Safeguarding the Future: How can we improve outcomes in ACS patients?

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Safeguard

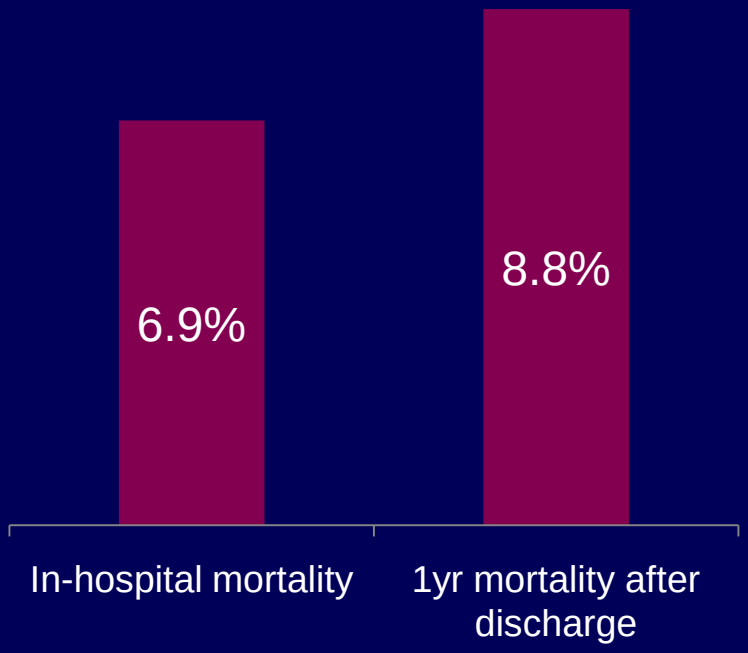
Contents

- Remnant risk in ACS treatment and numerous risk factors contribute to the risk of ACS
- Do we have any solutions to improve outcomes in ACS patients?
- Risk and Safety Management in ACS Patients

Remnant risk in ACS treatment and numerous risk factors contribute to the risk of ACS

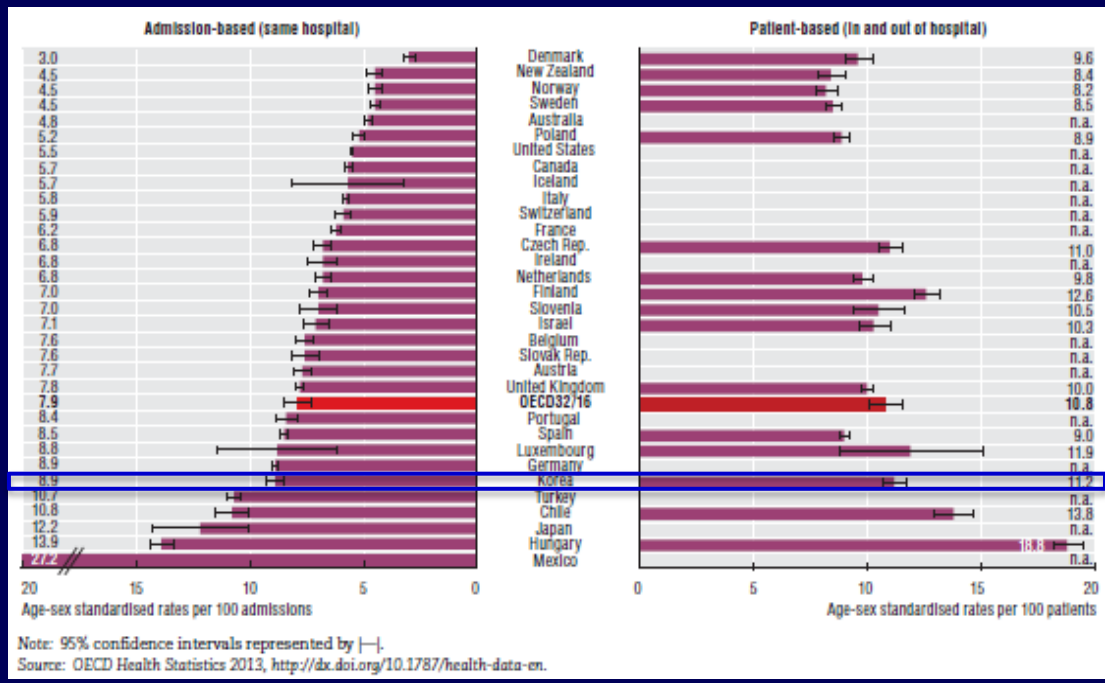
6.9%* AMI patients died in hospital and 8.8%* AMI patients died after discharge within 1 year in Korea

2012 AMI mortality in Korea



2013 HIRA data

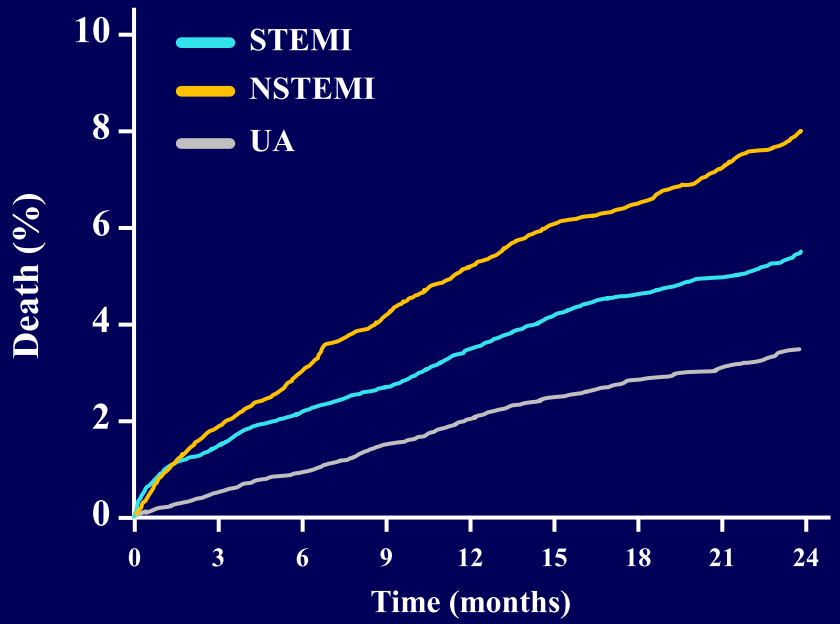
2011 30day AMI mortality rate after admission to hospital



Health At a Glance 2013: OECD Indicators

Source : OECD data in 2013 & HIRA data in 2013

Two-year outcomes post-discharge in Asian patients with ACS: finding from EPICOR Asia study



STEMI	at risk	6616	6460	6370	6267	6132	5977	5838	5600	536
NSTEMI	at risk	2570	2499	2460	2408	2351	2295	2229	2124	262
UA	at risk	3736	3692	3648	3582	3510	3421	3320	3171	376

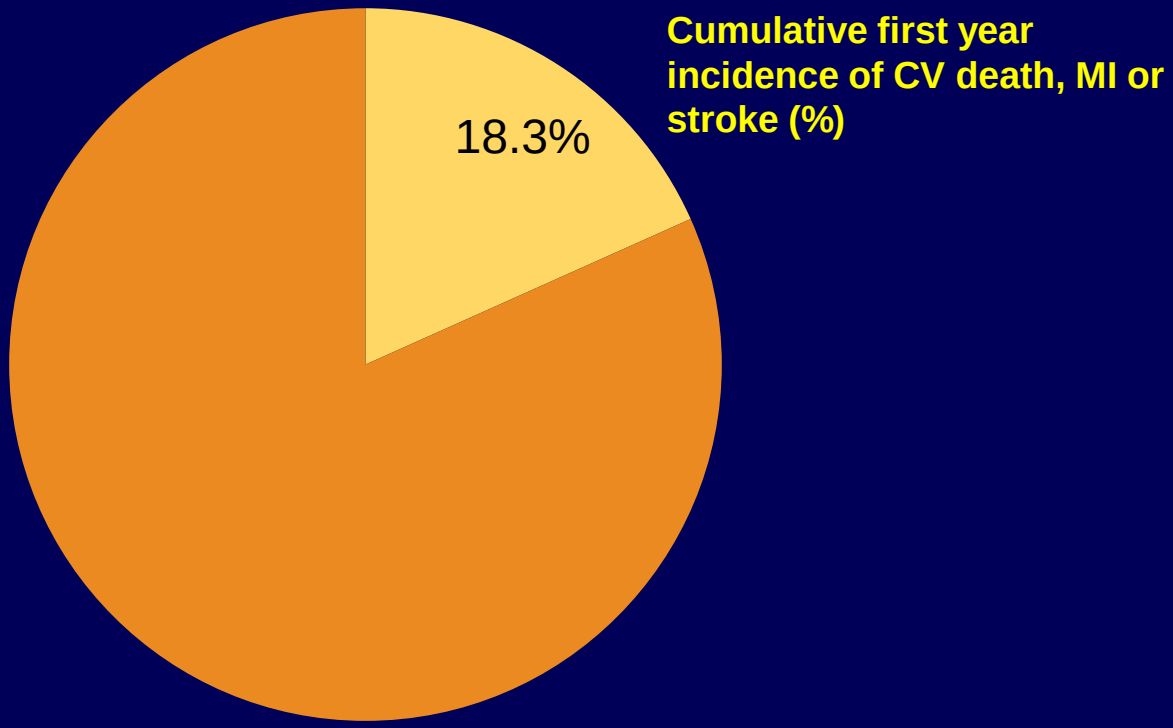
Over 2 years of follow-up post-discharge in EPICOR Asia, NSTEMI patients continue to experience more adverse outcomes, including greater mortality, compared with STEMI.

Mortality rates in Asia associated with ACS remain significant

Presented at the American college of Cardiology Congres March 14-16,2015, San Diego, California, USA

~1 in 5 patients will suffer from MI, stroke or CV death within the first year after MI

APOLLO HELICON Sweden analysis
Immediate post-MI survivors (n=97,254) [Jernberg 2014]



CV, cardiovascular; MI, myocardial infarction.
Jernberg T *et al.* Eur Heart J 2014;35(Suppl 1):363 (Abstract P2076).

Decision making for DAPT choice and duration: Ischemic risk vs Bleeding risk

Comprehensive Clinical Evaluation

UNFAVORABLE PROFILE

Clinical considerations:

- Short life expectancy
- Poor socio-economic status
- Poor expected DAPT adherence
- Poor mental status
- Malignancy
- End stage renal failure
- Smoker

BLEEDING RISK OUTWEIGHS ISCHEMIC RISK

Patient presentation:

- Clinically significant bleeding on DAPT
- Advanced age
- Female
- Liver disease
- Peptic ulcer disease
- Chronic oral nonsteroidal anti-inflammatory drug (NSAID) therapy
- Anemia and/or thrombocytopenia
- Uncontrolled hypertension
- Bleeding diathesis
- Prior major bleeding/ prior hemorrhagic stroke
- Atrial fibrillation/chronic anticoagulation therapy
- High bleeding risk score

ISCHEMIC RISK OUTWEIGHS BLEEDING RISK

Patient presentation:

- Recurrent ischemic event on DAPT
- Stent-related complications
- Acute coronary syndrome
- Male
- Diabetes mellitus
- Left ventricular dysfunction
- Chronic kidney disease
- Peripheral vascular disease
- Prior ischemic stroke
- Clopidogrel nonresponsiveness
- Prior myocardial infarction
- Lesion complexity
- Incomplete stent apposition
- Stent undersizing/ underexpansion
- Residual edge dissection
- Stent deployment in necrotic core
- Stent overlap

Montalescot, G. et al. J Am Coll Cardiol. 2015; 66(7):832–47.

Numerous Risk Factors Contribute to increase ischemic risk of ACS

Severity of Disease[1]
- Multivessel disease
- Calcification of the culprit vessel

Medical History[1,2]
- Previous MI
- Previous stroke or TIA

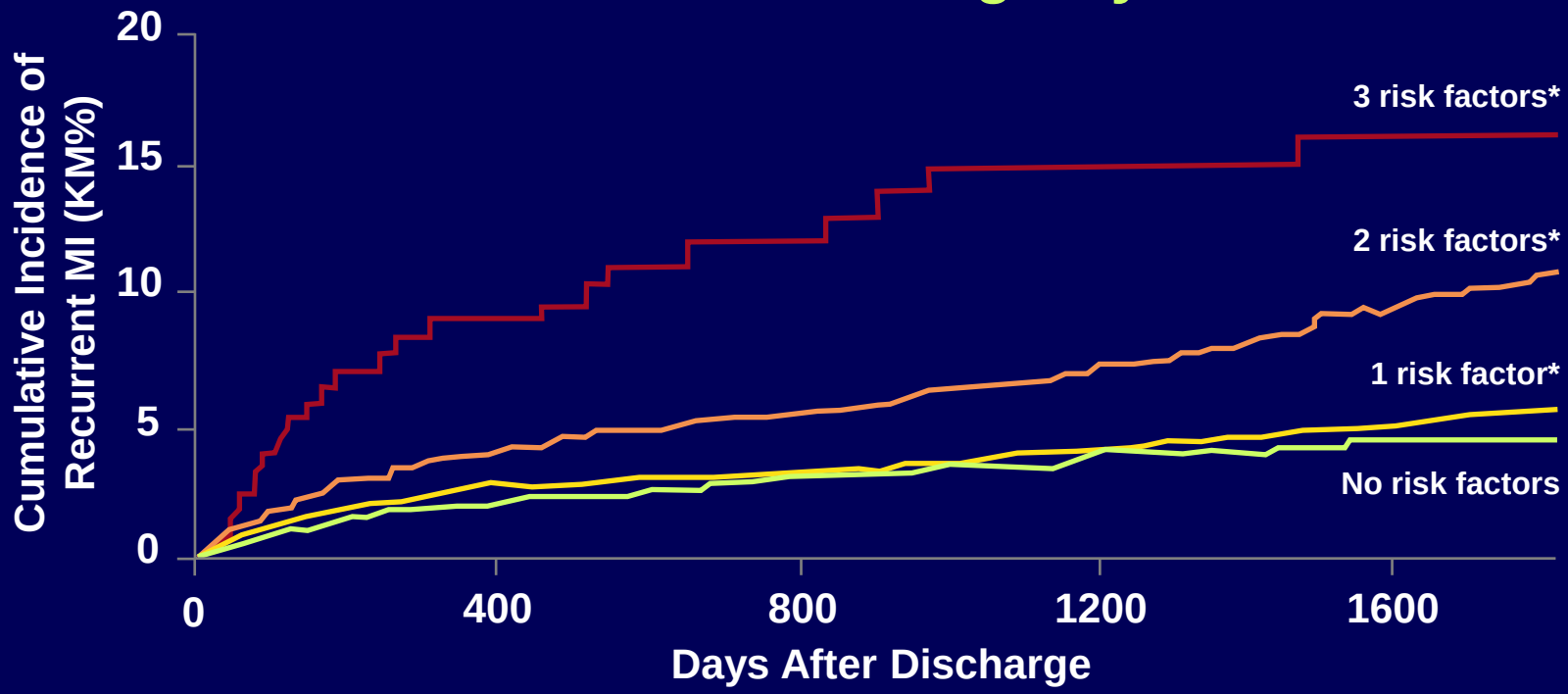
Comorbidities[1,2,3]
- Diabetes mellitus
- Chronic kidney disease
- Dyslipidemia
- Hypertension

Patient Characteristics[2,3,4,5]
- Older age
- Obesity
- Smoking

1. Kikkert WJ et al. *Am J Cardiol*. 2014;113:229-235. 2. Nakatani D et al. *Circ J.* 2013;77:439-446. 3. Thune JJ et al. *Eur J Heart Fail*. 2011;13:148-153. 4. Leander K et al. *Cardiovasc Prev Rehabil*. 2007;14:532–537. 5. Rea T et al. *Ann Intern Med.* 2002; 137:494–500.

