

Incontri al Fatebenefratelli

AGGIORNAMENTI IN MEDICINA INTERNA

BENEVENTO 12-13 GIUGNO 2013

Sindromi coronariche acute
nel paziente anziano con comorbidità.

Quale setting assistenziale :
UTIC, terapia intensiva medica o “corsia”?

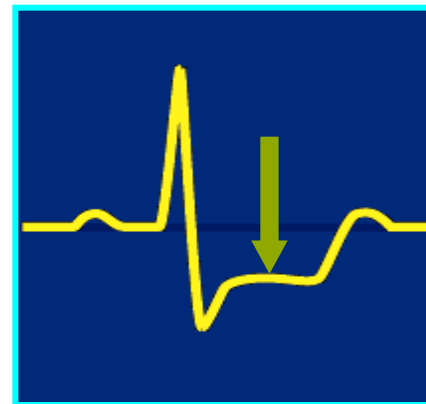
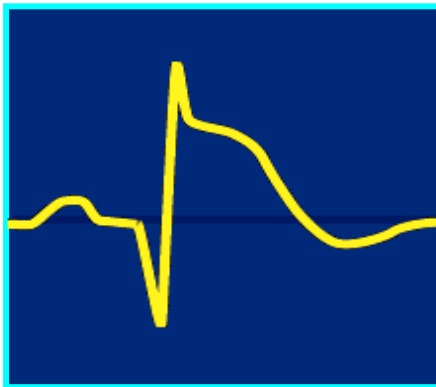
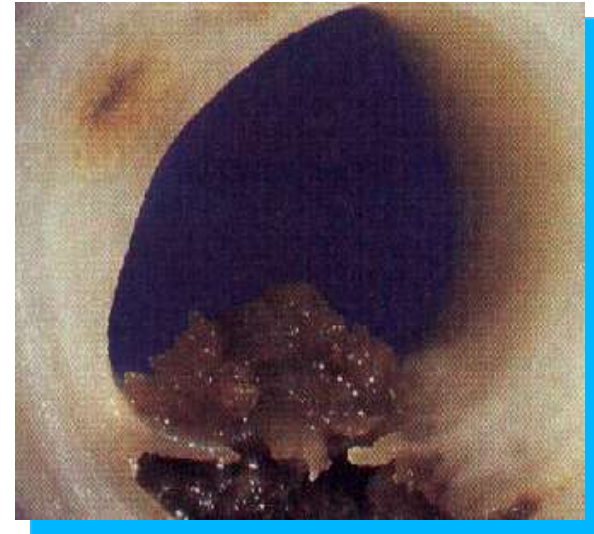
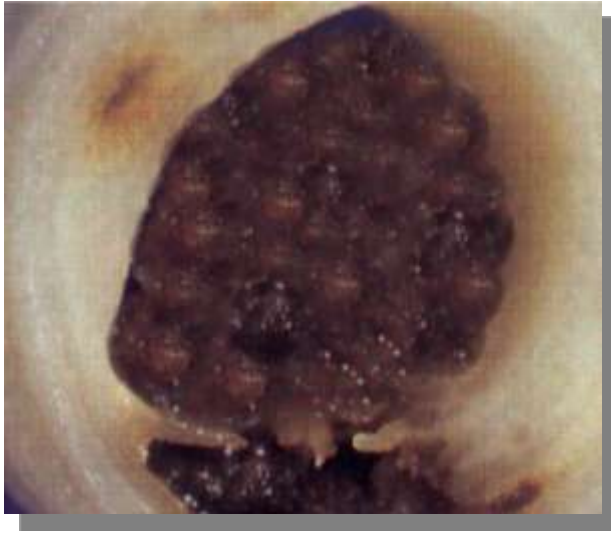
Domenico Panuccio
Ospedale Maggiore, Bologna

Nessun conflitto di interessi

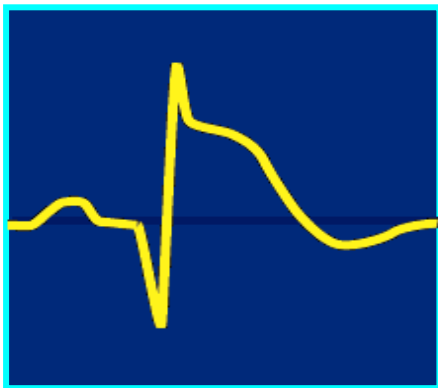


ACS with persistent ST-segment elevation

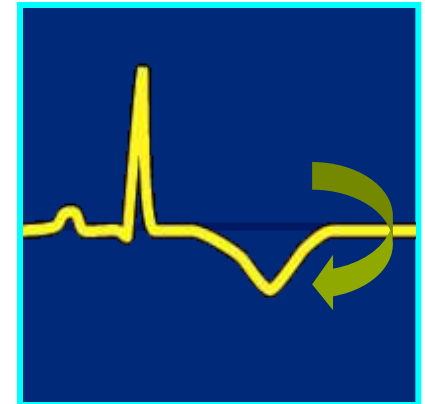
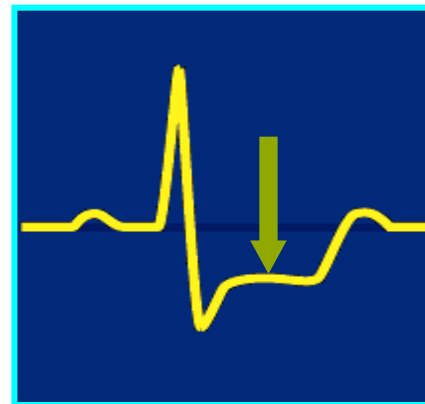
ACS without persistent ST-segment elevation



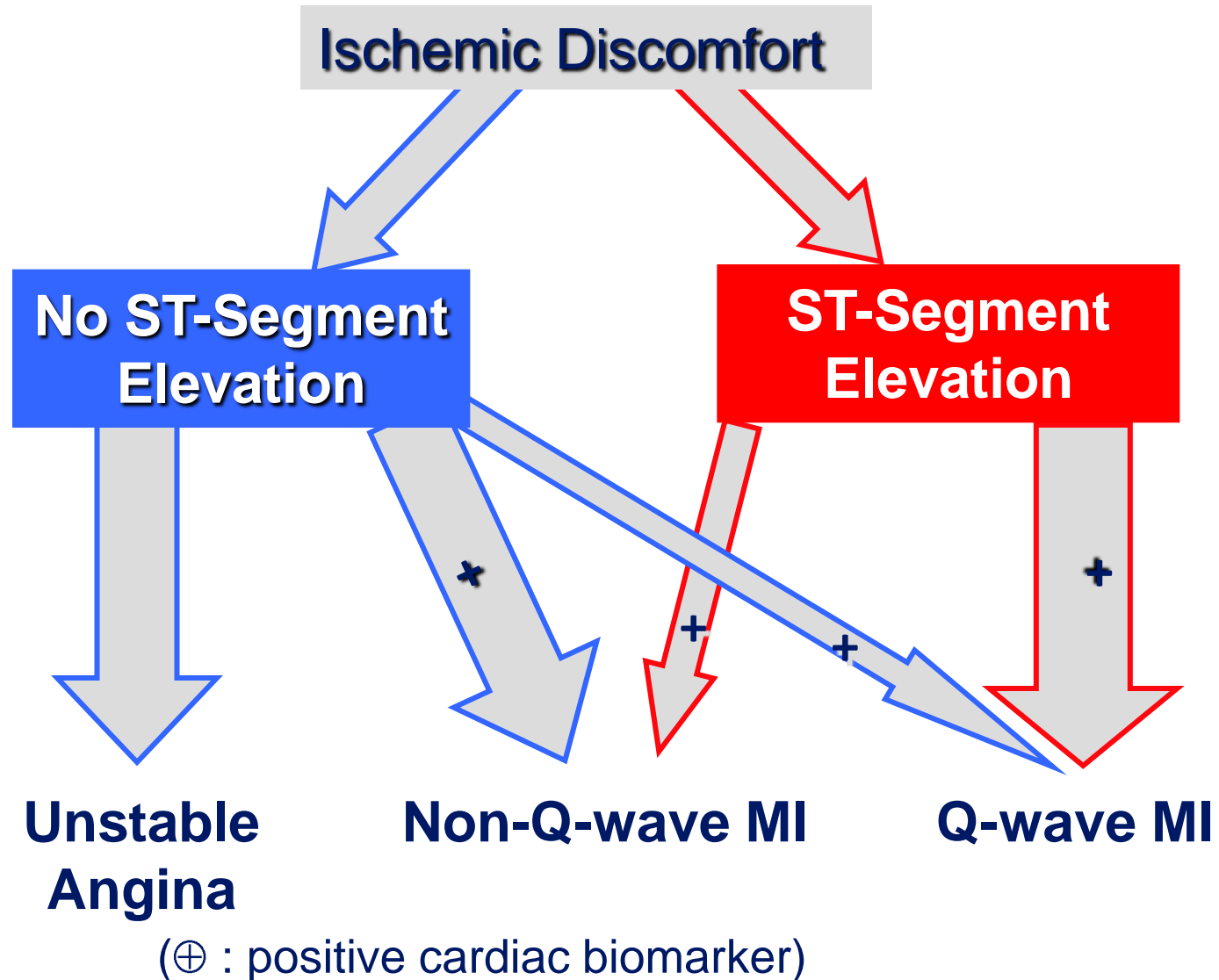
ACS with persistent ST-segment elevation



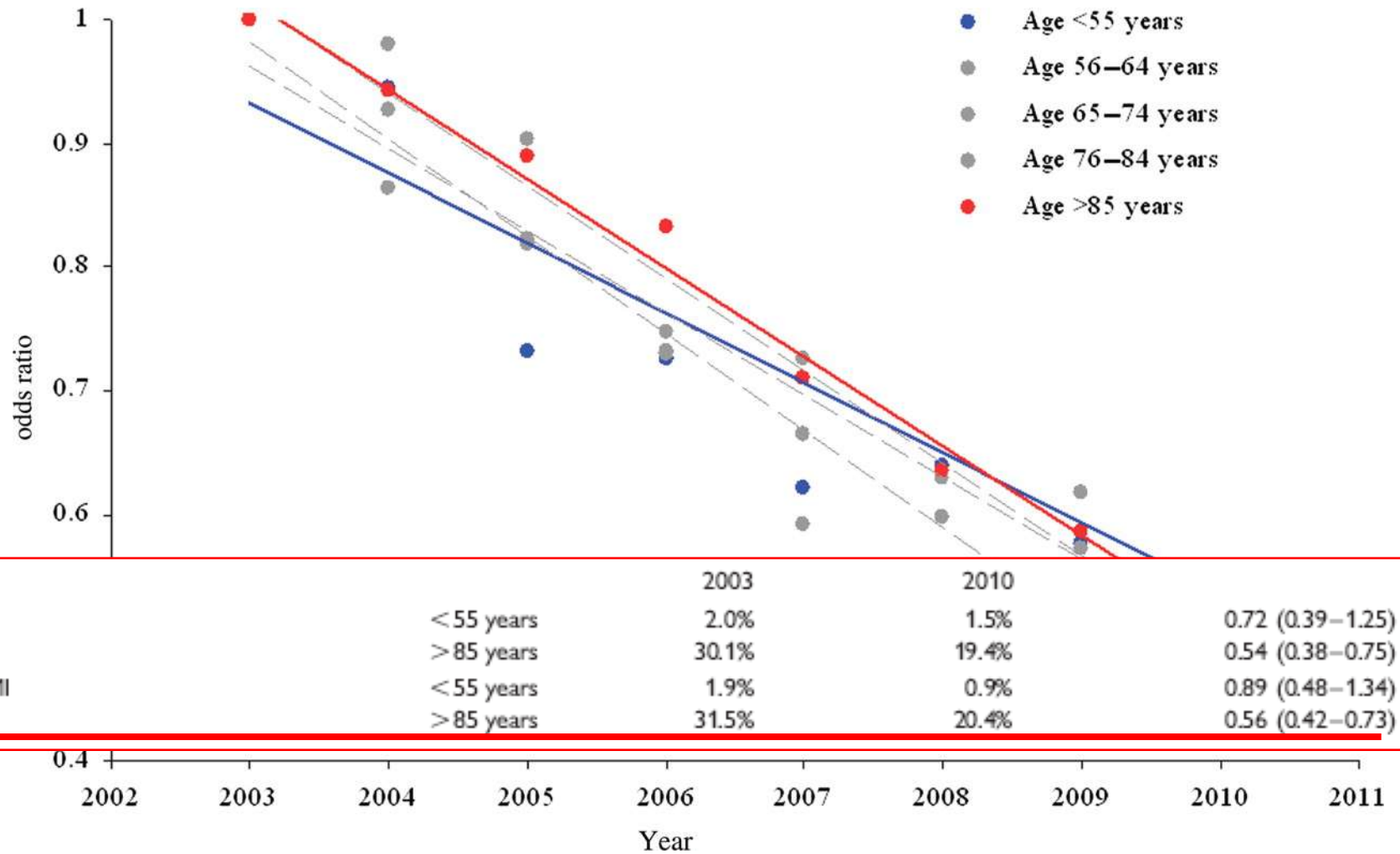
ACS without persistent ST-segment elevation



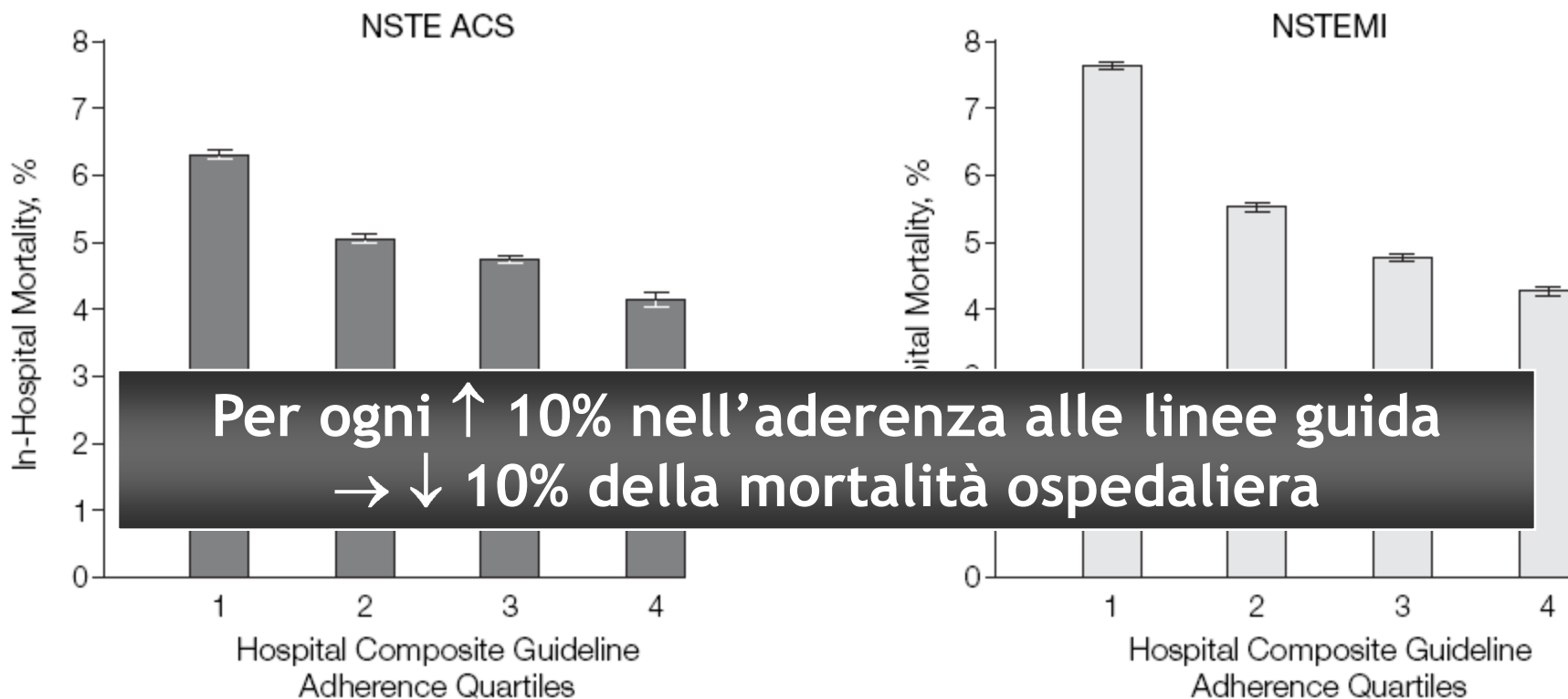
Spectrum of Acute Coronary Syndromes



STEMI and NSTEMI in-hospital all-cause mortality, stratified by age category



Association Between Guideline Adherence Rate and In-Hospital Mortality



Sospetto clinico di SCA

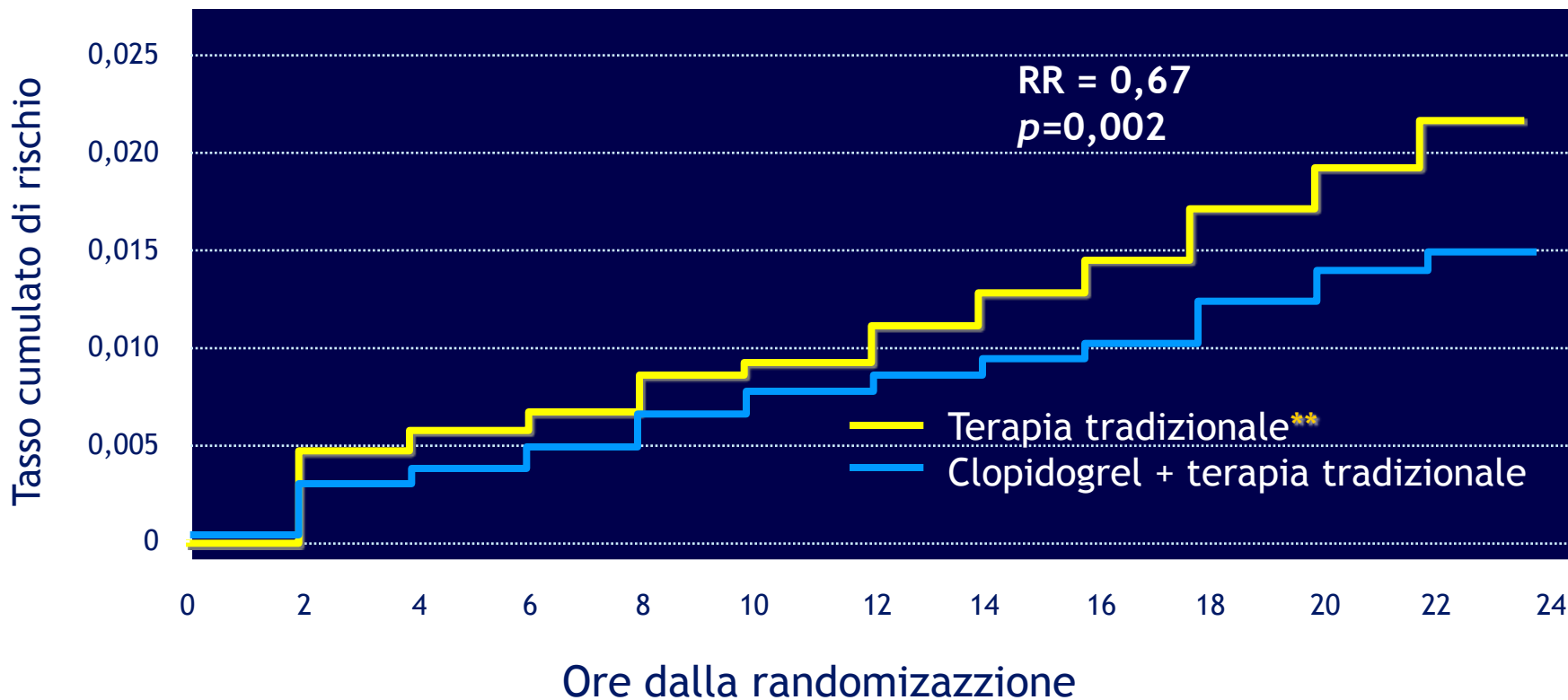


Esame fisico, monitoraggio ECG, prelievo ematico

**Sottoslivellamento o
sopraslivellamento
NON persistente ST**

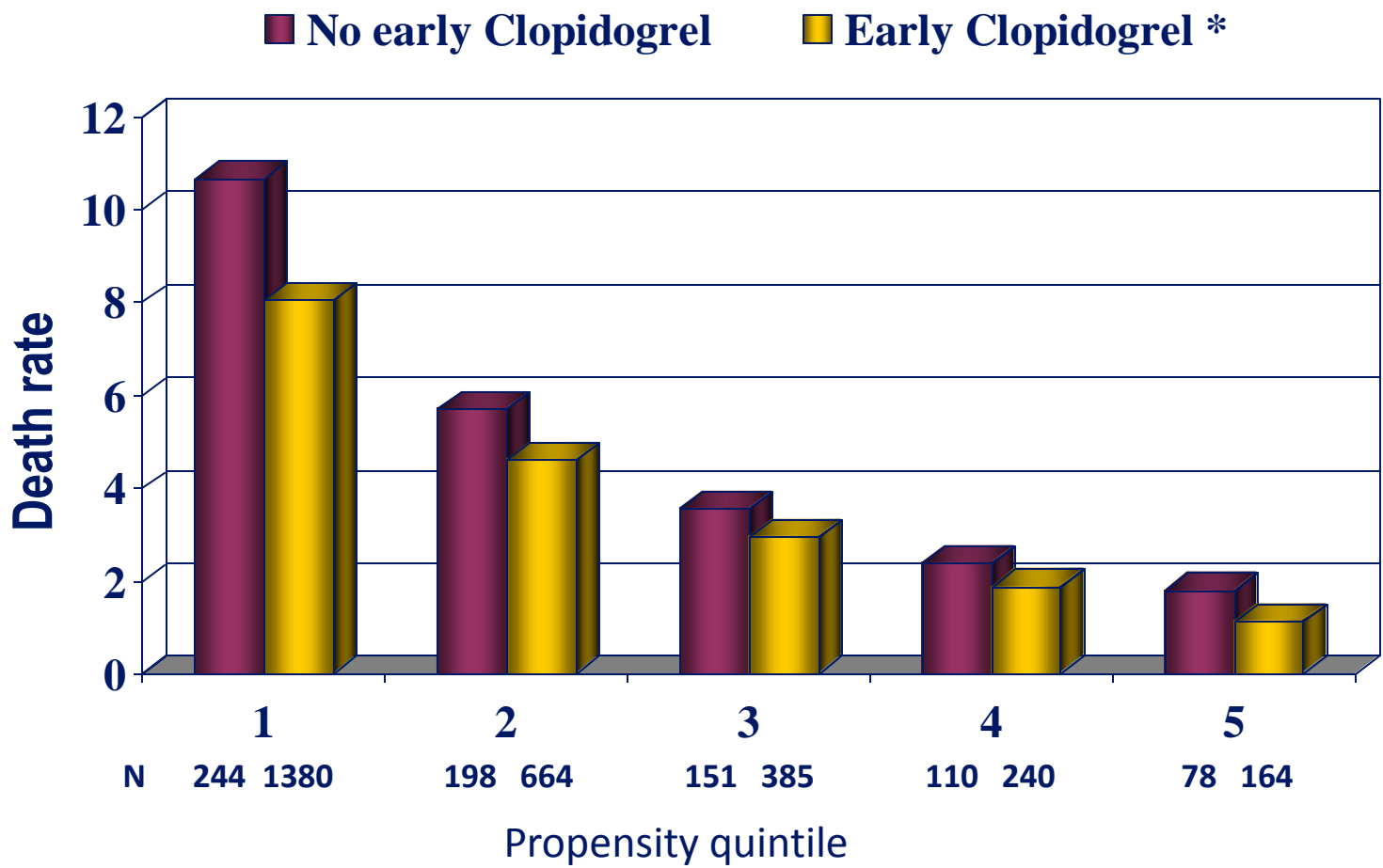
**EBPM o ENF o Fundaparinux, ASA,
Clopidogrel, β -bloccanti, Nitrati**

CURE- Morte CV/IMA/Ictus/Ischemia severa nelle 24 ore dalla randomizzazione



** comprendente ASA

Inhospital outcomes after early* clopidogrel therapy in patients not undergoing an early invasive strategy for treatment of NSTEMI: results from CRUSADE



* = within 24 hours

Sospetto clinico di SCA



Esame fisico, monitoraggio ECG, prelievo ematico

Sottoslivellamento o
sopraslivellamento
NON persistente ST

EBPM o ENF o Fundaparinux, ASA,
Clopidogrel, β -bloccanti, Nitrati

Alto Rischio

Basso Rischio

Anti IIb/IIIa
Angiografia coron.

