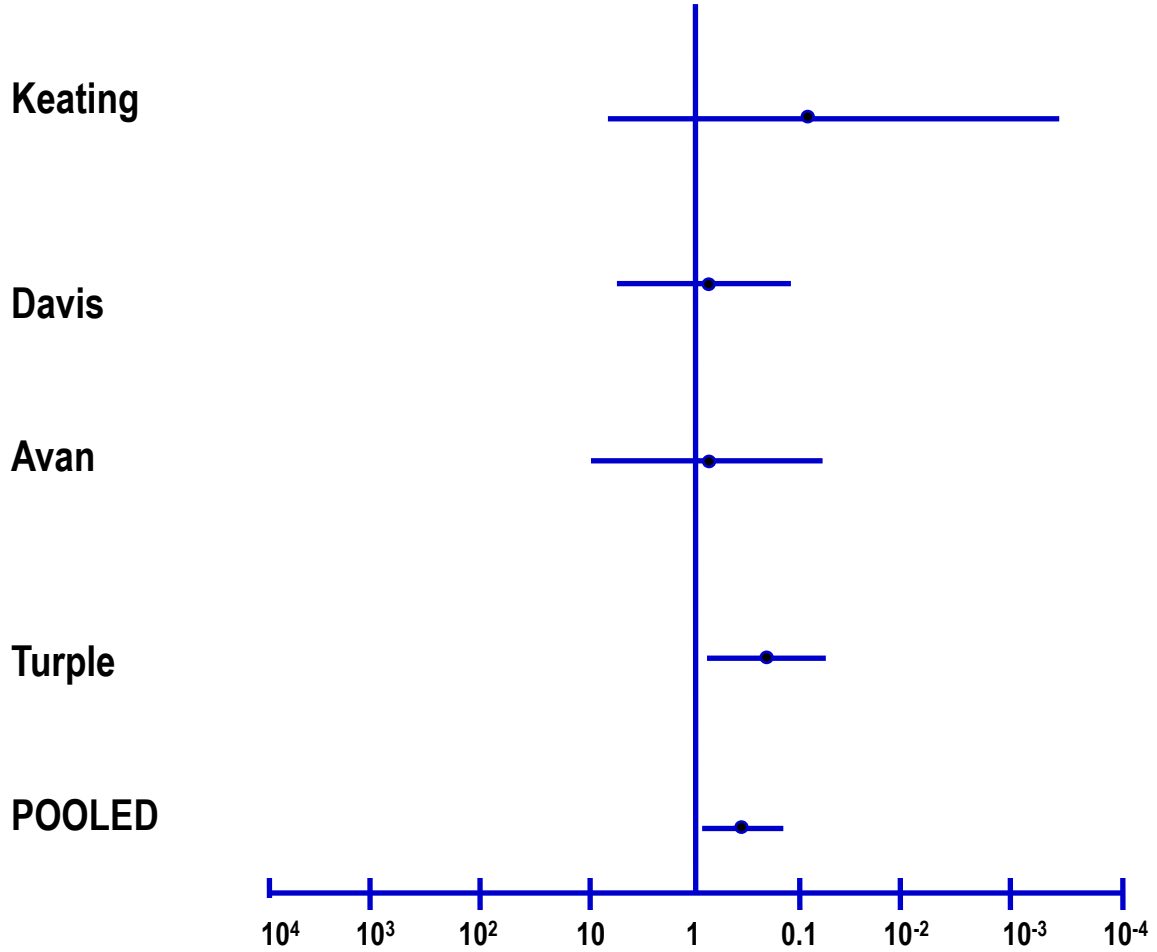
The embolic risk of echocardiographically demonstrated LVT after anterior AMI.
Pooled OR for risk of embolization for the 11 studies was 5 .45 (95% CI : 3 .02 to 9.83)



JACC 1993,22:1004-9

Anticoagulation of LVT in AMI : Meta-Analysis

OR and 95% confidence intervals (bars) for 4 studies addressing the efficacy of systemic anticoagulation in reducing the incidence of mural thrombi after anterior AMI was 0.35 .



JACC 1993,22:1004-9

LV thrombus in AMI : Guideline

2013 ACC/AHA STEMI guidelines

- Anticoagulation for patients with acute MI and asymptomatic LV mural thrombus (Class IIa, Level of Evidence: C)
- Anticoagulation and DAPT : lower INR goals 2.0 to 2.5 (Class IIb, LOE: C).

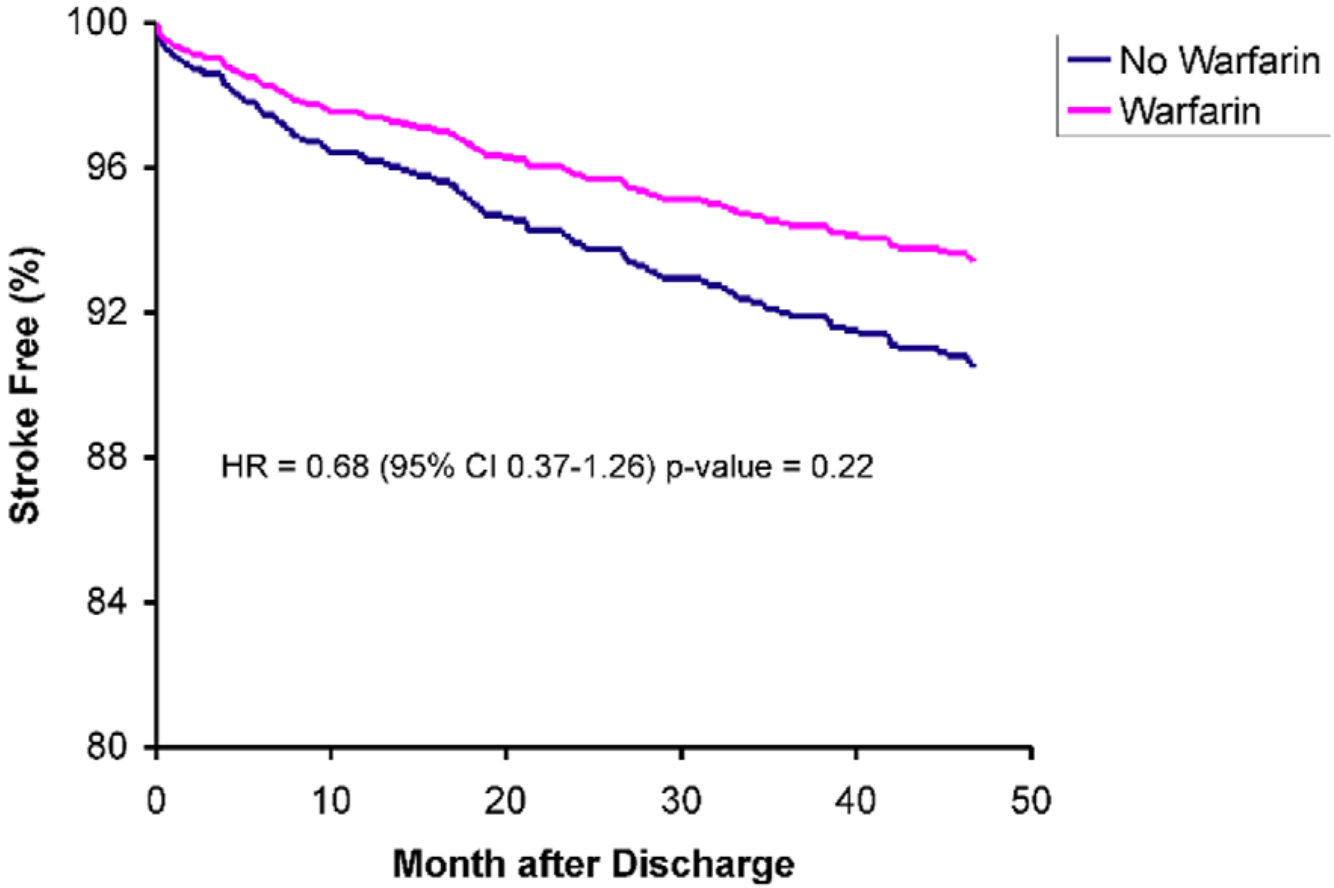
- Anticoagulation therapy may be considered for patients with STEMI and anterior apical akinesis or dyskinesis (Class IIb, LOE: C)

LV thrombus in AMI : Guideline

- **ACCP (American College of Chest Physicians) Clinical Practice Guidelines:**
  Patients with Ant. MI and LV thrombus, or at high risk for LV thrombus (EF < 40%, anteroapical wall motion abnormality), who undergo DES placement suggest triple therapy (warfarin INR 2.0-3.0, low-dose aspirin, clopidogrel 75 mg daily) for 3 to 6 months over alternative regimens and alternative durations of warfarin therapy (Grade 2 C)

Anticoagulation: really reduce stroke after anterior MI ?