Number of Risk Factors Incrementally Increased the Risk of Recurrent MI

The OACIS Registry



Prospective, observational multicenter study of 7870 Japanese patients with AMI enrolled between 1998 and 2008. During the 5-year follow-up period (median 3.9 years), 353 patients experienced a recurrent MI

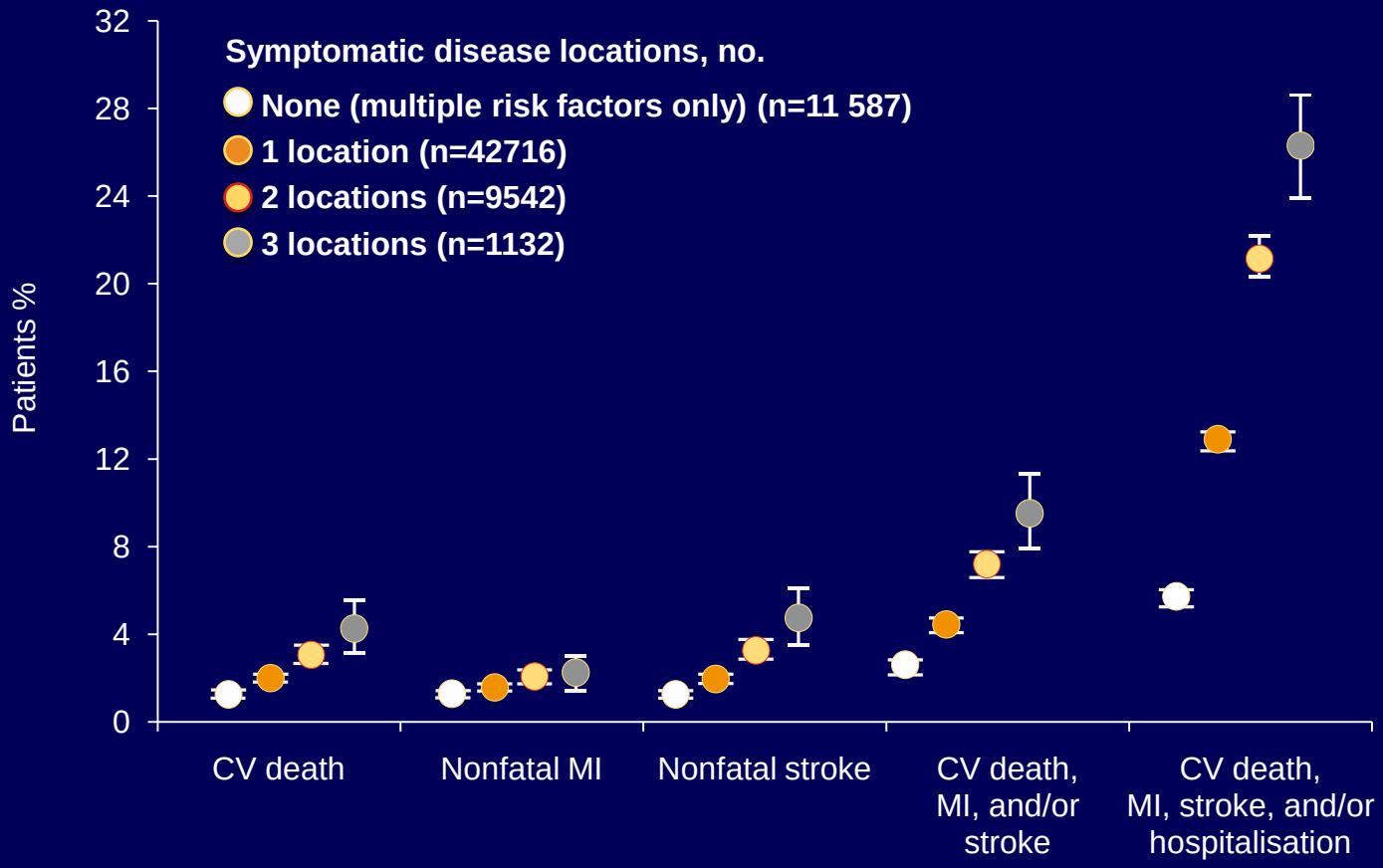
***Risk factors in this analysis were those that were independently associated with recurrent MI: DM, age, and prior MI.**

Nakatani D et al. *Circ J.* 2013;77:439-446.

The presence of atherosclerosis in multiple locations increases the risk of CV events

Multi vessel disease

REACH registry data



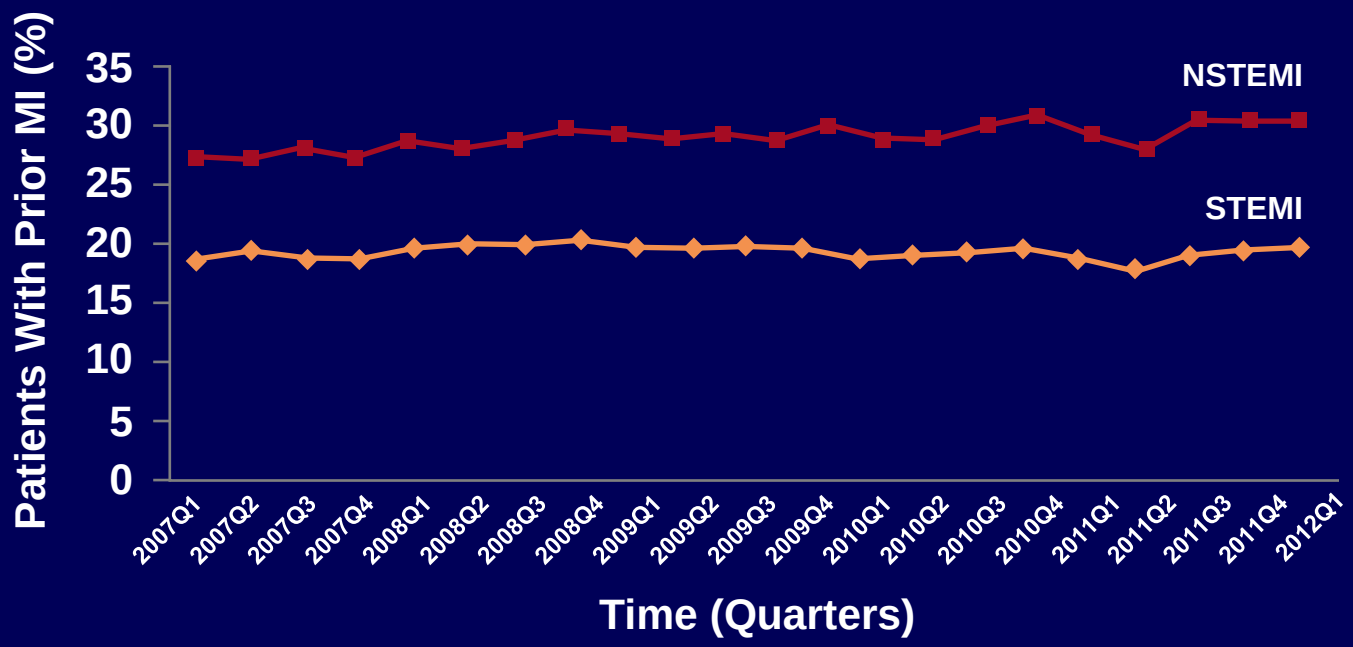
All p<001. Patients with at least 3 factors but no symptoms are counted as 0, even in the presence of asymptomatic carotid plaque or reduced ankle brachial index. Error bars represent 95% confidence intervals. CV, cardiovascular; MI, myocardial infarction; REACH, REduction of Atherothrombosis for Continued Health.

Steg PG *et al*. JAMA 2007;297:1197–1206.

Prior MI

Among Patients Presenting With AMI the Rate of Prior MIs Remained Consistent

NCDR ACTION Registry-GWTG



Over the entire study period 29% of NSTEMI and 19% of STEMI patients had a prior MI

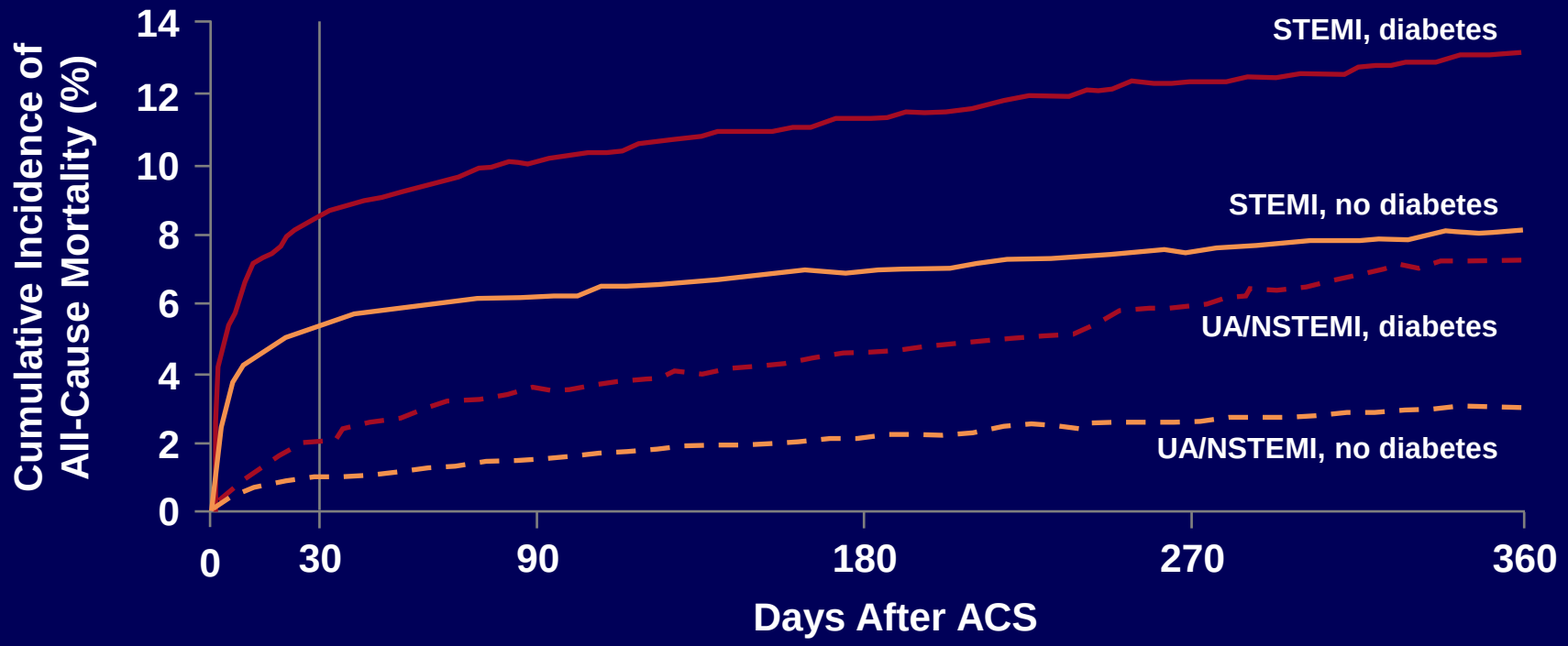
Observational study of 319,152 patients with a final diagnosis of STEMI (n=124,535) or NSTEMI (n=194,617) from 446 US hospitals

ACTION Registry-GWTG=Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With The Guidelines; NCDR=National Cardiovascular Data Registry; NSTEMI=non-ST-elevation myocardial infarction.

Adapted from Shen L et al. *Am Heart J.* 2014;167:840-845.