PCI, CABG o altro trattamento medico
in funzione dei dati clinici e angiografici

Criteria di alto rischio per le sindromi coronariche acute senza sopraslivellamento del tratto ST

Documento di Consenso FIC-GISE

- Presenza di scompenso cardiaco
- Presenza di aritmie ventricolari maggiori
- Età avanzata
- Associazione tra positività della troponina, sottoslivellamento del tratto ST e diabete
- TIMI risk score ≥ 5

TIMI Risk Score

- Age ≥ 65 years
- ≥ 3 CAD Risk Factors
- Prior Coronary Stenosis $>50\%$
- ST deviation
- ≥ 2 Anginal events ≤ 24 hours
- ASA in last 7 days
- Elevated Cardiac Markers (CK-MB or troponin)

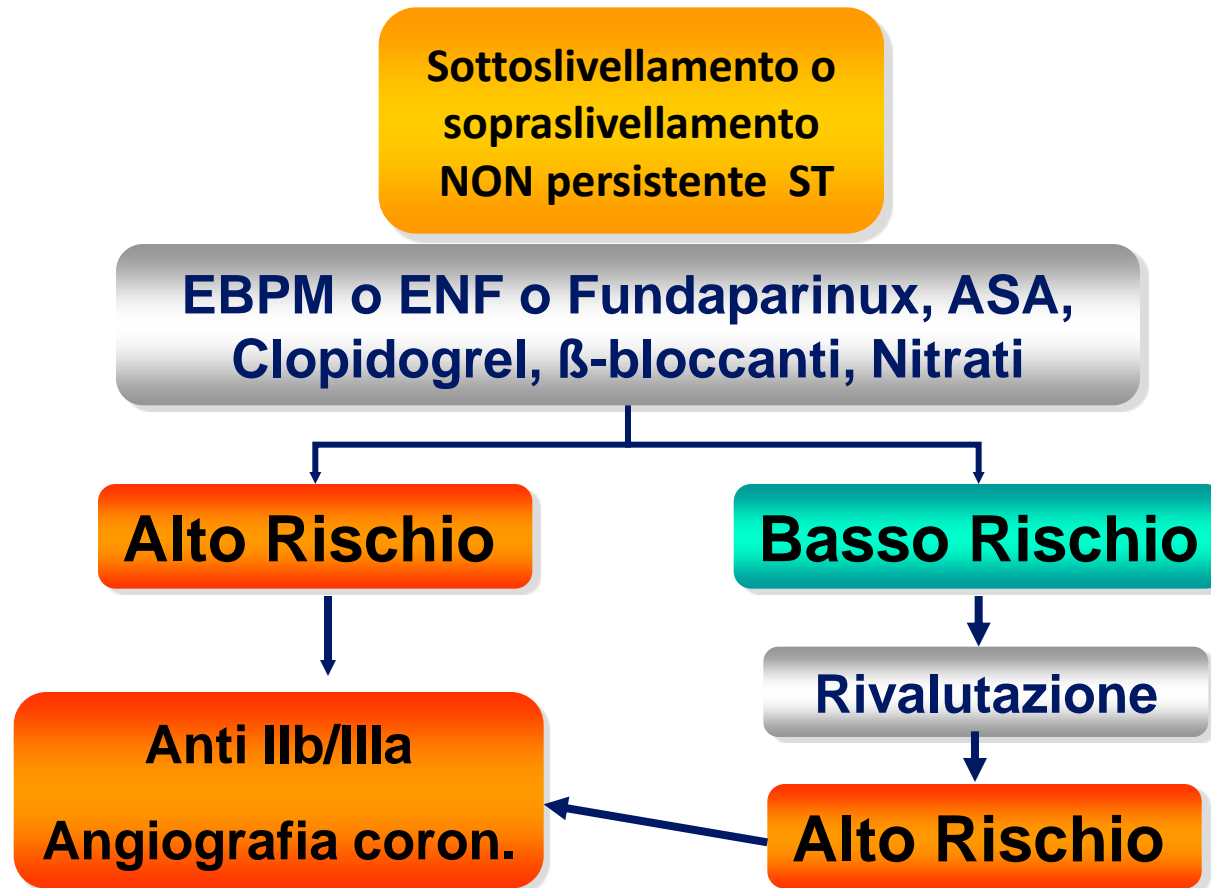
Mortalità Ospedaliera ed a 6 mesi in pazienti a Basso, Medio ed Alto Rischio in popolazioni di Registro secondo il GRACE Risk Score <http://www.outcomes.org/grace>

Categoria di Rischio (terzili)	GRACE Risk Score	Mortalità Ospedaliera (%)
Basso	<=108	<1
Medio	109-140	1-3
Alto	>140	>3
Categoria di Rischio (terzili)	GRACE Risk Score	Mortalità a 6 mesi (%)
Basso	<=88	<3
Medio	89-118	3-8
Alto	>118	>8

Sospetto clinico di SCA



Esame fisico, monitoraggio ECG, prelievo ematico

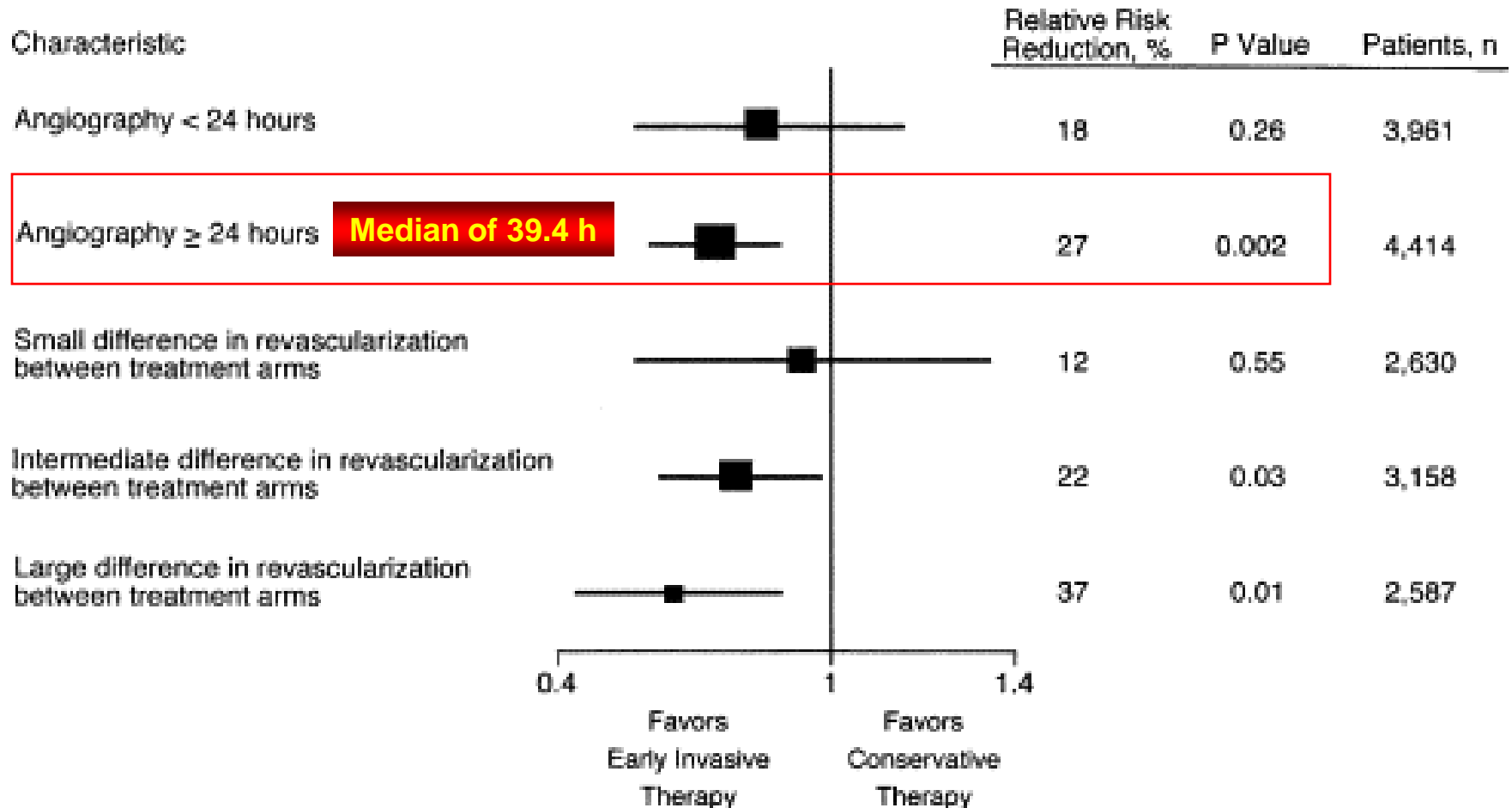


PCI, CABG o altro trattamento medico
in funzione dei dati clinici e angiografici

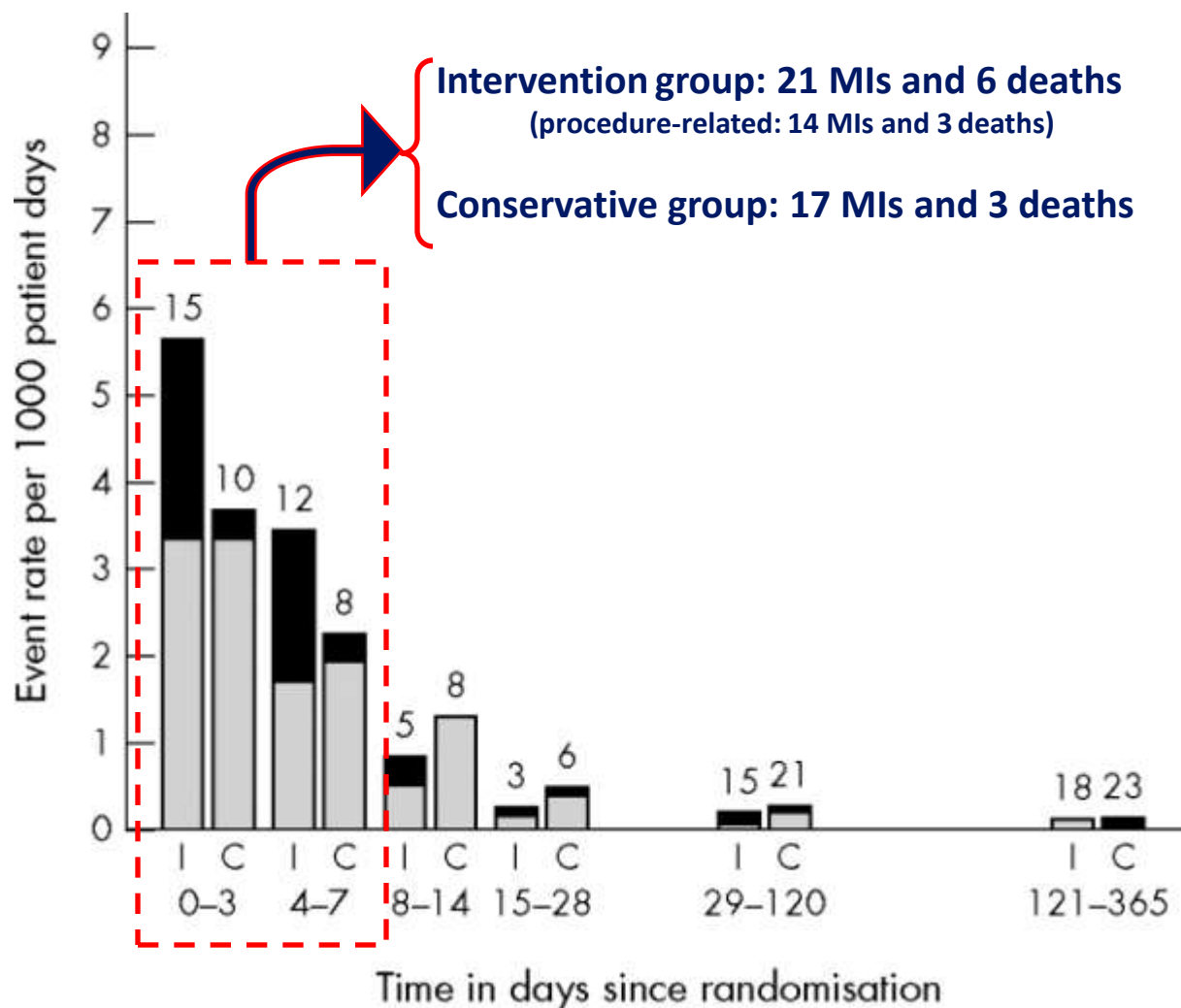


**Entro quanto
tempo deve
essere fatta la
PCI?**

Relative risk of all-cause mortality based on **time of angiography** and the extent of revascularization. Early invasive therapy compared with conservative therapy: a Meta-Analysis

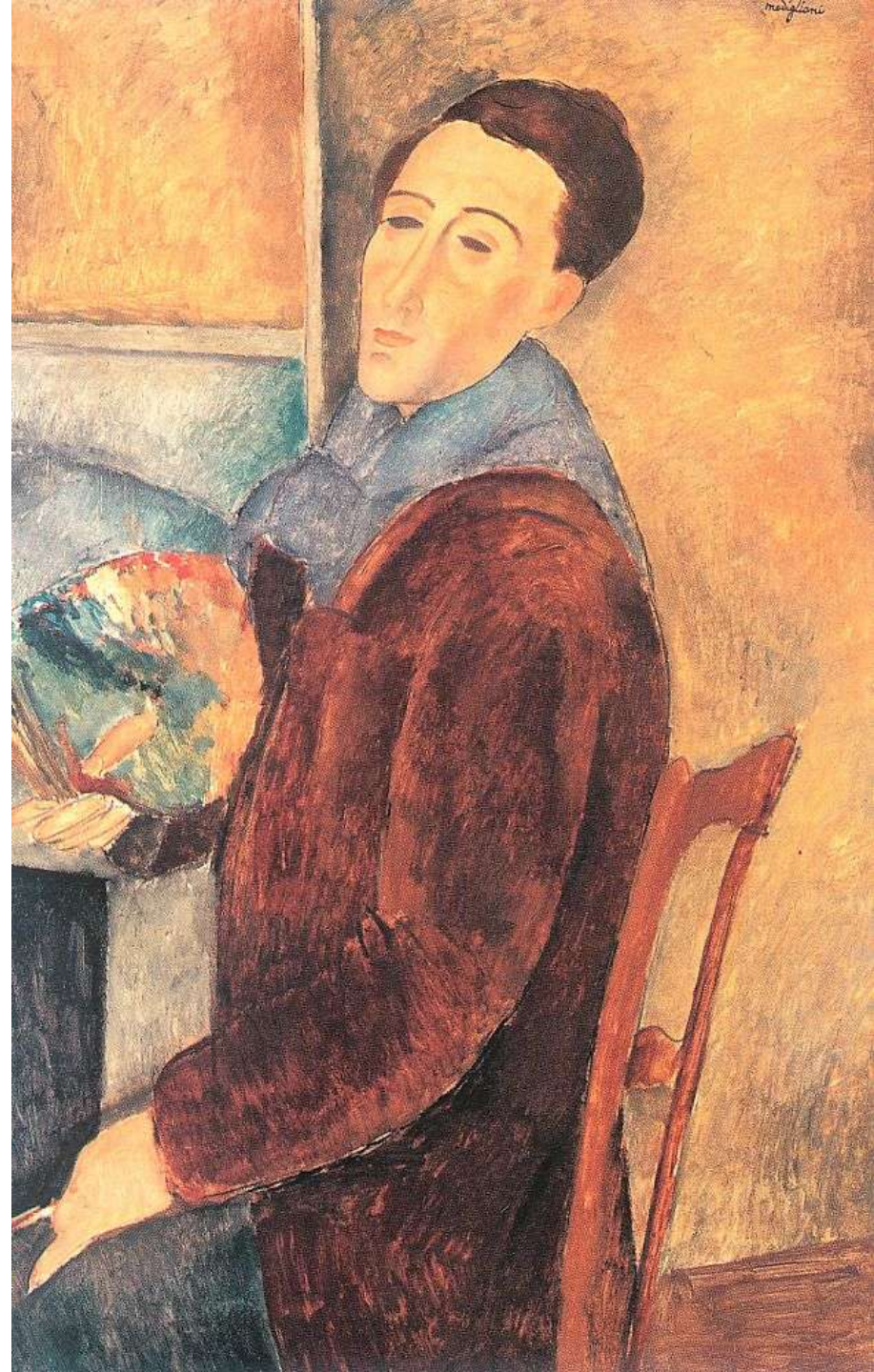


Rate of occurrence of death or myocardial infarction by time since randomisation and treatment group. RITA 3 trial



Quali sono i vantaggi della
strategia invasiva?

In quali pazienti?



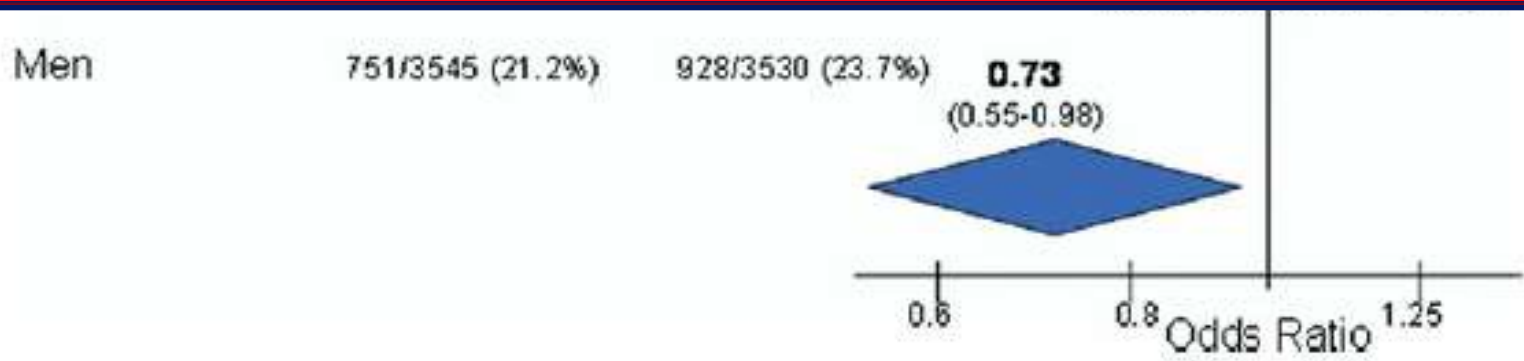
Modigliani, Self-Portrait

Death, MI, or Rehospitalization in NSTEMI-ACS Trials of an Invasive Versus Conservative Treatment Strategy.