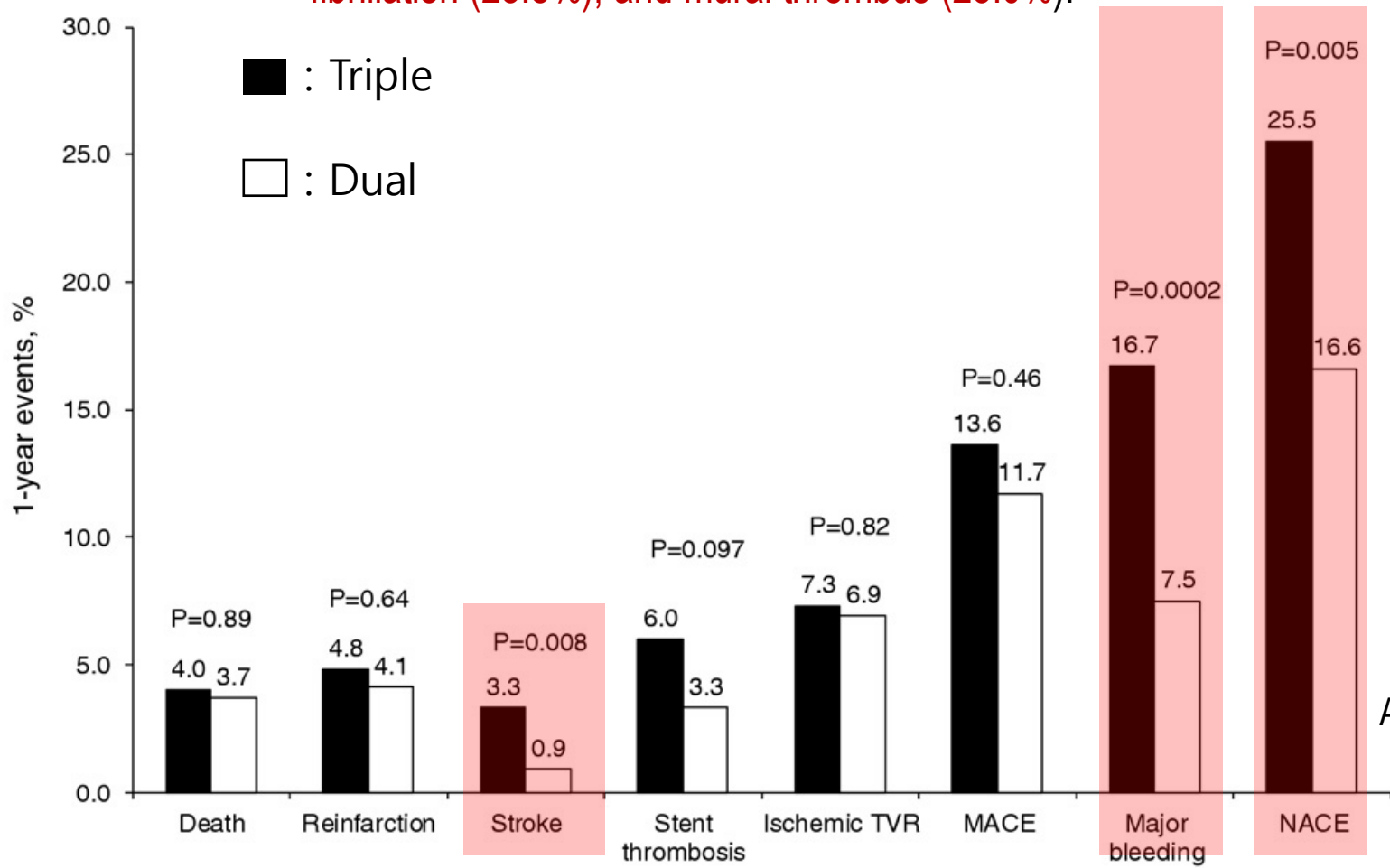
10,383 patients of acute MI in Ontario, Canada from 1999 to 2001.



PLoS ONE 2012 5(8): 12150

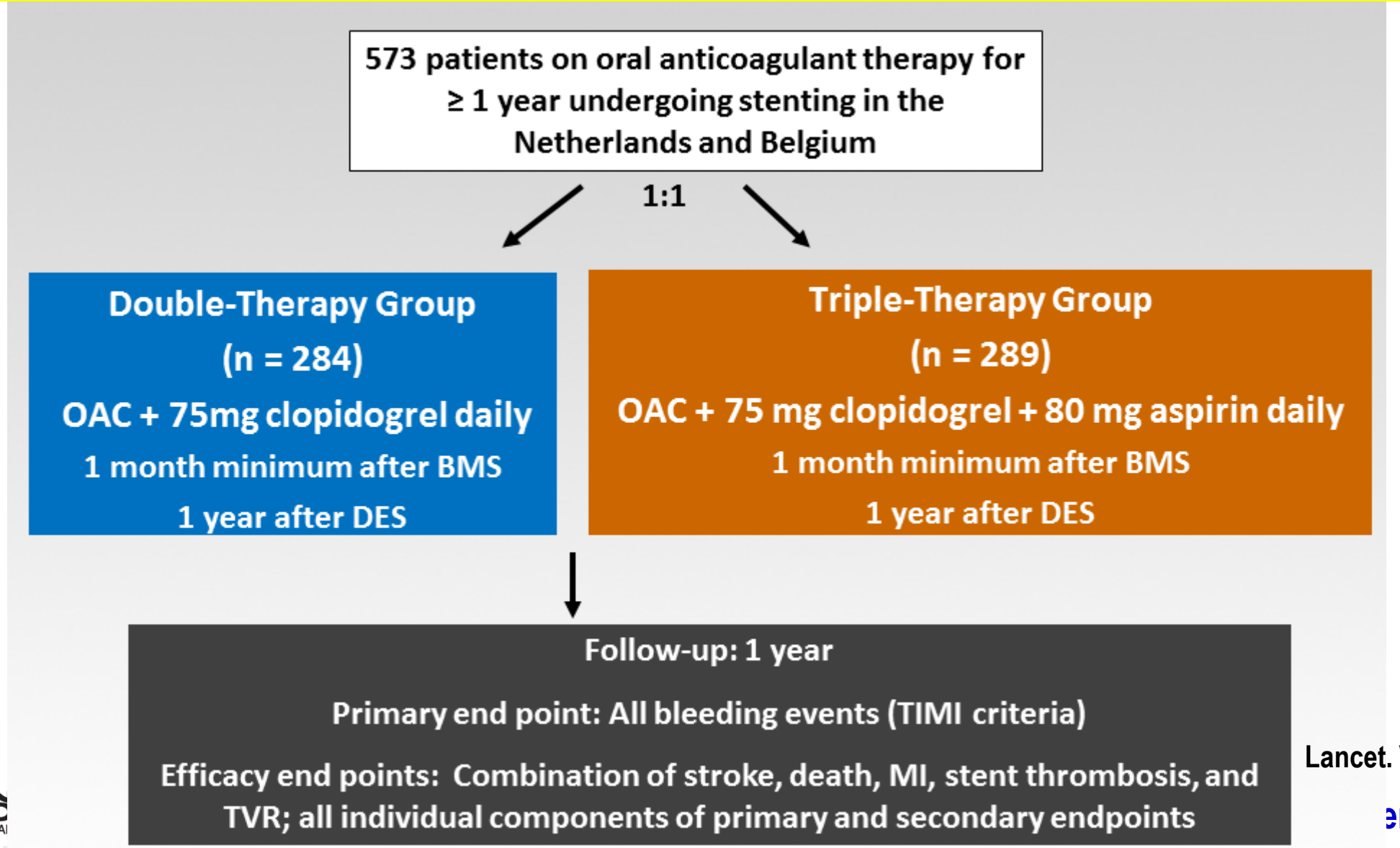
Recent data :
Triple Antithrombotic Therapy After PPCI for STEMI
HORIZONS-AMI Trial

Among the 3,320 patients with PPCI, 126 (3.8%) for triple therapy and 3,194 (96.2%) for dual antiplatelet therapy.
The most frequent indications for triple therapy were a severely reduced LVEF with a large akinetic area(53.2%), atrial fibrillation (23.8%), and mural thrombus (23.0%).



