From Guidelines to patient - ACS, AFIB, TVD Case

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Caesarea, November 2, 2010

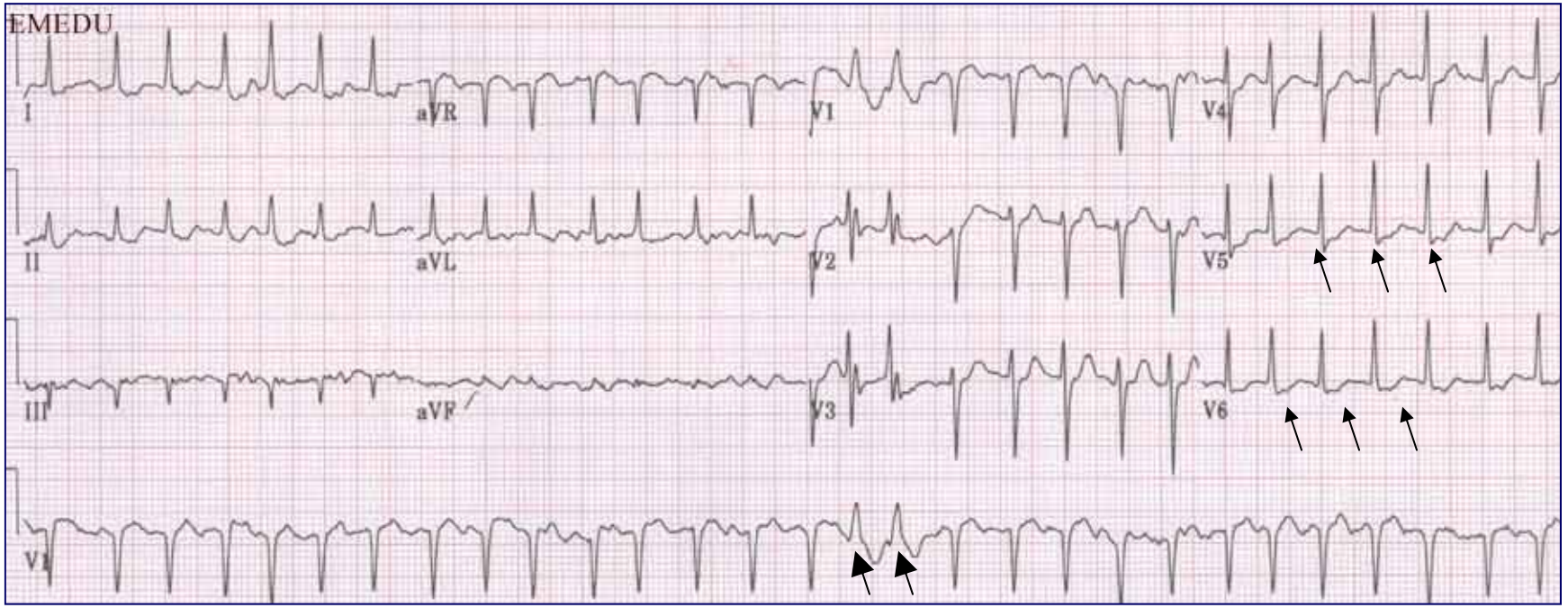
Case Presentation

- A 67 year-old hypertensive patient with a chief complain of undulating squeezing sub-sternal chest pain, which slightly subsided after 20-30 minutes
- Emergency mobile service treated him with aspirin 300 mg, nitroglycerin sublingual and nasal oxygen
- The pain was relieved and he was transferred to ER
- Current medications
  - Aspirin 100 mgX1
  - Atenolol (normiten) 25mgX1
  - Enalapril (enaladex) 20mgx1

Case Presentation

- The patients was initially comfortable but than experienced palpitations and chest pains.
  - Weight 65 kg, BP – 130/75 mmHg, HR: 150-170, irregular, T- 36.6^{o}C. SaO_2-99% (nasal O_2).
  - No JVD, normal lung exam.
  - Rapid, irregular heart rhythm, no gallop or murmurs.
  - Peripheral pulses – normal.
  - No peripheral edema.

ECG



WHAT TO DO at a glance

Recommendations for AF in acute coronary syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
DCC is recommended for patients with severe haemodynamic compromise or intractable ischaemia, or when adequate rate control cannot be achieved with pharmacological agents in patients with ACS and AF.	I	C	
Intravenous administration of amiodarone is recommended to slow a rapid ventricular response to AF in patients with ACS.	I	C	
Intravenous β-blockers are recommended to slow a rapid ventricular response to AF in patients with ACS.	I	C	

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Recommendations for AF in acute coronary syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
Intravenous administration of non-dihydropyridine calcium antagonists (verapamil, diltiazem) should be considered to slow a rapid ventricular response to AF in patients with ACS and no clinical signs of heart failure.	IIa	C	
Intravenous administration of digoxin may be considered to slow a rapid ventricular response in patients with ACS and AF associated with heart failure.	IIb	C	
Administration of flecainide or propafenone is not recommended in patients with AF in the setting of ACS.	III	B	124

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Labs

- Troponin-T on admission – 0.03 (n<0.01ng/dl, cutoff for MI >0.1ng/dl)
- CK – 110 (n<180)
- Glucose 105, Creatinine – 1.4
- K-3.9, Na-139
- HB 12.8, PLT – 285000, WBC – 11200 (N<10000)

Tn @ 24 hrs– 0.12 ng/dL

ECG @ day 2 showed AFIB with 90-110 ventricular response

ECG

What should we know about ECG changes during NSTEMI ACS?

ECG

- Normal ECG is recorded in up to half of all cases (normal ECG does not exclude diagnosis of ACS)
- New ST depression is both sensitive and specific for ACS. It is also a predictor for worse outcome
- New T wave inversion is sensitive but less specific (unless it is wide and deep)
- Isolated T wave inversion is associated with benign course, unless it is involved 5 or more leads
- Both ST depression and T wave inversion are usually transient and resolved when chest pain is over
- Persistent T wave inversion indicate NSTEMI

ECG – Risk Stratification

ST depression > T wave inversion > Normal ECG

ECG

What do we know about AFIB during NSTEMI ACS?

Comparison of Outcomes of Patients With Acute Coronary Syndromes With and Without Atrial Fibrillation

Rajendra H. Mehta, MD, MS, Omar H. Dabbous, MD, MPh, Christopher B. Granger, MD, Polina Kuznetsova, MS, Eva M. Kline-Rogers, MS, Frederick A. Anderson, Jr., PhD, Keith A.A. Fox, MB, CHB, Joel M. Gore, MD, Robert J. Goldberg, PhD, and Kim A. Eagle, MD, for the GRACE Investigators*

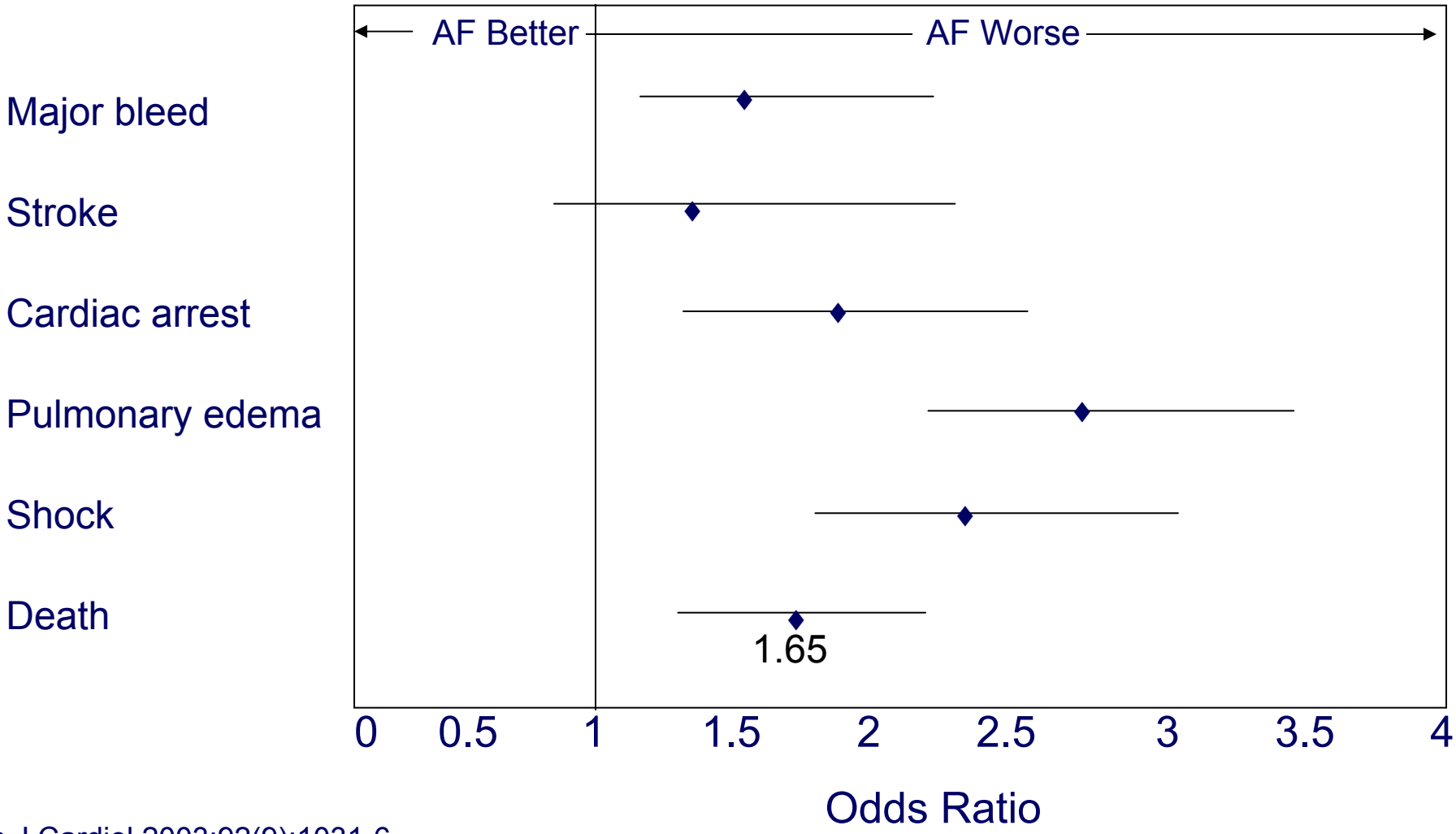
- Patient cohort: n=21,785
- STEMI 33%, NSTEMI 30%, UA 35%
- Previous AFIB: 7.9%
- New onset AFIB: 6.2%

Predictors for New-Onset of AFIB in ACS Patients

Predictors	OR	95% CI
Age (per 10 y)	1.58	1.49-1.67
Female gender	1.24	1.07-1.45
STEMI	2.08	1.74-2.49
NSTEMI	1.85	1.55-2.22
HTN	1.34	1.17-1.53
Admission HR (per 30 b/min)	1.65	1.53-1.79
Lower BP (per 20 mmHg)	1.16	1.12-1,21
Killip > I	1.36	1.17-1.56
Creatinine	1.07	1.01-1.15