A meta-analysis

Population	Invasive Strategy	Conservative Strategy	
All Patients	1075/5083 (21.1%)	1313/5067 (25.9%)	0.78 (0.61-0.98)

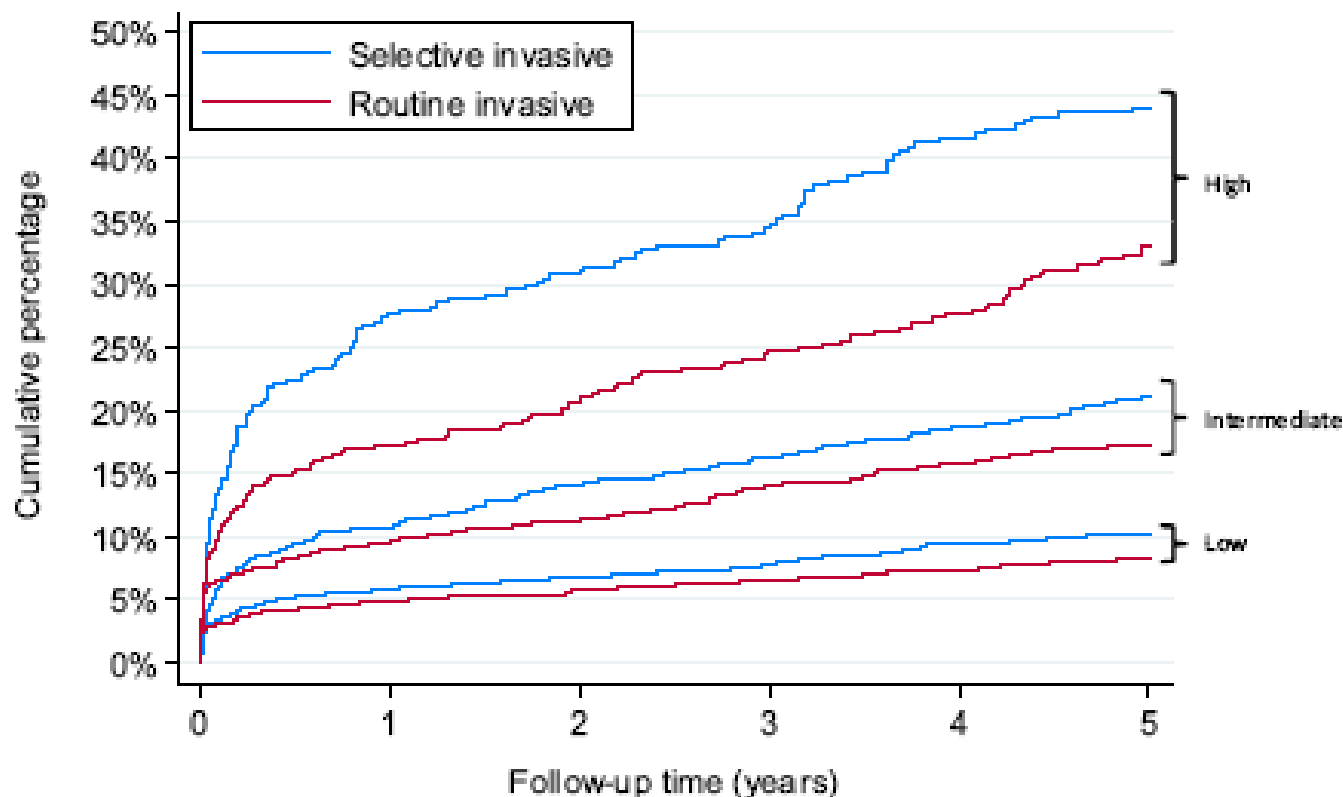
Men	Invasive Strategy	Conservative Strategy	Odds Ratio (95% CI)
Death, MI, or rehospitalization with ACS	751/3545 (21.2)	928/3530 (26.3)	0.73 (0.55-0.98)
Death or MI	433/3641 (11.9)	475/3619 (13.1)	0.87 (0.61-1.23)
Death	157/3641 (4.3)	165/3619 (4.6)	0.89 (0.58-1.35)
Nonfatal MI	284/3641 (7.8)	337/3619 (9.3)	0.81 (0.59-1.11)
Rehospitalization with ACS	444/3545 (12.5)	621/3530 (17.6)	0.66 (0.54-0.82)



Long-Term Outcome of a Routine Versus Selective Invasive Strategy in Patients With Non-ST-Segment Elevation ACS

A Meta-Analysis of Individual Patient Data

Cumulative Risk of CV Death or MI by risk group



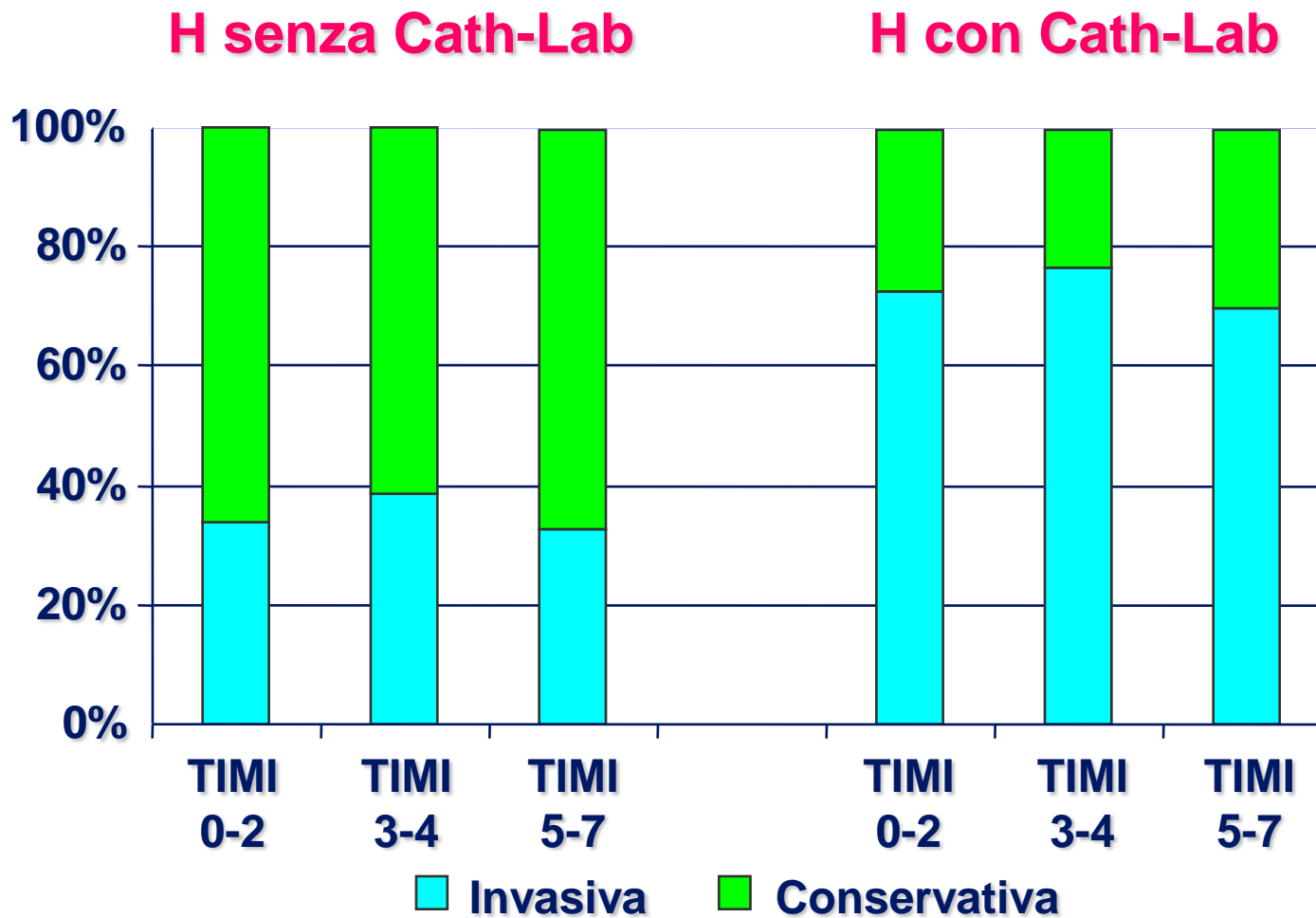
Selective invasive	2746	2452	2351	2178	2077	2005
Routine invasive	2721	2485	2410	2235	2166	2079

Tra il dire e il fare.....

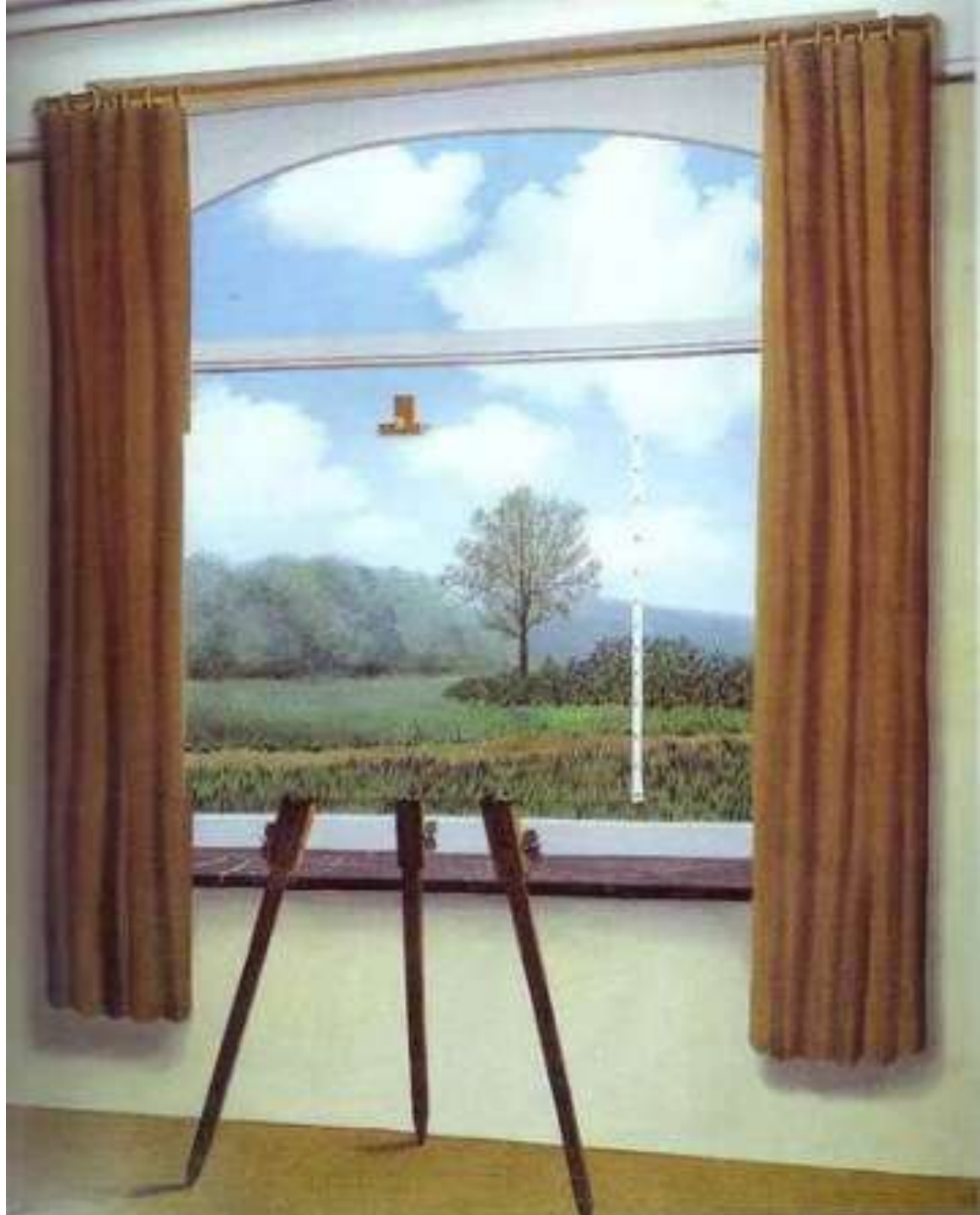


Hopper, Ground Swell

Scelta della Strategia Terapeutica Profilo di rischio ininfluente



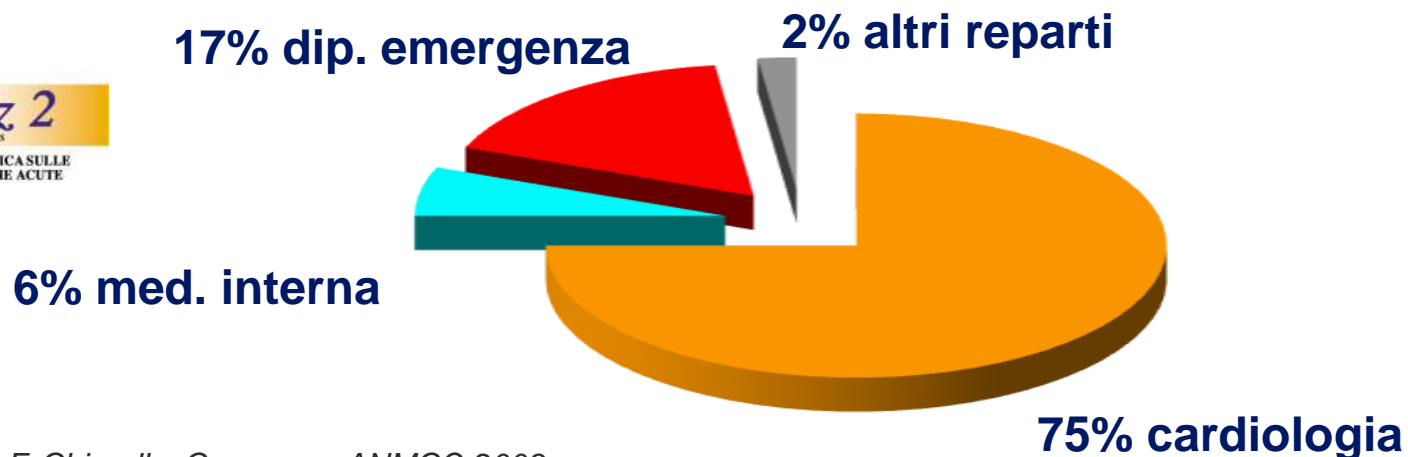
Il setting:
Cardiologia
o
Medicina?



Sindromi Coronariche Acute in Italia

- **I dati dello studio BLITZ 1 suggeriscono che, in Italia, circa il 30% dei pazienti con Infarto Miocardico Acuto vengono trattati al di fuori delle Unità Coronariche**

The Blitz study. Eur Heart J 2003;24:1616-1629



Influence of Inpatient Service Specialty on Care Processes and Outcomes for Patients With NonST-Segment Elevation ACS in the CRUSADE registry

Treatment Patterns by Primary Inpatient Service*

	Overall (n=55 994)	Cardiology (n= 35 374)	Noncardiology (n=20 620)	Adjusted OR (95% CI)
Acute (≤24 h) medications				
Aspirin	91.8 (n=52 399)	93.0 (n=33 789)	89.7 (n=18 610)	1.28 (1.17–1.39)
β-Blocker	78.5 (n=51 128)	80.1 (n=32 713)	75.6 (n=18 415)	1.28 (1.20–1.36)
Heparin	83.4 (n=53 159)	86.1 (n=34 224)	78.4 (n=18 935)	1.56 (1.43–1.70)
Unfractionated	52.9	57.6	44.3	1.50 (1.42–1.60)
Low-molecular weight	37.2	35.8	39.7	0.90 (0.84–0.95)
GP IIb/IIIa inhibitor	37.7 (n=49 350)	45.0 (n=32 091)	24.1 (n=17 259)	2.11 (1.95–2.27)
Clopidogrel	42.5 (n=55 428)	47.8 (n=35 187)	33.3 (n=20 241)	1.58 (1.49–1.69)
Invasive procedures				
Cardiac catheterization	72.7	81.4	57.8	2.55 (2.32–2.80)
Catheterization ≤48 h	51.5	61.2	34.9	2.25 (2.08–2.43)
PCI	41.7	49.2	28.9	1.86 (1.73–2.00)
PCI ≤48 h	30.0	37.1	17.8	2.06 (1.91–2.23)
CABG	13.3	14.0	12.1	1.13 (1.00–1.27)

Influence of Inpatient Service Specialty on Care Processes and Outcomes for Patients With NonST-Elevation ACS in the CRUSADE registry

In-Hospital Outcomes by Primary Inpatient Service

	Overall (n=55 994)	Cardiology (n=35 374)	Noncardiology (n=20 620)	Adjusted OR* (95% CI)
Death†	4.1	3.2	5.7	0.80 (0.73–0.88)
Reinfarction	3.0	2.8	3.4	0.74 (0.65–0.84)
Congestive heart failure	8.7	7.1	11.5	0.96 (0.87–1.06)
Cardiogenic shock	2.7	2.5	3.0	1.08 (0.95–1.23)
Non-CABG RBC transfusion	8.8	7.0	11.8	0.75 (0.69–0.82)

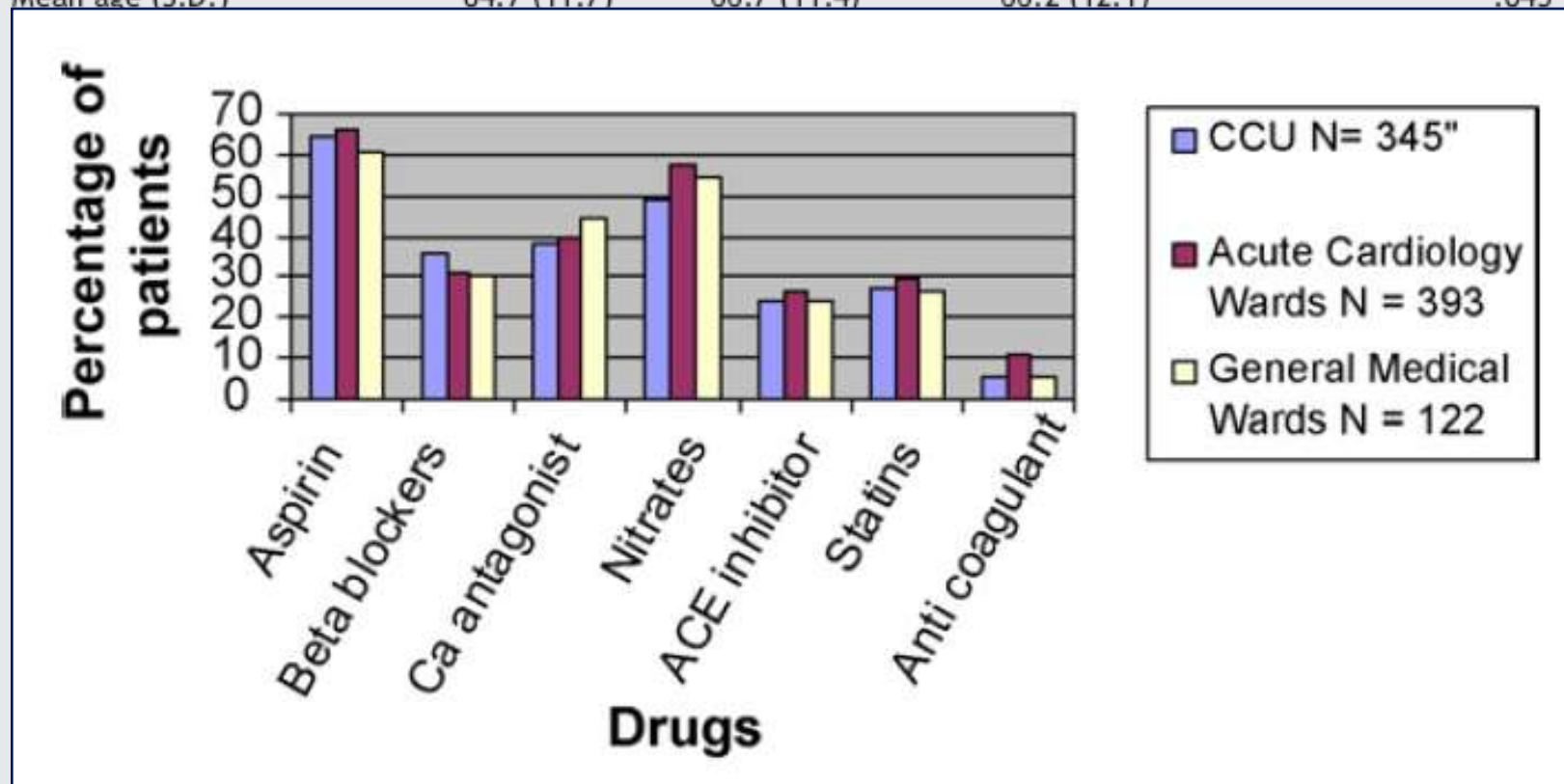
TABLE 1. Patient and Hospital Characteristics by Primary Inpatient Service

Variable		P
Demograph	<p>Conclusions. Results from the present analysis highlight the difficulties with accurately determining how specialty care is associated with treatment patterns and clinical outcomes for patients with acute coronary syndromes.</p>	
Age, y*		<0.0001
Female		<0.0001
Black race		11.0 9.7 13.3 <0.0001

Characteristics of patients with non-ST elevation ACS admitted to different settings in the 1990s. A secondary analysis of PRAIS (UK), a prospective, observational, multi-centred study

Table 1 Baseline characteristics of patients compared by care setting

	CCUs (N= 345)	Cardiology wards (N= 393)	General medical wards (N= 122)	χ^2 statistic	P-value
Mean age (S.D.)	64.7 (11.7)	66.7 (11.4)	66.2 (12.1)		.045



Prior statin use	29.9%	27%	26.2%	2.145	.709
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Studio IN-ACS Outcome: terapia farmacologica alla dimissione

	NSTE-SCA n. 3607	PCI n. 905	No PCI n. 2702	p
ASA, %	90.0	97.6	88.7	<0.0001
Clopidogrel, %	65.0	89.0	58.1	<0.0001
ASA+Clopidogrel, %	63.8	87.5	55.9	<0.0001
Ticlopidina, %	6.9	7.6	6.6	0.29
ASA+Clopidogrel/Ticlopidina, %	68.3	94.8	59.4	<0.0001
ASA/Clopidogrel/Ticlopidina, %	95.3	99.3	93.9	<0.0001
ACE-i, %	63.2	61.9	63.6	0.35
Sartani, %	9.9	9.0	10.3	0.25
ACE-i/Sartani, %	72.5	70.3	73.2	0.09
Beta-bloccanti, %	73.3	77.7	71.9	0.0006
Statine, %	73.9	82.0	71.2	<0.0001
n-3 PUFA, %	15.2	16.1	14.8	0.34