Diabetes Increased the Risk of Mortality in Patients With ACS

Pooled Analysis of TIMI ACS Trials



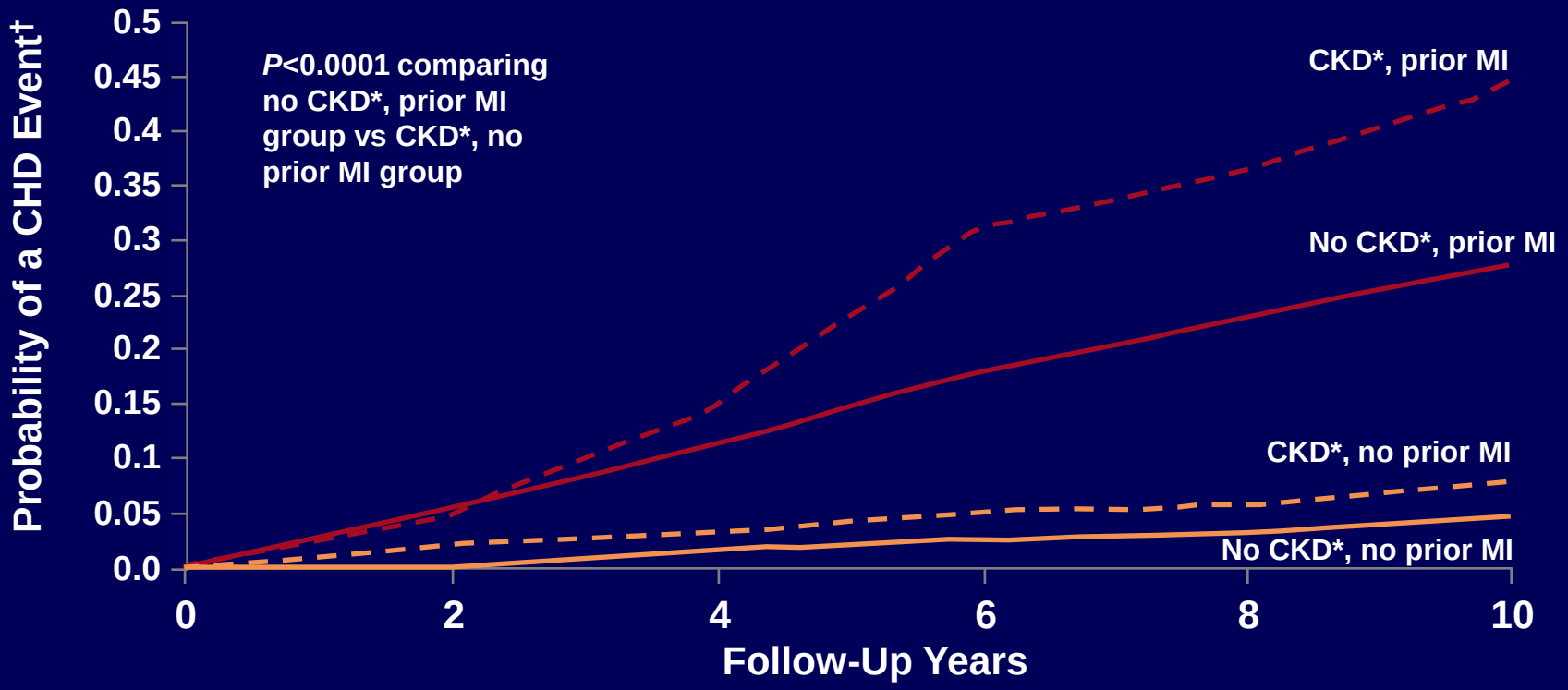
Patients with STEMI (n=46,577) and UA/NSTEMI (n=10,613) were pooled from 11 independent TIMI Study Group clinical trials that had at least 30 days of clinical follow-up from 1997-2006. 17.1% (n=10,613) of patients had diabetes

TIMI=Thrombolysis in Myocardial Infarction.

Donahoe SM et al. *JAMA*. 2007;298:765-775.

CKD Increased the Risk of Recurrent MI or Fatal CHD in Patients With Prior MI

The ARIC Study

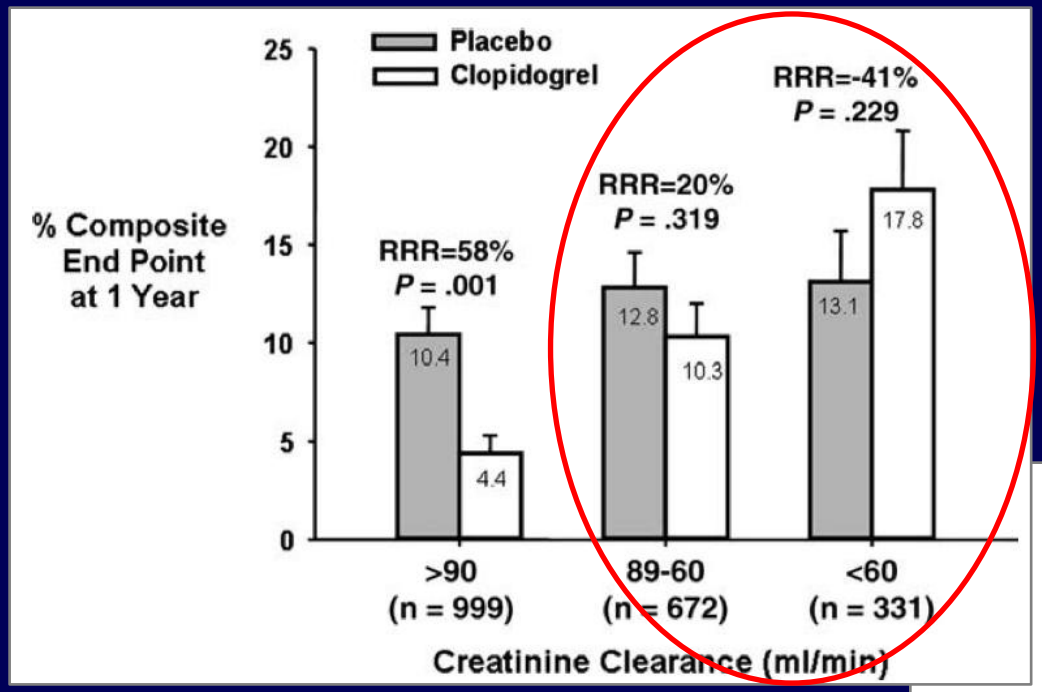


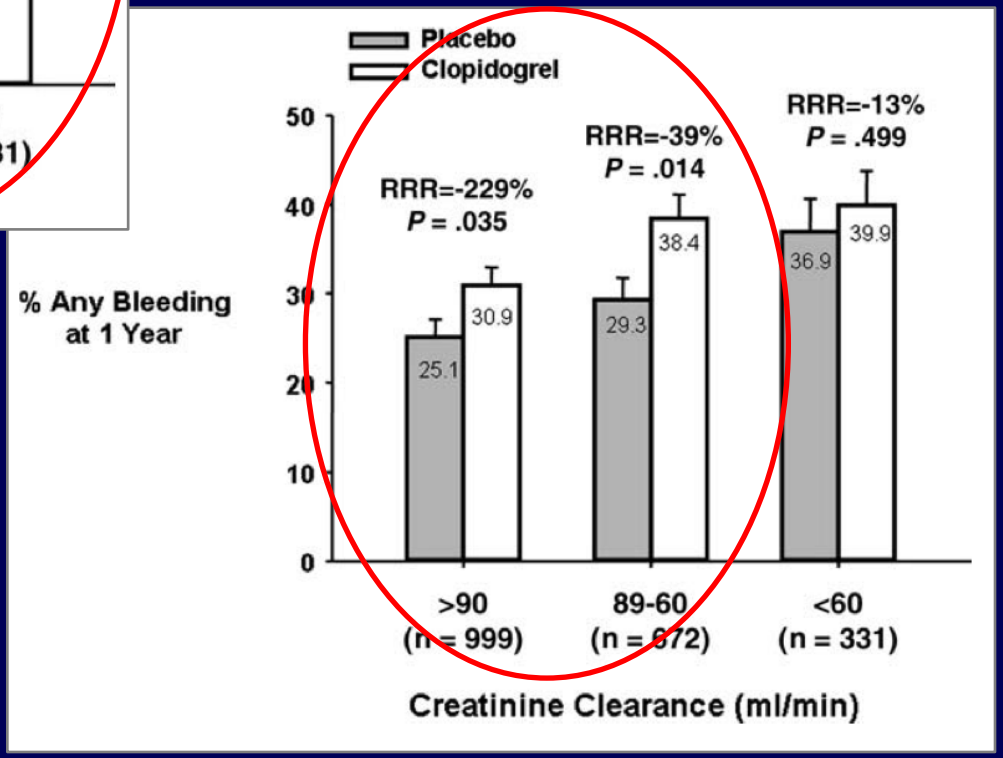
Prospective follow-up of over 10 years from 1987-2001 of 12,243 subjects. The cohort was re-examined approximately every 3 years

*Stage 3 CKD. †Definite or probable hospitalized MI or definite fatal CHD. ARIC=Atherosclerosis Risk in Communities.

Adapted from Wattanakit K et al. *J Am Coll Cardiol*. 2006;48:1183-1189.

CREDO study – CKD sub-group analysis

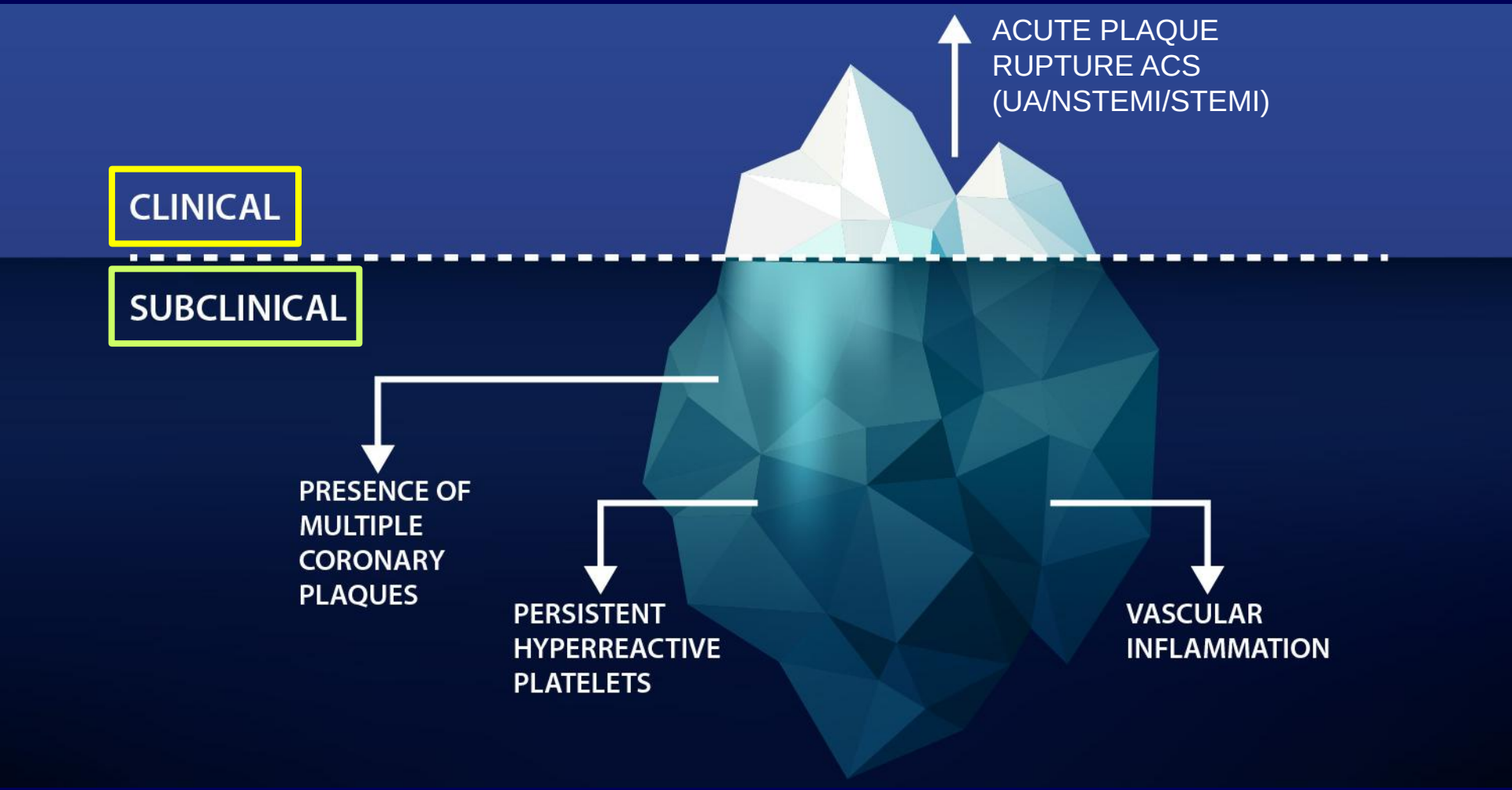




Best *et al*. *Am Heart J* 2008;155:687-93

Do we have any solutions to improve outcomes in ACS patients?