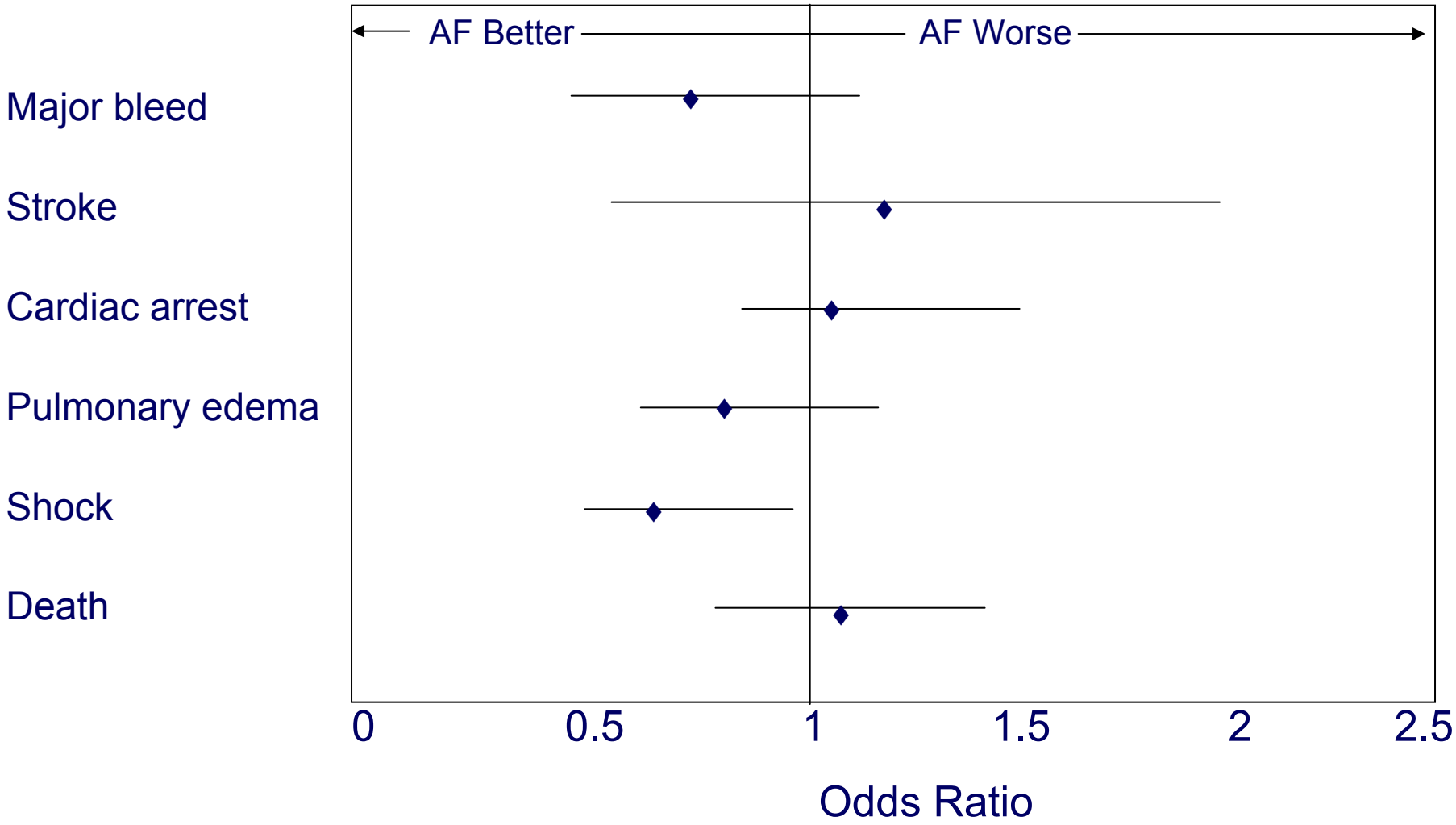
Am J Cardiol 2003;92(9):1031-6

Adjusted ORs for Hospital Events in Patients with ACS and New-Onset Atrial Fibrillation



Am J Cardiol 2003;92(9):1031-6

Adjusted ORs for Hospital Events in Patients with ACS and Previous Atrial Fibrillation



Am J Cardiol 2003;92(9):1031-6

Invasive or Non-invasive Strategy?

From Guidelines to patient - ACS, AFIB, TVD Case

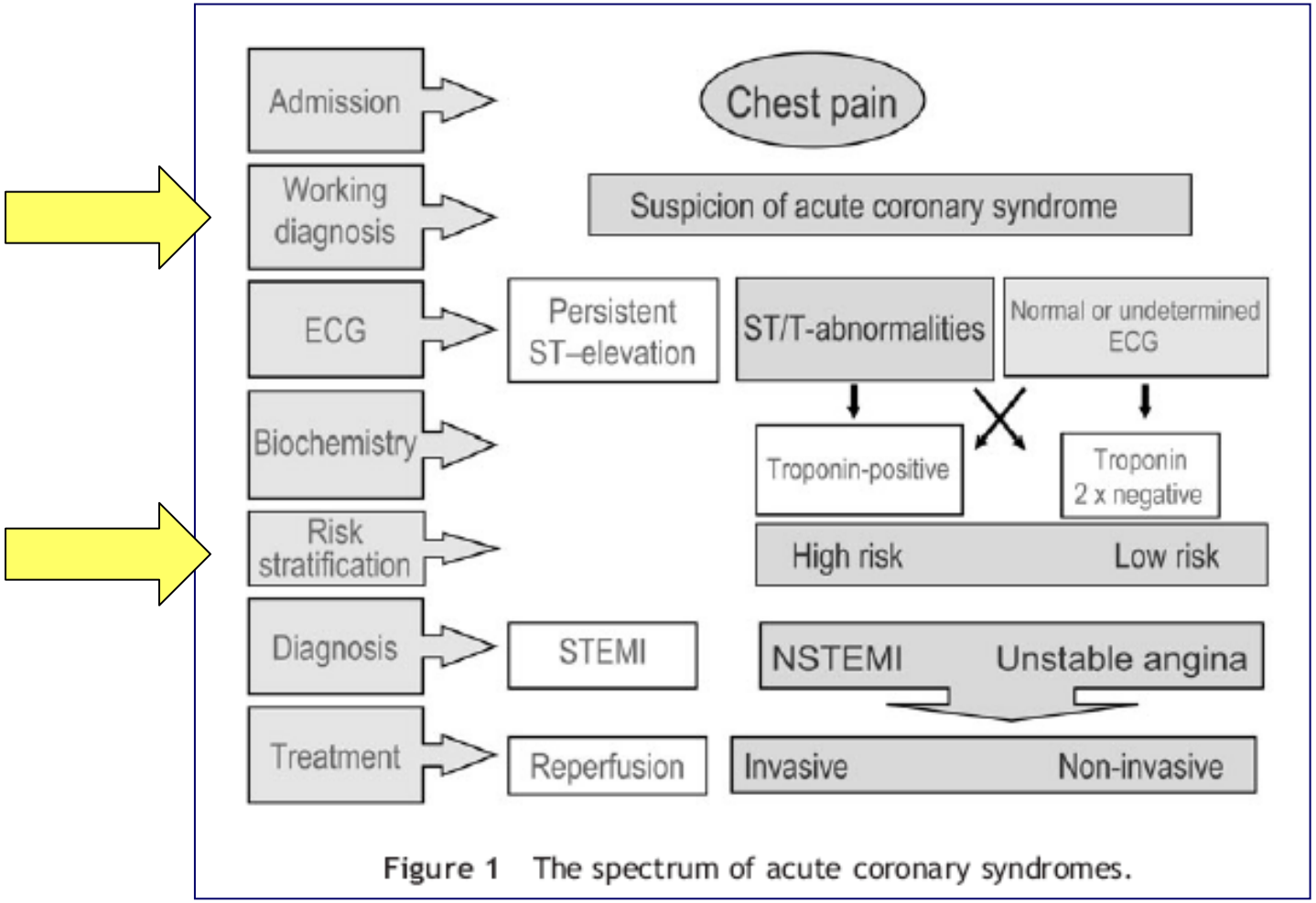
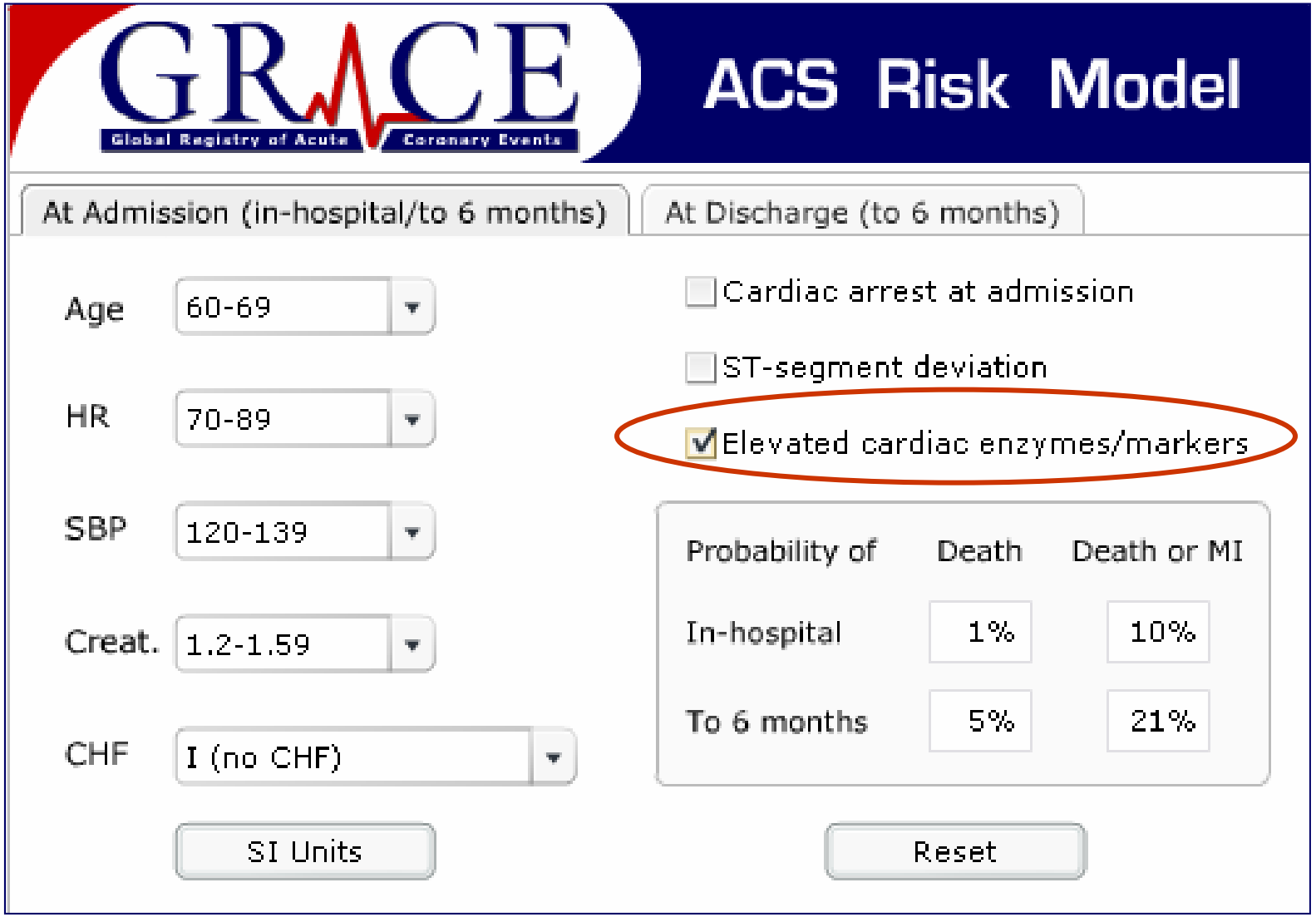


Figure 1 The spectrum of acute coronary syndromes.