AJC 2012 Mar 15;109(6):831-8

WOEST trial: aspirin omission in triple therapy



Lancet. Vol 381 March 30, 2013

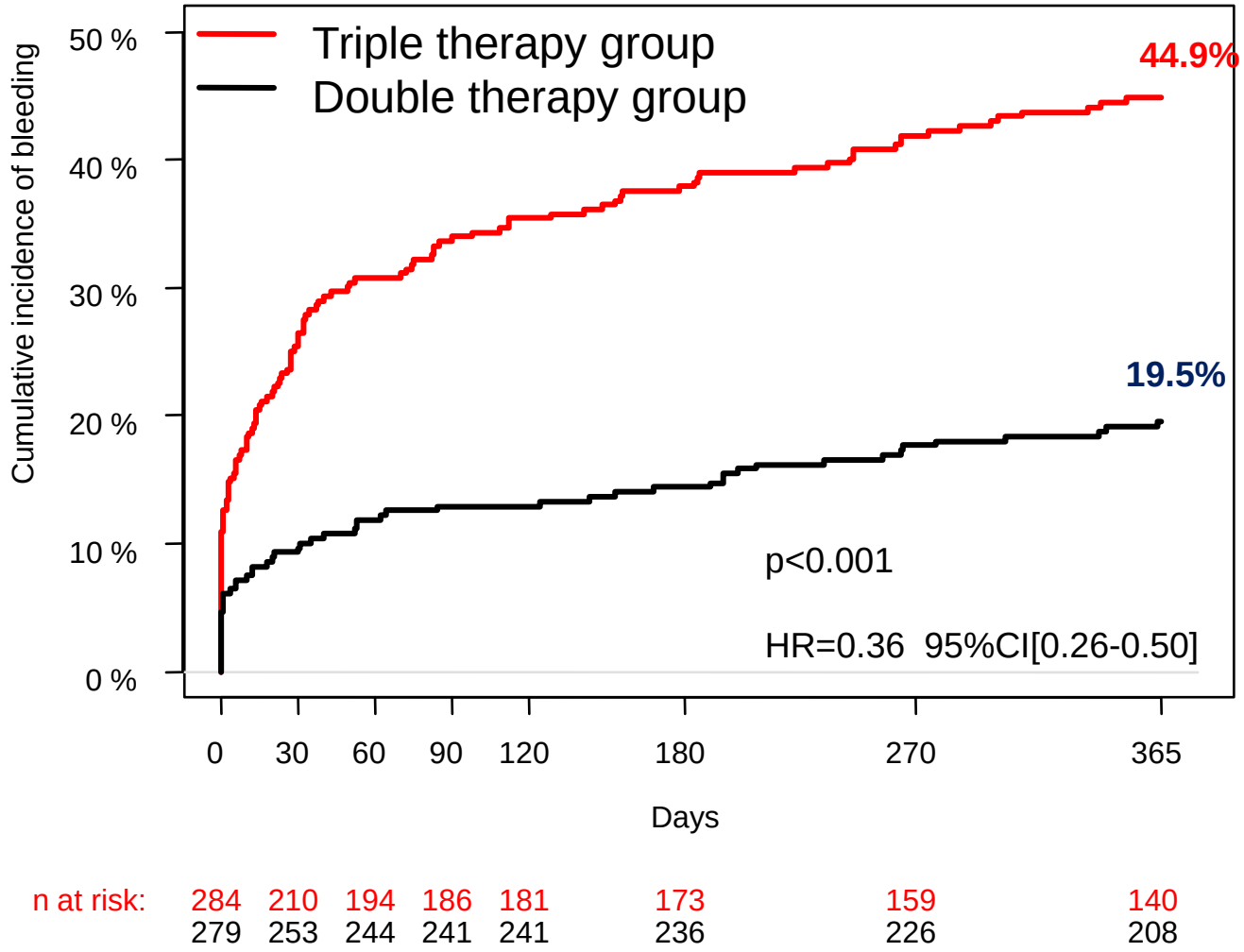
erence of the KSC

WOEST: Indication for oral anticoagulation

	Double therapy (n = 279)	Triple therapy (n = 284)
Atrial fibrillation/flutter	164/236 (69%)	164/234 (69%)
Mechanical valve	24/236 (10%)	25/234 (11%)
Apical aneurysm , PTE, PAD, EF< 30%	48/236 (20%)	47/234 (20%)