Sindromi coronariche
acute nel paziente
anziano con
comorbidità



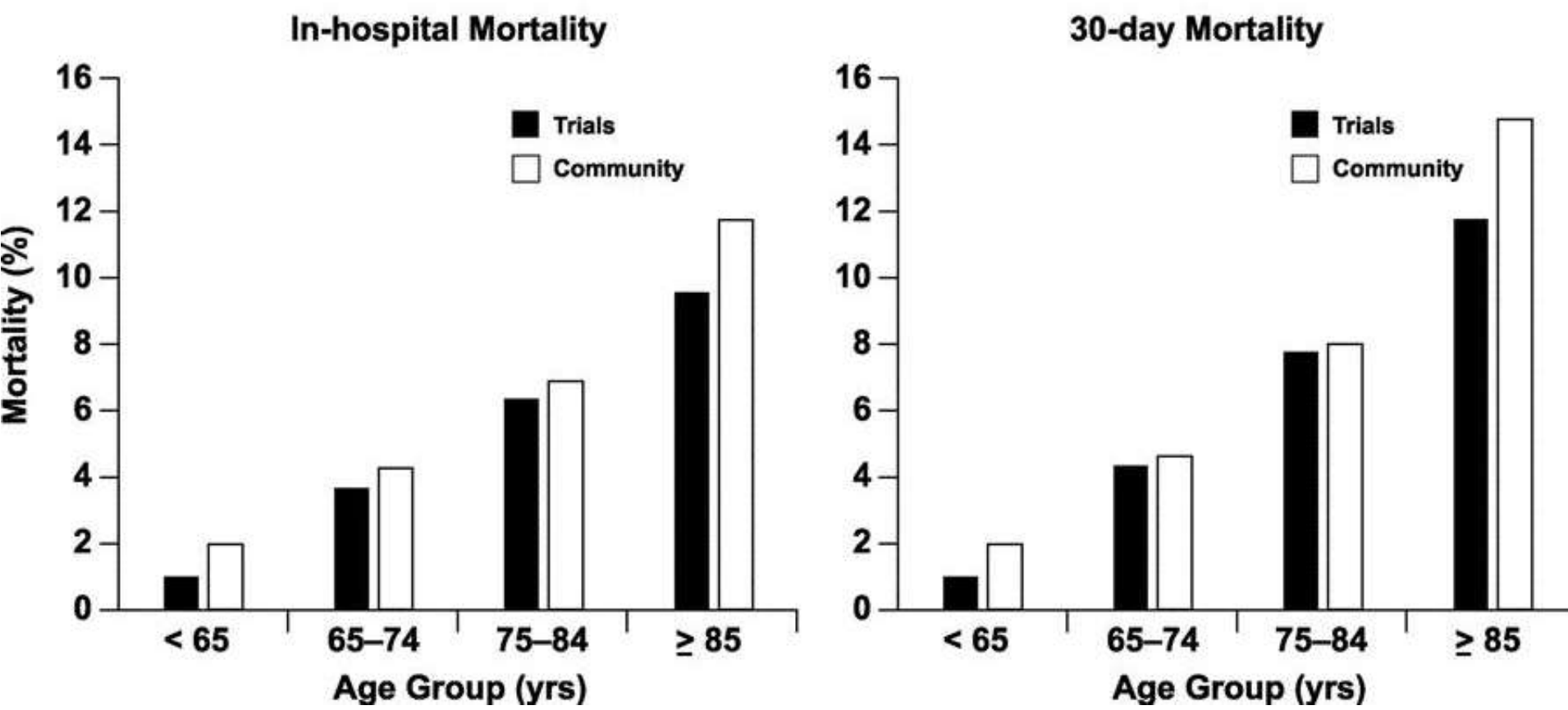
V. Van Gogh, vecchio che soffre

NSTE ACS - Representation of the subgroup >75 years as a proportion of the total trial and community populations

NSTE ACS Population	No. of Subjects	Age ≥ 75 y, %	Randomized Treatment
VIGOUR	34266	18%	NSTE ACS trials
GUSTO IIb	8011		Hirudin vs Heparin
PARAGON A	2282		GP IIb/IIIa Lamifiban vs UFH
PARAGON B	5225		GP IIb/IIIa Lamifiban vs placebo
PURSUIT	10948		GP IIb/IIIa Eptifibatide vs placebo
GUSTO IV ACS	7800		GP IIb/IIIa Abciximab vs placebo
NRMI 2-4	1076796	38%	NSTEMI registry
GRACE	11968		NSTE ACS registry
CRUSADE	56963		NSTE ACS QI initiative

In-hospital and 30-day mortality according to age groups

Summarized available data from trials (VIGOUR) and registries (GRACE, CRUSADE)



Influence of Comorbid Conditions on One-Year Outcomes in Non-ST-Segment Elevation Acute Coronary Syndrome

Variable	Hazard ratio (95% CI)	P value
Age (y/10)	1.7 (1.4-2.2)	.0001
Male sex	1.6 (1.0-2.5)	.06
Heart failure at admission	2.4 (1.5-4.0)	.0001
ST-segment depression	1.6 (1.1-2.5)	.01
White blood cell count >10 × 10 ⁹ /L	1.9 (1.2-2.8)	.01
Comorbid conditions		
Previous MI	1.4 (0.9-2.1)	.10
→ Previous heart failure	2.6 (1.6-4.3)	.0001
→ Peripheral artery disease	2.0 (1.2-3.3)	.01
→ Dementia	3.1 (1.2-8.2)	.01
→ Renal failure ^b		
Mild	1.6 (1.1-2.6)	.04
Severe	2.9 (1.5-6.0)	.01

Anemia

COPD

Cancer

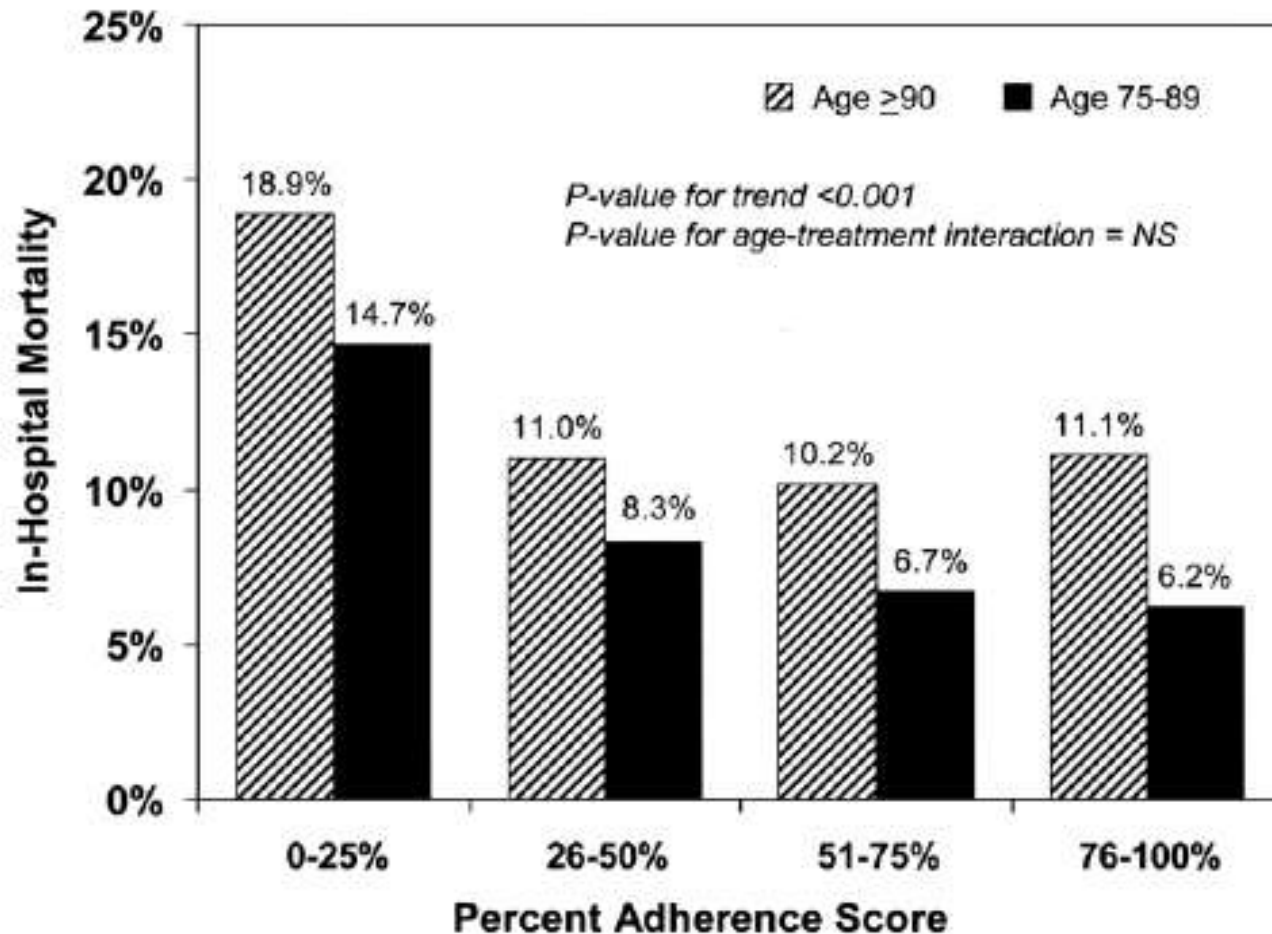
Elderly patients with acute coronary syndromes admitted to Italian intensive cardiac care units: a Blitz-3 Registry sub-analysis

Table 4 Treatment utilization for patients with ST-elevation acute coronary syndromes and non-ST-elevation acute coronary syndromes by age

	ST-elevation ACS			Non-ST-elevation ACS		
	Age <75 years (N=1 000) %	Age ≥75 years (N= 492) %	P	Age <75 years (N= 1254) %	Age ≥75 years (N= 890) %	P
Aspirin	96	90	<0.0001	93	85	<0.0001
Aspirin and clopidogrel association	84	63	<0.0001	75	59	<0.0001
Oral Anticoagulation Therapy	1.5	3.5	0.01	1.6	5.8	<0.0001
β-blockers	74	60	<0.0001	74	63	<0.0001
Iib/IIla inhibitors	45	29	<0.0001	25	15	<0.0001
ACE-inhibitors	61	55	0.02	57	55	0.33
Statins	86	68	<0.0001	82	69	<0.0001
Nitrates, intravenous	50	54	0.15	60	61	0.80
Inotropes, intravenous	6	17	<0.0001	2.2	5.4	<0.0001
Diuretics, intravenous	25	55	<0.0001	27	57	<0.0001
Insulin, subcutaneous	12	15	0.10	15	19	0.03
Insulin, intravenous	4.5	5.3	0.50	3.2	4.3	0.19
Transfusions	1.7	5.1	0.0002	2.1	6.1	<0.0001
No coronary reperfusion	34	52	<0.0001	NA	NA	NA
Primary PCI	49	37		NA	NA	
Thrombolysis	17	11		NA	NA	

ACE, angiotensin-converting enzyme; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention.

Relationship Between In-Hospital Mortality Across Each Age Group With Increasing Adherence to Recommended Therapies in the CRUSADE Initiative



ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

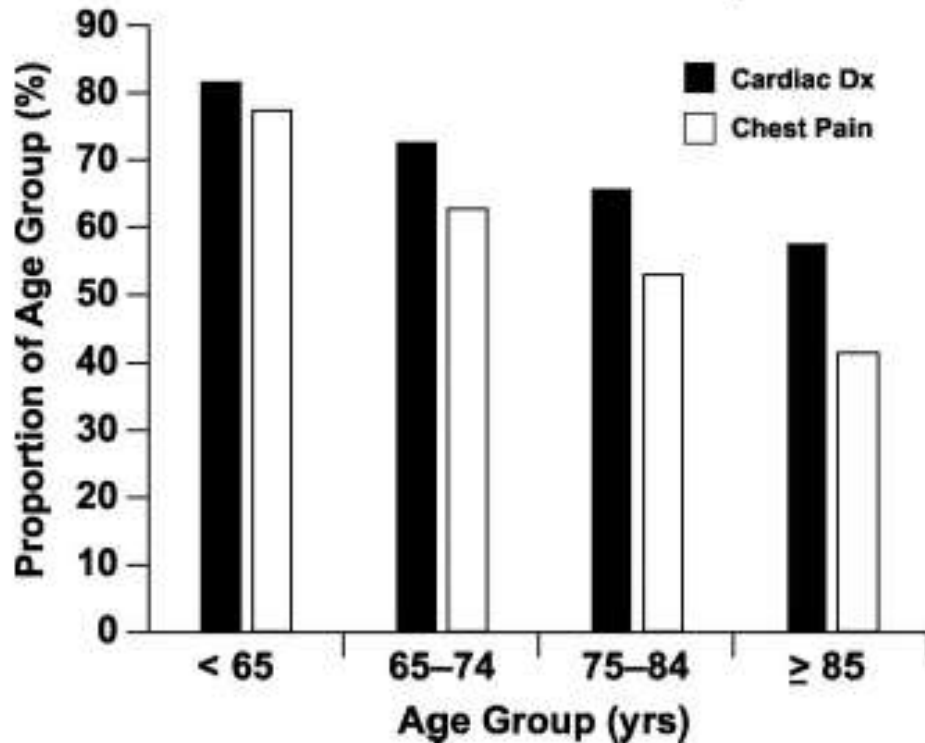
Recommendations for elderly patients

Recommendations	Class ^a	Level ^b
Because of the frequent atypical presentation, elderly patients (>75 years) should be investigated for NSTEMI-ACS at low level of suspicion	I	C
	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

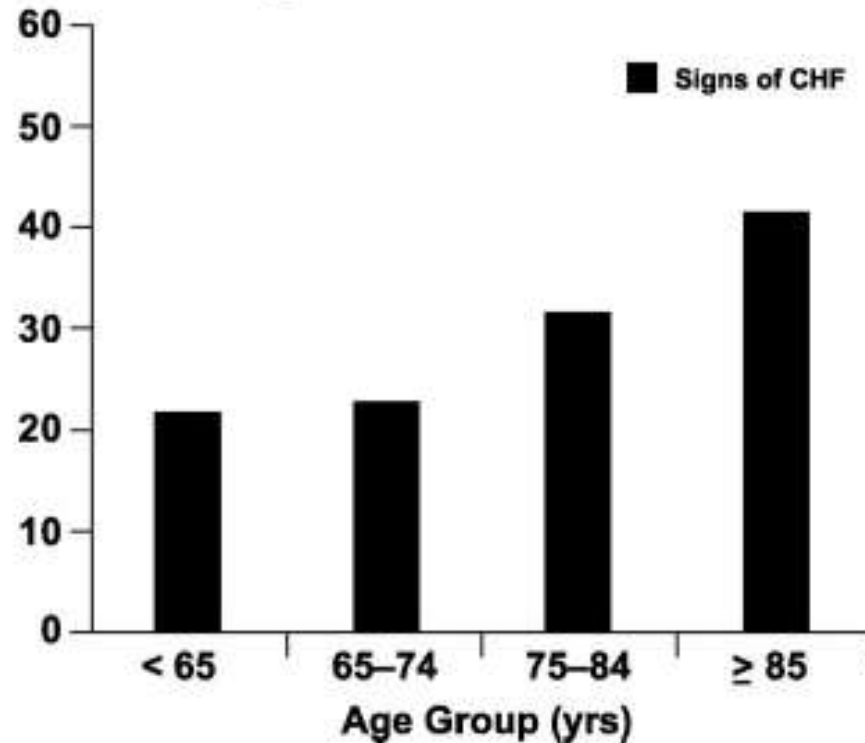
Admission signs, symptoms, and initial diagnosis according to age groups

Summarized available data from trials (VIGOUR) and registries (GRACE, CRUSADE)

Chest Pain and Initial Diagnosis



Signs of CHF on Admission



ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Cardiac and non-cardiac conditions that can mimic non-ST-elevation acute coronary syndromes

Cardiac	Pulmonary	Haematological	Vascular	Gastro-intestinal	Orthopaedic/ infectious
Myocarditis	Pulmonary embolism	Sickle cell crisis	Aortic dissection	Oesophageal spasm	Cervical discopathy
Pericarditis	Pulmonary infarction	Anaemia	Aortic aneurysm	Oesophagitis	Rib fracture
Cardiomyopathy	Pneumonia Pleuritis		Cerebrovascular disease	Peptic ulcer	Muscle injury/ inflammation
Valvular disease	Pneumothorax			Pancreatitis	Costochondritis
Tako-Tsubo cardiomyopathy				Cholecystitis	Herpes zoster
Cardiac trauma					

Effect of older age on diagnostic and prognostic performance of high-sensitivity troponin T in patients presenting to an emergency department

	Age ≥ 75 y n = 339	Age <75 y n = 509	HR (95% CI)	P
Non-ACS, n (%)	205 (60.5%)	237 (46.6%)	1.3 (1.1-1.5)	.0001
★ Cardiac	94 (27.7%)	112 (22.0%)	1.3 (1.0-1.6)	.048
Cardiomyopathy/takotsubo	1 (0.3%)	7 (1.4%)	0.2 (0.03-1.7)	NS
Valve disease	18 (5.3%)	12 (2.4%)	2.3 (1.1-4.6)	.03
Congestive heart failure	56 (16.5%)	46 (9.0%)	1.8 (1.3-2.6)	.0012
Endokarditis/myokarditis	1 (0.3%)	8 (1.6%)	0.2 (0.02-1.5)	.04
Brady/tachyarrhythmias	18 (5.3%)	32 (6.3%)	0.8 (0.5-1.5)	NS
Cardiac ablation/cardioversion	0	7 (1.4%)	0.1 (0.01-1.7)	.02
★ Extracardiac	111 (32.7%)	125 (24.6%)	1.3 (1.1-1.6)	.01
Hypertensive crisis	20 (5.9%)	7 (1.4%)	4.3 (1.8-10)	.0008
Renal failure	2 (0.6%)	3 (0.6%)	1.0 (0.17-5.9)	NS
Sepsis/SIRS	2 (0.6%)	3 (0.6%)	1.0 (0.17-5.9)	NS
Pneumonia	16 (4.7%)	23 (4.5%)	1.0 (0.6-1.9)	NS
Pulmonary embolism/PHT	9 (2.7%)	12 (2.4%)	1.1 (0.5-2.6)	NS
Non-ACS chest pain	24 (7.1%)	47 (9.2%)	0.8 (0.5-1.2)	NS
Syncope	13 (3.8%)	7 (1.4%)	2.8 (1.1-6.9)	.03
Unspecified dyspnea	4 (1.2%)	4 (0.8%)	1.5 (0.4-6.0)	NS
Else	21 (6.2%)	19 (3.7%)	1.7 (0.9-3.0)	NS

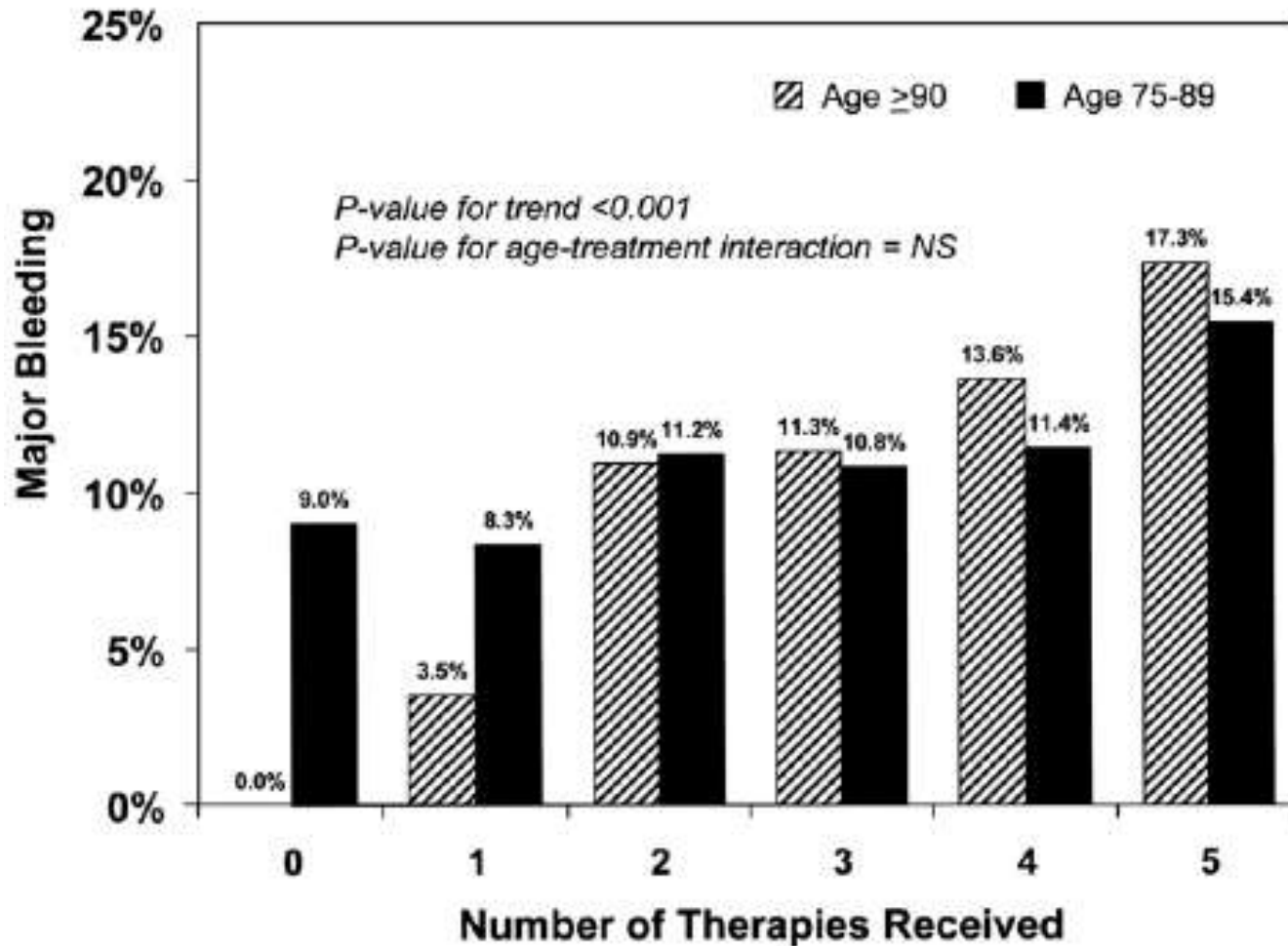
SIRS, Systemic inflammatory response syndrome; PHT, pulmonary hypertension.

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Recommendations for elderly patients

Recommendations	Class ^a	Level ^b
Choice and dosage of antithrombotic drugs should be tailored in elderly patients to prevent the occurrence of adverse effects.	I	C
Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.	