GRACE
Global Registry of Acute Coronary Events
ACS Risk Model
At Admission (in-hospital/to 6 months)
At Discharge (to 6 months)
Age
60-69
HR
70-89
SBP
120-139
Creat.
1.2-1.59
CHF
I (no CHF)
SI Units
Cardiac arrest at admission
ST-segment deviation
Elevated cardiac enzymes/markers
Probability of
Death
Death or MI
In-hospital
1%
10%
To 6 months
5%
21%
Reset

Global Registry of Acute Coronary Events risk model nomogram
Granger, C.B. et al. Arch Intern Med 2003; 163:2345-53.

Total points	≤60	70	80	90	100	110	120	130	140	150
Prob of in hospital Death%	≤0.2	0.3	0.4	0.6	0.8	1.1	1.6	2.1	2.9	3.9
Total points	160	170	180	190	200	210	220	230	240	≥250
Prob of in hospital death %	5.4	7.3	9.8	13	18	23	29	36	44	≥52

GRACE Study – In-hospital & Out of Hospital (6 mos) Deaths

Table 5 Mortality in hospital and at 6 months in low-, intermediate-, and high-risk categories in registry populations according to the GRACE risk score[8,117]

Risk category (tertiles)	GRACE risk score	In-hospital deaths (%)
Low	≤108	<1
Intermediate	109–140	1–3
High	>140	>3

Risk category (tertiles)	GRACE risk score	Post-discharge to 6 months deaths (%)
Low	≤88	<3
Intermediate	89–118	3–8
High	>118	>8

For calculations, see http://www.outcomes.org/grace.

Table 12 Recommendations for revascularization in non-ST-segment elevation acute coronary syndrome

Specification	Class[a]	Level[b]	Ref.[c]
An invasive strategy is indicated in patients with: • GRACE score >140 or at least one high-risk criterion. • recurrent symptoms. • inducible ischaemia at stress test.	I	A	64, 68–70
An early invasive strategy (<24 h) is indicated in patients with GRACE score >140 or multiple other high-risk criteria.	I	A	63, 64, 66, 70–72
A late invasive strategy (within 72 h) is indicated in patients with GRACE score <140 or absence of multiple other high-risk criteria but with recurrent symptoms or stress-inducible ischaemia.	I	A	59, 66, 68

ESC Guidelines 2010

Table 12 Recommendations for revascularization in non-ST-segment elevation acute coronary syndrome

Patients at very high ischaemic risk (refractory angina, with associated heart failure, arrhythmias or haemodynamic instability) should be considered for emergent coronary angiography (<2 h).	IIa	C	—
An invasive strategy should not be performed in patients: • at low overall risk. • at a particular high-risk for invasive diagnosis or intervention.	III	A	59, 68

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From Guidelines to patient - ACS, AFIB, TVD Case

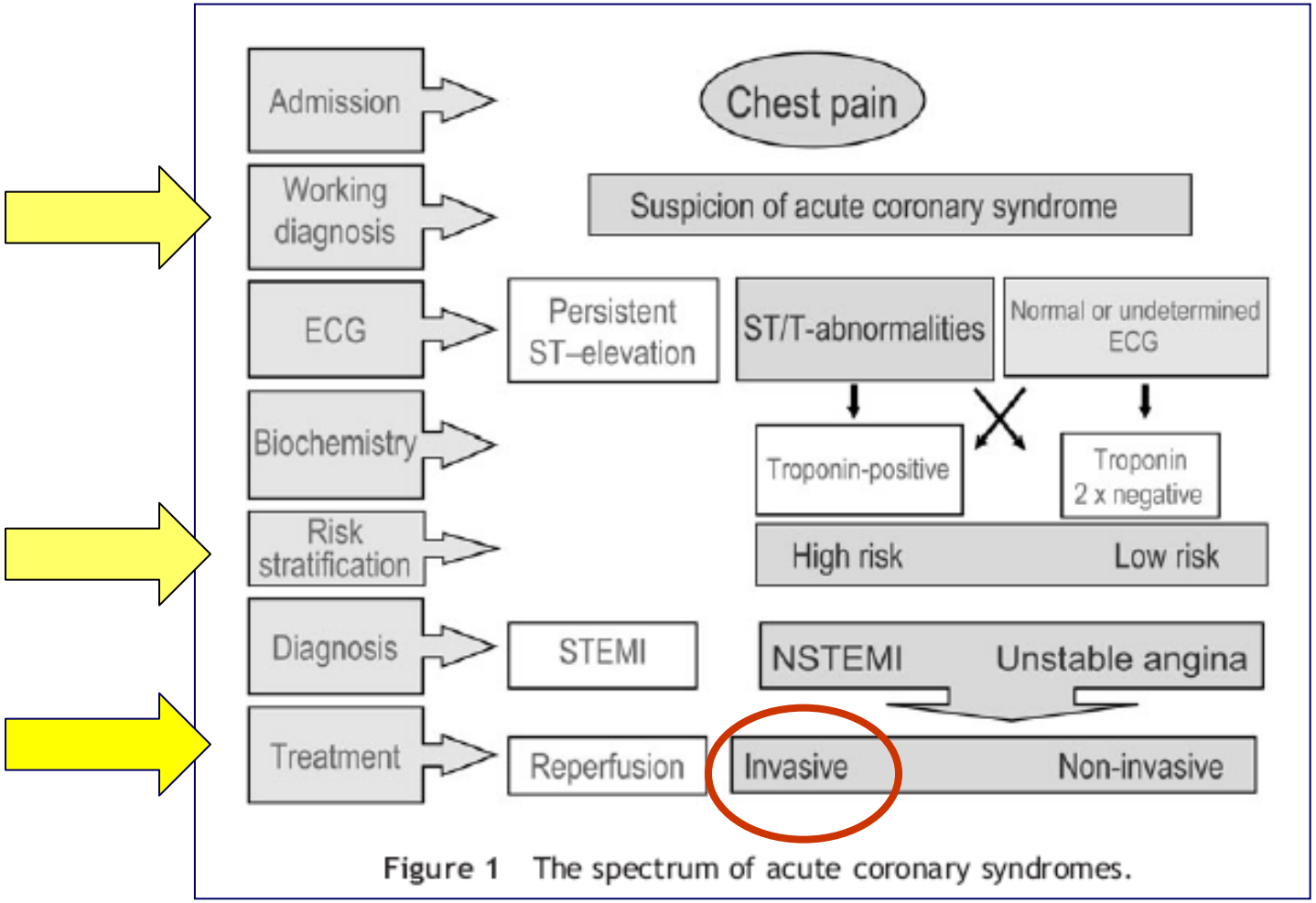

Figure 1 The spectrum of acute coronary syndromes.

What is the appropriate timing for cath?

Table 11 Indicators predicting high thrombotic risk or high-risk for progression to myocardial infarction, which indicate emergent coronary angiography

Ongoing or recurrent ischaemia.
Dynamic spontaneous ST changes (>0.1 mV depression or transient elevation).
Deep ST depression in anterior leads V2–V4 indicating ongoing posterior transmural ischaemia.
Haemodynamic instability.
Major ventricular arrhythmia.

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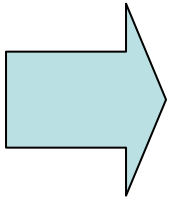
Timing of Catheterization

Validation

- Response to antianginal treatment
- Routine biochemistry, including troponins (on presentation and afte 6–12 h), poss. special markers (e.g. D-dimers, BNP/NT-pro-BNP)
- Repeat or continuous ST-segment monitoring
- Risk score assessment
- Bleeding risk assessment
- Differential diagnosis exclusion: echocardiogram, CT, MRI, nuclear imaging.



Urgent	▪ Persistent or recurrent angina with/without ST-changes (≥2mm) or deep neg. T resistant to anti-anginal treatment ▪ Clinical symptoms of heart failure or progressing haemodynamic instability ▪ Life-threatening arrhythmias (VF, VT)
Early (<72 h)	▪ Elevated troponin levels ▪ Dynamic ST- or T-wave changes (symptomatic or silent) ▪ Diabetes mellitus ▪ Renal dysfunction (GFR < 60 mL/min/1.73 m²) ▪ Reduced left ventricular function (EF < 40%) ▪ Early post-infarction angina ▪ Prior MI ▪ PCI within 6 months ▪ Prior CABG ▪ Intermediate to high GRACE risk score
No/ elective	▪ No recurrence of chest pain ▪ No signs of heart failure ▪ No new ECG changes (arrival and at 6–2 h) ▪ No elevation of troponins (arrival and at 6–12 h)

Decision Making in the Catheterization Laboratory

- Antiplatelets
- Anticoagulation
- PCI vs. CABG
- Culprit and non-culprit lesions
- Single vs. split procedures
- BMS vs. DES

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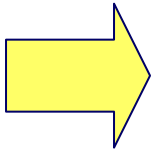


- What to use initially?
- Post procedure management (Dual vs Triple Therapy)
- Renal dose adjustment?

Clopidogrel in ACS Patients

Predictors	RRR PCI	RRR No PCI
CURE clopidogrel 300/75 vs placebo (CVD/MI)	30%[1]	19%[2]
STEMI clopidogrel 300/75 vs placebo (CVD/MI)	46%[3]	9%[4]
TRITON TIMI-38 clopidogrel 300/75 vs prasugrel (CVD/MI/Stroke)	19%[5]	NA

[1]Mehta, Lancet 2001
[2]Fox, Circulation 2004
[3]Sabatine, JAMA 2005
[4]Chen, Lancet 2005
[4]Boersma, Lancet 2005
[5]Wiviott, NEJM 2007

Dose Comparisons of Clopidogrel and Aspirin in Acute Coronary Syndromes

The CURRENT–OASIS 7 Investigators*

- 2x2 factorial, randomized trial studying the optimal doses of clopidogrel and aspirin in ACS patients with intent to perform PCI no later than 72 hours after randomization.
- 25,087 ACS pts (6346 STEMI)
- 17,232 patients underwent PCI,
- High-dose clopidogrel - 600-mg loading dose on day 1, 150 mg X1 for 7 days, followed by 75 mg X1 until 30d.
- Standard clopidogrel arm - 300-mg loading dose on day 1, followed by 75 mg once daily until 30 days.
- All patients were also assigned in an open-label manner to 75-100 or 300 to 325 mg of aspirin

Mehta, NEJM, 9.2010

CURRENT OASIS-7

All Patients

- 30d CV death/MI/Stroke was similar in the high and standard clopidogrel groups: 4.2% vs. 4.4%
- No differences in individual endpoints
- No changes between ASA groups
- Higher rates of bleeding

Bleeding Criteria	Standard n=12579	High N=12508	HR	P
TIMI Major	0.95	1.04	1.09	0.5
CURRENT Major	2.0	2.5	1.25	0.01
CURRENT Severe	1.5	1.9	1.23	0.03