ACS is the tip of the atherothrombotic 'iceberg'

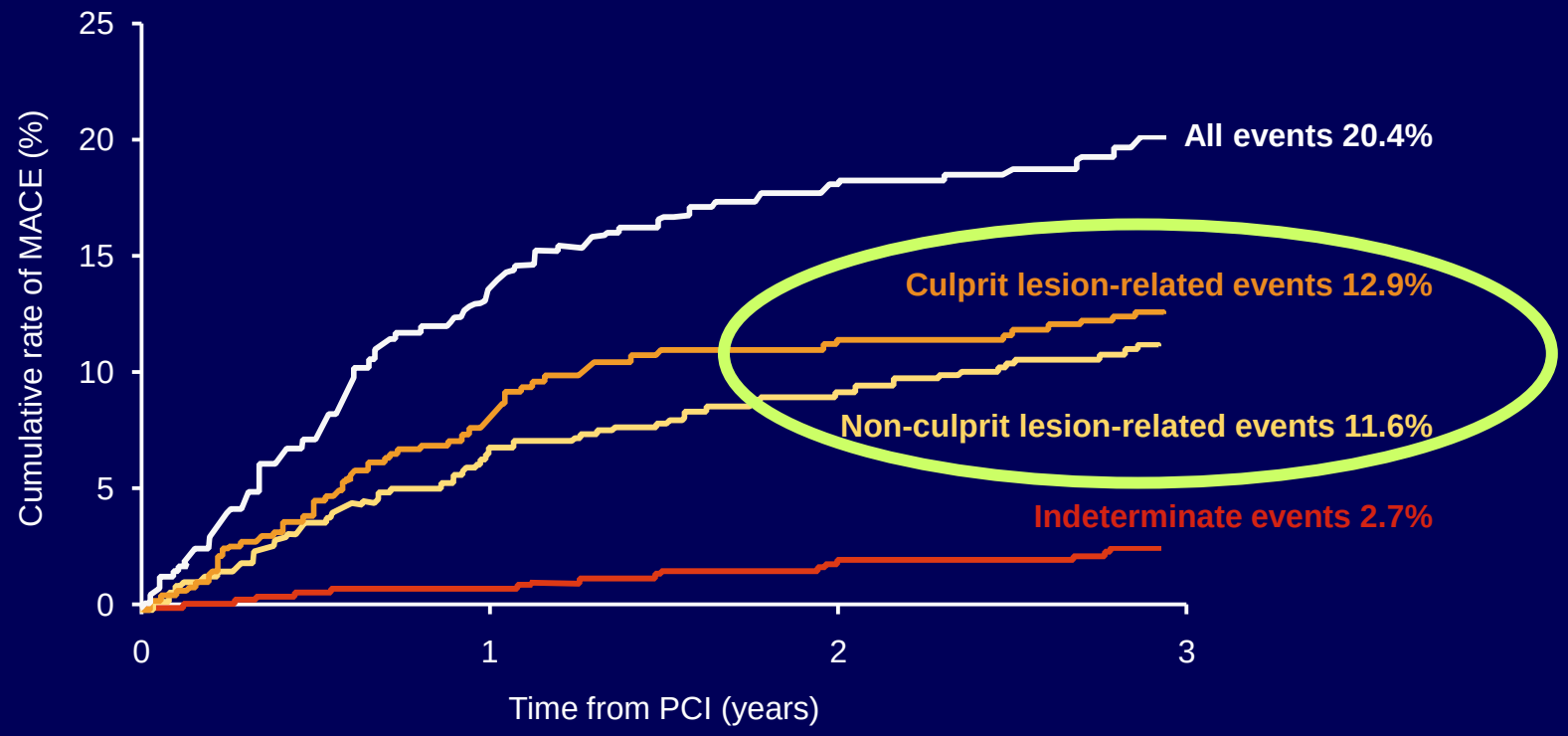


ACS, acute coronary syndrome; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

Goldstein JA. J Am Coll Cardiol 2002;39:1464–1467.

Recurrent events are as likely to originate from a new atherosclerotic plaque as they are from the initial culprit lesion

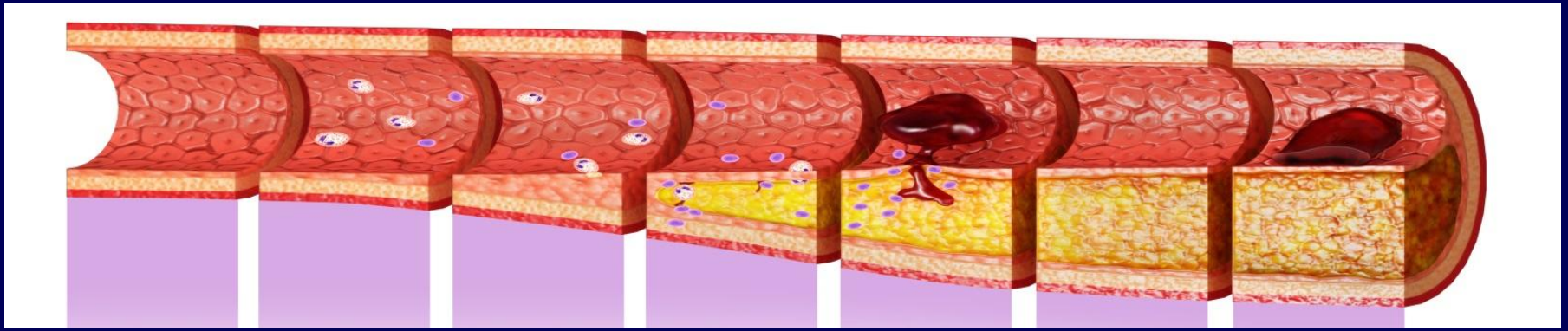
PROSPECT study: Prospective study of the natural history of atherosclerosis over 3 years in patients with ACS who underwent PCI (n=697)[Stone 2011]



ACS, acute coronary syndrome; MACE, major adverse cardiac events; PCI, percutaneous coronary intervention; PROSPECT, Providing Regional Observations to Study Predictors of Events in the Coronary Tree.
Stone GW *et al.* N Engl J Med 2011;364:226–235.

Platelets may be involved in all stages of atherothrombosis

Initiation and progression	Plaque rupture	Acute thrombus formation



Platelet adhesion & activation	Platelet activation	Platelet aggregation
• Release of inflammatory mediators, cell recruitment	• Release of inflammatory mediators, plaque instability	

Fuentes QE *et al.* Platelets 2013;24(4):255–262; Gawaz M. Eur Heart J Suppl 2008:10(Suppl 1);14–17.

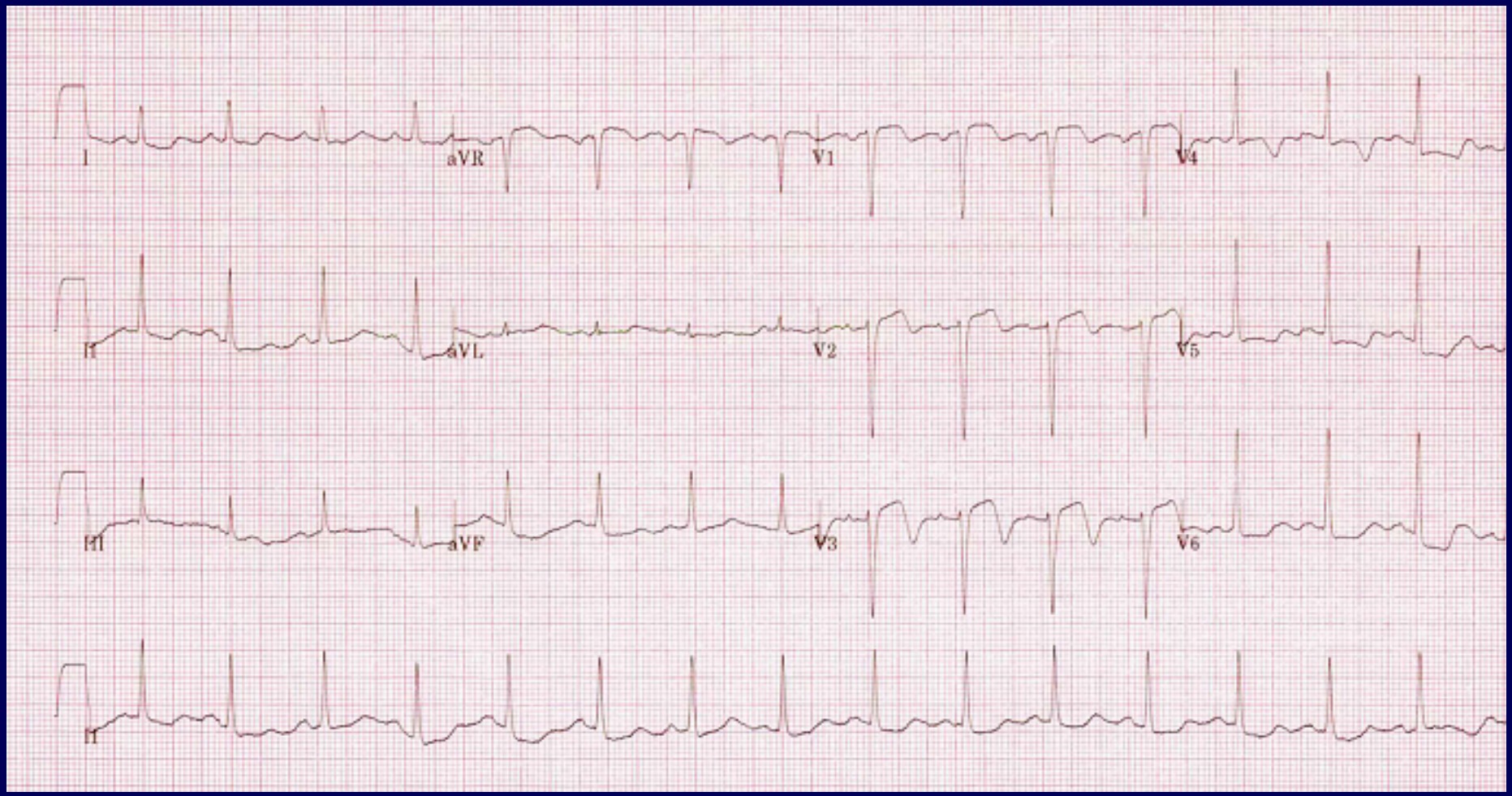
Case Presentation

- C/C ant chest pain (onset: 3 days ago)
- Age/Sex 77 / female
- HTN (+), no DM, no dyslipidemia
- Non-smoker

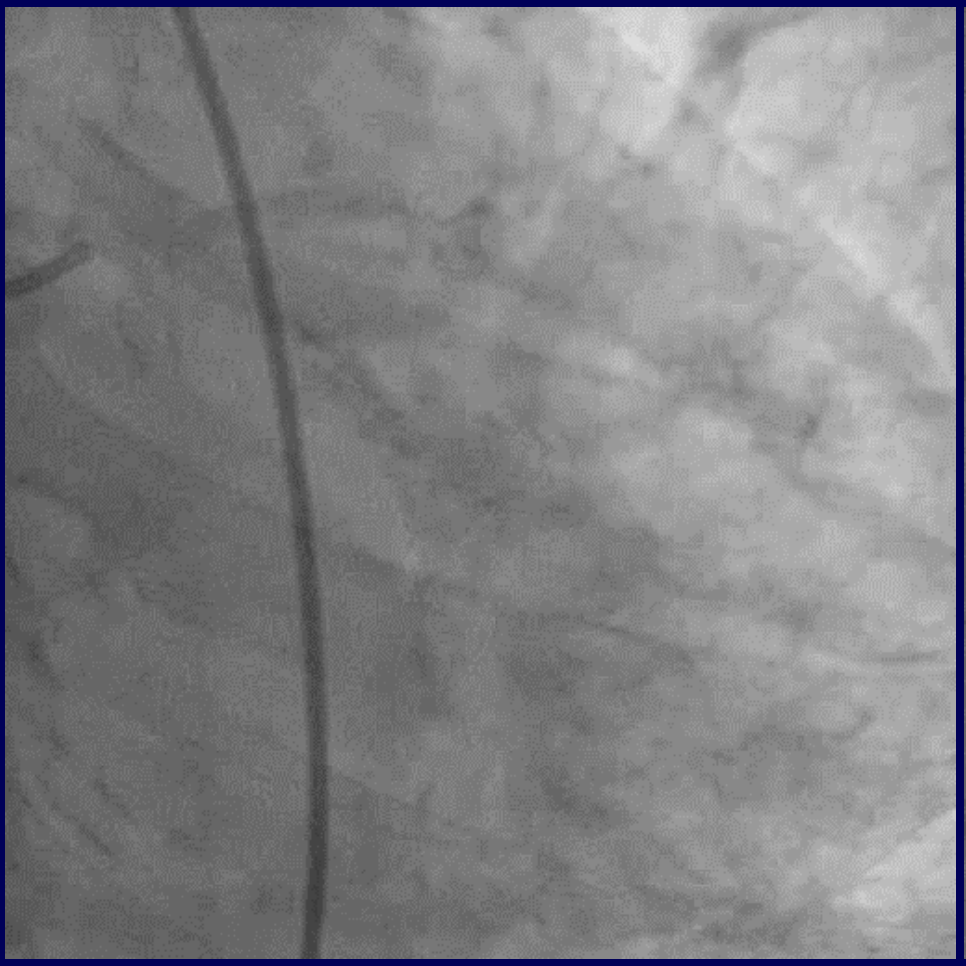
- CK-MB 15.45 ng/mL (0 - 6.22)
- hs Tropnin-T 2.25 ng/mL (0 – 0.013)

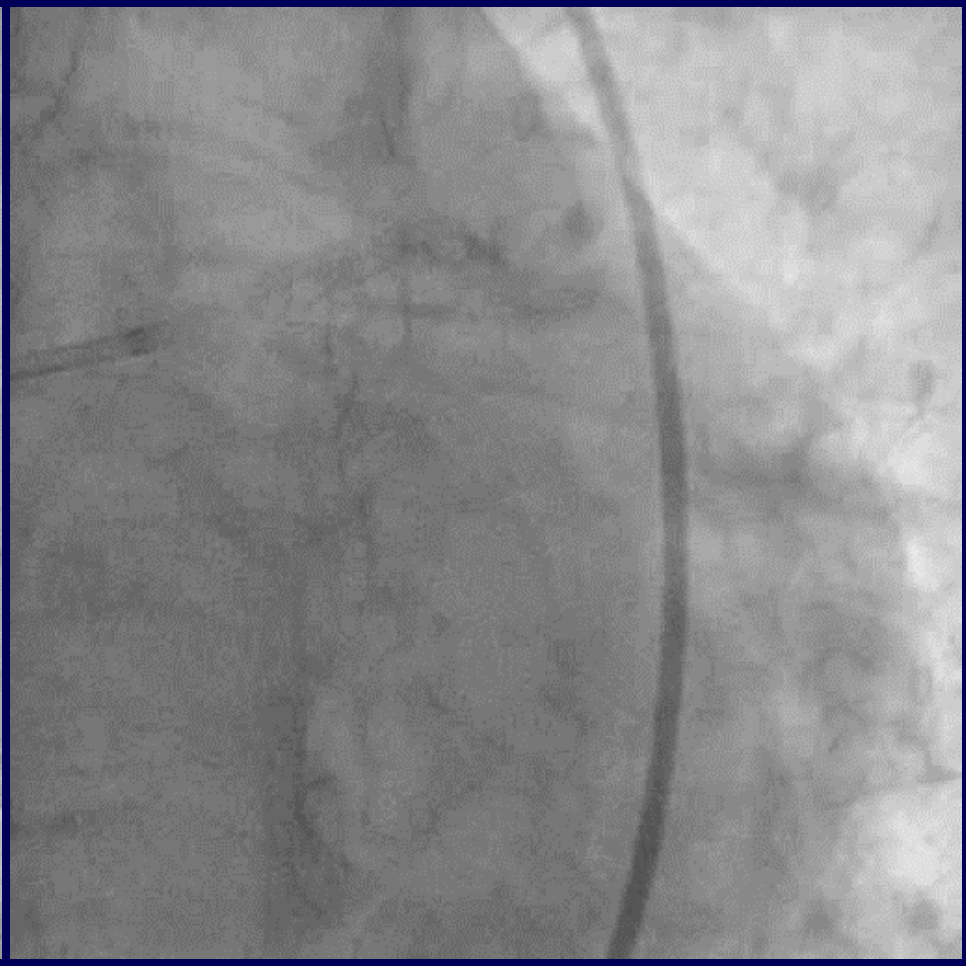
- 2DE HK in septum, apex, mid to apical ant LV wall
  IHD in LAD territory, EF=46%