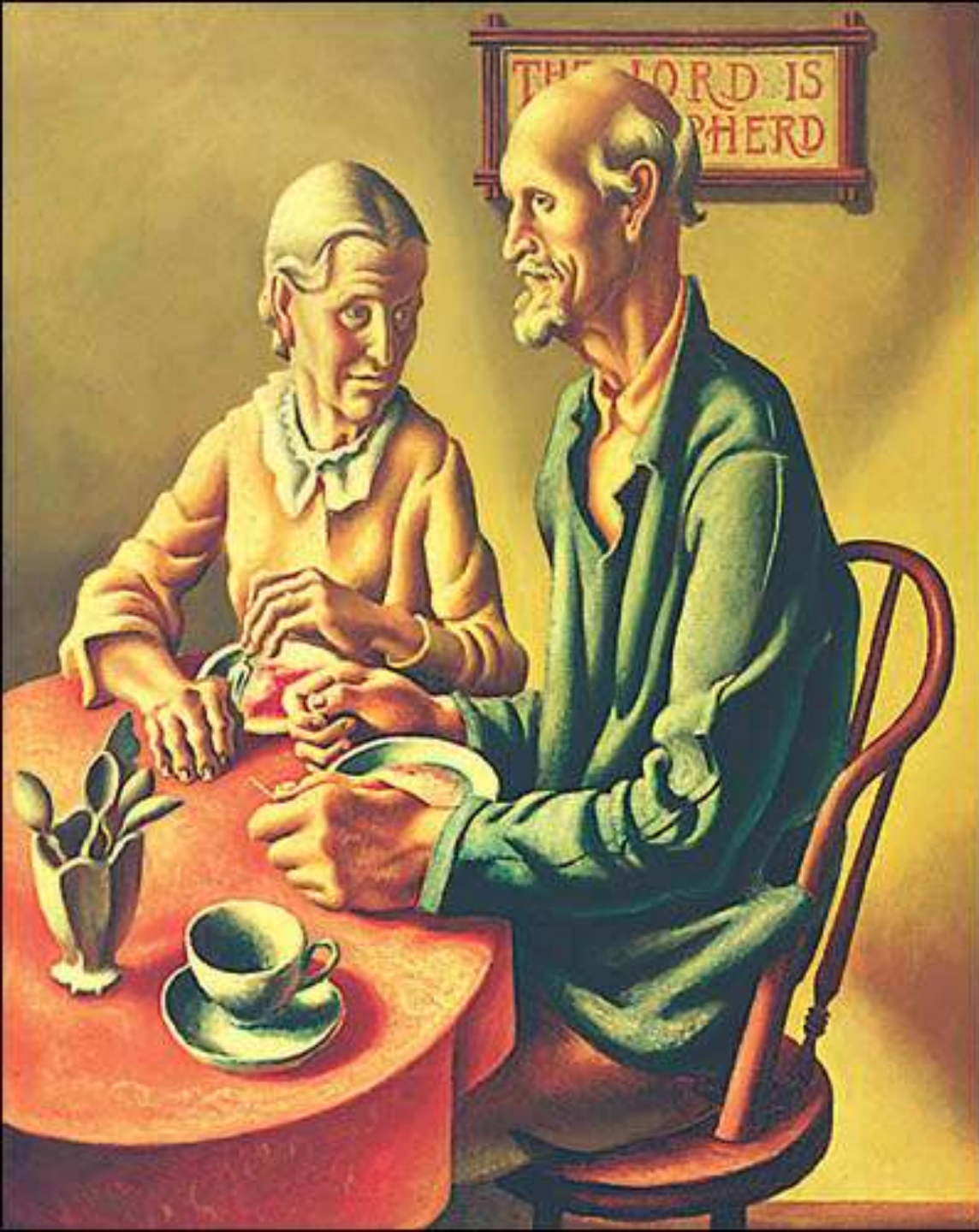
Relationship Between the Number of Therapies Provided and the Incidence of In-Hospital Major Bleeding in the CRUSADE Initiative



CRUSADE bleeding score

Predictor	Score	Predictor	Score
Baseline hematocrit, %		Systolic blood pressure, mm Hg	
31	9	90	10
31-33.9	7	91-100	8
34-36.9	3	101-120	5
37-39.9	2	121-180	1
40	0	181-200	3
Creatinine clearance, mL/min		<u>≥201</u>	5
15	39	Sex	
15-30	35	Male	0
30-60	28	Female	8
60-90	17	Signs of CHF at presentation	
90-120	7	No	0
120	0	Yes	7
Heart rate (bpm)		Prior vascular disease	
70	0	No	0
71-80	1	Yes	6
81-90	3	Diabetes mellitus	
91-100	6	No	0
101-110	8	Yes	6
111-120	10		
<u>≥121</u>	11		





Strategia invasiva anche negli anziani?

ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Recommendations for elderly patients

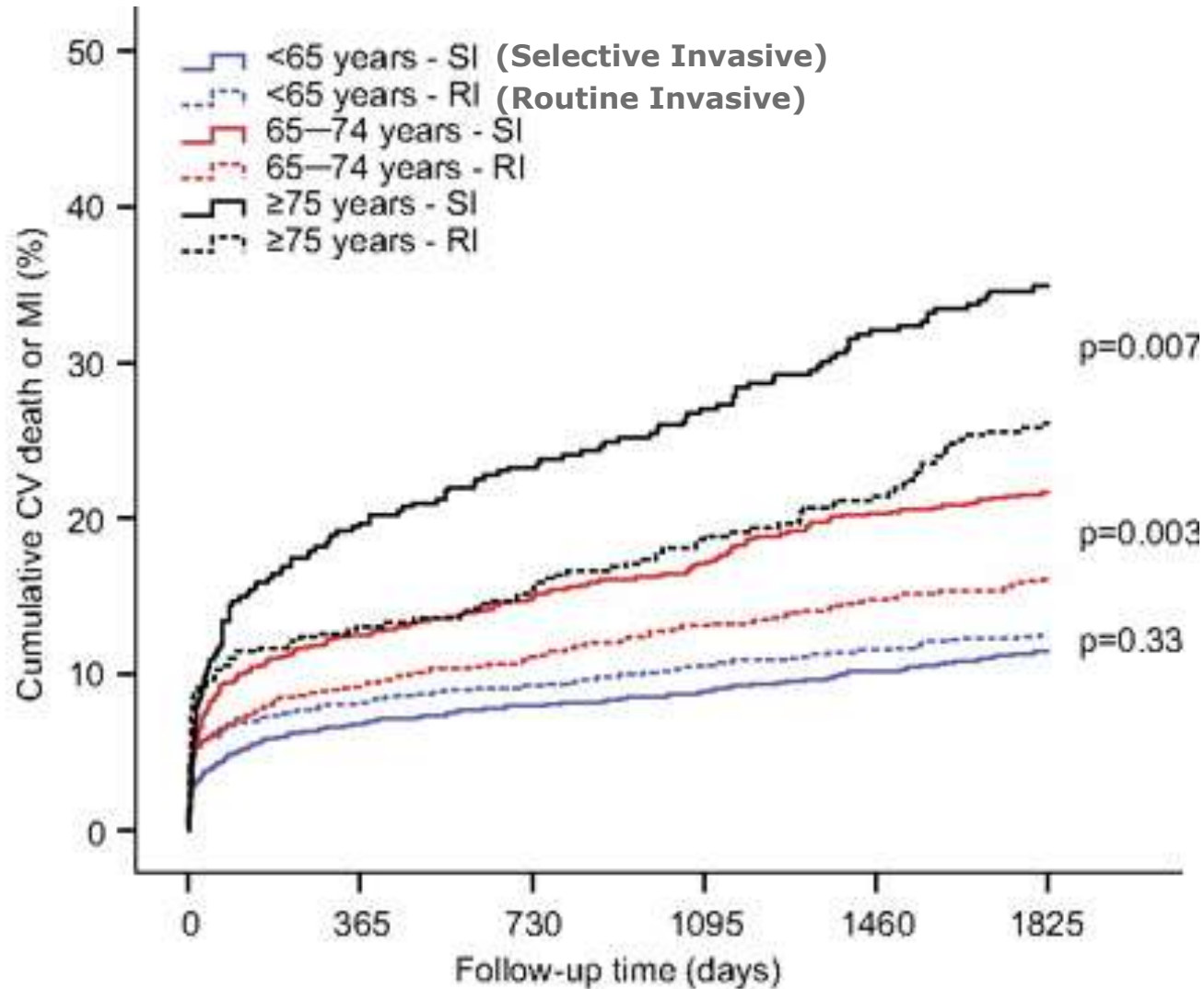
Recommendations	Class ^a	Level ^b
Elderly patients should be considered for an early invasive strategy with the option of possible revascularization, after careful weighing up of the risks and benefits.	IIa	B

Weight of evidence/opinion is in favour of usefulness/efficacy.

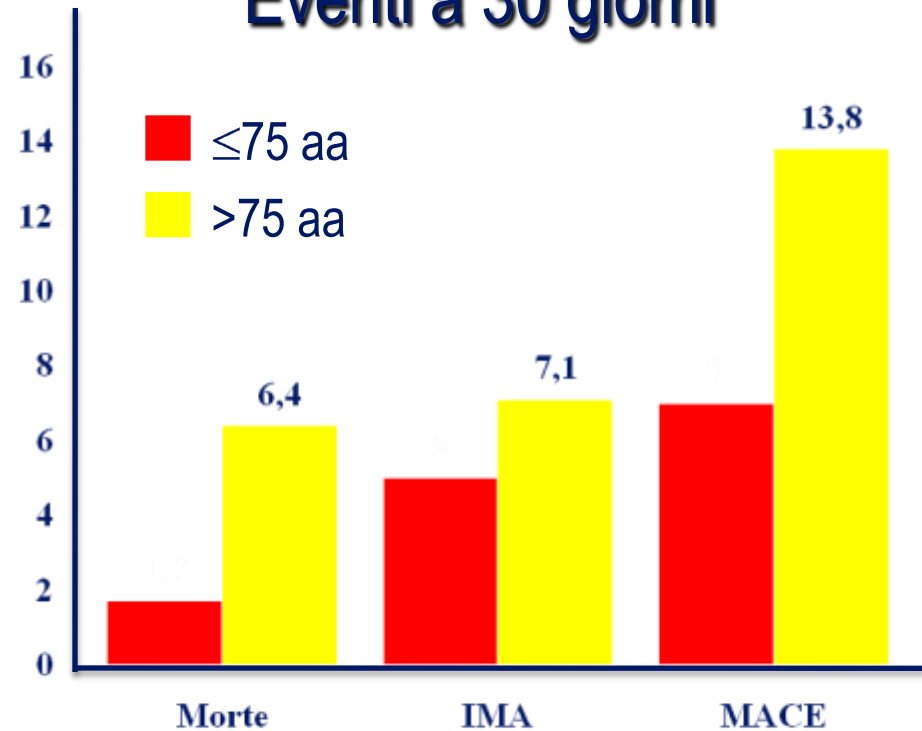
Data derived from a single randomized clinical trial or large non-randomized studies.

Cardiovascular death or myocardial infarction after a routine invasive or selective invasive strategy according to age.

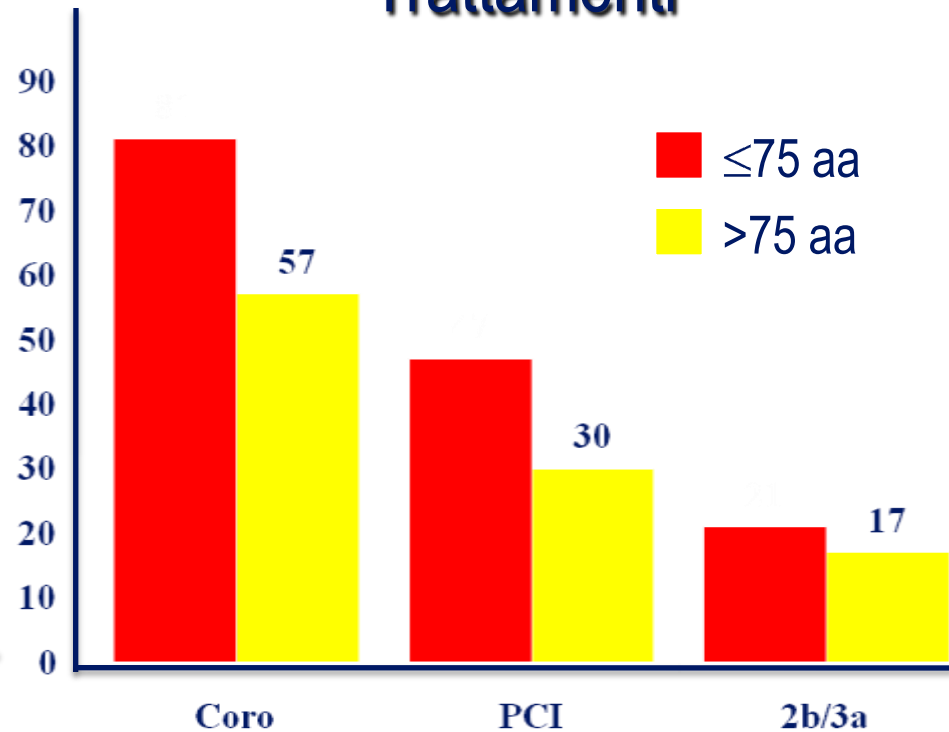
A meta-analysis from the FRISC II, ICTUS and RITA-3 trials.



Eventi a 30 giorni



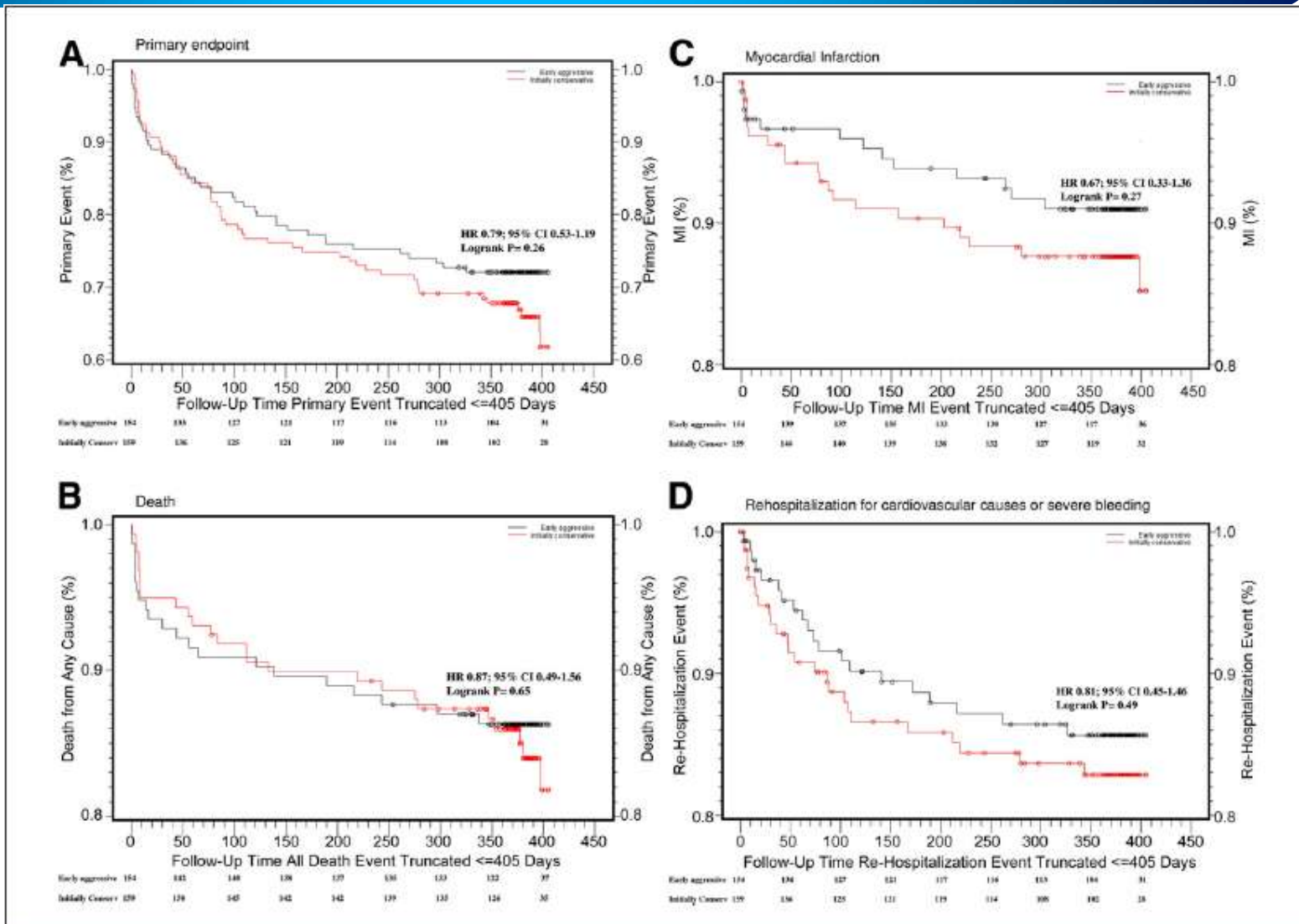
Trattamenti



Strategia Conservativa: OR 2,31 (1,20-4,48) eventi a 30 giorni

Early Aggressive Versus Initially Conservative Treatment in Elderly Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. A Randomized Controlled Trial

313 pts 75 years of age (mean 82 yrs)



ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

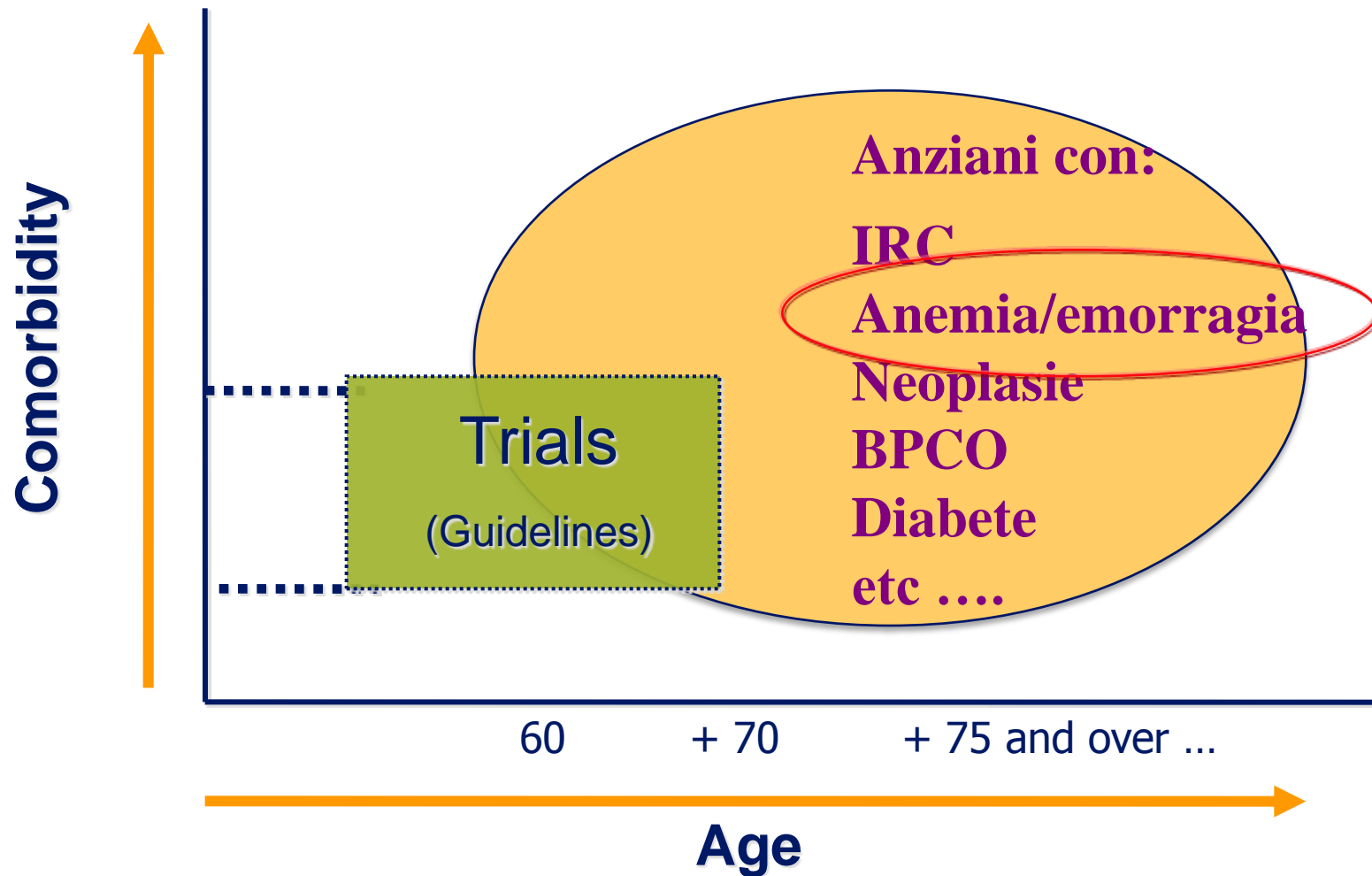
Recommendations for elderly patients

Recommendations	Class ^a	Level ^b
Treatment decisions in the elderly (>75 years) should be made in the context of estimated life expectancy, co-morbidities, quality of life, and patient wishes and preferences.	I	C

Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.

Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

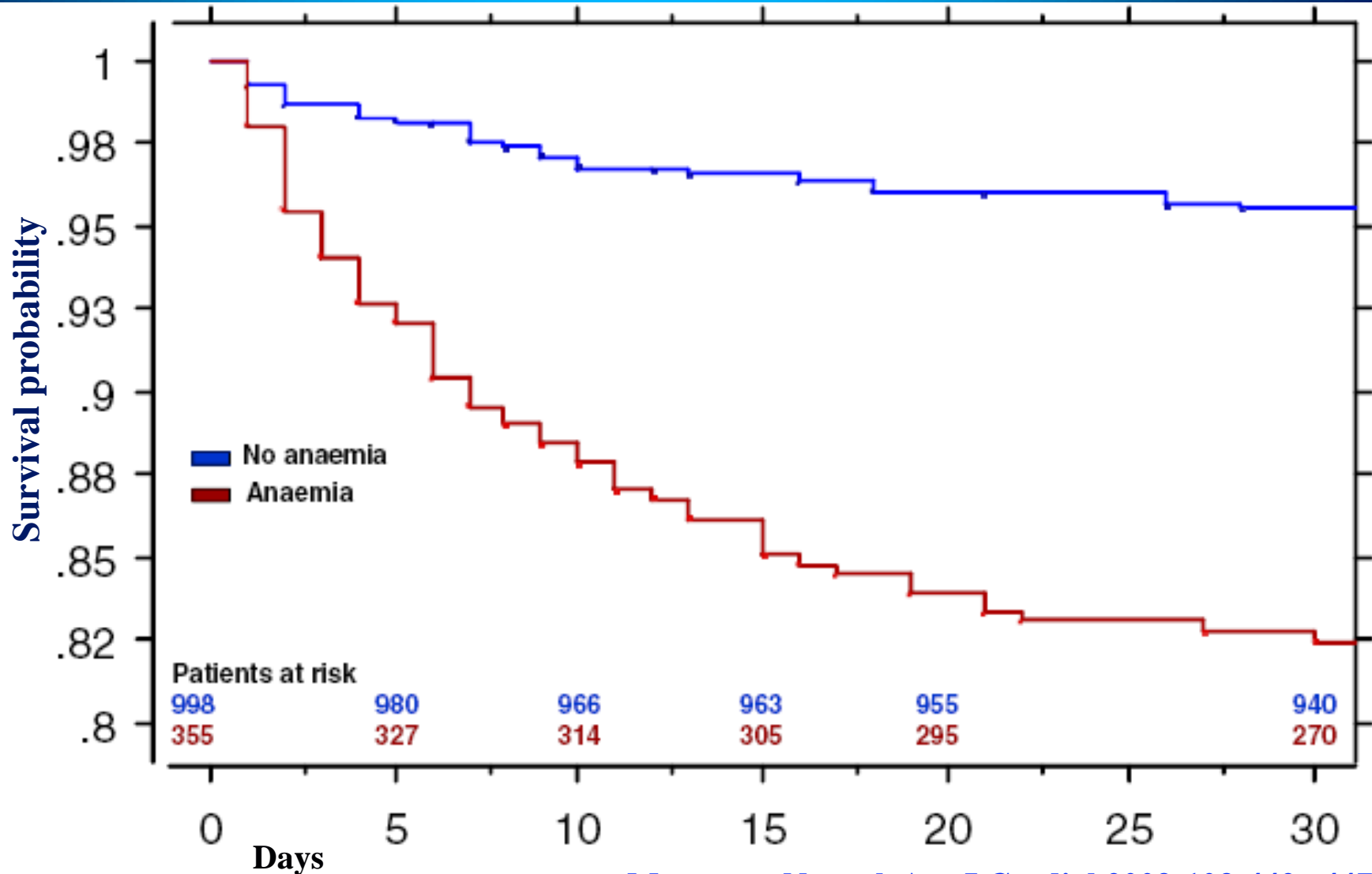
Applying Evidence-Based Medicine IN THE REAL WORD which proportion ?