Mehta, NEJM, 9.2010

CURRENT OASIS-7 – PCI Subgroup

Endpoint (30d)	Standard	High	HR	P
CVD/MI/Stroke	4.5	3.9	0.85	0.036
CVD	1.9	1.9	0.68	1.0
MI	2.6	2.0	0.78	0.012
Stroke	0.4	0.4	0.88	0.5
ST – definite/probable	2.3	1.6	0.71	0.002
TIMI Major	0.5	0.5	1.6	0.79
CURRENT Major	1.1	1.6	1.44	0.006
CURRENT Severe	0.8	1.1	1.39	0.034

Mehta, ESC, Spain

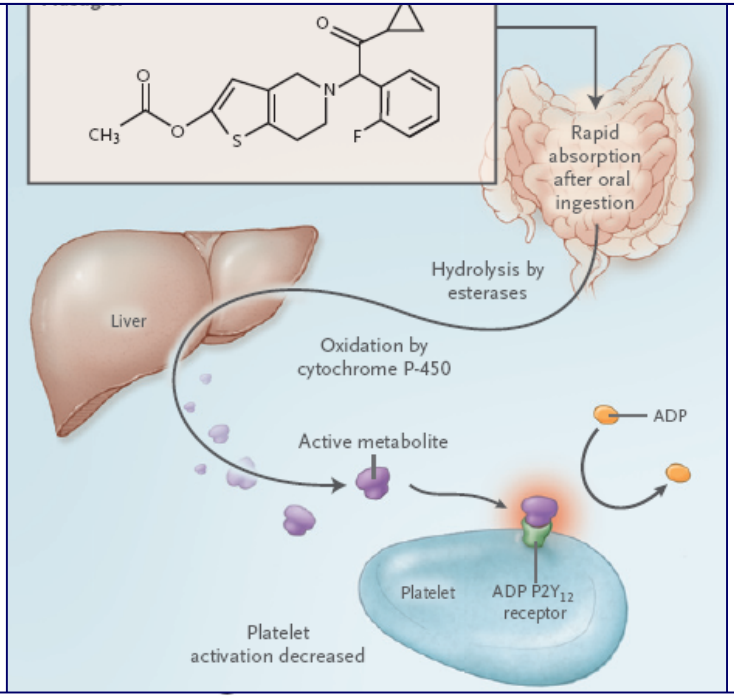
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

- 13608 ACS patients with scheduled PCI
- 10074 (74%) UA, NSTEMI, 3534 (26%) STEMI
- Prasugrel 60/10 mg vs. clopidogrel 300/75 mg

Wiviott, NEJM, 2007

Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes



Prasugrel is a prodrug with rapid and almost complete absorption after oral ingestion of a loading dose. It is metabolized into its active form, which binds irreversibly to the adenosine diphosphate (ADP) $P2Y_{12}$ receptor on platelets for their lifespan, thereby inhibiting their activation and decreasing subsequent platelet aggregation. Hydrolysis by intestinal carboxylesterases and oxidation by intestinal and hepatic cytochrome P-450 enzymes convert prasugrel into its active metabolite. Prasugrel has a greater antiplatelet effect than clopidogrel because it is metabolized more efficiently. Genetic polymorphisms affecting the cytochrome P-450 system may explain some of the differences in metabolism between prasugrel and clopidogrel.

Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

	Prasugrel	Clopidogrel	HR	P
CVD/MI/Stroke	9.9	12.1	0.81	<0.001
CVD	2.1	2.4	0.89	0.31
MI	7.3	9.5	0.76	<0.001
Stroke	1.0	1.0	1.02	0.93
Urgent Revasc	2.5	3.7	0.66	<0.001
ST	1.1	2.4	0.48	<0.001
TIMI Major Bleeding				
Non-CABG	2.4	1.8	1.32	0.03
Non-CABG, fatal	0.4	0.1	4.19	0.002
CABG-related	13.4	3.2	4.73	<0.001

Wiviott, NEJM, 2007

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

Lars Wallentin et al for the PLATO Investigators

N Engl J Med 2009; 361:1045-1057September 10, 2009

Ticagrelor - an oral 1st reversible, direct inhibitor of the P2Y12 receptor

- Multicenter, double-blind, randomized trial
- 18,624 patients admitted to the hospital with an ACS, with or without ST-segment elevation
- Ticagrleor – 180 mg loading dose, 90 mg twice daily thereafter or clopidogrel (300-to-600-mg loading dose), 75 mg daily thereafter

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

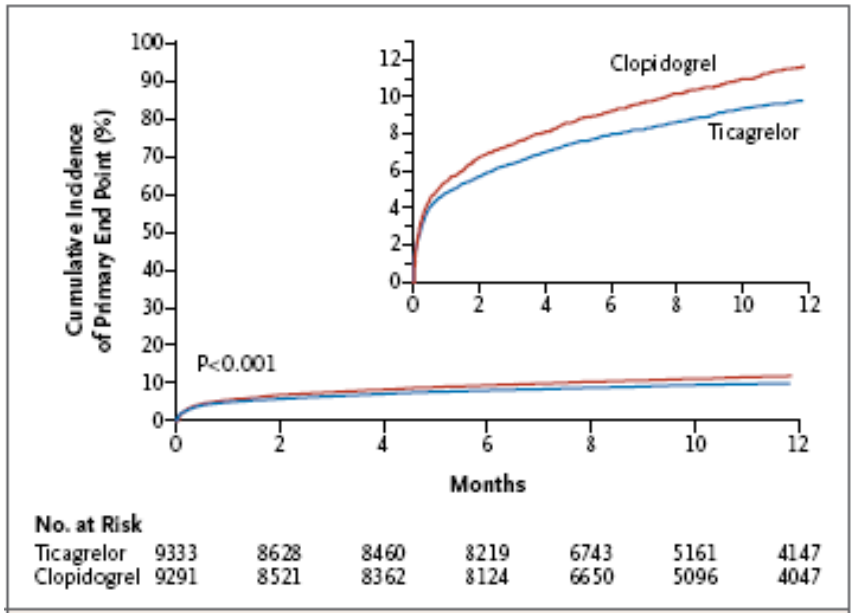


Figure 1. Cumulative Kaplan–Meier Estimates of the Time to the First Adjudicated Occurrence of the Primary Efficacy End Point.

The primary end point — a composite of death from vascular causes, myocardial infarction, or stroke — occurred significantly less often in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12 months; hazard ratio, 0.84; 95% confidence interval, 0.77 to 0.92; P<0.001).

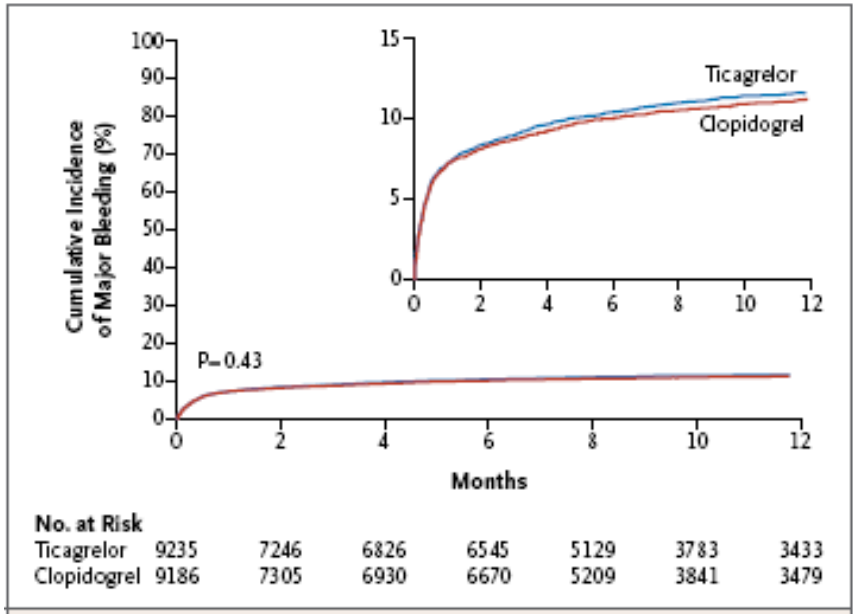


Figure 2. Cumulative Kaplan–Meier Estimates of the Time to the First Major Bleeding End Point, According to the Study Criteria.

The time was estimated from the first dose of the study drug in the safety population. The hazard ratio for major bleeding, defined according to the study criteria, for the ticagrelor group as compared with the clopidogrel group was 1.04 (95% confidence interval, 0.95 to 1.13).

ESC Guidelines for Revascularization in NSTE ACS

Recommendations for Oral Antiplatelet Drugs

ASA	I	C
Clopidogrel (with 600 mg loading dose as soon as possible)	I	C
Clopidogrel (for 9–12 months after PCI)	I	B
Prasugrel[d] 60 mg loading, followed by 10 mg daily	IIa	B
Ticagrelor[d] 180 mg loading, followed by 90 mg bid	I	B
+ GPIIb–IIIa antagonists (in patients with evidence of high intracoronary thrombus burden)		
Abciximab (with DAPT)	I	B
Tirofiban, Eptifibatide	IIa	B
Upstream GPIIb–IIIa antagonists	III	B

ESC Guidelines, Revascularization, 2010

ESC Guidelines for Revascularization in NSTE ACS

Anticoagulation During Catheterization

The patient's creatinine 1.4

CRF

Antiplatelet therapy	
ASA	No specific recommendations.
Clopidogrel	No information in patients with renal dysfunction.
Prasugrel[a]	No dosage adjustment is necessary for patients with renal impairment, including patients with end stage renal disease.
Ticagrelor[a]	No dose reduction required in patients with GFR <60 mL/min/1.73 m^2.
GPIIb–IIIa antagonists	
Abciximab	No specific recommendations for the use or dose adjustment in the case of renal failure.
Tirofiban	Dose adaptation required in patients with renal failure: 50% of the dose with GFR of <30 mL/min/1.73 m^2.
Eptifibatide	Dose adaptation in moderate renal impairment (GFR <60 mL/min/1.73 m^2). Contraindicated in severe renal dysfunction.

Dosage

↔

↓

ESC Guidelines for Revascularization in NSTE ACS

Anticoagulation During Catheterization

- The golden rule is to continue the initial anticoagulant and avoid switching between antithrombins (UFH, enoxaparin, bivalirudin [with the exception of adding UFH (50-100 U/Kg)to fondaparinox]

ESC Guidelines, Revascularization, 2010

ESC Guidelines for Revascularization in NSTE ACS

Recommendations for Anticoagulation

Anticoagulation			
Very high-risk of ischaemia[e]	UFH (+GPIIb–IIIa antagonists) or	I	C
	Bivalirudin (monotherapy)	I	B
Medium-to-high-risk of ischaemia[e]	UFH Initial bolus 60 U/Kg	I	C
	Bivalirudin Initial bolus 0.1mg/Kg, infusion 0.25mg/kg/h	I	B
	Fondaparinux 2.5 mg s.c/ daily	I	B
	Enoxaparin 1mg (0.75 in >75 years , s.c bid	IIa	B
Low-risk of ischaemia[e]	Fondaparinux	I	B
	Enoxaparin	IIa	B

ESC Guidelines, Revascularization, 2010

ESC Guidelines for Revascularization in NSTE ACS

Anticoagulation During Catheterization

CRF

Anticoagulation	
UFH	Dose reduction necessary based on frequent aPTT measurements to control therapeutic range.
Enoxaparin (and other LMWHs)	In case of severe renal failure (GFR <30 mL/min/1.73 m^2) either to be avoided or 50% dose reduction and control of therapeutic levels by factor Xa-activity measurements. In patients with reduced GFR (range 30–60 mL/min/1.73 m^2) dose reduction to 75% of the recommended full dose.
Fondaparinux	Contraindicated in severe renal failure (<30 mL/min/1.73 m^2); drug of choice in patients with reduced renal function (GFR 30–60 mL/min/1.73 m^2) due to lower risk of bleeding complications compared with enoxaparin.
Bivalirudin	Consider reduction of infusion rate to 1.0 mg/kg/h in patients with severe renal dysfunction; consider use in patients with NSTE-ACS and reduced renal function (GFR 30–60 mL/min/1.73 m^2) undergoing angiography ± PCI due to lower bleeding risk compared with UFH + GPIIb–IIIa antagonists.