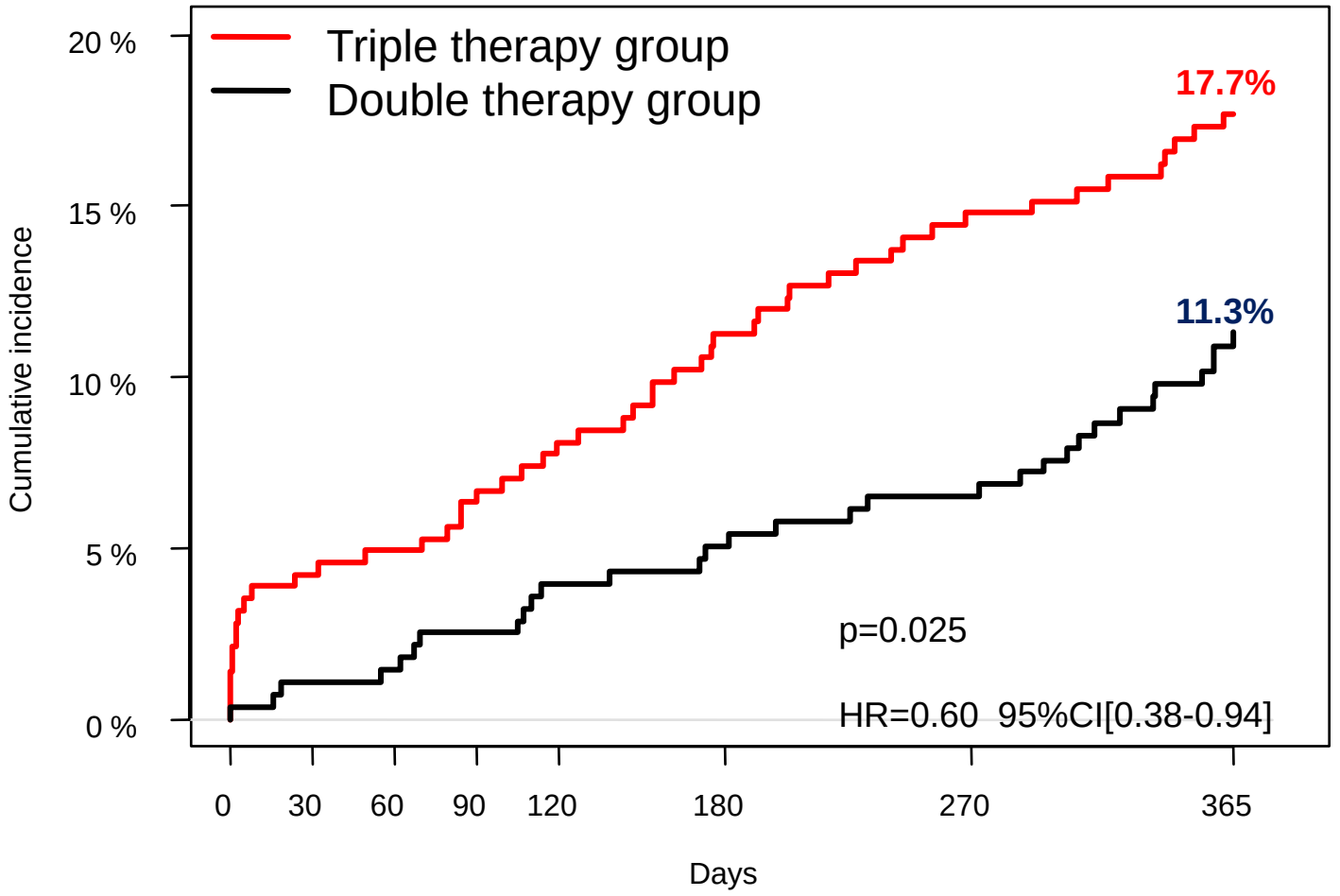
Lancet. Vol 381 March 30, 2013

WOEST: Primary Endpoint -Total number of TIMI bleeding events



Lancet. Vol 381 March 30, 2013

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



Lancet. Vol 381 March 30, 2013

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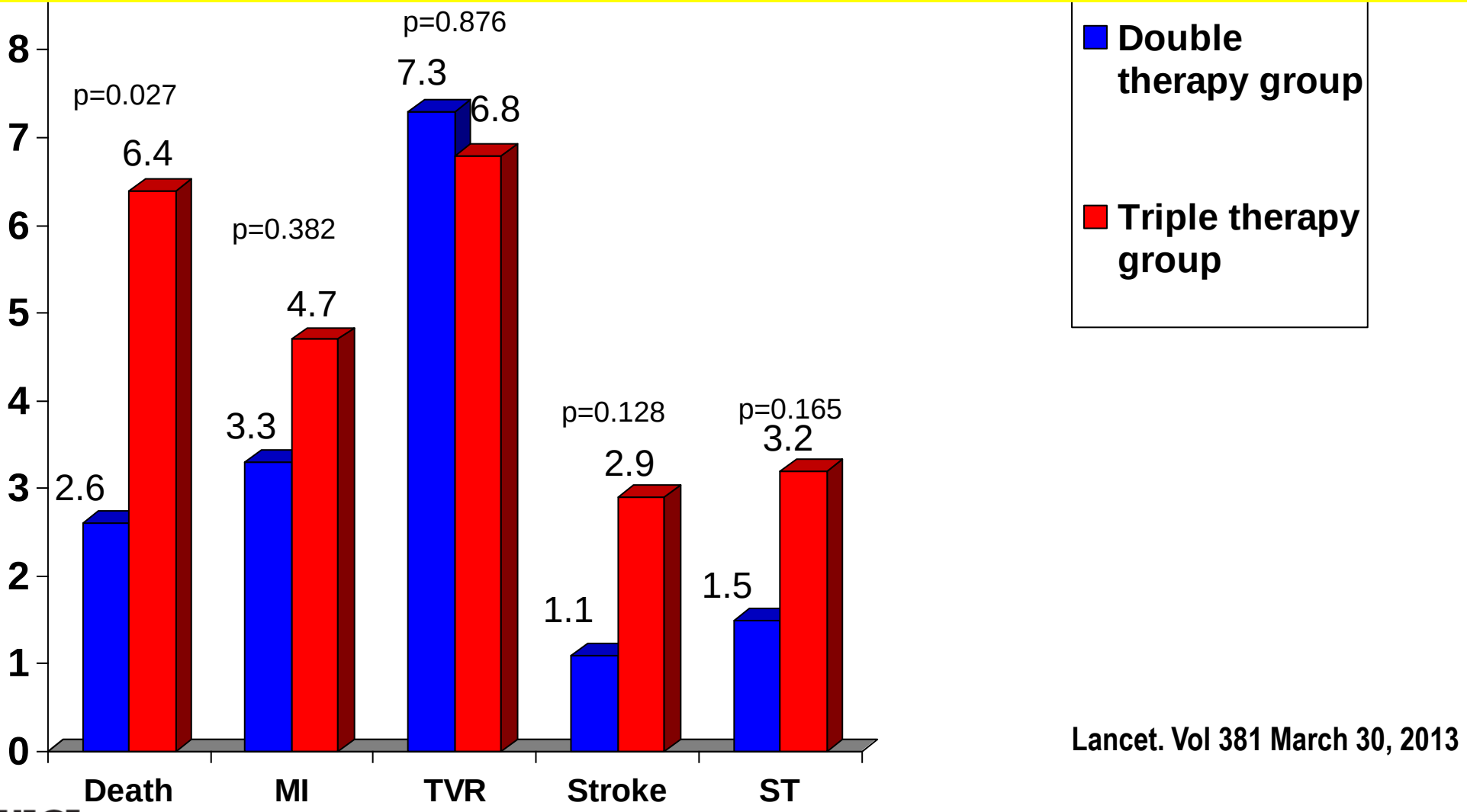
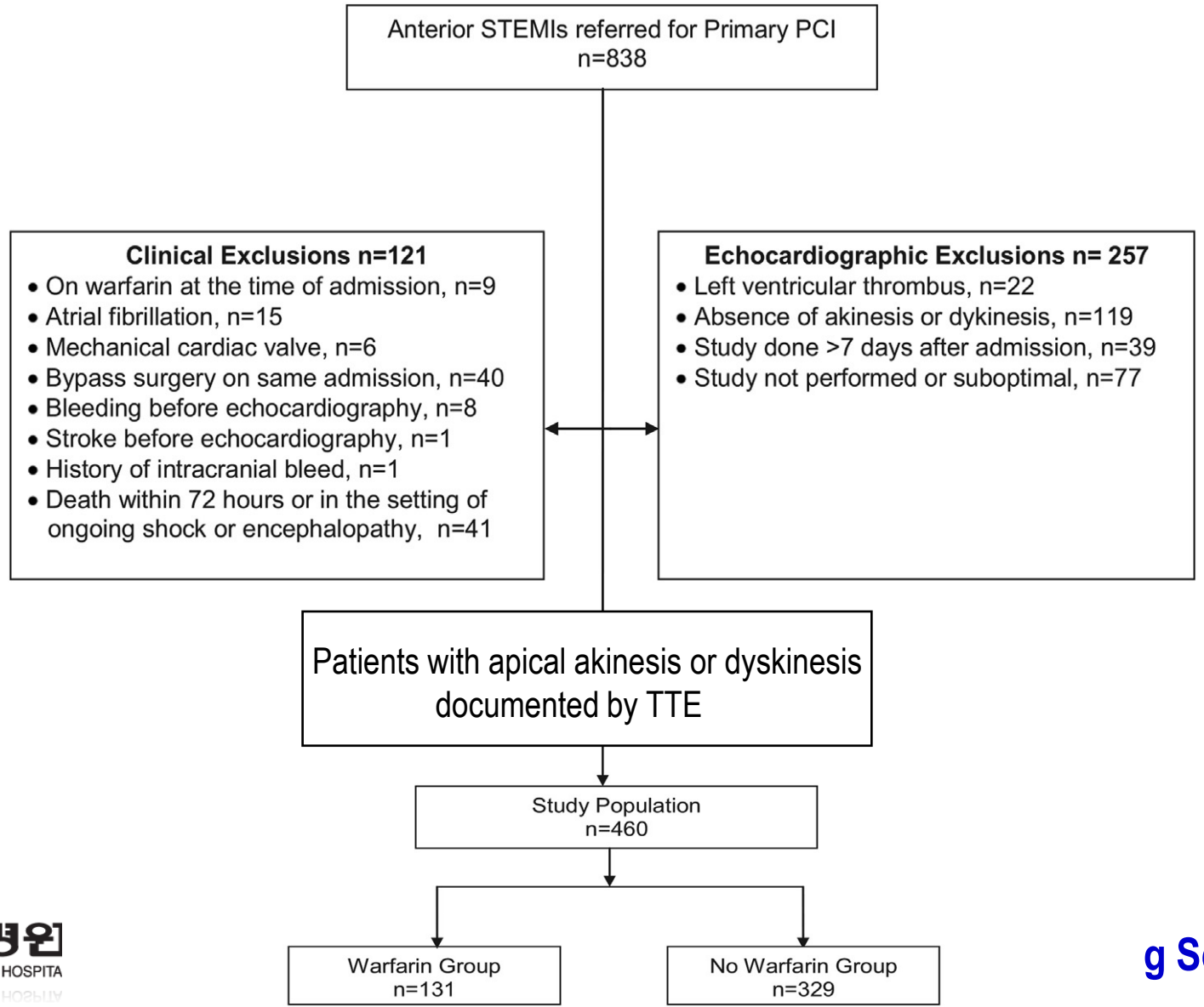


Lancet. Vol 381 March 30, 2013

Prophylactic Warfarin Therapy After PPCI for Anterior STEMI



JACC Intv 2015;8:155–62

Prophylactic Warfarin Therapy After PPCI for Anterior STEMI

Outcomes	Warfarin (n = 131)	No Warfarin (n = 329)	p Value
In-hospital			
Death	0 (0.0)	0 (0.0)	–
Reinfarction	1 (0.8)	0 (0.0)	0.29
Stroke	1 (0.8)	1 (0.3)	0.49
Hemorrhagic	0 (0)	0 (0)	
Blood transfusion	4 (3.1)	0 (0.0)	0.006
Major bleeding	4 (3.1)	0 (0.0)	0.006
Death, reinfarction or stroke	2 (1.5)	1 (0.3)	0.20
Death, reinfarction, stroke or major bleeding	6 (4.6)	1 (0.3)	0.003
Stent thrombosis	1 (0.8)	0 (0.0)	0.29
Cardiogenic shock	14 (10.7)	10 (3.0)	0.002
Length of stay, days	8 (7-11)	5 (4-7)	<0.001