L'anemia è presente nel 15-30% dei soggetti con sindrome coronarica acuta

Tale percentuale aumenta durante il ricovero ospedaliero e tende ad essere superiore a quella basale al momento della dimissione.

Kaplan-Meier curves of 30-day survival probability according to the presence of anemia at admission in patients with Acute Coronary Syndromes



Comparison of clinical characteristics according to the presence of anemia at admission in the Registre Franc Comtois des Syndromes Coronariens Aigus

Variable	Overall Cohort (n = 1,410)	Anemia (n = 381)	No Anemia (n = 1,029)	p Value
Non-ST elevation myocardial infarction	845 (60%)	262 (69%)	583 (57%)	<10 ⁻⁴
Men	926 (65%)	231 (61%)	695 (68%)	0.015
Age* (yrs)	70 ± 14	75 (13%)	66 (13%)	0.001
Diabetes mellitus	330 (23%)	126 (33%)	204 (20%)	<10 ⁻⁴
High blood pressure	794 (56%)	253 (66%)	541 (53%)	<10 ⁻⁴
Hypercholesterolemia	664 (47%)	167 (44%)	497 (48%)	0.13
Current smoker	359 (25%)	102 (27%)	257 (25%)	0.24
Previous myocardial infarction	263 (19%)	93 (24%)	170 (17%)	0.0007
Killip class				<0.0001
I	1,202 (85%)	286 (75%)	916 (89%)	
II	127 (9%)	65 (17%)	62 (6%)	
III	50 (4%)	19 (5%)	31 (3%)	
IV	31 (2%)	11 (3%)	20 (2%)	
Previous coronary angioplasty	197 (14%)	58 (15%)	139 (13%)	0.41
Previous coronary bypass	70 (5%)	30 (8%)	40 (4%)	0.002
Stroke	79 (6%)	29 (8%)	50 (5%)	0.005
Peripheral vessel disease	174 (12%)	73 (19%)	101 (10%)	<10 ⁻⁴
Glomerular filtration rate (ml/min/1.73 m ²)				
>60	899 (64%)	166 (44%)	733 (71%)	<10 ⁻⁴
30–60	431 (31%)	164 (43%)	267 (26%)	<10 ⁻⁴
<30	80 (5%)	51 (13%)	29 (3%)	<10 ⁻⁴
Fasting glucose (mmol/L)	6.4 ± 1.8	6.6 ± 1.4	6.2 ± 1.4	0.02
B-Type natriuretic peptide* (pg/ml)	287 (104–891)	730 (283–1727)	196 (81–542)	<10 ⁻⁴
High-sensitivity C-reactive protein* (mg/dl)	6.5 (3–23)	16.2 (4.7–73)	5.2 (2.1–15)	<10 ⁻⁴
Serum creatinine (μmol/L)	107 ± 61	129 ± 82	99 ± 51	<10 ⁻⁴



Perché l'anemia peggiora la prognosi delle SCA?

Tamara De Lempicka

1. Modifiche della terapia

2. Alterazioni emodinamiche

3. Cause ischemiche

- Effetti pro-infiammatori
- Effetti pro-trombotici

} Instabilizzazione della placca

4. Aumento delle emorragie

Hospital therapies and procedures according to presence of anemia

(Worcester Heart Attack Study)

1

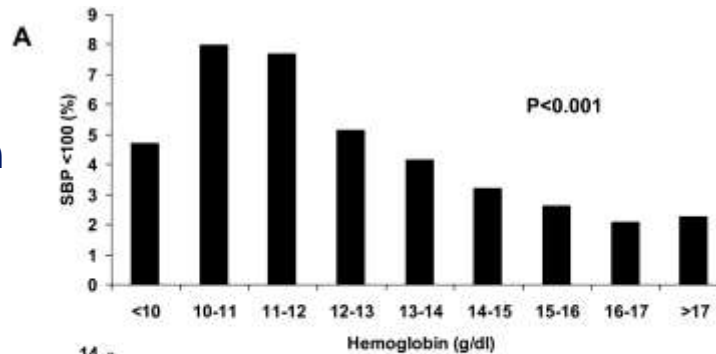
Modifiché Tx

Therapy	Anemia		p Value
	Present (n = 1,681)	Absent (n = 3,697)	
ACE inhibitors	52.9%	53.3%	0.83
Aspirin	87.9%	93.3%	<0.001
β Blockers	79.4%	85.3%	<0.001
Calcium channel blockers	31.4%	26.4%	<0.005
Digoxin	33.6%	24.9%	<0.001
Lipid-lowering agents	39.4%	44.7%	<0.005
Thrombolytics	7.9%	17.6%	<0.001
Warfarin	15.0%	14.3%	0.49
Cardiac catheterization	34.4%	52.3%	<0.001
Coronary angioplasty	17.7%	29.4%	<0.001
Coronary bypass surgery	5.1%	6.8%	<0.05

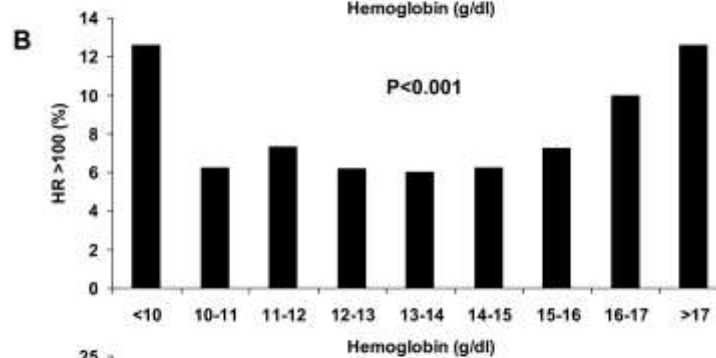
Prevalence of hypotension, tachycardia and Killip class 2 to 4 in patients with STEMI stratified by baseline hemoglobin values.

2

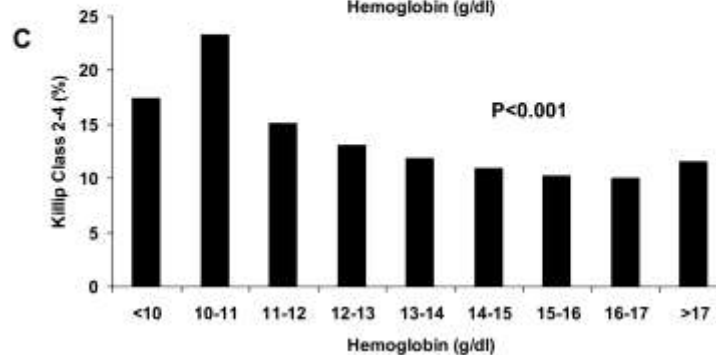
Alterazioni emodinamiche Hypotension



Tachycardia



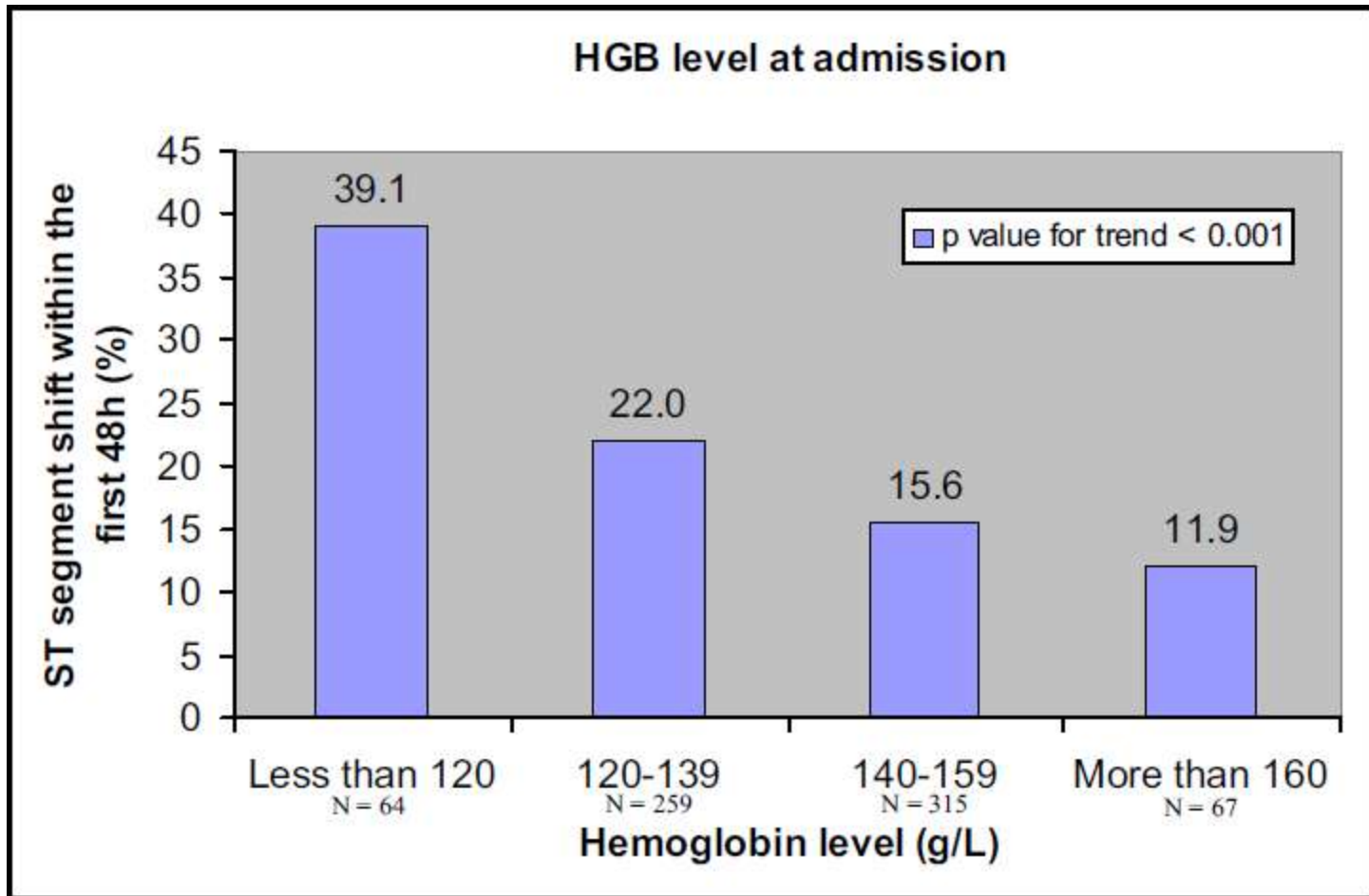
Killip class 2 to 4



Relation Between Hemoglobin Level and Recurrent Myocardial Ischemia in ACS Detected by Continuous Electrocardiographic Monitoring

3

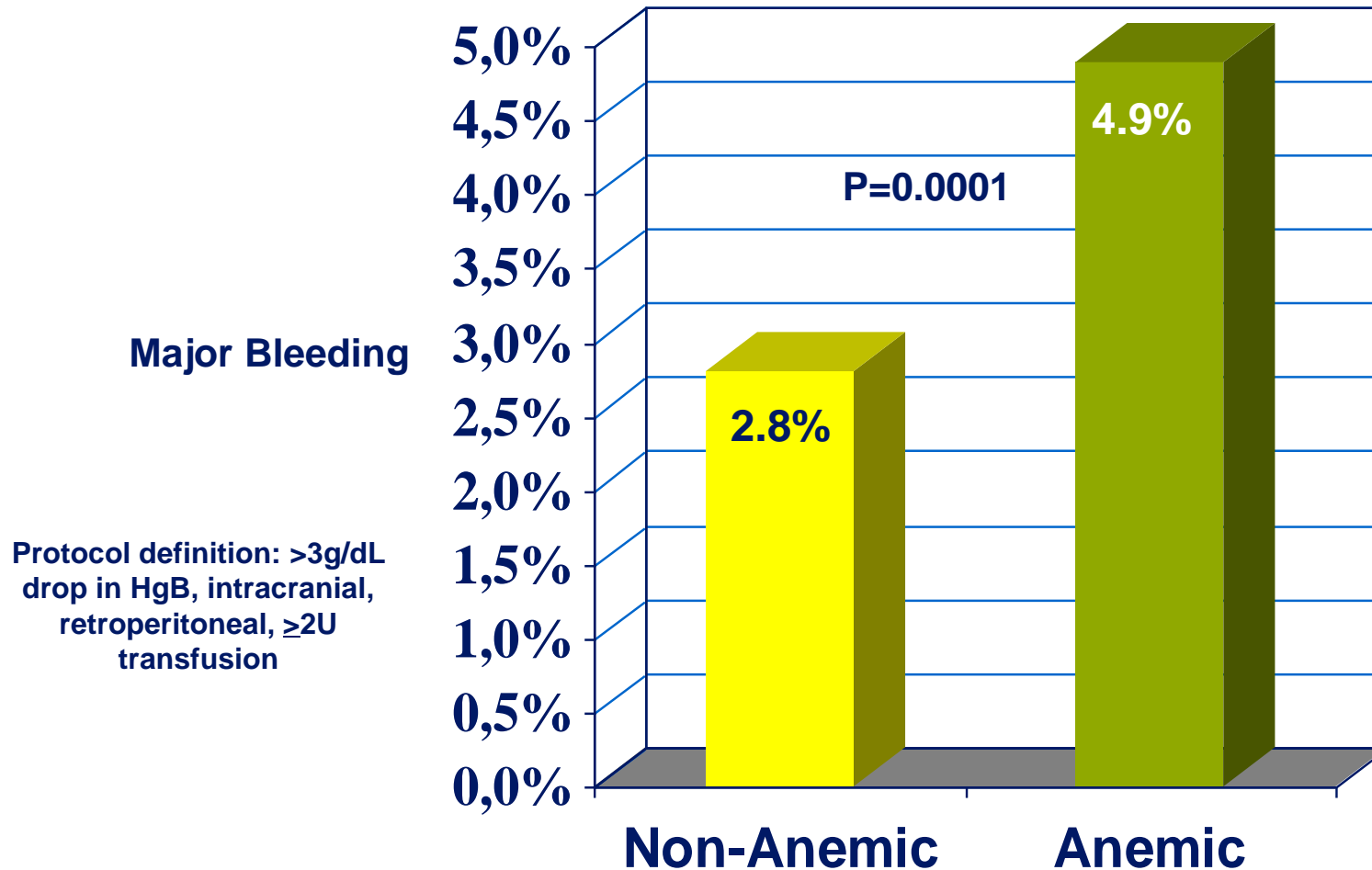
Induzione ischemia



Major Bleeding and Anemia in PCI

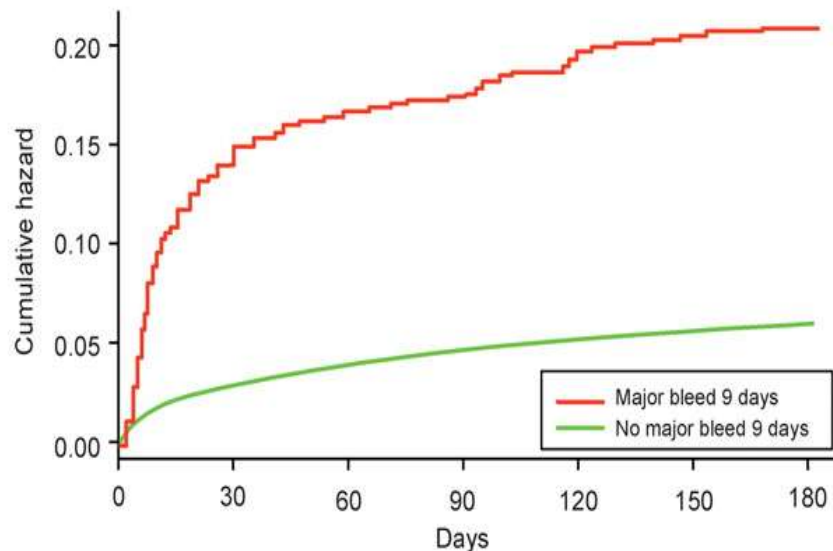
The REPLACE-2 Trial (N=6,010)

4



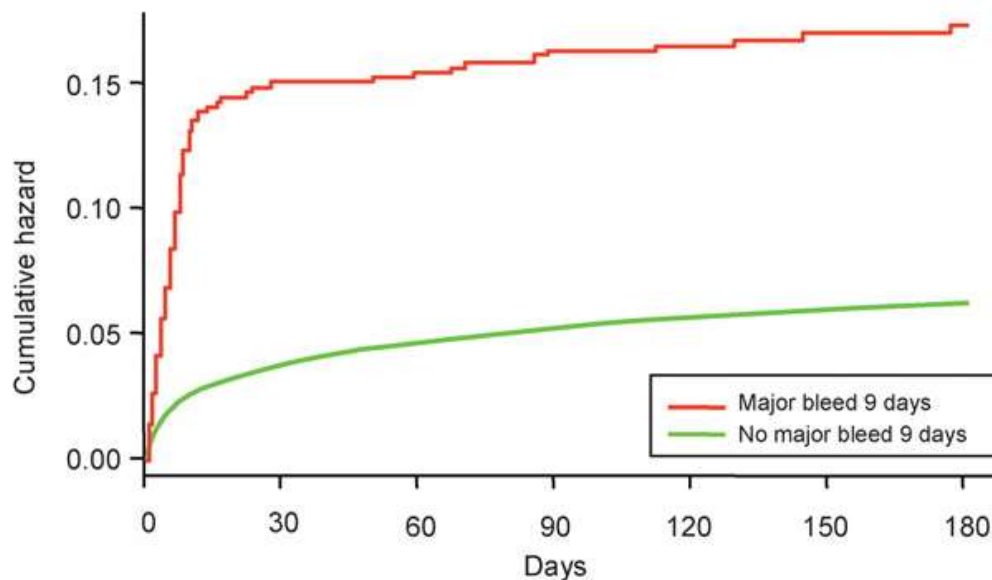
Emorragia nelle SCA: effetti sulla prognosi

(A) Mortality



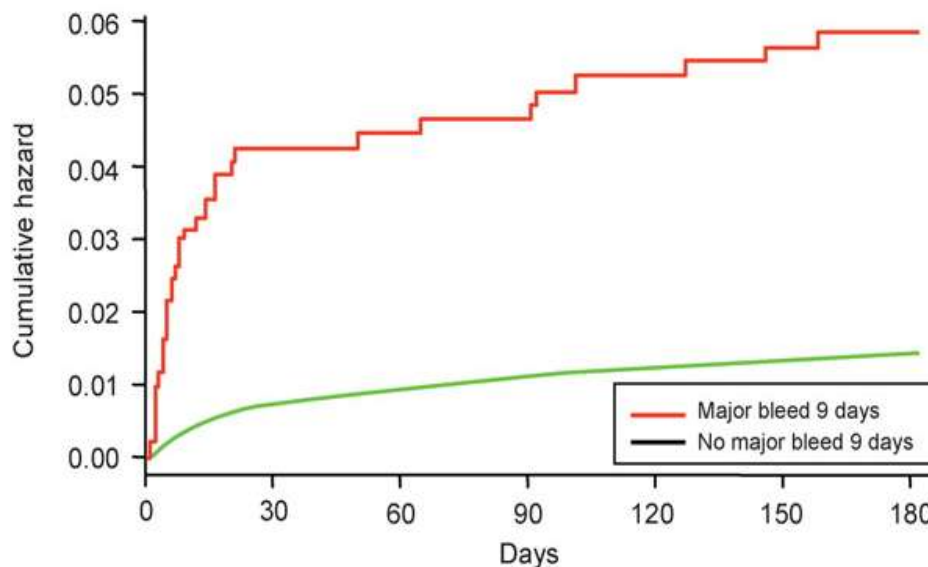
Adjusted HR (95% CI) at day 30: 5.06 (4.59–5.62); at day 180: 3.16 (2.92–3.44)

(B) Myocardial infarction



Adjusted HR (95% CI) at day 30: 5.01 (4.56–5.57); at day 180: 2.99 (2.75–3.28)

(C) Stroke



Adjusted HR (95% CI) at day 30: 4.77 (3.95–6.00); at day 180: 3.30 (2.82–3.97)

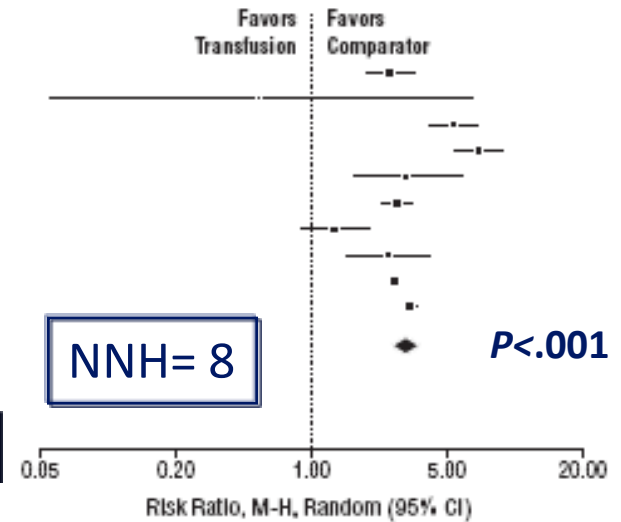
Trasfondere o non trasfondere?