Dosage

Patient's Status

- The patient is asymptomatic, hemodynamically stable
- ECG – AFIB, ventricular response 80-95 b/min
- Echocardiography revealed mildly reduced LV systolic function with hypokinesis of infero-lateral wall

Current medications

- ASA, clopidogrel, enoxaparin, enalapril, normiten, simvastatin, ompradex

Decision Making in the Catheterization Laboratory

- Antiplatelets
- Anticoagulation
- PCI vs. CABG
- Culprit and non-culprit lesions
- Single vs. split procedures
- BMS vs. DES

ESC Guidelines for Management of NSTE ACS

Recommendations for Revascularization

5.4.4 Coronary artery bypass graft

The proportion of patients with NSTE-ACS undergoing bypass surgery during initial hospitalization is about 10%.[314] It is important to consider the risk of bleeding complications in patients who undergo bypass surgery, although initially treated with aggressive antiplatelet treatment.[330,331]

5.4.5 Respective indications for percutaneous coronary intervention or coronary artery bypass graft

With the exception of an urgent procedure, the choice of revascularization technique in NSTE-ACS is the same as for elective revascularization procedures. From the randomized controlled trials comparing multivessel-stented PCI with bypass surgery, there was no interaction between the presence of NSTE-ACS, treatment strategy, and outcome.[331,332]

Similar recommendations are made by the 2010 ESC revascularization guidelines

ESC Guidelines, 2007

ESC Guidelines for Management of NSTE ACS

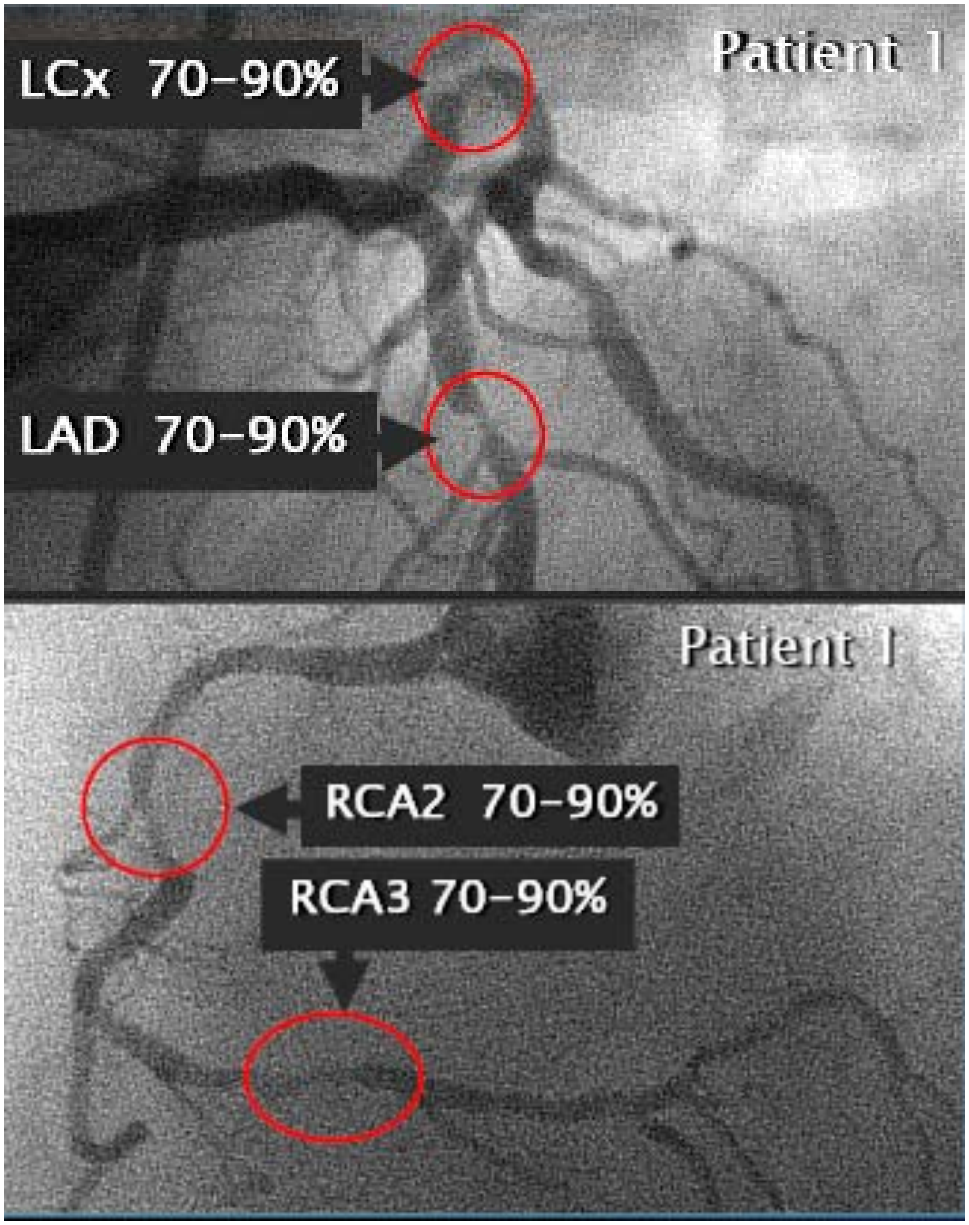
Recommendations for Revascularization

- In stable NSTE ACS patients, the mode of revascularization should be based on the distribution and severity of the CAD
- PCI should, preferably be performed within 72 hrs, while the benefit from CABG is greatest after several days of medical stabilization

Table 3 Recommended risk stratification scores to be used in candidates for percutaneous coronary intervention or coronary artery bypass grafting

Score	Calculation	Number of variables used to calculate risk		Validated outcomes	Class[a]/level[b]		Ref.[c]
		Clinical	Angiographic		PCI	CABG	
EuroSCORE	www.euroscore.org/calc.html	17	0	Short- and long-term mortality	IIb B	I B	2, 3, 6
SYNTAX score	www.syntaxscore.com	0	11 (per lesion)	Quantify coronary artery disease complexity	IIa B	III B	4
Mayo Clinic Risk Score	(7, 8)	7	0	MACE and procedural death	IIb C	III C	—
NCDR CathPCI	(5)	8	0	In-hospital mortality	IIb B	—	5
Parsonnet score	(9)	16	0	30-day mortality	—	III B	9
STS score[d]	http://209.220.160.181/STSWebRiskCalc261/	40	2	Operative mortality, stroke, renal failure, prolonged ventilation, deep sternal infection, re-operation, morbidity, length of stay <6 or >14 days	—	I B	10
ACEF score	[Age/ejection fraction (%)] + 1 (if creatinine >2 mg/dL)(11)	2	0	Mortality in elective CABG	—	IIb C	—

From Guidelines to patient - ACS, AFIB, TVD Case



Patient Profiling

SYNTAX

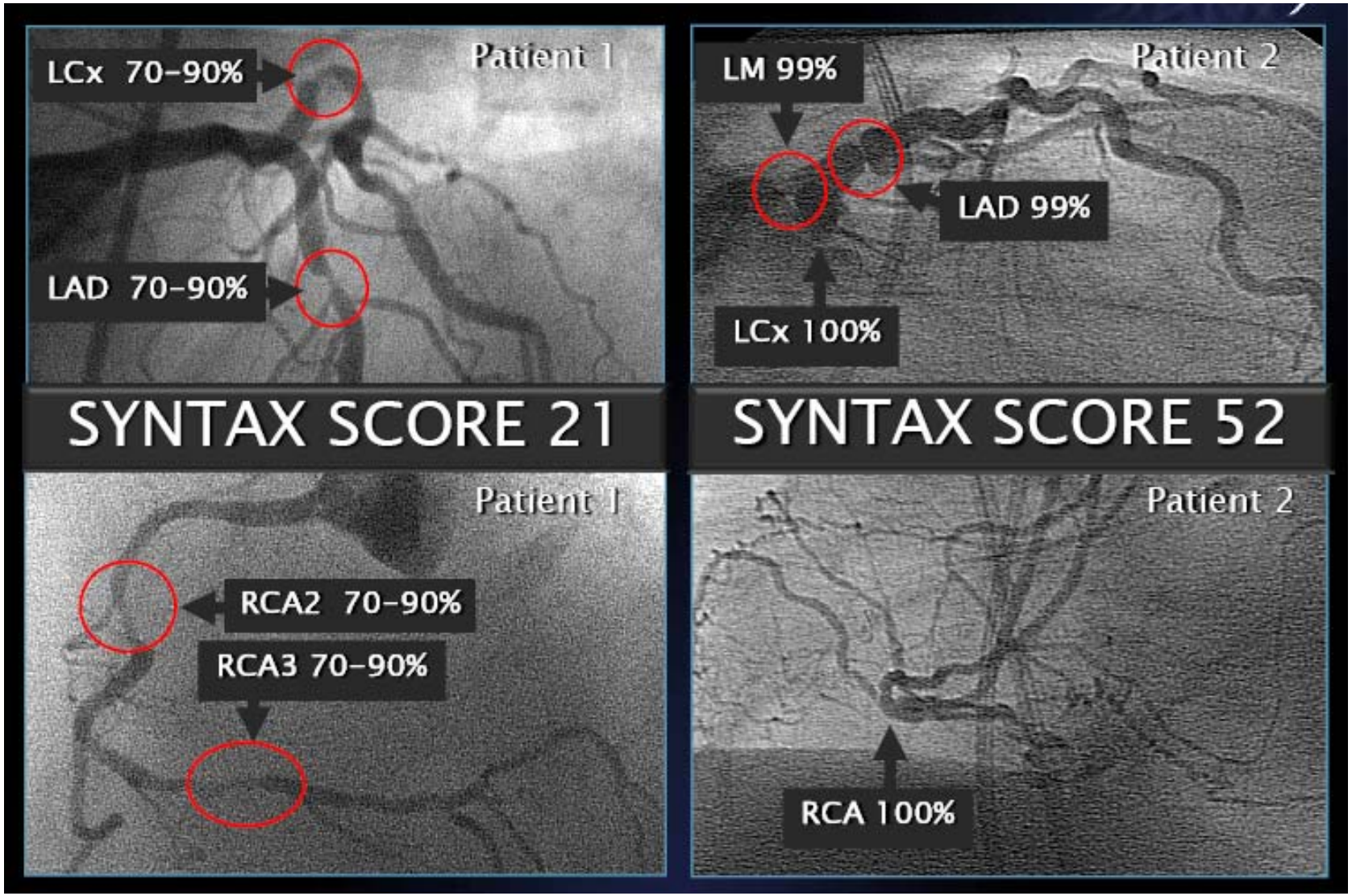
Local Heart team (surgeon & interventional cardiologist) assessed each patient in regards to :