ECG at ER



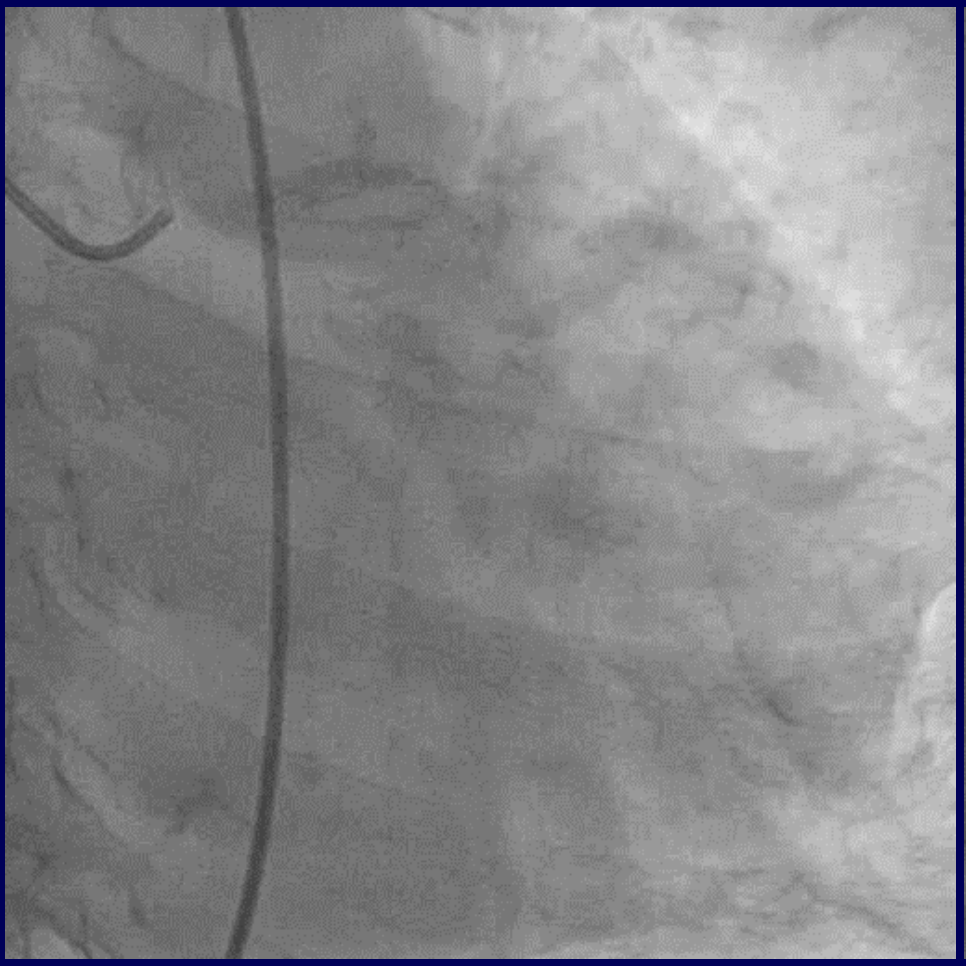
PCI for pLAD

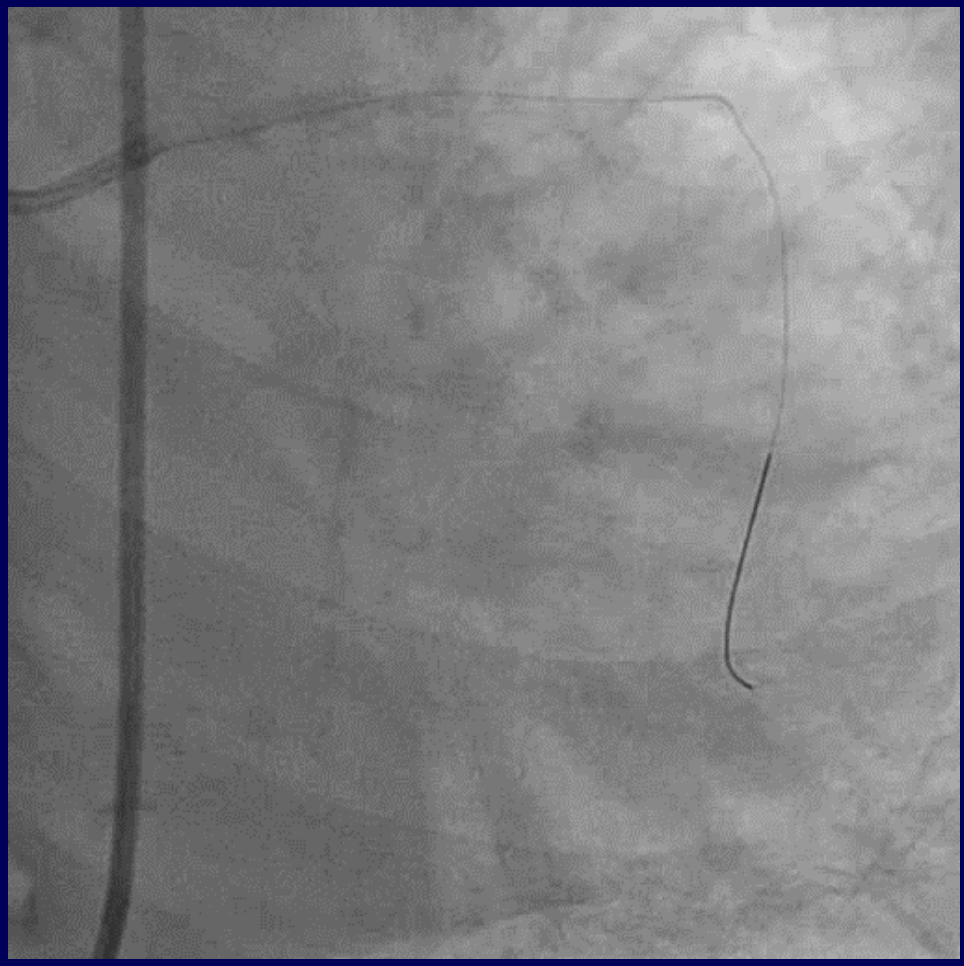




PCI for pLAD using 3.0*15mm R onyx
Aspirin 100mg MD and clopidogrel 75mg MD

ER revisit d/t Ant. chest pain 1-M later





POBA using 3.0*8 mm NC balloon for subacute stent thrombosis in pLAD

병원정보SYSTEM(병동 OCS) - [임상병리 결과조회(w_cpl31q01) (192.168.10.25)]

화일관리(F) OCS사용자기준정보 처방 차트관련 기타환자관련 원내전화번호조회 창(W)

등록번호 여자 77 주민등록번호 혈액검사결과COPY

구분	과	처방일자	접수일자
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입원	EN	16/01/01	16/01/01

미생물

생화학 | 응급검사 | 종합검증 | 혈액학검사 | 면역혈청 | 염기서열

염기서열

출력일자 : 2016/02/22 17:12

등록번호: 환자명: (77 / F) 의뢰과: CO ERI VER 검체번호: 1601290971

의뢰일자: 2016/01/29 의뢰의: 검체종류:B2 검사명: CYP2C19 유전형

검사결과

1. 검사방법: PCR. sequencing of CYP2C19 [c.681G>A(*2), c.636G>A(*3)]
2. 검사결과:
CYP2C19 유전형: *1/*2, intermediate metabolizer

Genotype	predicted phenotype	Frequency (%)	95% CI
CYP2C19*1/*1	EM	37.86	29.72-45.99
CYP2C19*1/*2, CYP2C19*1/*3 and CYP2C19*2/*3	IM	51	43-60
CYP2C19*2/*2 and CYP2C19*3/*3	PM	10.7	5.5-15

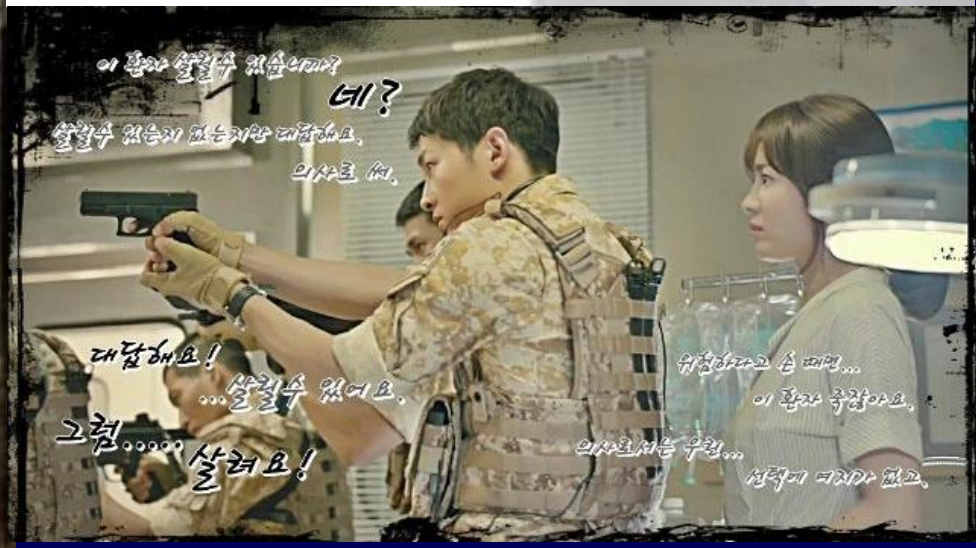
Ulrarapid Metabolizer	The CYP2C19 has fast enzyme activity. Individuals with ultrarapid metabolizer phenotype may be at increased risk of drug failure due to increased drug elimination with drugs that are substrates of CYP2C19. For prodrugs such as clopidogrel (Plavix), these individual may be at increased risk of overdose toxicity due to increased exposure to active metabolites.
Normal (extensive) Metabolizer	CYP2C19 enzyme of these patients is fully functioning. Individuals with normal metabolizer status may be administered drugs following standard dosing guidelines.
Intermediate Metabolizer	Intermediate metabolizers have reduced CYP2C19 enzymatic activity. These individuals may be at increased risk of overdose toxicity due to decreased drug elimination for medications metabolized by CYP2C19. Conversely, when administered prodrugs such as clopidogrel (Plavix) that require activation by CYP2C19, these individuals may be at increased risk of therapeutic failure.
Poor Metabolizer	Poor metabolizers have no CYP2C19 enzyme activity. These patients are likely to be at increased risk of overdose toxicity using drugs that are metabolized by CYP2D6. In addition, these individuals are likely to be at risk of therapeutic failure when administered prodrugs such as clopidogrel (Plavix) that require activation by CYP2C19.

결론 및 의견

1. CYP2C19 유전형: *1/*2로, intermediate metabolizer 입니다.
2. Clopidogrel 투여시 CYP2C19 intermediate metabolizer와 poor metabolizer의 경우 용량을 증량하거나 다른 약물로 대체할 필요가 있습니다.

일반결과지 출력 | 미생물 결과지 출력 | 외국결과지 출력 | 외국기본형결과지 출력 | 수혈 LIST | 혈의학(체외) 결과지 | F6 조회 | F8 종료


BOOK ONE OF THE HITCHHIKER STRAIN
MORTALITY
KELLIE SHERIDAN


네?
대답해요!
...살릴수 없어요.
그럼.....살려요!