Association of Blood Transfusion With Increased Mortality in Myocardial Infarction. A Meta-analysis

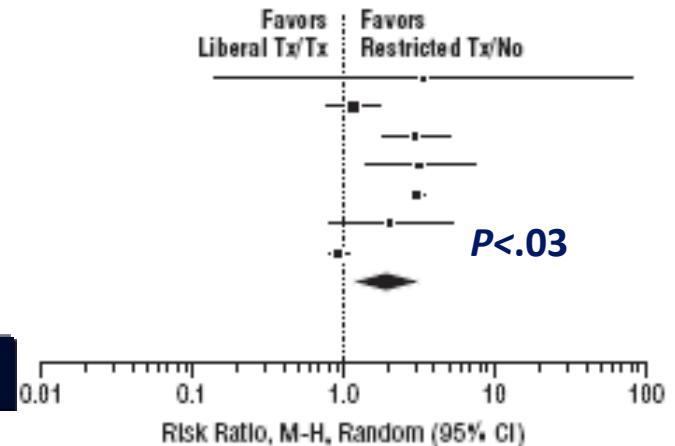
Source	Transfusion or Liberal		No Transfusion or Restricted		Weight. %	Risk Ratio, M-H, Random (95% CI)
	Events	Total	Events	Total		
Aronson et al, ³⁰ 2008	54	192	250	2134	11.4	2.40 (1.86-3.10)
Cooper et al, ³¹ 2011	1	21	2	24	0.5	0.57 (0.06-5.86)
Jani et al, ³² 2007	150	1033	108	3590	11.8	4.83 (3.81-6.12)
Jolicoeur et al, ³³ 2009	53	204	203	4984	11.1	6.38 (4.88-8.34)
Nikolsky et al, ³⁴ 2009	11	82	87	1891	5.3	2.92 (1.62-5.24)
Rao et al, ³⁵ 2004	192	2401	669	21711	13.6	2.60 (2.22-3.03)
Shishebor et al, ³⁶ 2009	39	292	67	651	8.8	1.30 (0.90-1.88)
Singla et al, ³⁷ 2007	29	110	29	260	7.1	2.36 (1.49-3.76)
Wu et al, ³⁸ 2001	1778	3690	14432	75 284	15.3	2.51 (2.42-2.61)
Yang et al, ³⁹ 2005	1463	12724	2751	72387	15.1	3.03 (2.85-3.21)
Total (95% CI)		20749		182916	100.0	2.91 (2.46-3.44)
Total events	3770		18598			
Heterogeneity: $\tau = 0.05$; $\chi^2 = 110.72$ ($P < .001$), $I^2 = 92\%$						
Test for overall effect: $z = 12.48$ ($P < .001$)						

Risk for all-cause mortality

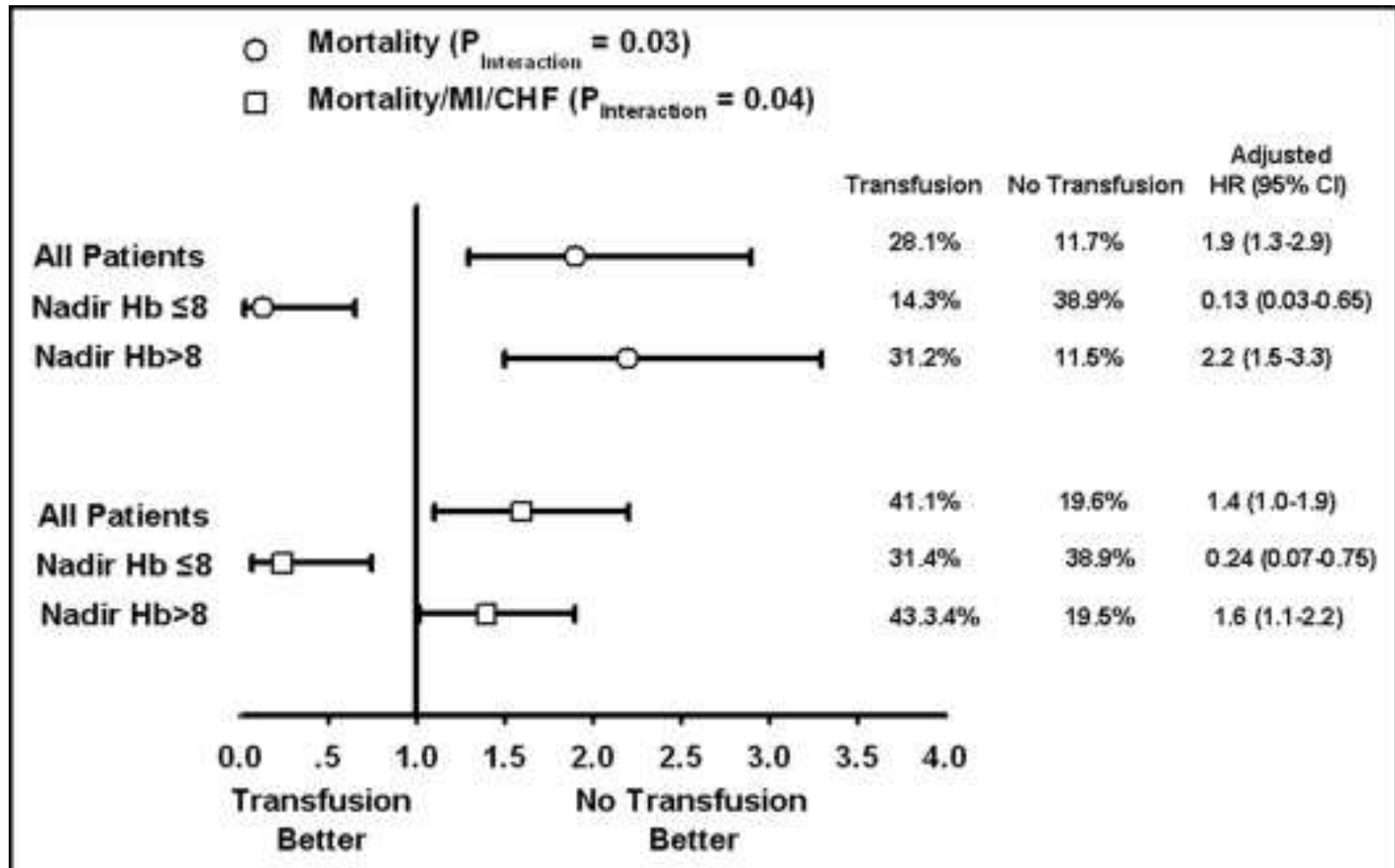


Source	Transfusion or Liberal		No Transfusion or Restricted		Weight. %	Risk Ratio M-H, Random (95% CI)
	Events	Total	Events	Total		
Cooper et al, ³¹ 2011	1	21	0	24	3.5	3.41 (0.15-79.47)
Jani et al, ³² 2007	35	1033	102	3590	17.0	1.19 (0.82-1.74)
Jolicoeur et al, ³³ 2009	16	204	128	4984	16.3	3.05 (1.85-5.04)
Nikolsky et al, ³⁴ 2009	6	82	44	1975	14.0	3.28 (1.44-7.49)
Rao et al, ³⁵ 2004	604	2401	1771	21711	18.0	3.08 (2.84-3.35)
Singla et al, ³⁷ 2007	8	110	9	260	13.3	2.10 (0.83-5.30)
Yang et al, ³⁹ 2005	242	12724	1447	72387	17.9	0.95 (0.83-1.09)
Total (95% CI)		16575		104931	100.0	2.04 (1.06-3.93)
Total events	912		3501			
Heterogeneity: $\tau = 0.62$; $\chi^2 = 246.84$ ($P < .001$), $I^2 = 98\%$						
Test for overall effect: $z = 2.14$ ($P = .03$)						

Risk for myocardial infarction



Impact of Red Blood Cell Transfusion on Clinical Outcomes in Patients With Acute Myocardial Infarction



Perché le
emorragie e le
trasfusioni
peggiorano la
prognosi?

Boldini, Lady Colin Campbell



Intracranial bleeding

Blood transfusion

↓ O₂ delivery
Prothrombotic?
Proinflammatory?

Ischemic events

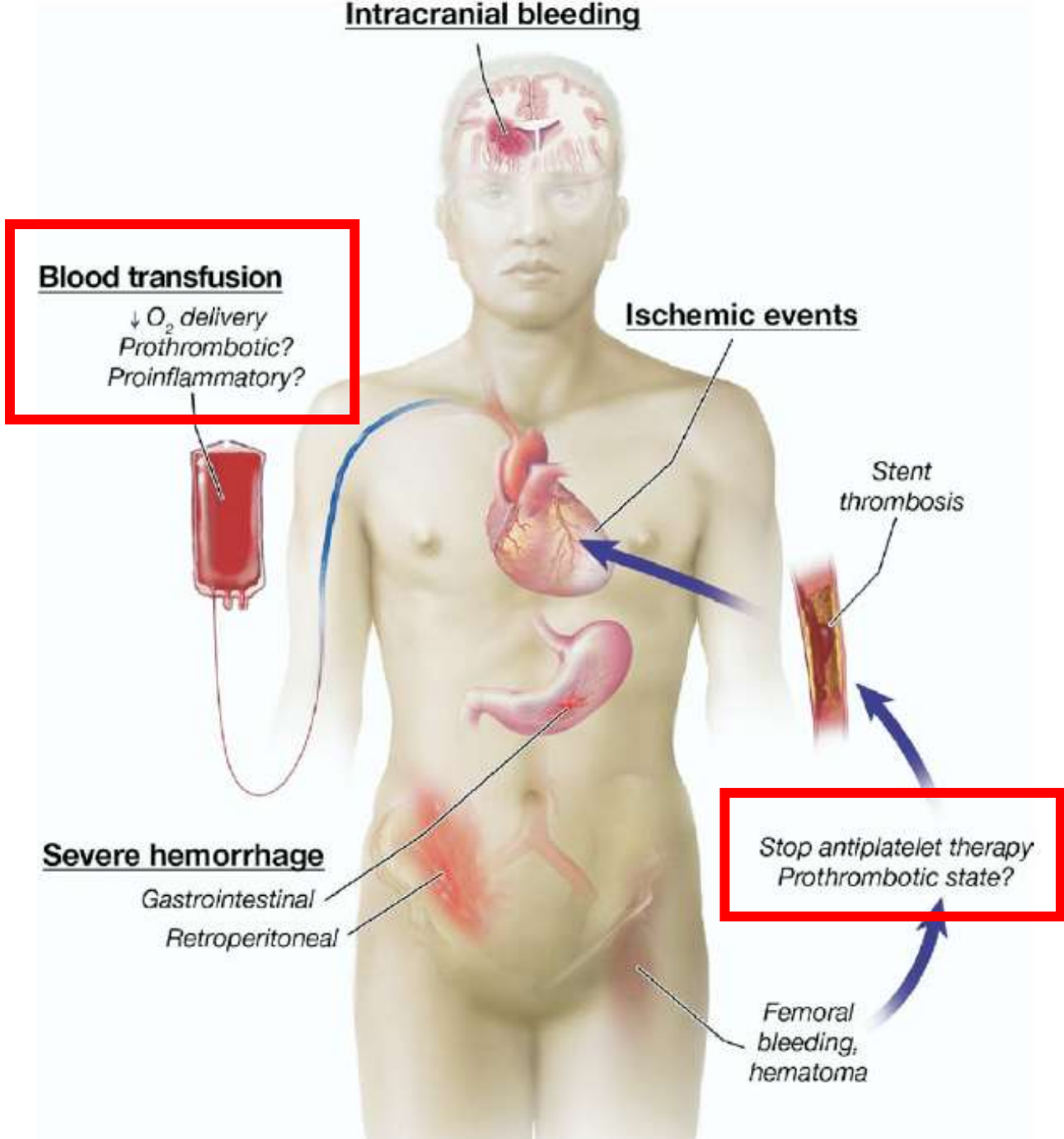
Stent thrombosis

Severe hemorrhage

Gastrointestinal
Retroperitoneal

Stop antiplatelet therapy
Prothrombotic state?

Femoral bleeding,
hematoma



Emorragia
in corso di SCA:

sospendere gli
antiaggreganti?

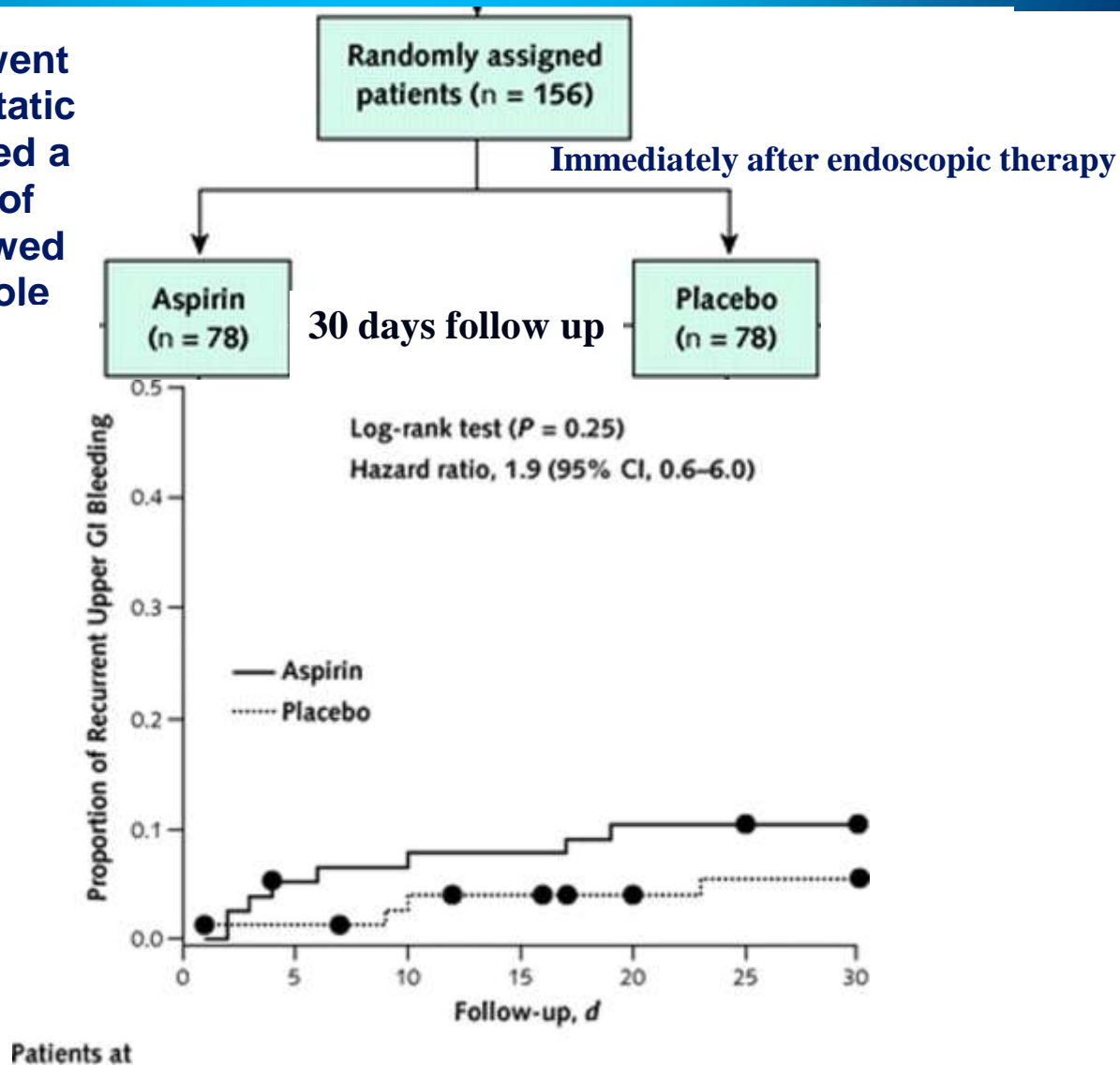
SI

...ma per quanto
tempo?



Continuation of Low-Dose Aspirin Therapy in Peptic Ulcer Bleeding A Randomized Double Blinded placebo-controlled Trial

All patients underwent endoscopic hemostatic therapy and received a 72-hour infusion of pantoprazole followed by oral pantoprazole

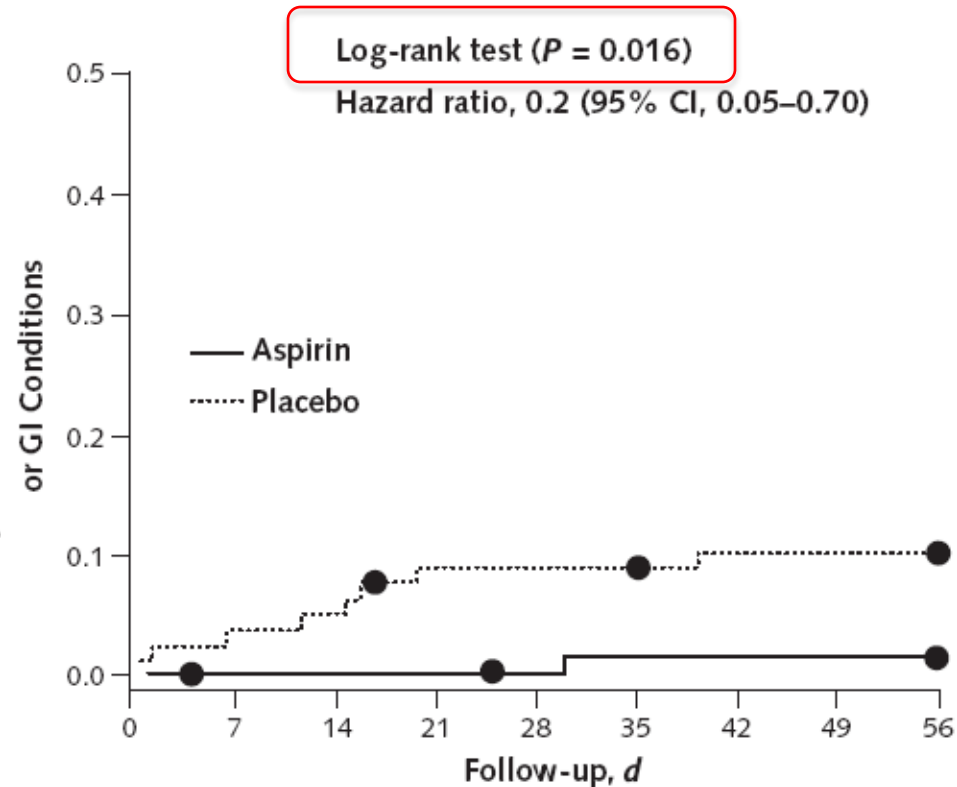
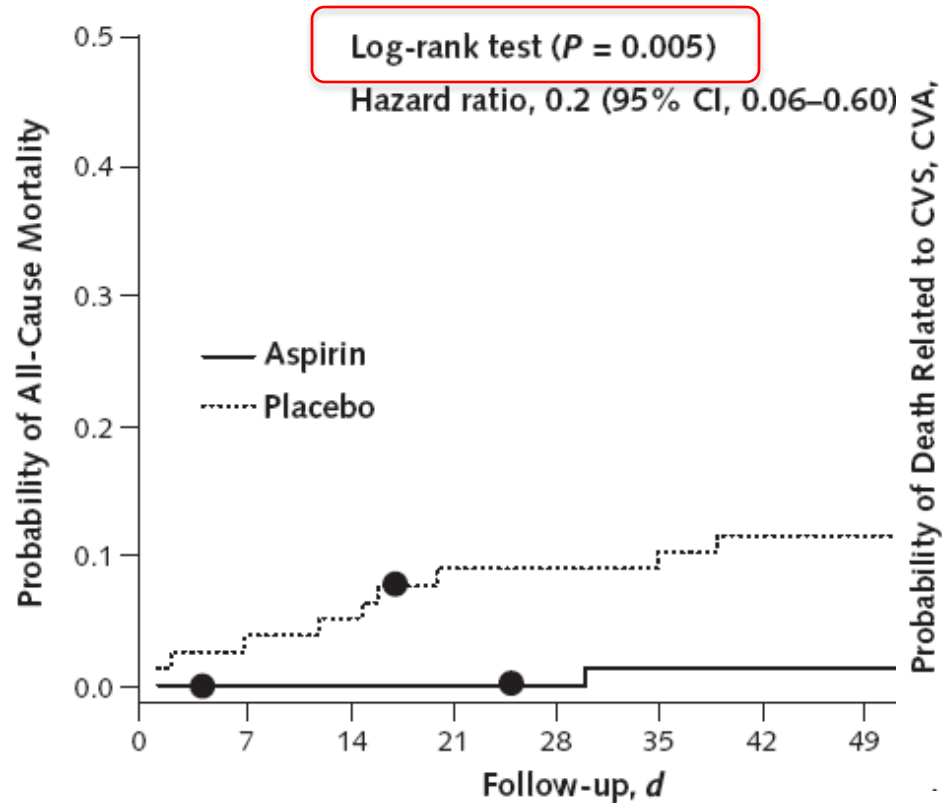


Continuation of Low-Dose Aspirin Therapy in Peptic Ulcer Bleeding A Randomized Double Blinded placebo-controlled Trial

EDITORIAL

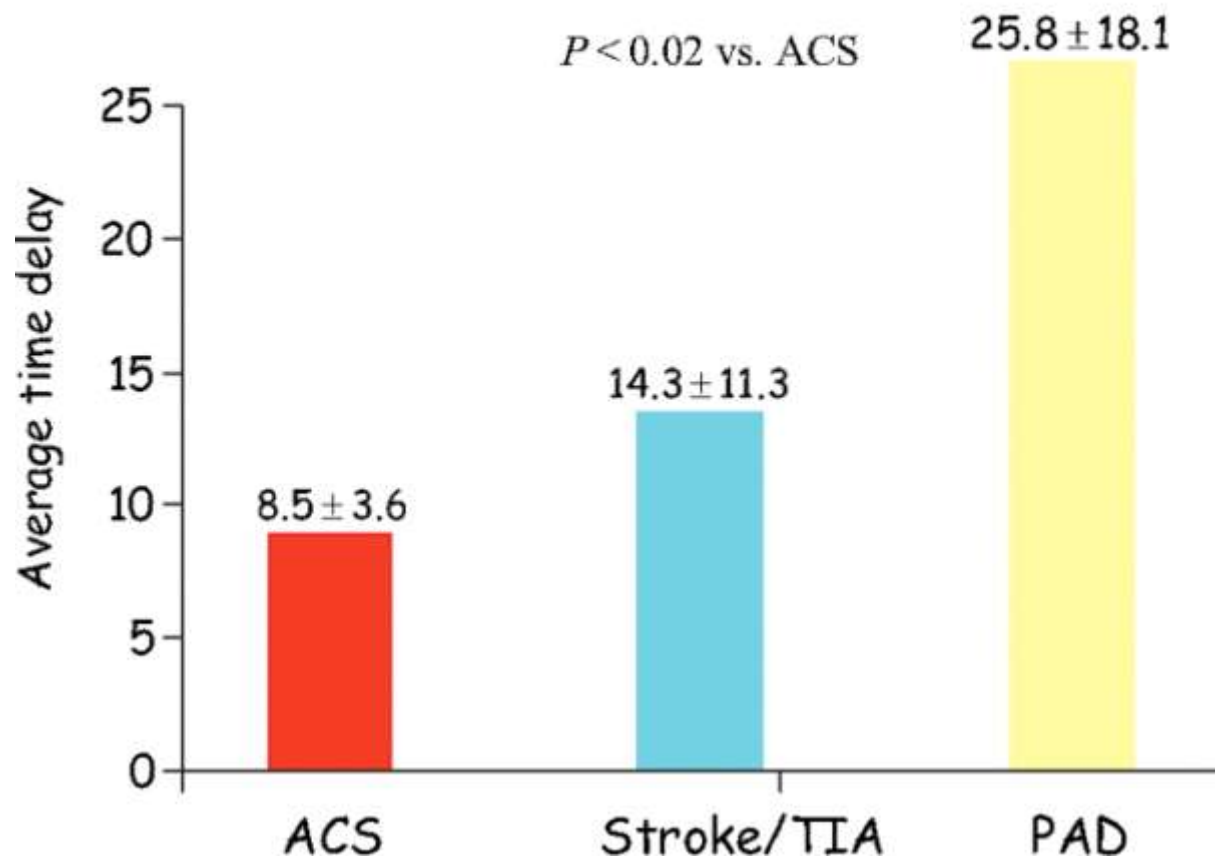
Annals of Internal Medicine

Aspirin Withdrawal in Acute Peptic Ulcer Bleeding: Are We Harming Patients?