- Patient's operative risk (EuroSCORE & Parsonnet score)
- Coronary lesion complexity (Newly developed SYNTAX score)
- Goal: SYNTAX score to provide guidance on optimal revascularization strategies for patients with high risk lesions

Sianos et al, EuroIntervention 2005;1:219–227
Valgimigli et al, Am J Cardiol 2007;99:1072–1081
Serruys et al, EuroIntervention 2007;3:450–459

BARI classification of coronary segments
Leaman score, Circ 1981;63:285–299
Lesions classification ACC/AHA , Circ 2001;103:3019–3041
Bifurcation classification, CCI 2000;49:274–283
CTO classification, J Am Coll Cardiol 1997;30:649–656

Differences in Angiographic Complexity

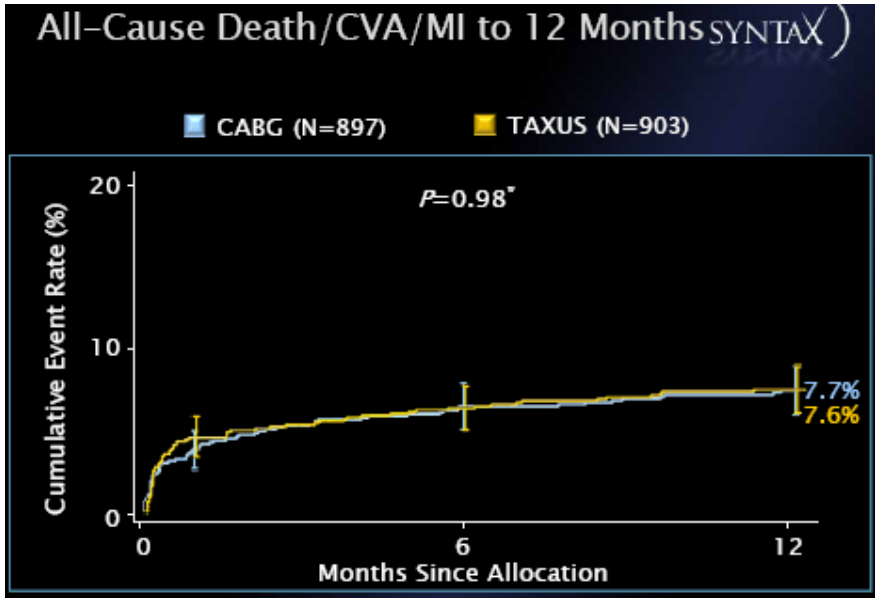


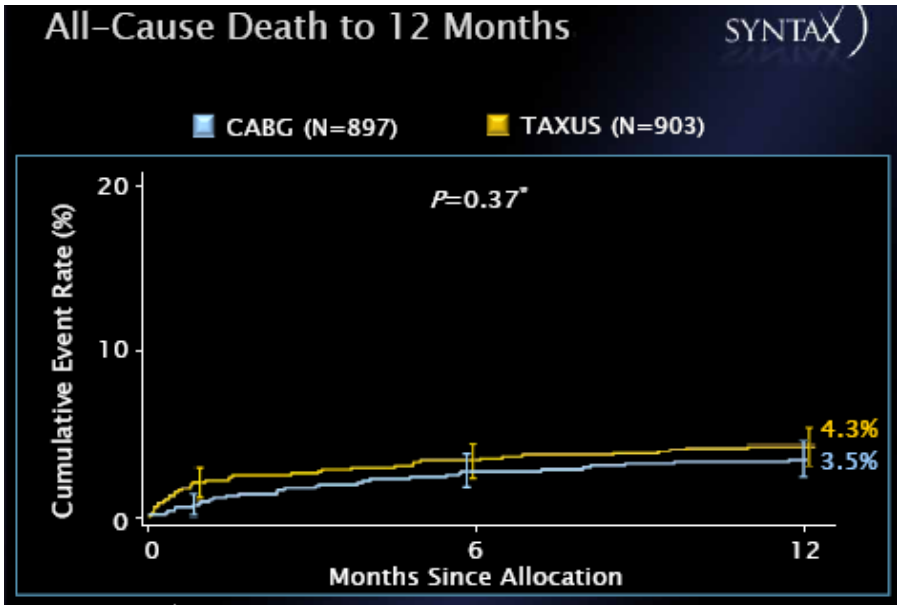
Patient Characteristics (I)
Randomized Cohort

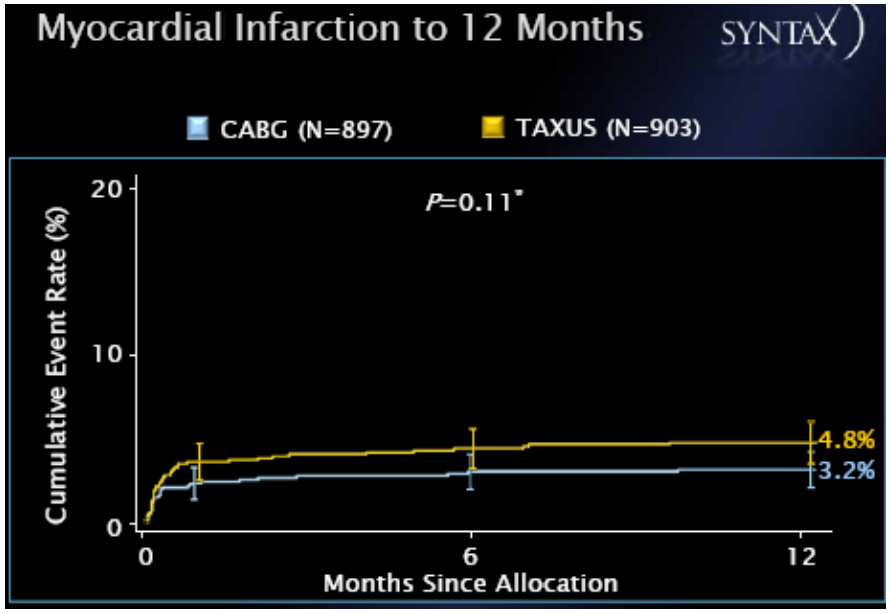
SYNTAX

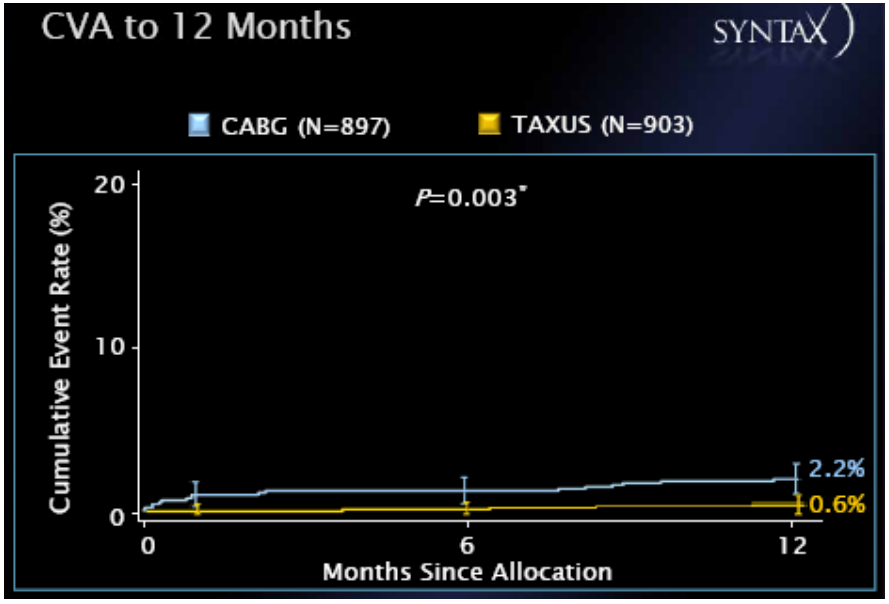
	CABG N=897	TAXUS N=903	*P* value
Age, mean • •SD (y)	65.0 • •9.8	65.2 • •9.7	0.55
Male, %	78.9	76.4	0.20
BMI, mean • •SD	27.9 • •4.5	28.1 • •4.8	0.37
Diabetes, %	28.5	28.2	0.89
Hypertension, %	77.0	74.0	0.14
Hyperlipidemia, %	77.2	78.7	0.44
Current smoker, %	22.0	18.5	0.06
Prior MI, %	33.8	31.9	0.39
Unstable angina, %	28.0	28.9	0.67
Additive EuroSCORE, mean • •SD	3.8 • •2.7	3.8 • •2.6	0.78
Total Parsonnet score , mean • •SD	8.4 • •6.8	8.5 • •7.0	0.76

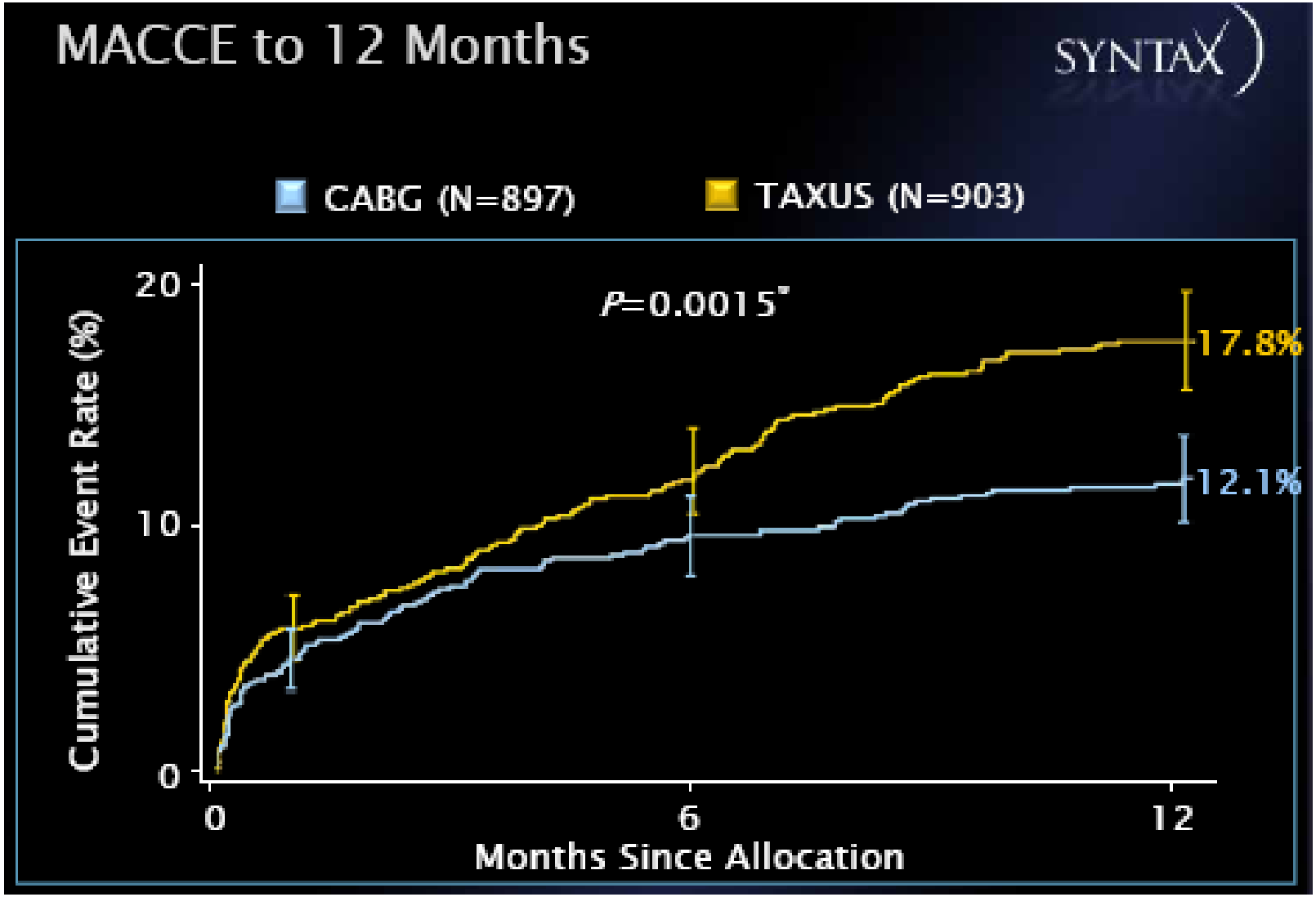
From Guidelines to patient - ACS, AFIB, TVD Case