그럼.....
살려요

Mortality outcomes with clopidogrel

Study	Treatment	Primary efficacy endpoint RR (95% CI)	Mortality outcome (secondary endpoint) RR (95% CI)	Major bleeding (primary safety endpoint) RR (95% CI)
CURE[1]	Clopidogrel + ASA versus ASA	0.80 (0.72–0.90); ***P*<0.001**	CV death: 0.93 (0.79–1.08); ***P*=NS** All-cause death: No data	1.38 (1.13–1.67); ***P*=0.001**
PCI -CURE[2]	Clopidogrel + ASA versus ASA	0.75 (0.56–1.00); ***P*=0.047**	CV death: 1.07 (0.65–1.75); ***P*=NS** All-cause death: No data	1.12 (0.70–1.78); ***P*=0.64**
CLARITY-TIMI 28[3]	Clopidogrel + ASA + lysis versus ASA + lysis	0.64 (0.53–0.76); ***P*<0.001**	CV death: no data All-cause death: 1.17 (0.75–1.82); ***P*=0.49**	No RR available; ***P*=0.64**
PCI-CLARITY[4]	Clopidogrel + ASA + lysis versus ASA + lysis	0.59 (0.43–0.81); ***P*=0.001**	CV death: 0.49 (0.24–1.03); ***P*=NS** All-cause death: No data	No RR available; ***P*=0.21**
CHARISMA[5]	Clopidogrel + ASA versus ASA	0.93 (0.83–1.05); ***P*=0.22**	CV death: 1.04 (0.87–1.25); ***P*=0.68** All-cause death: 0.99 (0.86–1.14); ***P*=0.90**	1.25 (0.97–1.61); ***P*=0.09**
CURRENT[6]	Standard dose versus high-dose clopidogrel	0.94 (0.83–1.06); ***P*=0.30**	CV death: 0.95 (0.81–1.13); ***P*=0.57** All-cause death: 0.96 (0.82–1.13); ***P*=0.61**	1.24 (1.05–1.46); ***P*=0.01**

NS, not significant; RR, risk reduction

1. Yusuf S et al. N Engl J Med 2001;345:494–502; 2. Mehta SH et al. Lancet 2001;8;358:527–533;
3. Sabatine MS. N Engl J Med 2005;352;1179–1189; 4. Sabatine MS. JAMA 2005;294;1224–1232;
5. Bhatt DL et al. N Engl J Med 2006;354:1706–1717; 6. Mehta et al. N Engl J Med 2010;363:930–942

Mortality outcomes with prasugrel

Prasugrel/TRITON-TIMI 38 – mortality and safety outcomes (15 months)

Endpoint	Prasugrel, n (%) (N=6813)	Clopidogrel, n (%) (N=6795)	*HR (95% CI)	*P* value
Primary endpoint (CV death, MI or stroke)	643 (9.9%)	781 (12.1%)	0.81 (0.73–0.90)	<0.001
CV death	133 (2.1%)	150 (2.4%)	0.89 (0.70–1.12)	0.31
MI	475 (7.3)	620 (9.5)	0.76 (0.67–0.85)	<0.001
Stroke	61 (1.0)	60 (1.0)	1.02 (0.71–1.45)	0.93
All-cause death	188 (3.0%)	197 (3.2%)	0.95 (0.78–1.16)	0.64
Key safety endpoint (major bleeding)	146 (2.4%)	111 (1.8%)	1.32 (1.03–1.68)	0.03

*HR <1 favours prasugrel

Wiviott SD et al. N Engl J Med 2007;357:2001–2015

PLATO main analysis – major efficacy outcomes

	Ticagrelor (n=9333)	Clopidogrel (n=9291)	HR* (95% CI)	*P* value
Primary endpoint, n (%)				
CV death + MI + stroke	864 (9.8)	1014 (11.7)	0.84 (0.77–0.92)	**<0.001**
Secondary endpoints, n (%)				
Total death + MI + stroke	901 (10.2)	1065 (12.3)	0.84 (0.77–0.92)	**<0.001**
CV death + MI + stroke + ischaemia + TIA + arterial thrombotic events	1290 (14.6)	1456 (16.7)	0.88 (0.81–0.95)	**<0.001**
MI	504 (5.8)	593 (6.9)	0.84 (0.75–0.95)	**0.005**
CV death	**353 (4.0)**	**442 (5.1)**	**0.79 (0.69–0.91)**	**0.001**
Stroke	125 (1.5)	106 (1.3)	1.17 (0.91–1.52)	**0.22**
All-cause death	**399 (4.5)**	**506 (5.9)**	**0.78 (0.69–0.89)**	**<0.001**

*HR <1 favours ticagrelor
CI, confidence interval; HR, hazard ratio
Wallentin L et al. N Engl J Med 2009;361:1045–1057

Mortality outcomes in PLATO sub-group analyses

Reduction in CV death observed with ticagrelor versus clopidogrel, irrespective of intended treatment strategy*

ACS treatment strategy	RRR	*P* value
PLATO overall[1]	–21%	**0.001**
PLATO – intended for invasive management[2] (PCI and CABG)	–18%	**0.025**
PLATO – intended for non-invasive management[3] (medically managed)	–24%	**0.019**

*Results should be regarded as exploratory and hypothesis generating only; PLATO sub-group analyses were not powered to show statistical significance
Mortality outcomes in main PLATO trial:[1] CV death: HR (95% CI) = 0.79 (0.69–0.91) *P*<0.001; all-cause death: HR (95% CI) = 0.78 (0.69–0.89) *P*<0.001
Note: CV and all-cause death were secondary efficacy endpoints; RRR, relative risk reduction
1. Wallentin L et al. N Engl J Med 2009;361:1045–1057; 2. Cannon CP et al. Lancet 2010;375:283–293; 3. James S et al. BMJ 2011;342:d3527
RRR values calculated based on data in references cited

2014 AHA/ACC guideline in NSTE-ACS

Early management strategy (initial ischaemia-guided or early invasive strategy) before definition of coronary anatomy

Recommendation	Class	Level	Evidence
$P2Y_{12}$ inhibitor (**either clopidogrel or ticagrelor**) in addition to aspirin, for up to 12 months in patients treated initially with either an early invasive or ischaemia-guided strategy	I	B	CURE[1], CURRENT-OASIS 7[2], PLATO[3], PLATO non-invasive substudy[4]
new It is reasonable to choose **ticagrelor in preference to clopidogrel** for patients treated with an early invasive or ischaemia-guided strategy	IIa	B	PLATO[3], PLATO non-invasive substudy[4]

Contraindications and other label requirements still apply

1. Yusuf S et al. N Engl J Med 2001;345:494–502
2. Mehta SR et al. N Engl J Med 2010;363:930–942
3. Wallentin L et al. N Engl J Med 2009;361:1045–1057
4. James SK et al. BMJ 2011;342:d3527

Risk and Safety Management in ACS Patients

Modes of DAPT Cessation

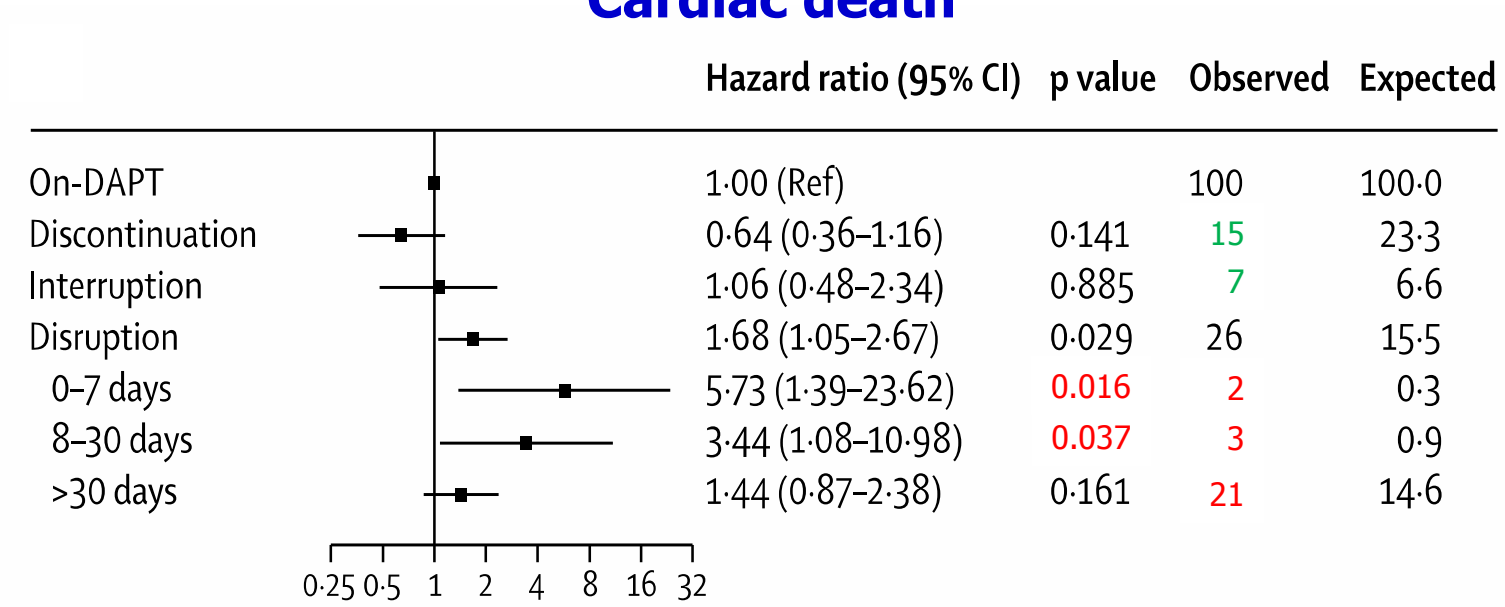
- **Discontinuation**
  - Patients had discontinued DAPT as per recommendation of their physician who felt the patient no longer needed therapy
- **Interruption**
  - Patients had interrupted DAPT use on a voluntary basis and as guided by a physician due to (e.g.surgery)
  - DAPT was then reinstituted within 14 days
- **Disruption**
  - Patients had disrupted DAPT use due to bleeding or non-compliance

Mehran et al. Lancet. 2013;382:1714–1722

PARIS Registry – Risk of Ischaemic Endpoints After Stent Implantation

2-year results from the PARIS registry - a prospective observational study of patients undergoing PCI with stent implantation (n = 5,018) in 15 clinical sites in the USA and Europe between July 1, 2009, and Dec 2, 2010

Cardiac death



For each relevant HR, the expected number of MACE events was the observed number divided by HR

Mehran et al. Lancet. 2013;382:1714–1722

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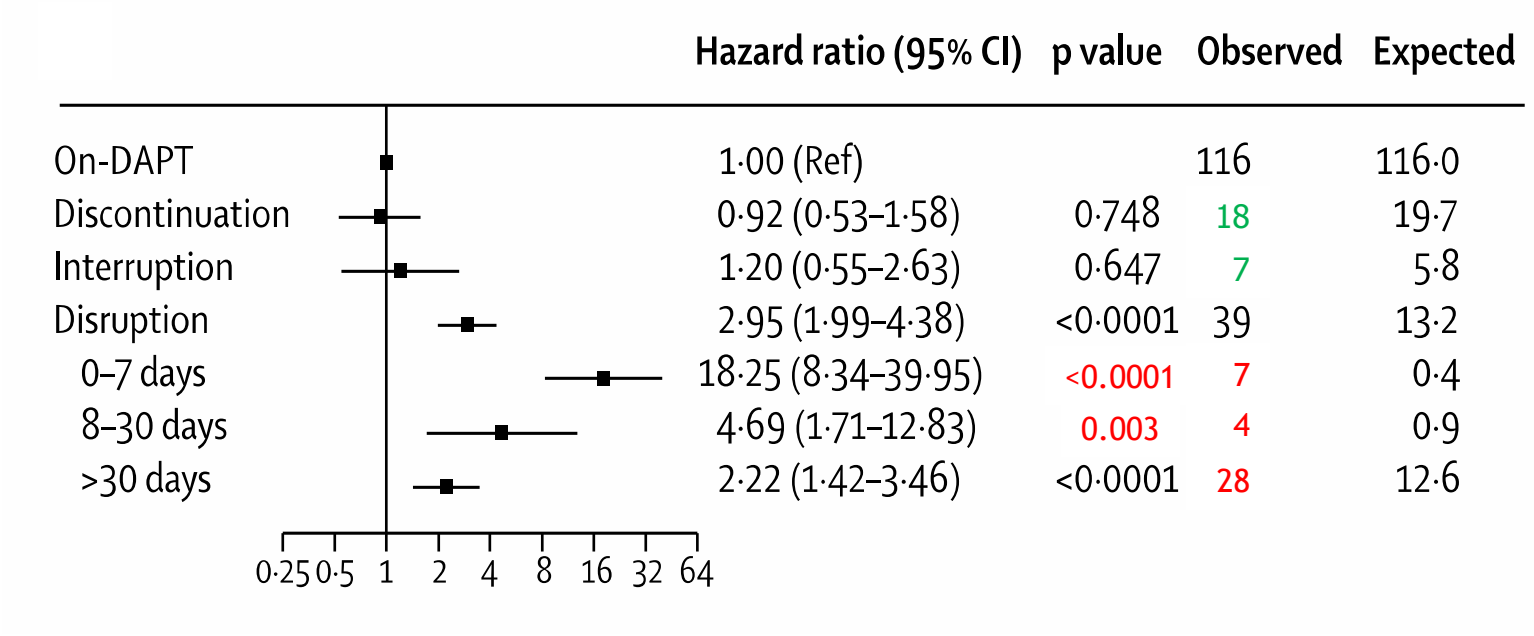
2-year results from the PARIS registry - a prospective observational study of patients undergoing PCI with stent implantation (n = 5,018) in 15 clinical sites in the USA and Europe between July 1, 2009, and Dec 2, 2010

Spontaneous myocardial infarction

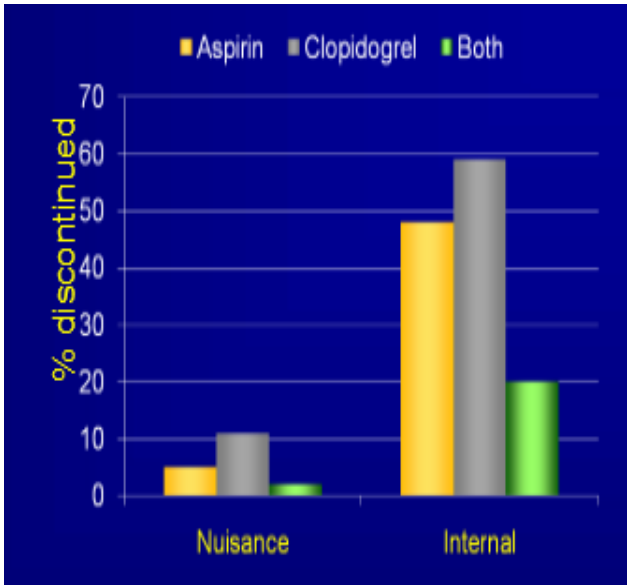


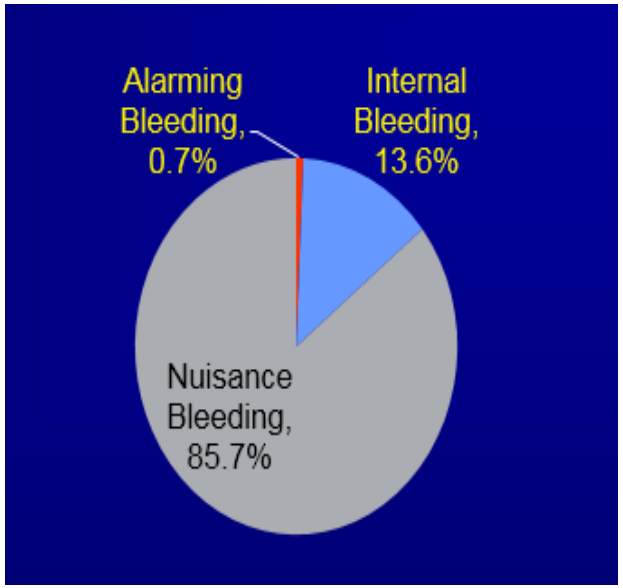
For each relevant HR, the expected number of MACE events was the observed number divided by HR