JACC Intv 2015;8:155–62

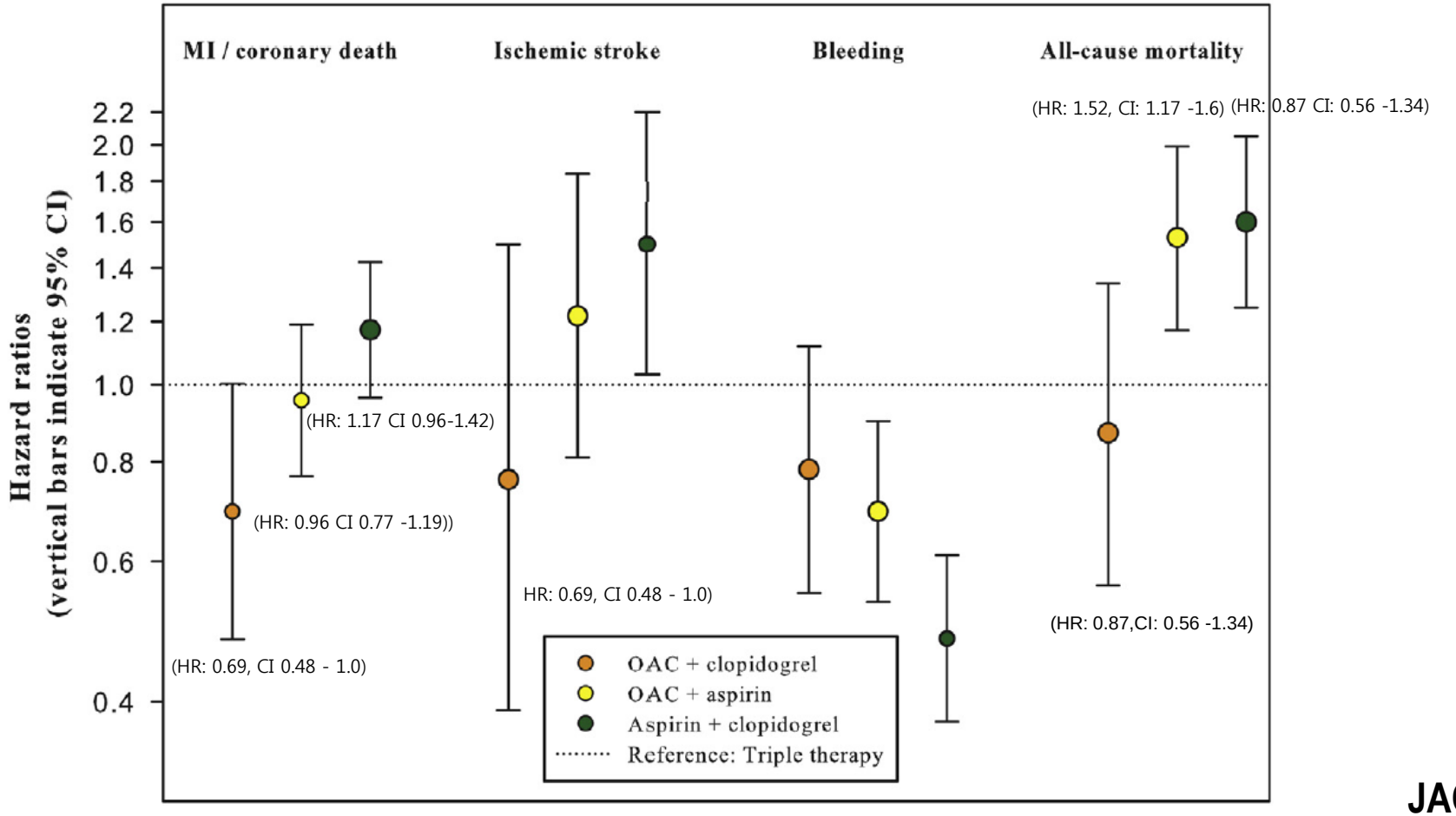
Prophylactic Warfarin Therapy After PPCI for Anterior STEMI

Outcomes	Warfarin (n = 131)	No Warfarin (n = 329)	p Value
Cumulative events at 180 days			
Death	7 (5.4)	5 (1.5)	0.04
Reinfarction	2 (1.6)	5 (1.5)	1.00
Stroke	4 (3.1)	1 (0.3)	0.02
Hemorrhagic	2 (1.5)	0 (0)	0.08
Blood transfusion	10 (7.8)	6 (1.8)	0.004
Major bleeding	11 (8.5)	6 (1.8)	<0.0001
Death, reinfarction or stroke	12 (9.3)	9 (2.8)	0.005
Primary outcome: death, reinfarction, stroke, or major bleeding	19/129 (14.7)	15/327 (4.6)	0.001
Stent thrombosis	1/129 (0.8)	3/327 (0.9)	1.000
Hospital readmission	25 (19.4)	30 (9.2)	0.004

JACC Intv 2015;8:155–62

OAC and Antiplatelets in Atrial Fibrillation Patients After AMI and Coronary Intervention

A total of 12,165 AF patients hospitalized with MI and/or undergoing PCI between 2001 and 2009 were identified by nationwide registries (60.7% male; mean age 75.6 years).



JACC 2013;62:981–9

Triple therapy with NOAC for LVT in AMI

Short duration rivaroxaban effective in patient under dual antiplatelet therapy

Rivaroxaban dissolves postinfarction left ventricular thrombus

Assadullah Azizi, Serban Puricel, Stéphane Cook, Nicolas Brugger

Department of Cardiology, Fribourg, University and Hospital, Switzerland

In summary,

- The incidence of LVT in AMI significantly decreased with reperfusion therapies, contemporary studies note LV thrombus in 4% of anterior MI treated with PPCI.
- Although guidelines recommend anticoagulation for patients with LVT and risk group of LVT in acute MI , it is unknown if the benefits of anticoagulation outweigh the known bleeding risks in current practice.
- Recent data showed triple therapy increase bleeding and mortality without embolic event prevention.
- Routine use of anticoagulation in patients with anterior MI with apical dysfunction without evidence of mural thrombus seems dangerous in recent study. Given the bleeding risks, triple therapy should probably be avoided in these patients.
- The combination of clopidogrel and warfarin showed more safe and effective result than triple therapy in AMI with coronary intervention patients. Randomized studies should be considered to investigate this strategy.
- If anticoagulation is used after anterior MI, clinicians should probably consider omitting aspirin, adding proton pump inhibitors, targeting lower INR ranges, shortening the anticoagulation course.

Thank you for listening.

Oral Anticoagulation and Antiplatelets in Atrial Fibrillation Patients After Myocardial Infarction and Coronary Intervention

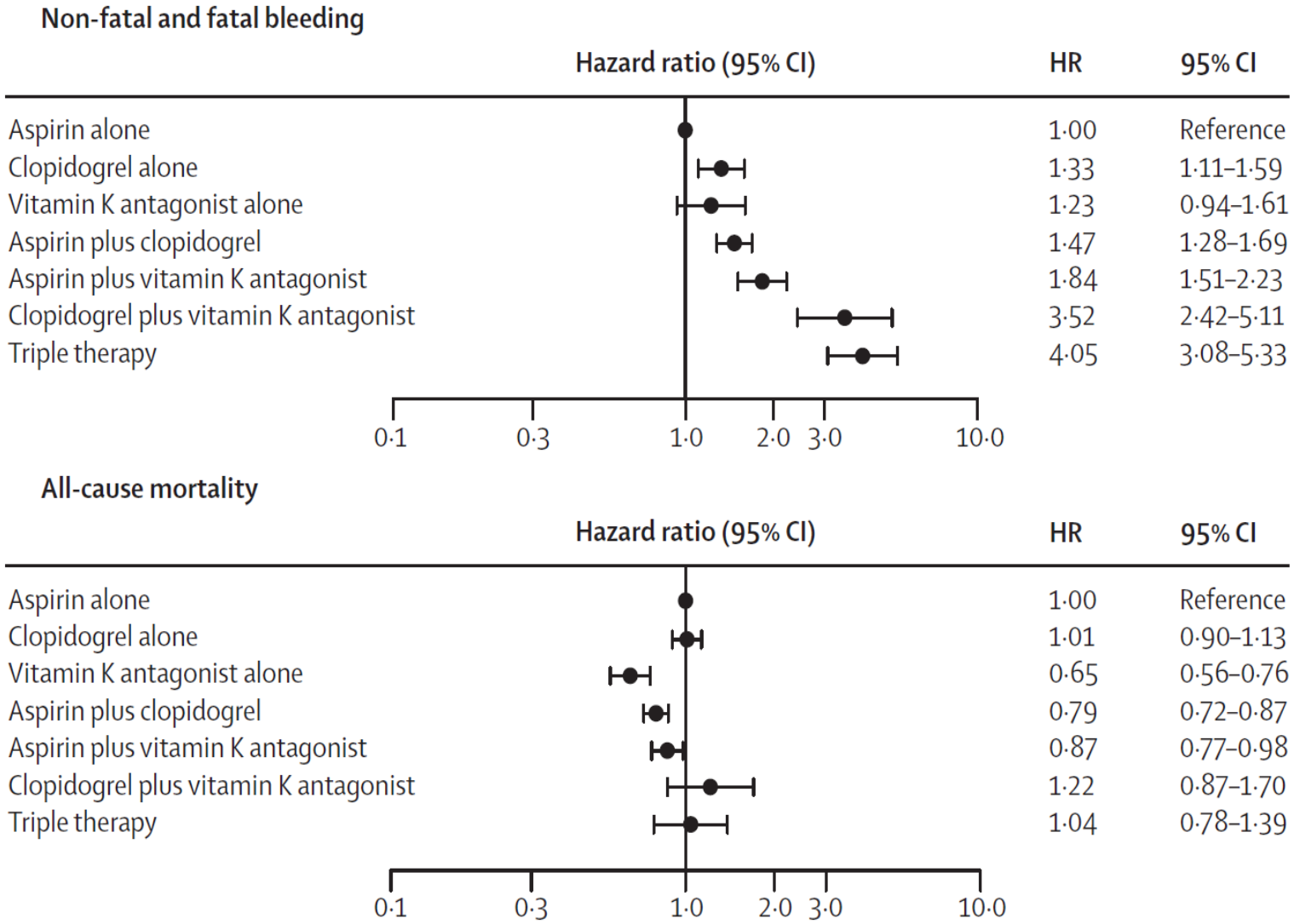
A total of 12,165 AF patients hospitalized with MI and/or undergoing PCI between 2001 and 2009 were identified by nationwide registries (60.7% male; mean age 75.6 years).