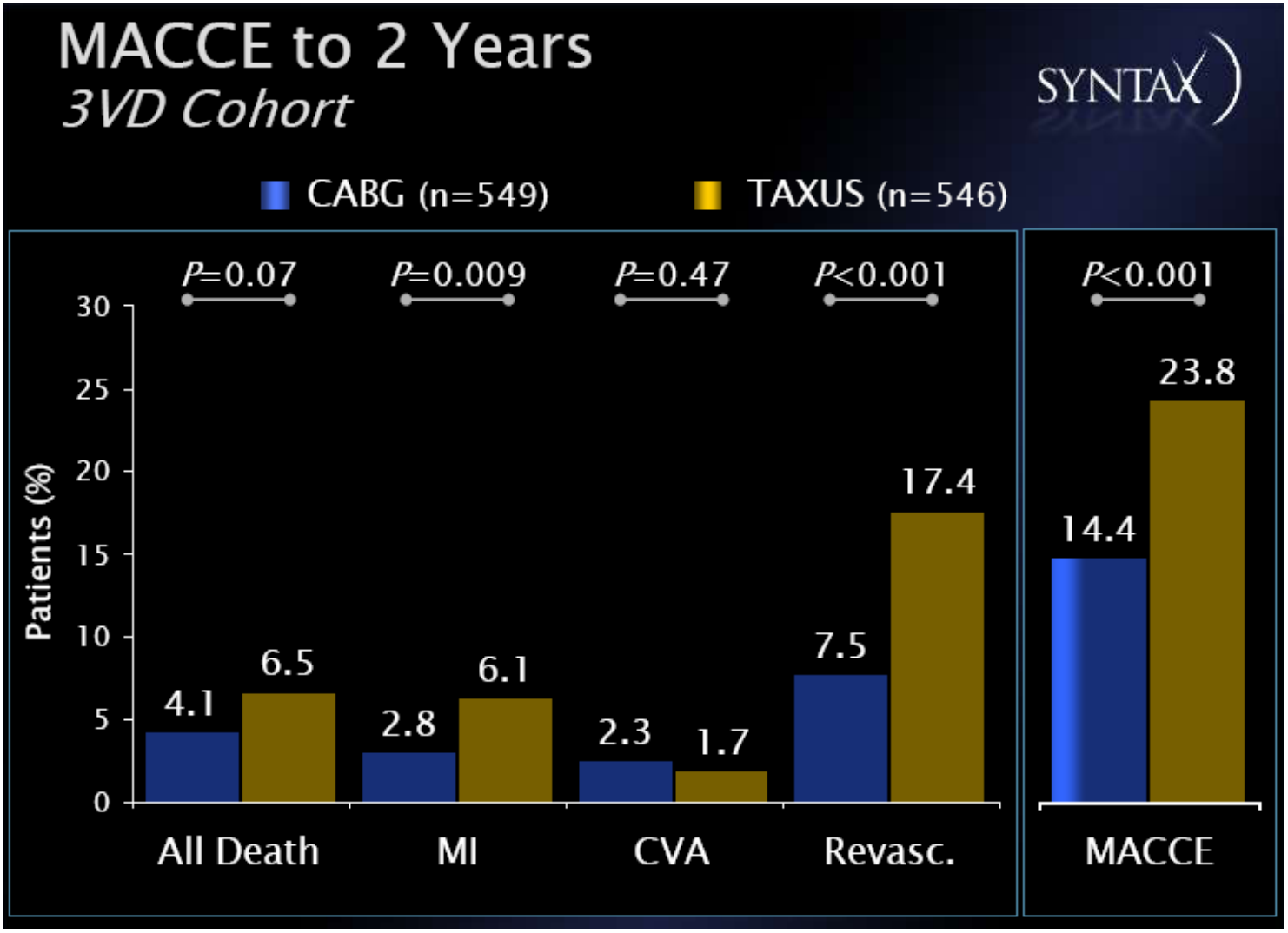







MACCE to 12 Months
SYNTAX
CABG (N=897)
TAXUS (N=903)
P=0.0015*
17.8%
12.1%
Cumulative Event Rate (%)
20
10
0
0
6
12
Months Since Allocation

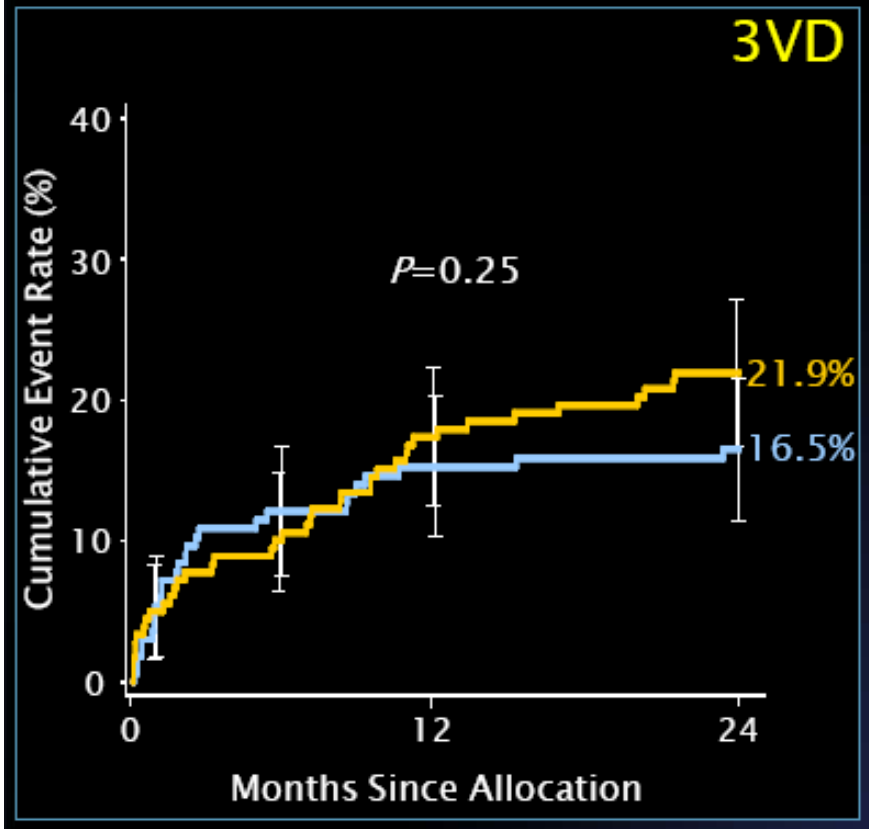
SYNTAX Trial – the Impact of SYNTAX Score



MACCE to 2 Years by SYNTAX Score Tercile *Low Scores (0–22)*

SYNTAX

CABG (N=171)
TAXUS (N=181)

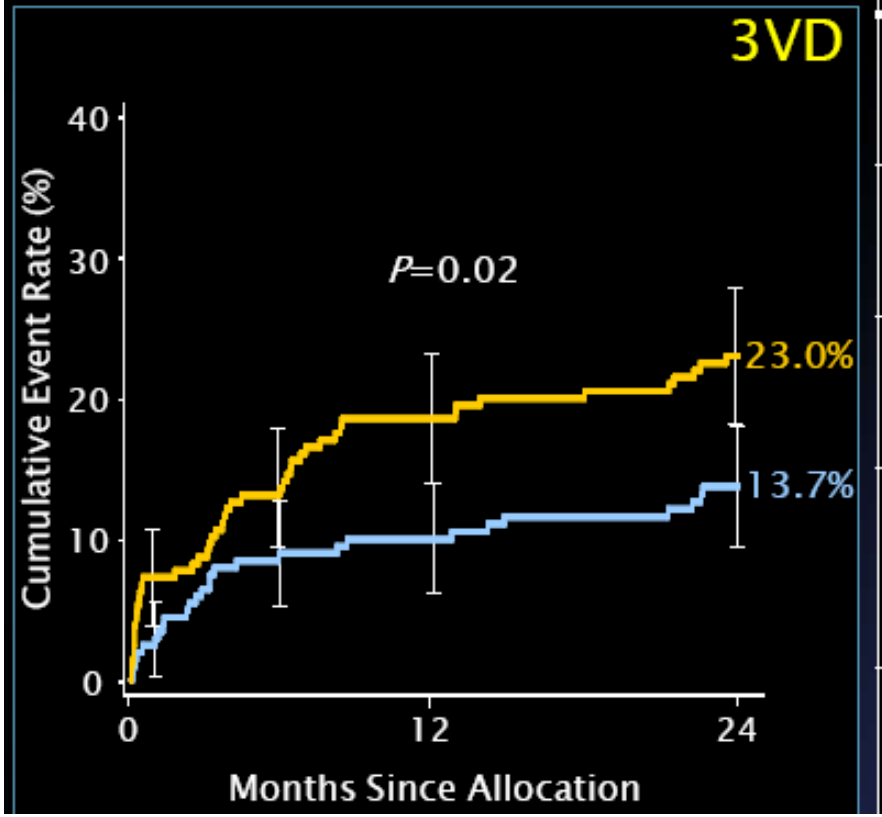


	CABG	PCI	*P* value
Death	5.5%	5.1%	0.85
CVA	1.9%	1.2%	0.57
MI	4.2%	3.9%	0.90
Death, CVA or MI	9.7%	8.4%	0.67
Revasc.	7.6%	17.1%	0.01

MACCE to 2 Years by SYNTAX Score Tercile *Intermediate Scores (23–32)*

SYNTAX

CABG (N=208)
TAXUS (N=207)