Temporal relationship between oral antiplatelet agent interruption and recurrent vascular event

Aspirin withdrawal precedes up to 10.2% of acute cardiovascular syndromes



International Consensus Recommendations on the Management of Patients With Nonvariceal Upper Gastrointestinal Bleeding

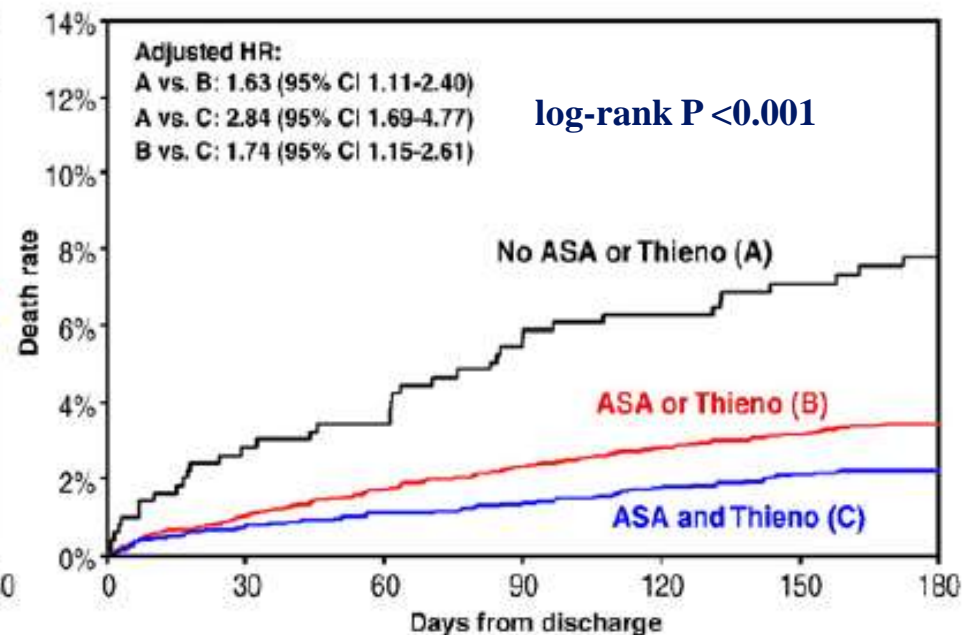
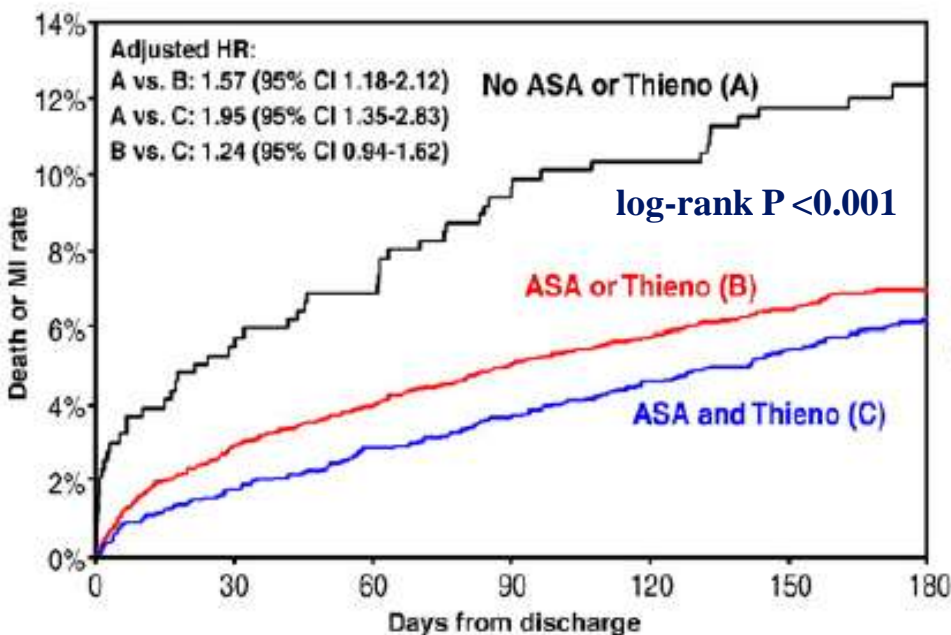
Alan N. Barkun, MD, MSc (Clinical Epidemiology); Marc Bardou, MD, PhD; Ernst J. Kuipers, MD; Joseph Sung, MD; Richard H. Hunt, MD; Myriam Martel, BSc; and Paul Sinclair, MSc, for the International Consensus Upper Gastrointestinal Bleeding Conference Group*

Statement E3

In patients who receive low-dose ASA and develop acute ulcer bleeding, ASA therapy should be restarted as soon as the risk for cardiovascular complication is thought to outweigh the risk for bleeding.

(Agree, 100% [Vote: a, 70%; b, 30%]. Grade: Moderate, 1b, **“do it”**)

Antiplatelet prescription at discharge and late outcomes among 8,582 patients with bleeding during ACS: a pooled analysis from PURSUIT, PARAGON-A, PARAGON-B, and SYNERGY.



Intracranial bleeding

Blood transfusion

↓ O₂ delivery
Prothrombotic?
Proinflammatory?

Ischemic events

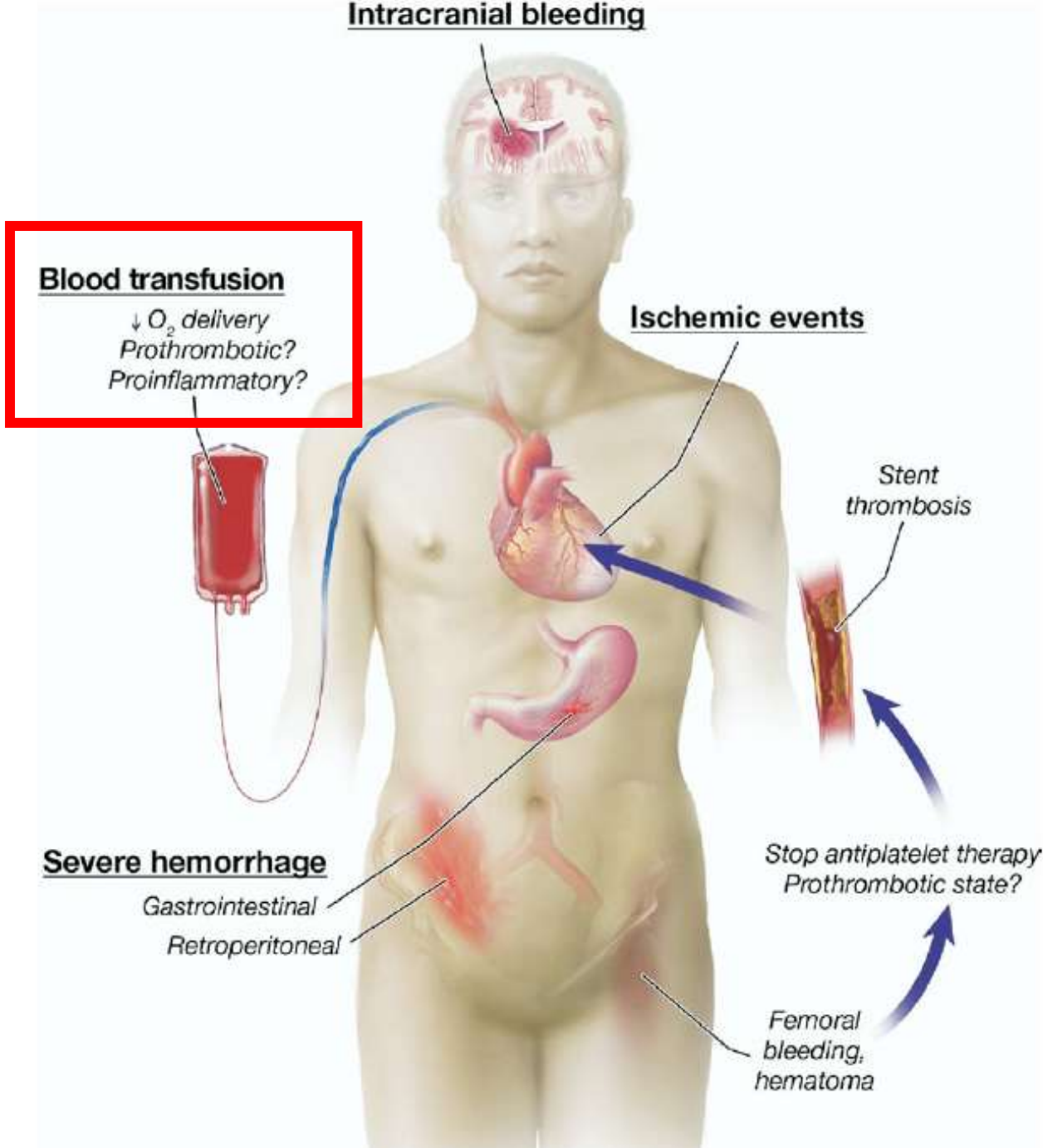
Stent
thrombosis

Severe hemorrhage

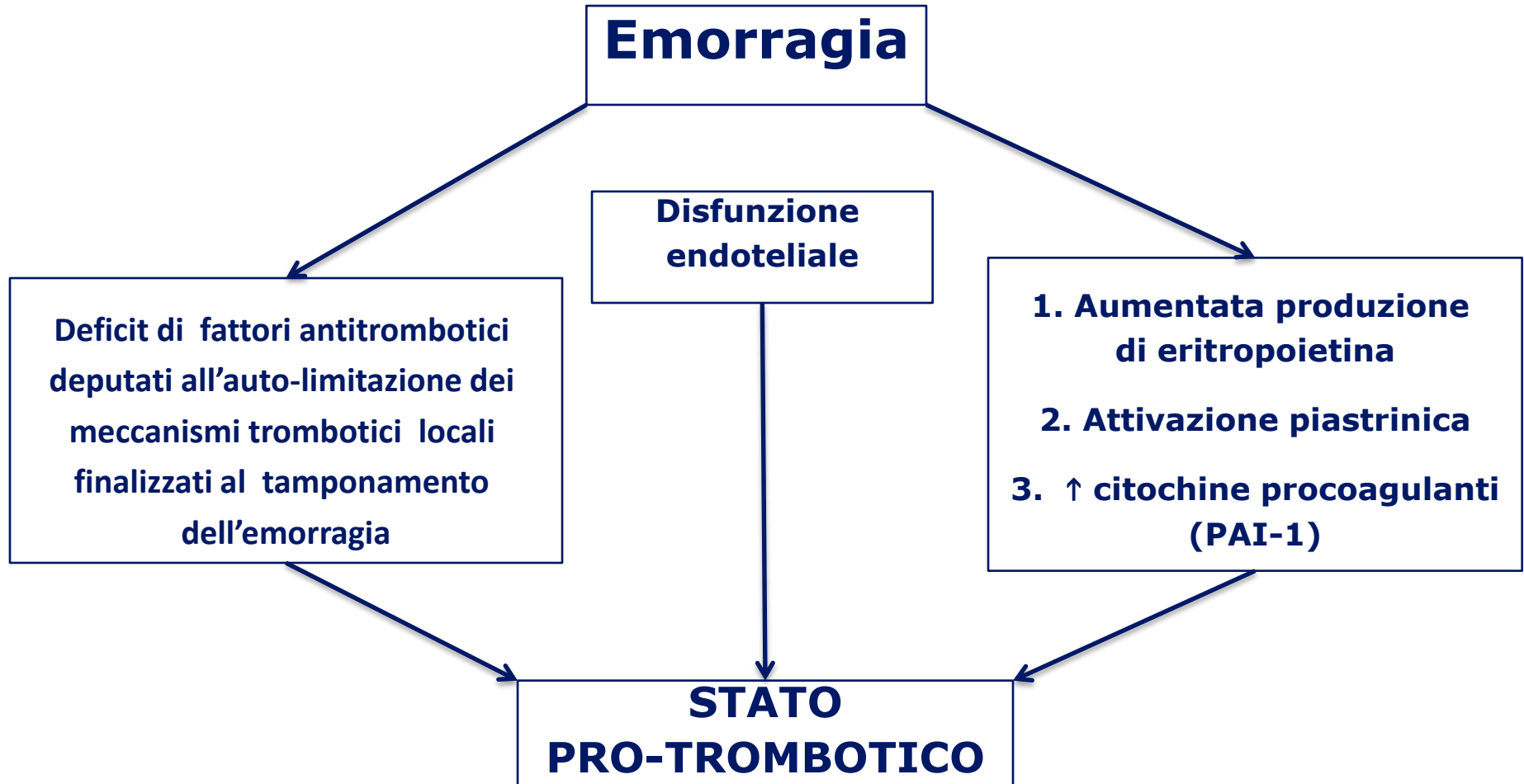
Gastrointestinal
Retroperitoneal

Stop antiplatelet therapy
Prothrombotic state?

Femoral
bleeding,
hematoma



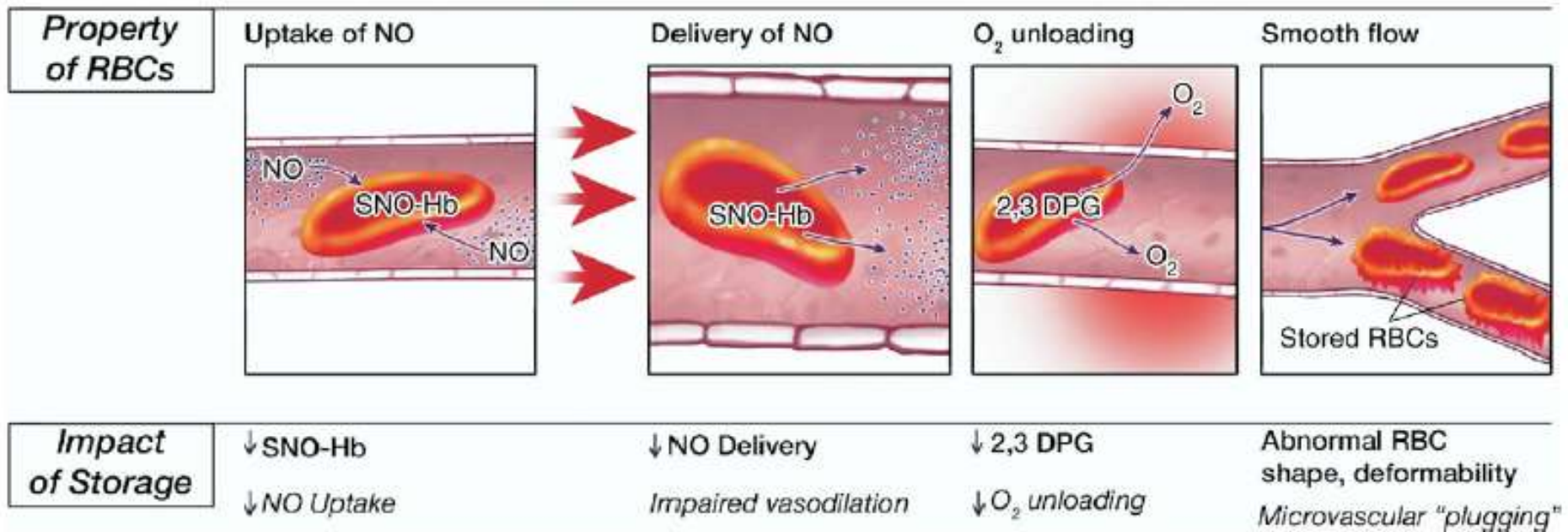
Stato protrombotico post-emorragia nelle SCA



Lane DA, et al. Blood 2005;106:2605–12.
Taylor JE, et al. Lancet 1991;338:1361–2.
Smith KJ, et al. Cardiovasc Res 2003;59:538–48.

Trasfusioni e rischio trombotico. 1

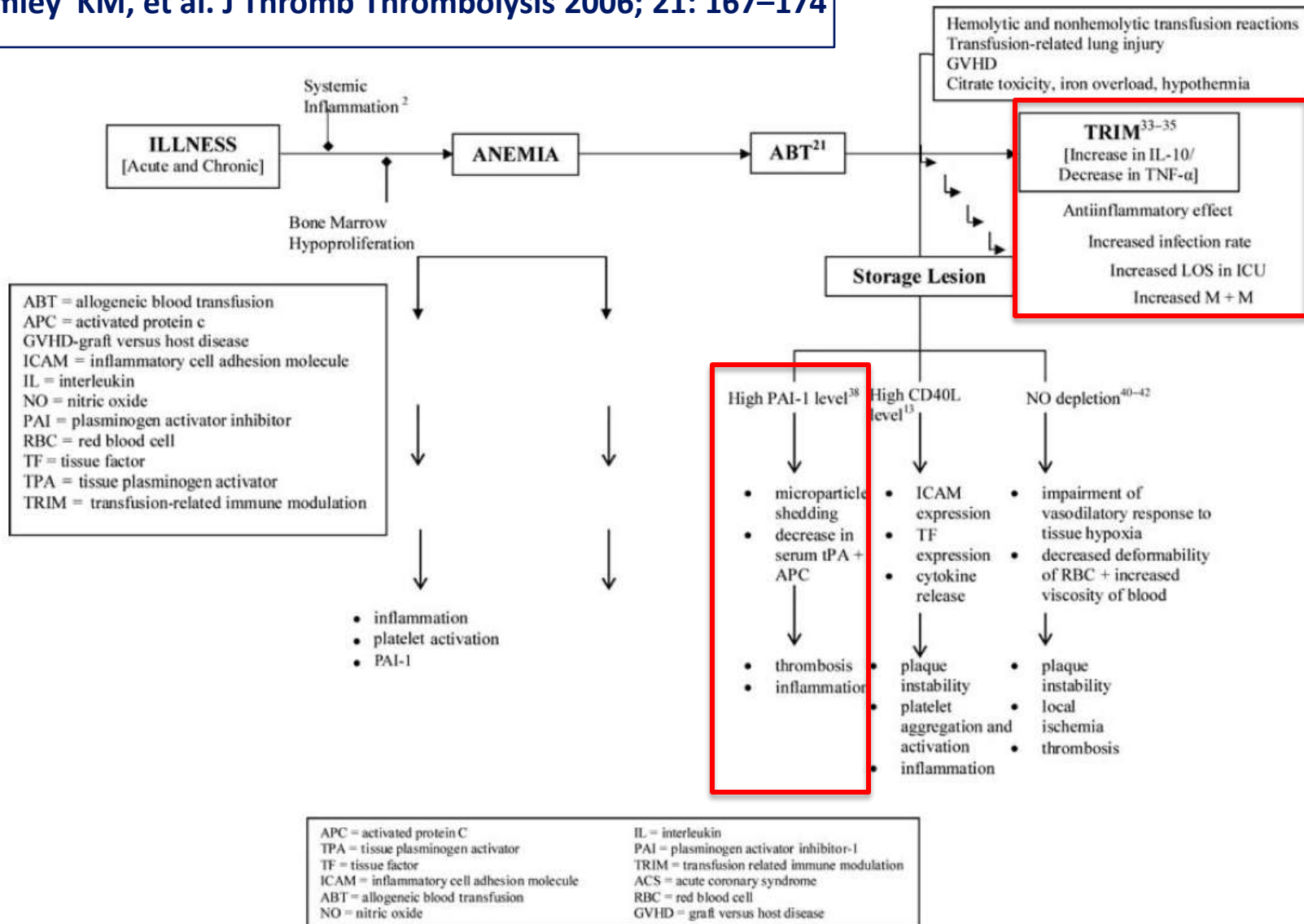
Impact of Storage on RBCs and Tissue Oxygen Delivery



DPG = diphosphoglycerate; Hb = hemoglobin; NO = nitric oxide; RBC = red blood cell; SNO = S-nitrosothiol.

Trasfusioni e rischio trombotico. 2

Twomley KM, et al. J Thromb Thrombolysis 2006; 21: 167–174



A scenic view of the Dolomites mountains. The central focus is a large, rugged mountain peak with a snowfield at its base. The foreground is filled with dense green forest, and a small town is visible in the valley to the left. The sky is filled with large, white clouds.

**Molte grazie
per la cortese attenzione**