Table 2 Benefit and Safety Outcomes in Multiple Antithrombotic Regimens Within 1 Year in AF Patients After MI/PCI

	Dual Therapy						Triple Therapy	
	Aspirin + Clopidogrel		OAC + Aspirin		OAC + Clopidogrel		OAC + Aspirin + Clopidogrel	
	n (IR)	HR (95% CI)	n (IR)	HR (95% CI)	n (IR)	HR (95% CI)	n (IR)	HR (95% CI)
Benefit outcomes								
MI/coronary death (n = 2,255)	484 (21.3)	Reference	230 (17.7)	0.78 (0.66–0.91)	36 (9.6)	0.56 (0.40–0.79)	129 (16.2)	0.83 (0.68–1.00)
Ischemic stroke (n = 680)	151 (6.3)	Reference	75 (5.6)	0.81 (0.61–1.08)	11 (2.8)	0.51 (0.28–0.95)	34 (4.1)	0.67 (0.46–0.98)
All-cause mortality (n = 2,356)	430 (17.5)	Reference	215 (15.6)	0.91 (0.77–1.08)	28 (7.1)	0.54 (0.35–0.76)	76 (8.9)	0.61 (0.47–0.77)
Coronary death or fatal ischemic stroke (n = 605)	130 (5.3)	Reference	54 (3.9)	0.78 (0.57–1.08)	9 (1.2)	0.63 (0.32–1.24)	21 (2.5)	0.58 (0.36–0.92)
Coronary death or fatal ischemic stroke or fatal bleeding (n = 671)	133 (5.4)	Reference	64 (4.6)	0.92 (0.68–1.24)	11 (2.8)	0.74 (0.40–1.37)	27 (3.2)	0.72 (0.48–1.09)
Safety outcomes								
Bleeding (n = 769)	166 (6.9)	Reference	129 (9.7)	1.44 (1.14–1.83)	41 (10.9)	1.63 (1.15–2.30)	117 (14.3)	2.08 (1.64–2.65)
Fatal bleeding (n = 78)	6 (0.3)	Reference	11 (0.8)	3.90 (1.43–10.66)	2 (0.5)	2.73 (0.54–13.70)	8 (0.9)	4.80 (1.64–14.02)
Fatal/nonfatal intracranial bleeding (n = 89)	9 (0.4)	Reference	15 (1.1)	2.98 (1.28–6.92)	5 (1.3)	3.80 (1.26–11.44)	12 (1.5)	4.05 (1.69–9.71)
Fatal/nonfatal GI bleeding (n = 320)	70 (2.9)	Reference	53 (4.0)	1.36 (0.94–1.96)	13 (3.5)	1.24 (0.68–2.25)	47 (5.7)	1.99 (1.37–2.90)
Fatal bleeding defined as death within 30 days (n = 399)	75 (3.1)	Reference	75 (5.3)	1.51 (1.09–2.11)	13 (3.5)	1.23 (0.68–2.22)	44 (5.4)	1.85 (1.27–2.70)

Values are number of events (n), and incidence rates (IR) are events per 100 person-years within 1 year.
CI = confidence interval; GI = gastrointestinal; HR = hazard ratio; other abbreviations as in Table 1.

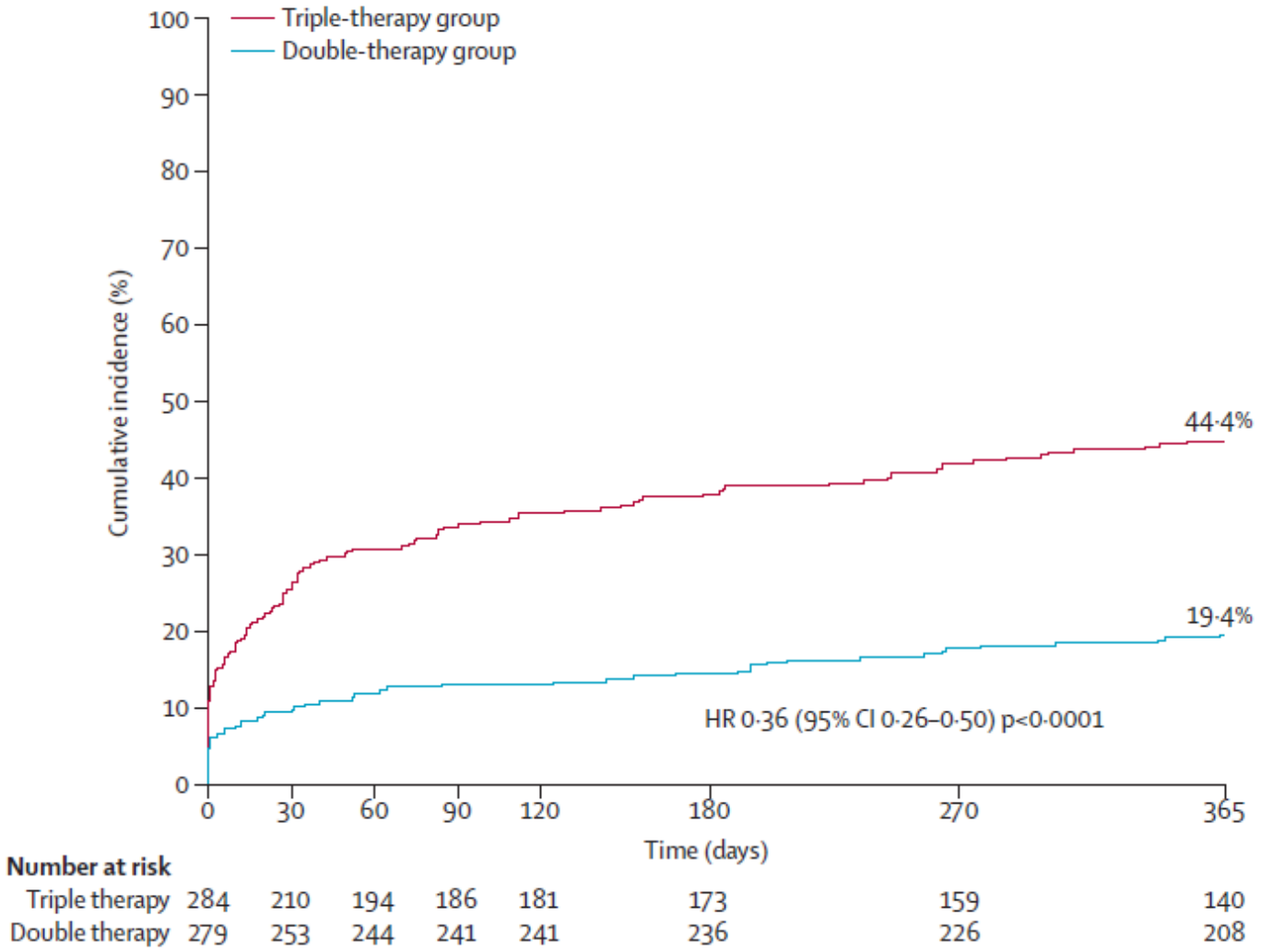
Risk of bleeding in AMI patients with different combinations of aspirin, clopidogrel, and vitamin K antagonists