Mehran et al. Lancet. 2013;382:1714–1722

“Nuisance” Bleeding and Drug Discontinuation

- N=2360 unselected pts. receiving DES
- Prospective data collection
- Major events adjudicated
- Serebruany bleeding classification*





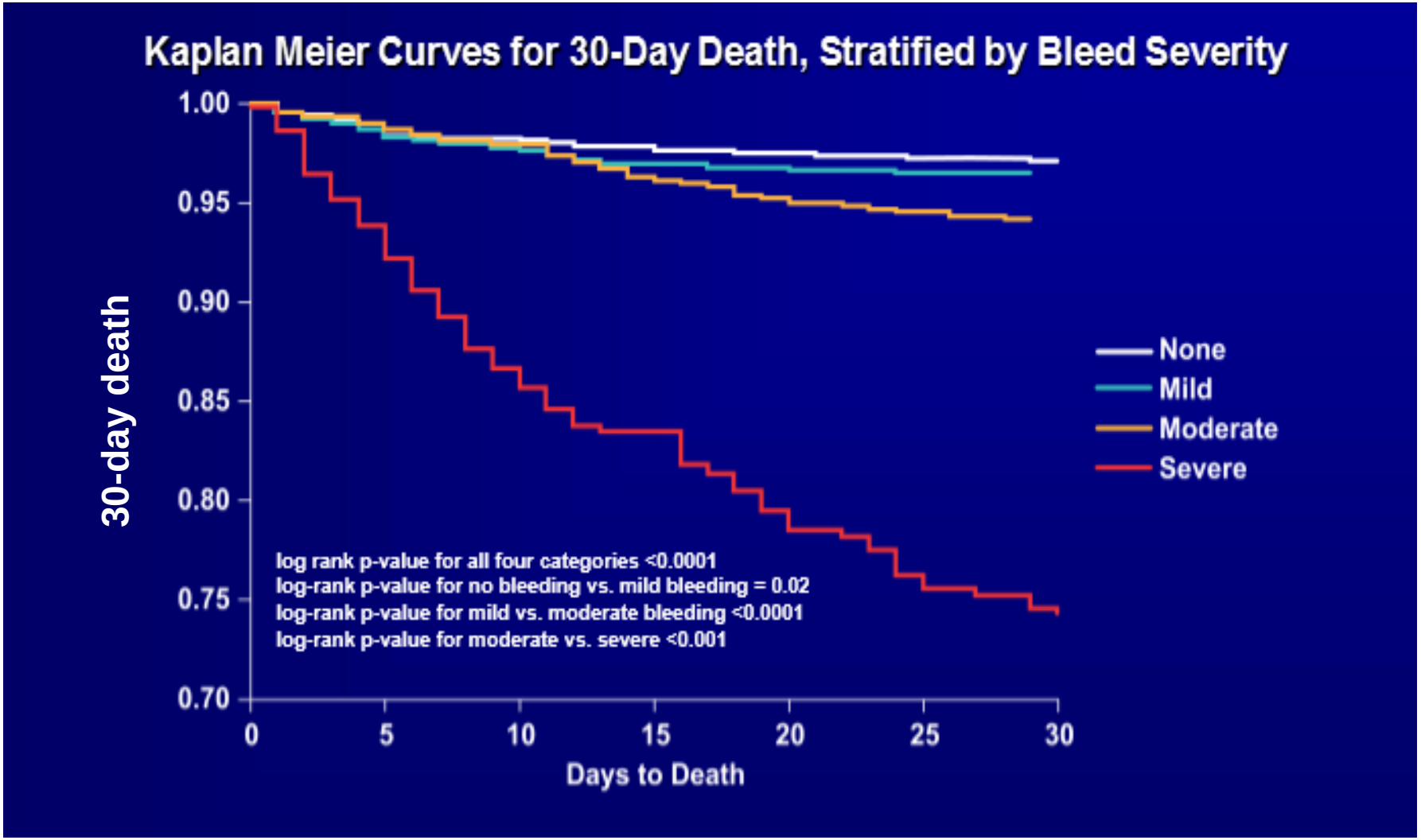
***Alarming bleeding** = ICH, life-threatening, + transfusion
Internal bleeding = hematoma, epistaxis, mouth or vaginal, Melena, IO, hematuria or hematemesis
Nuisance bleeding = bruising, petechiae, ecchymosis

Overall rate of bleeding=32.4%

Roy P, et. al. AJC 2008

Bleeding in ACS & Outcomes

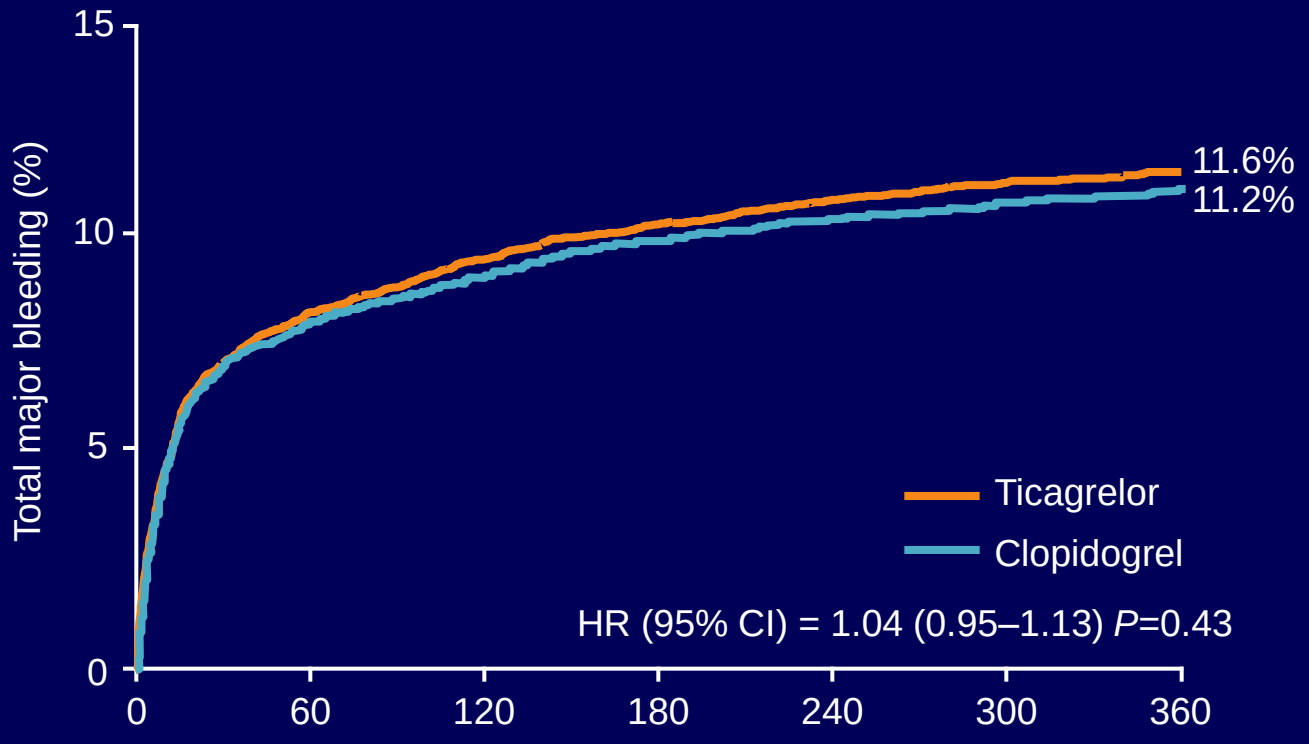
N=26,452 pts from PURSUIT, GUSTO IIb, PARAGON A & B



Rao SV, et al. *Am J Cardiol*. 2005

PLATO main analysis – primary safety endpoint

Total PLATO-defined major bleeding



No. at risk							
Ticagrelor	9235	7246	6826	6545	5129	3783	3433
Clopidogrel	9186	7305	6930	6670	5209	3841	3479

PLATO – causes of death

Death caused by or related to infection or bleeding

	Ticagrelor, n/N (%)	Clopidogrel, n/N (%)	HR* (95% CI)
Infection	51/9235 (0.5)	76/9186 (0.8)	0.67 (0.47–0.95) ***P*=0.03**
Bleeding	42/9333 (0.5)	42/9291 (0.5)	0.99 (0.65–1.53) ***P*=1.00**

- Significantly fewer cases of infection as either the direct or contributing cause of death with ticagrelor versus clopidogrel
- No significant difference in deaths due to bleeding

Varenhorst C et al. Eur Heart J 2013;34(Suppl 1):827 (data presented at ESC, 2013)

Dyspnea by Ticagrelor?

- **Dyspnea in the PLATO trial**

	Ticagrelor	Clopidogrel	*P* Value
Dyspnea adverse events	13.8 %	7.8 %	<0.001
- Discontinued treatment d/t dyspnea	0.9 %	0.1 %	<0.001
- COPD pts	26.1%	16.3%	0.001
- Asians	11.6%	6.7%	0.005
- Women	16.3%	9.0%	<0.001
- Old Age (≥ 75 years old)	18.8%	12.2%	<0001
- Creatinine clearance <60ml/min	16.4%	11.5%	0.008
- STEMI	12.6%	8.4%	<0.001
- Discontinued treatment	0.5%	0.1%	<0.001

Wallentin L, et al. *N Engl J Med*. 2009;361:1045–1057.
Storey R, et al. *J Am Coll Cardio.* 2010;55 (Suppl 1):A108.E1007.
Andell P et al., J Am Heart Assoc. 2015 Oct 9;4(10):e002490
James S et al., Circulation. 2010 Sep 14;122(11):1056-67
Steg PG et al., Circulation. 2010 Nov 23;122(21):2131-41
Kang HJ et al., Am Heart J. 2015 Jun;169(6):899-905
Husted S et al., Eur Heart J. 2014 Jun 14;35(23):1541-50.
Husted S et al., Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):680-8.

Clinical characteristics of dyspnea

Features of ticagrelor-related dyspnea
Sudden and unexpected air hunger or unsatisfied inspiration (usually at rest)
Can vary widely from very brief episodes lasting minutes, generally starting in the first week of ticagrelor treatment, to sustained or intermittent episodes occurring over several weeks – most episodes reported as mild

Features generally NOT associated with ticagrelor-related dyspnea:
Wheezing, orthopnea, paroxysmal nocturnal dyspnea, chest tightness or pain
Related to exertion

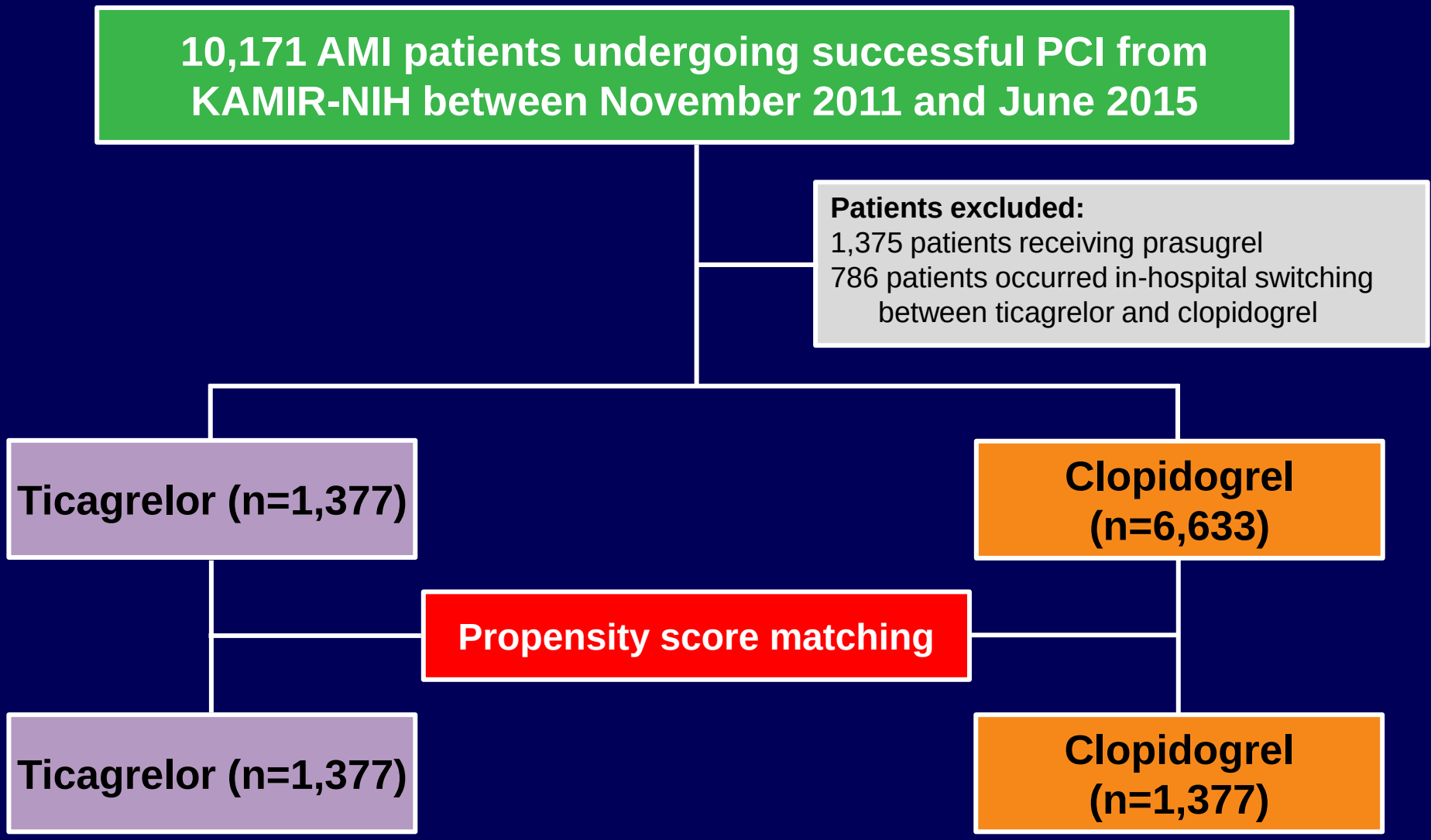
Dyspnea by Ticagrelor?