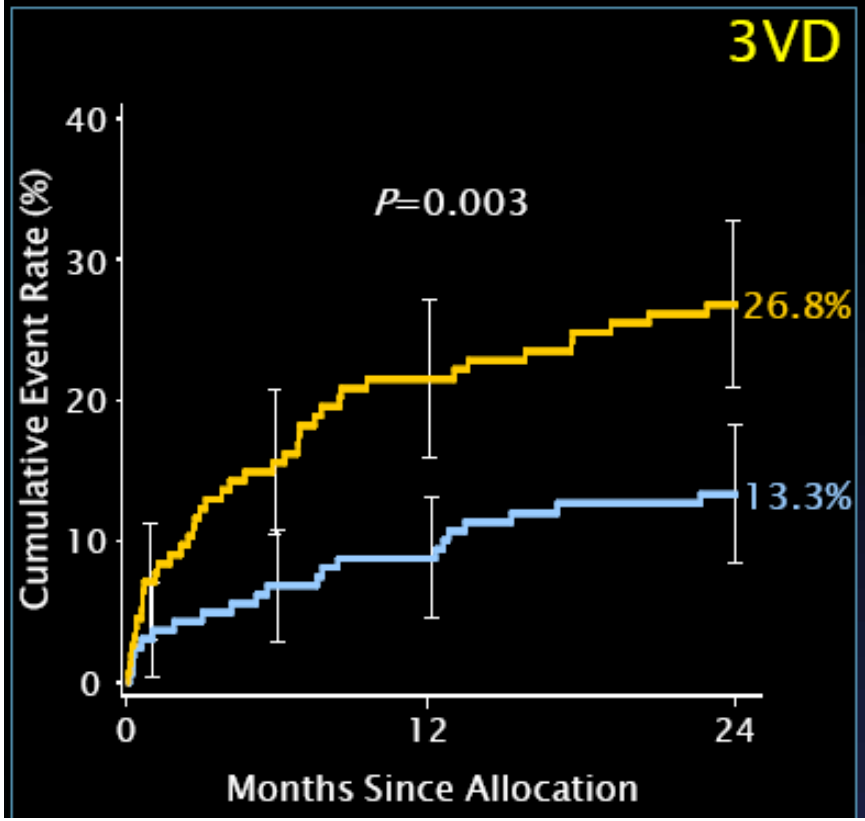


	CABG	PCI	*P* value
Death	4.1%	6.4%	0.30
CVA	3.1%	2.0%	0.50
MI	2.6%	7.4%	0.03
Death, CVA or MI	8.6%	11.7%	0.29
Revasc.	7.3%	16.1%	0.006

MACCE to 2 Years by SYNTAX Score Tercile *High Scores (≥33)*

SYNTAX

CABG (N=166)
TAXUS (N=155)



	CABG	PCI	*P* value
Death	2.5%	8.5%	0.02
CVA	1.9%	2.1%	0.95
MI	1.9%	7.2%	0.02
Death, CVA or MI	6.3%	13.7%	0.03
Revasc.	7.7%	19.3%	0.002

Summary – SYNTAX Trial

- In the randomized SYNTAX cohort, there were comparable overall safety outcomes (Death, CVA, MI,) in CABG and PCI patients at 12 months (7.7 *vs.* 7.6 %).
- Per protocol rates of symptomatic graft occlusion and stent thrombosis were similar.
- There was a significantly higher rate of revascularization in the PCI group (13.7 *vs.* 5.9 %), and a significantly higher rate of CVA in the CABG group (2.2 *vs.* 0.6 %).
- Overall MACCE in the PCI group was higher (17.8 *vs.*12.1 %) due to an excess of redo revascularization compared with CABG.
- The SYNTAX score will help stratify patients for the appropriate revascularization option.

PCI vs CABG

- In stable NSTE ACS patients, the mode of revascularization should be based on the distribution and severity of the CAD
- TVD – significant advantage for CABG when SYNTAX score >22
- LM``- Up to 80% of patients with LM disease also have multivessel disease and up to 80% of LM disease involves the bifurcation
  - There is no differences in mortality and MACCE.
  - Repeat revascularization is significantly higher with PCI (HR ~5.1 at 5 year F/U in the MAIN-COMPARE study)
  - PCI may be consider in isolated (or with 1VD) ostial/prox LM disease

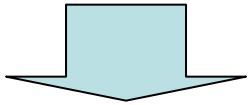
Decision Making in the Catheterization Laboratory

- Antiplatelets
- Anticoagulation
- PCI vs. CABG
- Culprit and non-culprit lesions
- Single vs. split procedures
- BMS vs. DES

ESC Guidelines for Management of NSTE ACS

Recommendations for Revascularization

ment strategy.[28] Multivessel stenting for suitable significant stenoses rather than stenting the culprit lesion only has not been evaluated appropriately in a randomized fashion. The optimal



There are no specific guidelines regarding PCI-based revascularization of non-culprit lesions

Decision Making in the Catheterization Laboratory

- Antiplatelets
- Anticoagulation
- PCI vs. CABG
- Culprit and non-culprit lesions
- Single vs. split procedures
- BMS vs. DES

Indications for drug-eluting stent

DES with proven efficacy should be considered by default in nearly all clinical conditions and lesion subsets, except if there are concerns or contraindications for prolonged DAPT

Table 35 Relative clinical contraindications to the use of drug-eluting stents

• Clinical history difficult to obtain, especially in the setting of acute severe clinical conditions (STEMI or cardiogenic shock).
• Expected poor compliance with DAPT, including patients with multiple comorbidities and polypharmacy.
• Non-elective surgery required in the short term that would require interruption of DAPT.
• Increased risk of bleeding.
• Known allergy to ASA or clopidogrel/prasugrel/ticagrelor.
• Absolute indication for long-term anticoagulation.

ASA = acetylsalicylic acid; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; STEMI = ST-segment elevation myocardial infarction.

What is the risk of bleeding in patients on DAT + oral anticoagulation?

From Guidelines to patient - ACS, AFIB, TVD Case

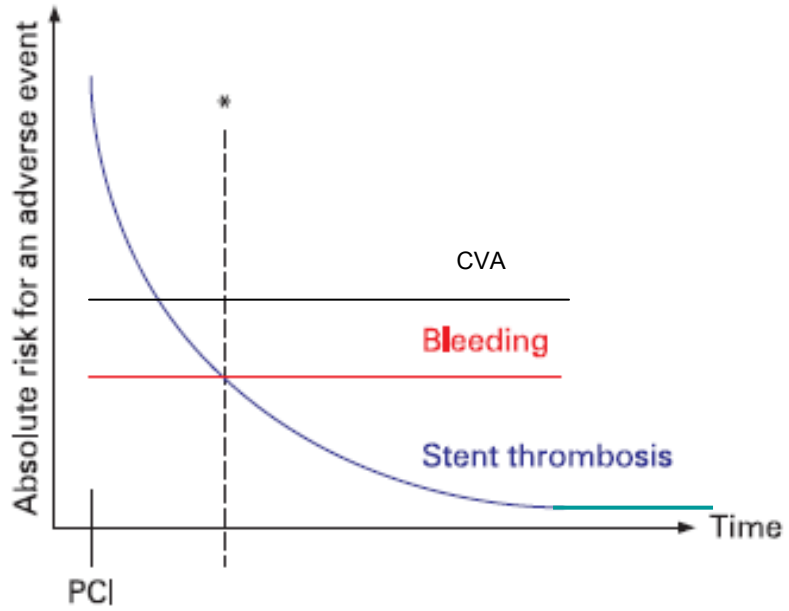


Figure 1 The bleeding risk of patients on triple therapy is grossly time independent, while the risk for stent thrombosis diminishes clearly over time. The asterisk marks a theoretical time point, at which the absolute bleeding risk exceeds the risk of stent thrombosis. At this time point, triple therapy could be reduced to oral anticoagulation (OAC) + single agent antiplatelet therapy in patients with an indication for lifelong OAC. PCI, percutaneous coronary intervention.

- Overall warfarin reduced stroke rate by 60%
- Antiplateletes reduced stroke rate by 20%

Recommendations for antithrombotic therapy in AF and ACS/PCI

Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

SBP >160 mmHg

e.g. Antiplatelets

Scoe ≥ 3 indicates 'high risk'

ESC Guidelines, AFIB, 2010

From Guidelines to patient - ACS, AFIB, TVD Case

CHA_2DS_2-VASc score	Patients (n = 7329)	Adjusted stroke rate (%/year)[b]
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc
(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

Recommendations for antithrombotic therapy in AF and ACS/PCI

between VKA-treated and non-treated patients. The prevalence of major bleeding with triple therapy (VKA, aspirin, and clopidogrel) is 2.6–4.6% at 30 days, which increases to 7.4–10.3% at 12 months. Thus triple therapy seems to have an acceptable risk–benefit ratio provided it is kept short (e.g. 4 weeks) and the bleeding risk is low.

A systematic review and consensus document published by the ESC Working Group on Thrombosis, endorsed by the EHRA and the European Association of Percutaneous Cardiovascular Interventions (EAPCI), suggests that drug-eluting stents should be avoided and triple therapy (VKA, aspirin, and clopidogrel) used in the short term, followed by longer therapy with VKA plus a single antiplatelet drug (either clopidogrel or aspirin) (*Table*

ESC Guidelines, AFIB, 2010

Recommendations for antithrombotic therapy in AF and ACS/PCI

Recommendations	Class[a]	Level[b]
Following elective PCI in patients with AF with stable coronary artery disease, BMS should be considered, and drug-eluting stents avoided or strictly limited to those clinical and/or anatomical situations (e.g. long lesions, small vessels, diabetes, etc.), where a significant benefit is expected when compared with BMS.	IIa	C
Following elective PCI, triple therapy (VKA, aspirin, clopidogrel) should be considered in the short term, followed by more long-term therapy (up to 1 year) with VKA plus clopidogrel 75 mg daily (or, alternatively, aspirin 75–100 mg daily, plus gastric protection with PPIs, H_2 antagonists, or antacids).	IIa	C
Following elective PCI, clopidogrel should be considered in combination with VKA plus aspirin for a minimum of 1 month after implantation of a BMS, but longer with a drug-eluting stent (at least 3 months for a sirolimus-eluting stent and at PPIs, H_2 antagonists, or antacids).		
In anticoagulated patients at very high risk of thrombo-embolism, uninterrupted therapy with VKA as the preferred strategy and radial access used as the first choice even during therapeutic anticoagulation (INR 2–3).	IIa	C
When VKA is given in combination with clopidogrel or low-dose aspirin, careful regulation of the anticoagulation dose intensity may be considered, with an INR range of 2.0–2.5.	IIb	C
Following revascularization surgery in patients with AF, VKA plus a single antiplatelet drug may be considered in the initial 12 months, but this strategy has not been evaluated thoroughly and is associated with an increased risk of bleeding.	IIb	C
In patients with stable vascular disease (e.g. >1 year, with no acute events), VKA monotherapy may be considered, and concomitant antiplatelet therapy should not be prescribed in the absence of a subsequent cardiovascular event.	IIb	C

Following an ACS with or without PCI in patients with AF, triple therapy (VKA, aspirin, clopidogrel) should be considered in the short term (3–6 months), or longer in selected patients at low bleeding risk, followed by long-term therapy with VKA plus clopidogrel 75 mg daily (or, alternatively, aspirin 75–100 mg daily, plus gastric protection with PPIs, H_2 antagonists, or antacids).

ESC Guidelines, AFIB, 2010

Table 11 Antithrombotic strategies following coronary artery stenting in patients with AF at moderate to high thrombo-embolic risk (in whom oral anticoagulation therapy is required)

Haemorrhagic risk	Clinical setting	Stent implanted	Anticoagulation regimen
Low or intermediate (e.g. HAS-BLED score 0–2)	Elective	Bare-metal	1 month: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Lifelong: VKA (INR 2.0–3.0) alone
	Elective	Drug-eluting	3 (-olimus[a] group) to 6 (paclitaxel) months: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone
	ACS	Bare-metal/ drug-eluting	6 months: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone
High (e.g. HAS-BLED score ≥3)	Elective	Bare-metal[c]	2–4 weeks: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Lifelong: VKA (INR 2.0–3.0) alone
	ACS	Bare-metal[c]	4 weeks: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone

From Guidelines to patient - ACS, AFIB, TVD Case

Thank You

& Good Luck