Lancet 2009; 374: 1967–74

WOEST trial: aspirin omission in triple therapy

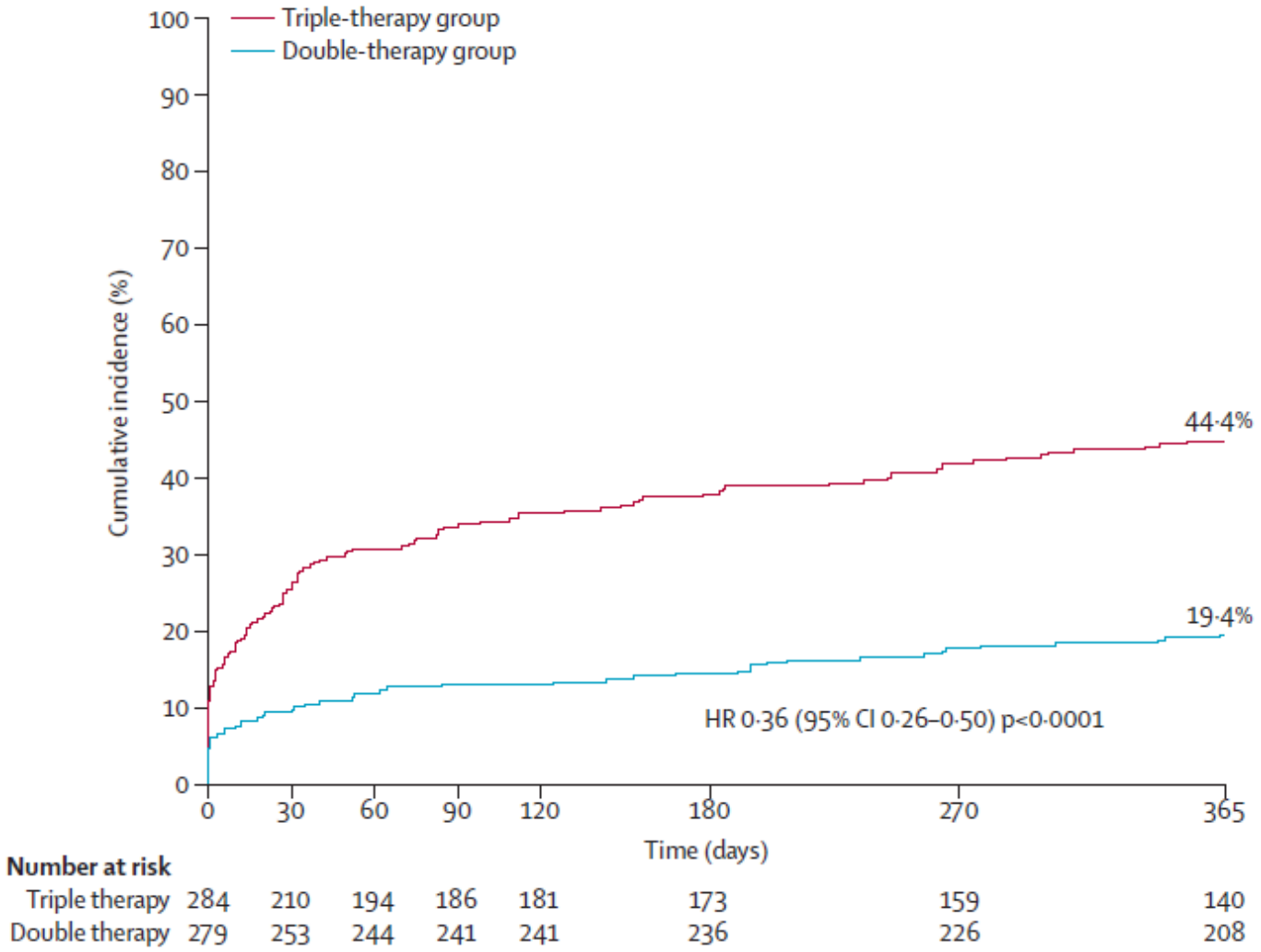
Use of clopidogrel with or without aspirin in 573 patients taking oral anticoagulant therapy and undergoing PCI



	Double therapy (n=297)	Triple therapy (n=284)	Hazard ratio (95% CI)	p value
Combined secondary endpoint	31 (11·1%)	50 (17·6%)	0·60 (0·38–0·94)	0·025
Death				
All-cause	7 (2·5%)	18 (6·3%)	0·39 (0·16–0·93)	0·027
Cardiac	3 (1·1%)	7 (2·5%)	0·43 (0·11–1·66)	0·207
Non-cardiac	4 (1·4%)	11 (3·9%)	0·36 (0·11–1·13)	0·069
Myocardial infarction				
Any	9 (3·2%)	13 (4·6%)	0·69 (0·29–1·60)	0·382
STEMI	1 (0·4%)	3 (1·1%)	0·34 (0·04–3·25)	0·325
Non-STEMI	8 (2·9%)	10 (3·5%)	0·79 (0·31–2·01)	0·625
Target-vessel revascularisation				
PCI or CABG	20 (7·2%)	19 (6·7%)	1·05 (0·56–1·97)	0·876
PCI	17 (6·1%)	16 (5·6%)	1·06 (0·54–2·10)	0·869
CABG	3 (1·1%)	3 (1·1%)	1·00 (0·20–4·90)	0·998
Stroke				
Any	3 (1·1%)	8 (2·8%)	0·37 (0·10–1·40)	0·128
Ischaemic	2 (0·7%)	8 (2·8%)	0·25 (0·05–1·17)	0·056
Haemorrhagic	1 (0·4%)	0	NA	0·321
Disabling	2 (0·7%)	2 (0·7%)	0·99 (0·14–6·99)	0·988
Non-disabling	1 (0·4%)	7 (2·5%)	0·14 (0·02–1·16)	0·034
Stent thrombosis				
Any	4 (1·4%)	9 (3·2%)	0·44 (0·14–1·44)	0·165
Definite	1 (0·4%)	3 (1·1%)	0·33 (0·03–3·22)	0·319
Probable	0	2 (0·7%)	NA	0·161
Possible	3 (1·1%)	4 (1·4%)	0·75 (0·17–3·30)	0·708

WOEST trial: aspirin omission in triple therapy

Use of clopidogrel with or without aspirin in 573 patients taking oral anticoagulant therapy and undergoing PCI



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PCI or CABG	20 (7·2%)	19 (6·7%)	1·05 (0·56–1·97)	0·876
PCI	17 (6·1%)	16 (5·6%)	1·06 (0·54–2·10)	0·869
CABG	3 (1·1%)	3 (1·1%)	1·00 (0·20–4·90)	0·998
Stroke				
Any	3 (1·1%)	8 (2·8%)	0·37 (0·10–1·40)	0·128
Ischaemic	2 (0·7%)	8 (2·8%)	0·25 (0·05–1·17)	0·056
Haemorrhagic	1 (0·4%)	0	NA	0·321
Disabling	2 (0·7%)	2 (0·7%)	0·99 (0·14–6·99)	0·988
Non-disabling	1 (0·4%)	7 (2·5%)	0·14 (0·02–1·16)	0·034
Stent thrombosis				
Any	4 (1·4%)	9 (3·2%)	0·44 (0·14–1·44)	0·165
Definite	1 (0·4%)	3 (1·1%)	0·33 (0·03–3·22)	0·319
Probable	0	2 (0·7%)	NA	0·161
Possible	3 (1·1%)	4 (1·4%)	0·75 (0·17–3·30)	0·708