- Ticagrelor-associated dyspnea was mostly **mild to moderate in severity** and **did not** reduce efficacy
- **Not** associated with new or worsening heart or lung disease
  - not related with wheezing, orthopnea, paroxysmal nocturnal dyspnea, chest tightness, dyspnea on exertion
- Most events were reported as **single episode** occurring early after starting treatment
- **Label precautions and warnings**: use with caution in patients with history of asthma and COPD

Wallentin L, et al. *N Engl J Med*. 2009;361:1045–1057.
Storey R, et al. *J Am Coll Cardio.* 2010;55 (Suppl 1):A108.E1007.

Ticagrelor vs. Clopidogrel in KAMIR-NIH

Study Flow Chart



Baseline Clinical Characteristics (PSM)

	Ticagrelor (n=1,377)	Clopidogrel (n=1,377)	p-value
Age, years	62.30±12.06	62.24±12.53	0.895
Age ≥75 years (%)	259 (18.8)	272 (19.8)	0.530
Body weight, kg	66.35±11.92	65.98±11.59	0.402
Body weight <60 kg (%)	382 (27.7)	385 (28.0)	0.865
Male gender (%)	1,070 (77.7)	1,086 (78.9)	0.460
Hypertension (%)	635 (46.1)	646 (46.9)	0.674
Diabetes (%)	327 (23.7)	314 (22.8)	0.558
Dyslipidemia (%)	155 (11.3)	156 (11.3)	0.952
Current smoker (%)	581 (42.2)	588 (42.7)	0.787
Previous CVA (%)	64 (4.6)	58 (4.2)	0.578
Previous MI (%)	73 (5.3)	63 (4.6)	0.379
Family Hx of CAD (%)	83 (6.0)	82 (6.0)	0.936
Killip class (%)			0.749
I	1,174 (85.3)	1,168 (84.8)	
II to IV	203 (14.7)	209 (15.2)	
Final diagnosis			0.563
Non ST elevation MI	581 (42.2)	596 (43.3)	
ST elevation MI	796 (57.8)	781 (56.7)	
LV ejection fraction, %	52.90±10.23	53.19±10.01	0.454
LV ejection fraction <50% (%)	464 (33.7)	481 (34.9)	0.495
Creatinine clearance, ml/min/1.73m^2	82.75±40.32	82.61±36.85	0.924
Creatinine clearance <60 ml/min/1.73m^2 (%)	368 (26.7)	373 (27.1)	0.830

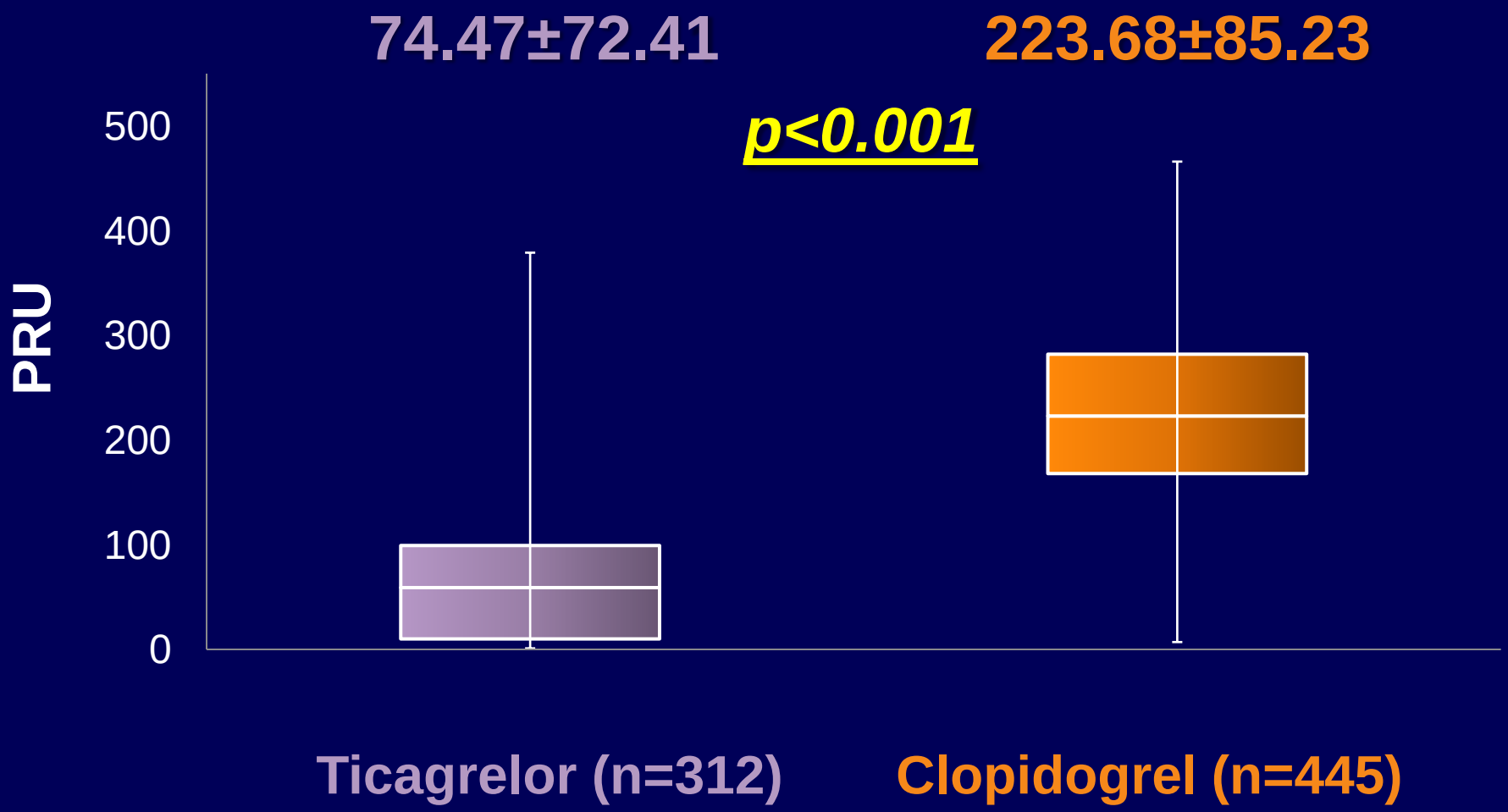
Baseline Procedural Characteristics (PSM)

	Ticagrelor (n=1,377)	Clopidogrel (n=1,377)	p-value
Vascular access (%)			0.789
Transradial approach	638 (46.3)	645 (46.8)	
Transfemoral approach	739 (53.7)	732 (53.2)	
Infarct-related artery (%)			0.724
LAD	631 (45.8)	602 (43.7)	
LCX	255 (18.5)	264 (19.2)	
RCA	465 (33.8)	486 (35.3)	
LM	26 (1.9)	25 (1.8)	
Involved vessel number (%)			0.879
Single vessel	683 (49.6)	687 (49.9)	
LM or MVD	694 (50.4)	690 (50.1)	
ACC/AHA Type B2/C (%)	1,251 (90.8)	1,252 (90.9)	0.947
Treatment at target lesion (%)			0.926
Balloon angioplasty	93 (6.8)	89 (6.5)	
Bare metal stent	30 (2.2)	32 (2.3)	
Drug-eluting stent	1,254 (91.1)	1,256 (91.2)	
Glycoprotein IIb/IIIa inhibitor (%)	242 (17.6)	225 (16.3)	0.388

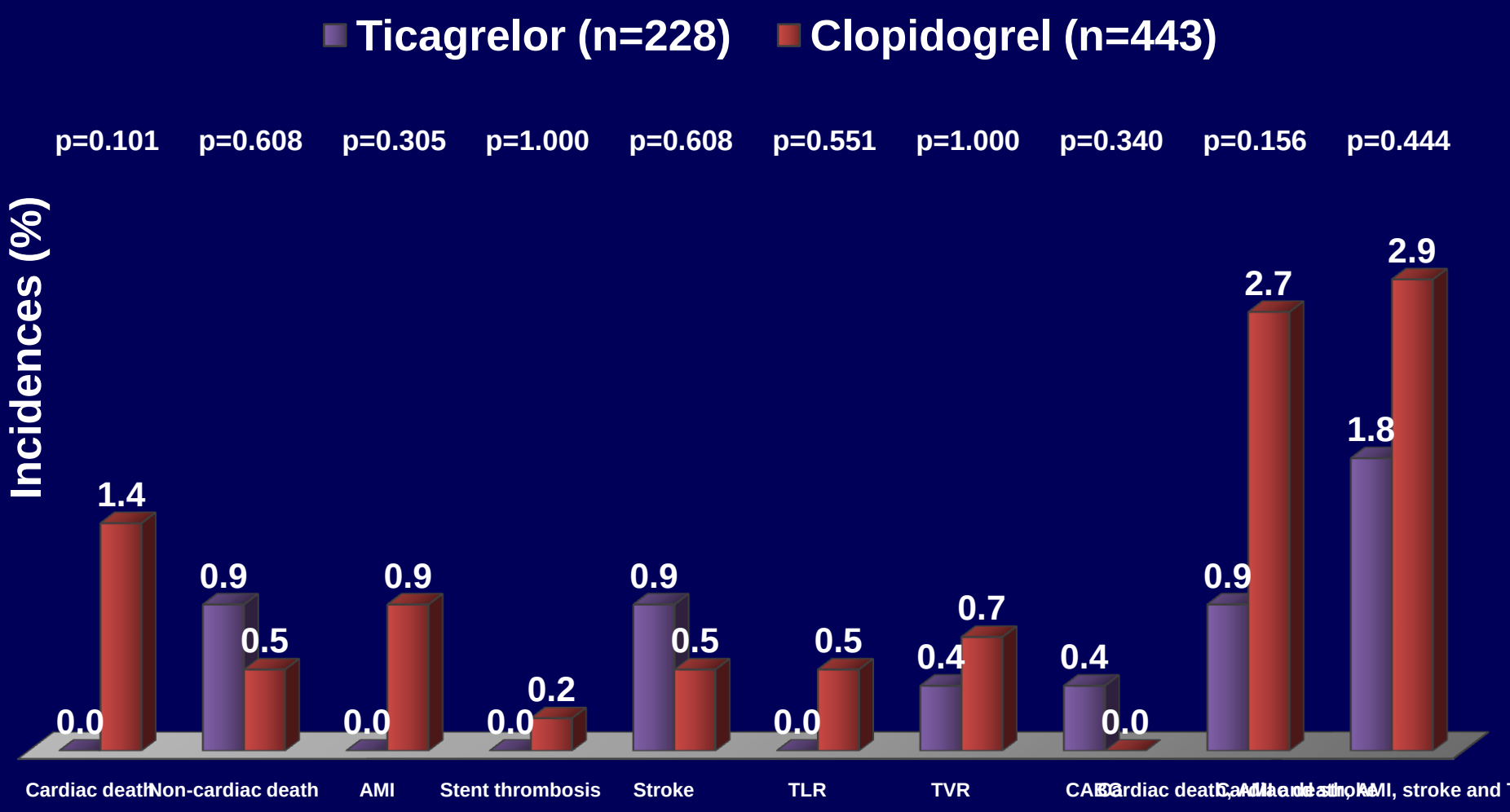
In-hospital Medication (PSM)

	Ticagrelor (n=1,377)	Clopidogrel (n=1,377)	p-value
Aspirin (%)	1,376 (99.9)	1,377 (100)	1.000
Cilostazol (%)	7 (0.5)	226 (16.4)	<0.001
Beta-blocker (%)	1,165 (84.6)	1,150 (83.5)	0.435
Calcium channel blockers (%)	56 (4.1)	65 (4.7)	0.403
ACEi or ARB (%)	1,104 (80.2)	1,112 (80.8)	0.701
Statin (%)	1,317 (95.6)	1,316 (95.6)	0.926

PRU between Ticagrelor vs. Clopidogrel



6-month Clinical Outcomes in Ticagrelor



Summary

- **The highest risk of subsequent CV events occurs in the first year following an MI**
- **Numerous risk factors can contribute to the recurrence of CV events such as multi vessel CAD, diabetes mellitus, CKD and older age**
- **Ticagrelor has been associated with a unique long-term reduction in mortality following ACS across a wide range of moderate-to-high risk subgroups**
- **Ticagrelor did not increase the risk of overall major bleeding (primary safety endpoint) compared with clopidogrel**
- **Ticagrelor-associated dyspnea was mostly mild to moderate in severity and did not reduce efficacy**

ACS, acute coronary syndromes; CV, cardiovascular; MI, myocardial infarction.

Fox KA *et al*. Eur Heart J 2010;31:2755–2764; Norgaard ML *et al*. Diabetologia 2010;53:1612–1619; Kikkert WJ *et al*. Am J Cardiol 2014;113:229–235; Nakatani D *et al*. Circ J 2013;77:439–446; Jernberg T *et al*. Eur Heart J 2014;35(Suppl 1):363 (Abstract P2076).

Thank You For Your Attention