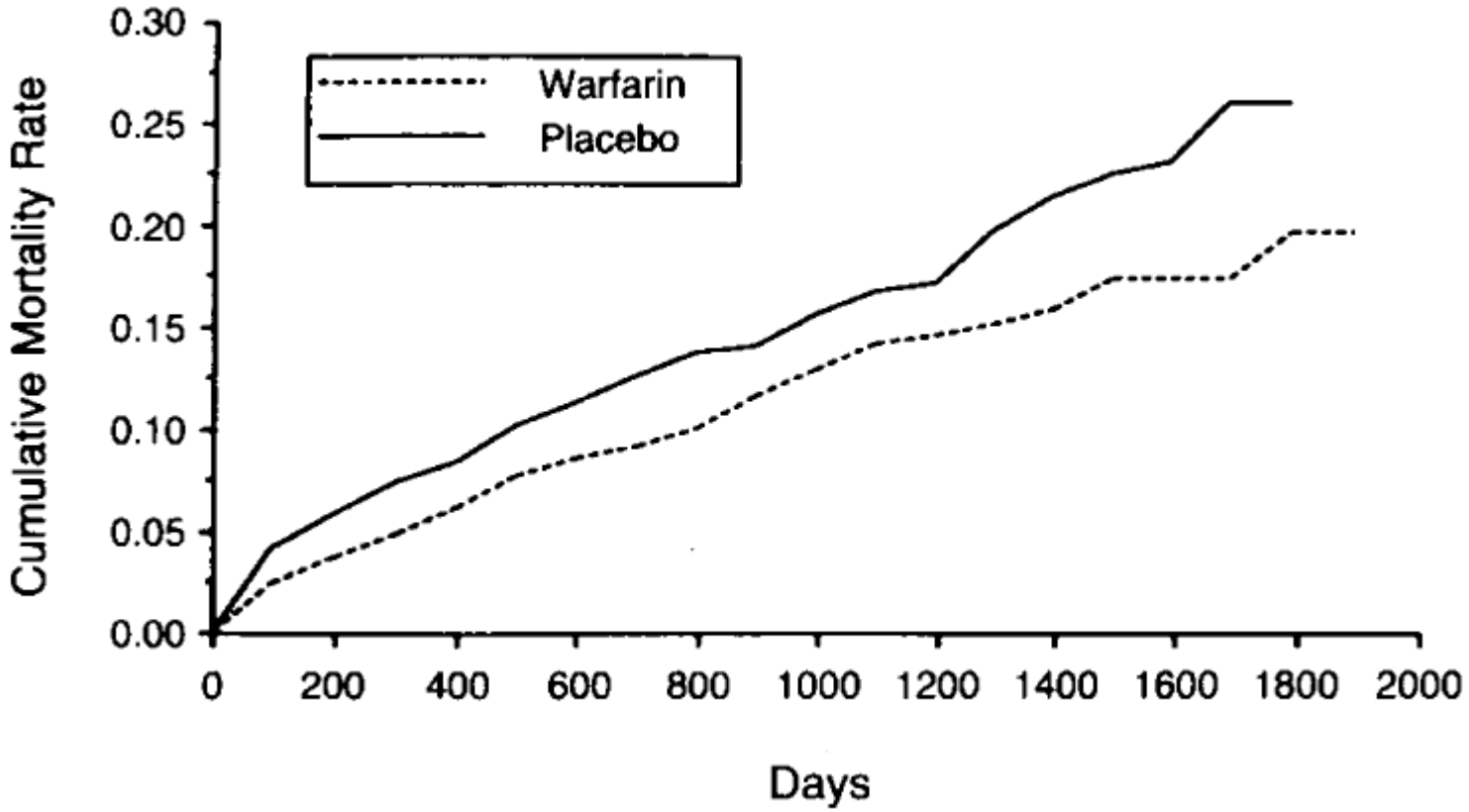
Brief summary

- Until such a trial is conducted, if anticoagulation is used after anterior MI, clinicians should probably consider omitting aspirin, adding proton pump inhibitors, targeting lower international normalized ratio ranges, shortening the anticoagulation course (3 months),

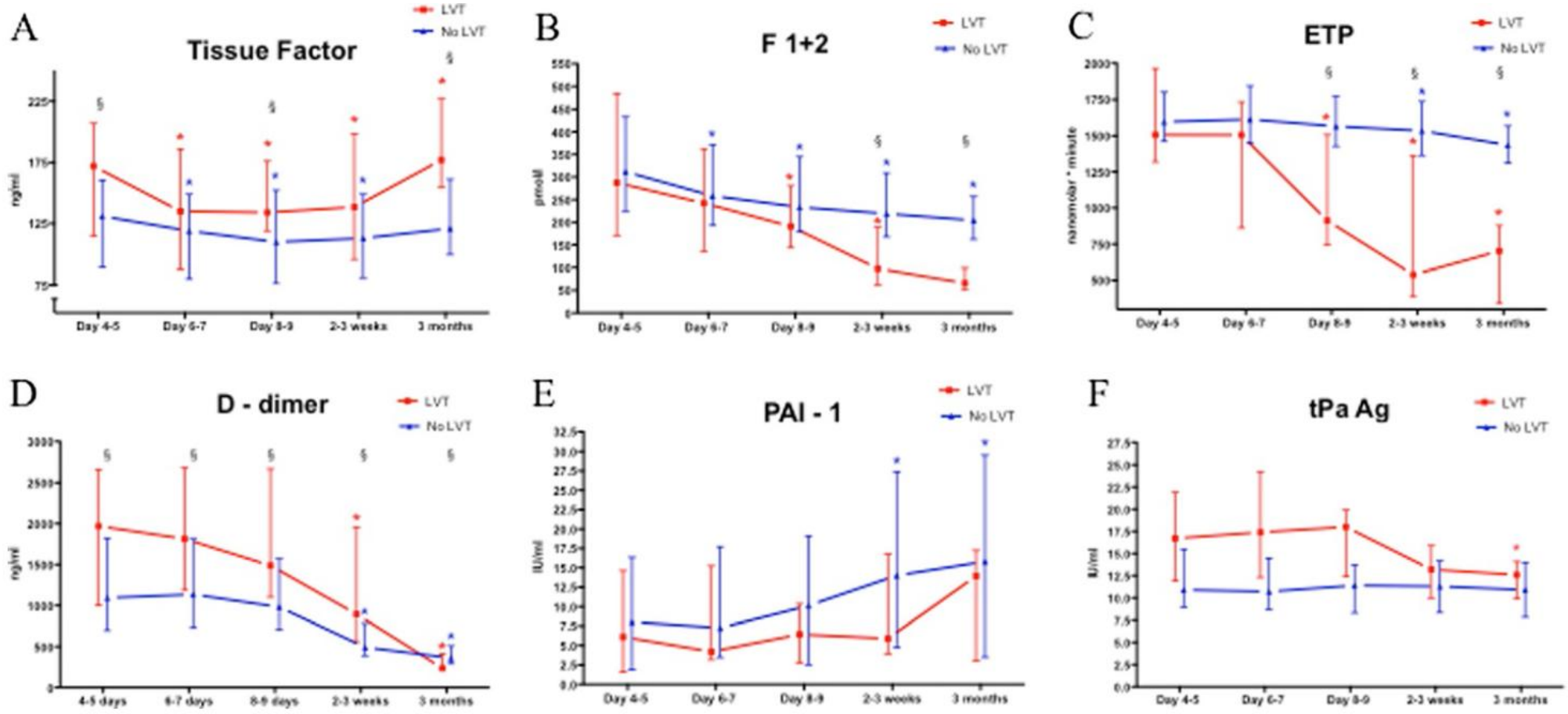
- it should be noted that the safety of the novel anticoagulant and antiplatelet therapies in this setting has not been tested.

- Ultimately, better risk assessment tools are needed to guide therapeutic decisions balancing the risk of LV thrombus formation and thromboembolism with the risk of bleeding.

Wafarin reduce the incidence of stroke and mortality after acute MI in randomized studies from the pre-thrombolytic era



Prothrombotic markers in patients with AMI and LV treated with PCI and DAPT.



Incidence of LV thrombus in AMI in thrombolytic era

A GISSI-2 Connected Study

The overall incidence of left ventricular thrombi in this population treated with thrombolytic agents was 28%.

TABLE 5. Influence of Treatment With Acetylsalicylic Acid on Left Ventricular Thrombi: Occurrence, Time of Appearance, and Disappearance

	ASA		No ASA	
	n	%	*n*	%
LV thrombi total	43/150	29	8/30	23
LV thrombi <48 hr	29/150	19	5/30	17
LV thrombi >48 hr	14/134	10	3/32	9
Disappearance	5/32	16	2/5	40

ASA, acetylsalicylic acid; LV, left ventricular; LV thrombi <48 hr, LV thrombi appearance at the first echocardiographic examination; LV thrombi >48 hr, LV thrombi appearance at the second examination; Disappearance, LV thrombi disappearance at the second examination.

TABLE 2

Clinical data on patients with left ventricular thrombus (LVT) within 48 hr of acute myocardial infarction (AMI), with LVT after 48 hr of AMI, and without LVT

	Age (years)	Sex (No. of men)	Killip class III or IV (No. of patients)	CK (IU/l)	MB (IU/l)	LDH (IU/l)	Mortality (No. of patients)
LVT within 48 hr of AMI (n = 11)	66 ± 8	9 (82%)	7 (64%)	2448 ± 920	281 ± 114	2087 ± 667	10 (91%)
LVT after 48 hr of AMI (n = 13)	59 ± 13	12 (92%)	3 (23%)	2368 ± 772	268 ± 64	1695 ± 555	2 (15%)[A]
No LVT (n = 34)	64 ± 13	23 (68%)	4 (12%)[A]	1935 ± 886	232 ± 146	1440 ± 582[B]	4 (12%)[B]

[A]$p < .005$ compared with patients with LVT within 48 hr of AMI; [B]

The incidence of clinically evident systemic embolic events was low: one of the 24 patients with left ventricular thrombus experienced transient ischemic attacks, and no embolic events were detected in patients without thrombus.

TABLE 4

Causes of death in 16 study patients

	LVT within 48 hr of AMI (No. of patients)	LVT after 48 hr of AMI (No. of patients)	No LV (No. o patient
Cardiogenic shock	5	1	2
Reinfarction	1	1	2