L'algoritmo per una gestione moderna dell'angina stabile

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PL. Temporelli

Istituti Clinici Scientifici Maugeri
Divisione di Cardiologia Riabilitativa, Veruno

AP maschio a. 71

Paziente dimesso in Va giornata con diagnosi di SCA STEMI inferiore in monovaso Dx trattata con PTCA primaria e impianto di BMS. FE 54%
Stenosi subcritica 50% su Cx media.
Ipertensione, dislipidemia, abitudine tabagica.

Terapia:
Pantoprazolo 20 mg 1 cp al mattino a digiuno
Metoprololo 100 mg1/2 cp ore 8-20
Ramipril 2.5 mg 1 cp ore 8
Cardioaspirina 1 cp dopo pranzo
Ticagrelor 1 cp mattina e sera
Atorvastatina 80 mg 1 cp dopo cena

Raccomandazioni per sospensione fumo
Programma di controllo ambulatoriale a 30 giorni

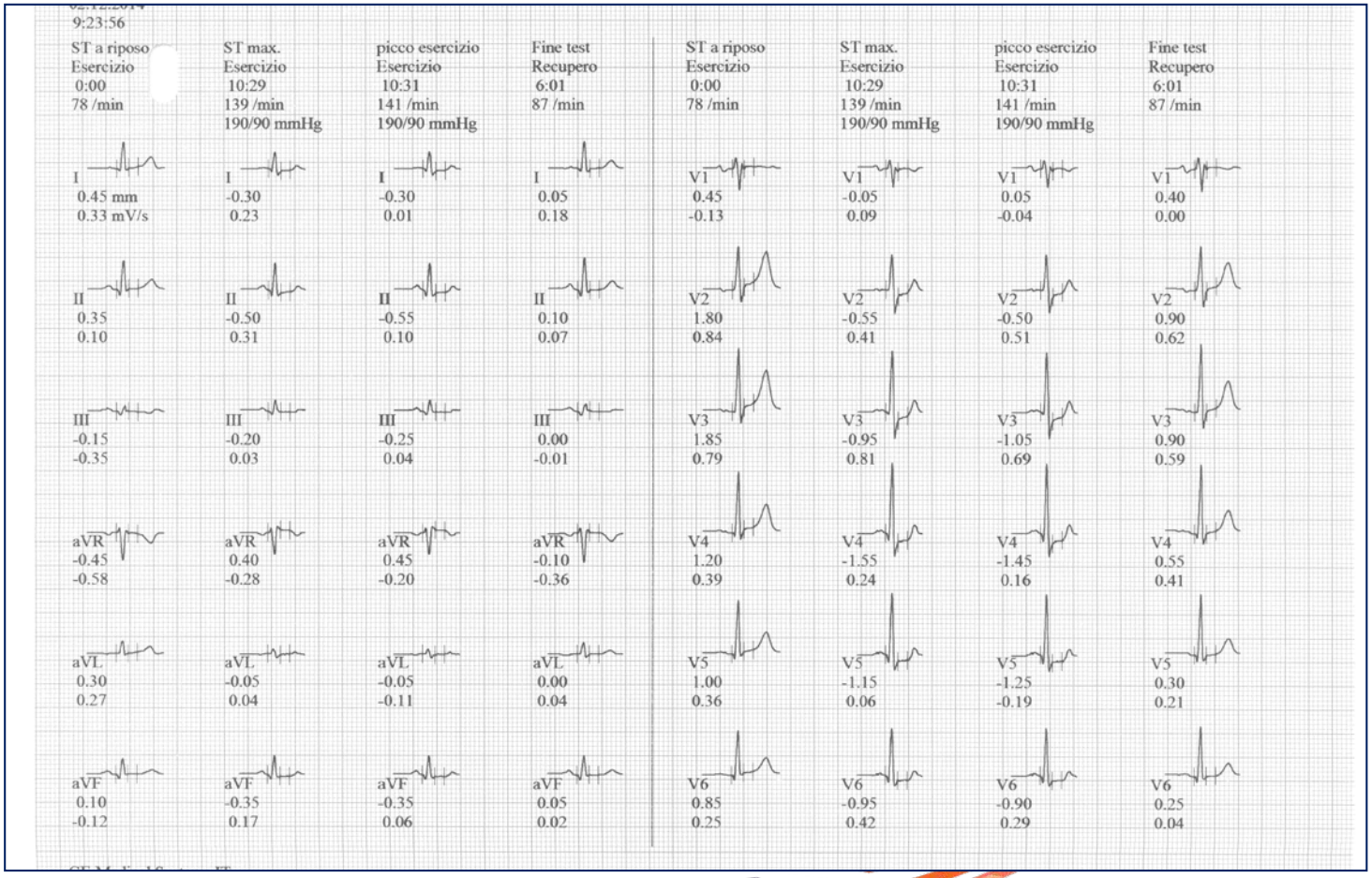
AP maschio a. 71

- ✓ Visita a 30 giorni: confermata terapia in atto e ribadite raccomandazioni per sospensione fumo
- ✓ A 6 mesi circa il cardiologo curante, in assenza di sintomi, decide di far eseguire test ergometrico in sospensione parziale terapia betabloccante (24 h)
- ✓ Il paziente ha ridotto ma non sospeso il fumo
- ✓ Nel frattempo ridotta atorvastatina a 20 mg/die
- ✓ LDL 94 mg/dl; altri parametri ematochimici nella norma

Test da sforzo al cicloergometro

Test interrotto a **125 w 1 min** (prot. 25 w ogni 3') per fatica muscolare, FC max 141 bpm (a riposo 67 bpm), con incremento PAS da 120 a riposo a 190 mmHg al picco, in presenza di **lieve sotto-ST asintomatico al max carico** (<1 mm) in V3-V6 (**DP 26.600**) a rapido recupero.

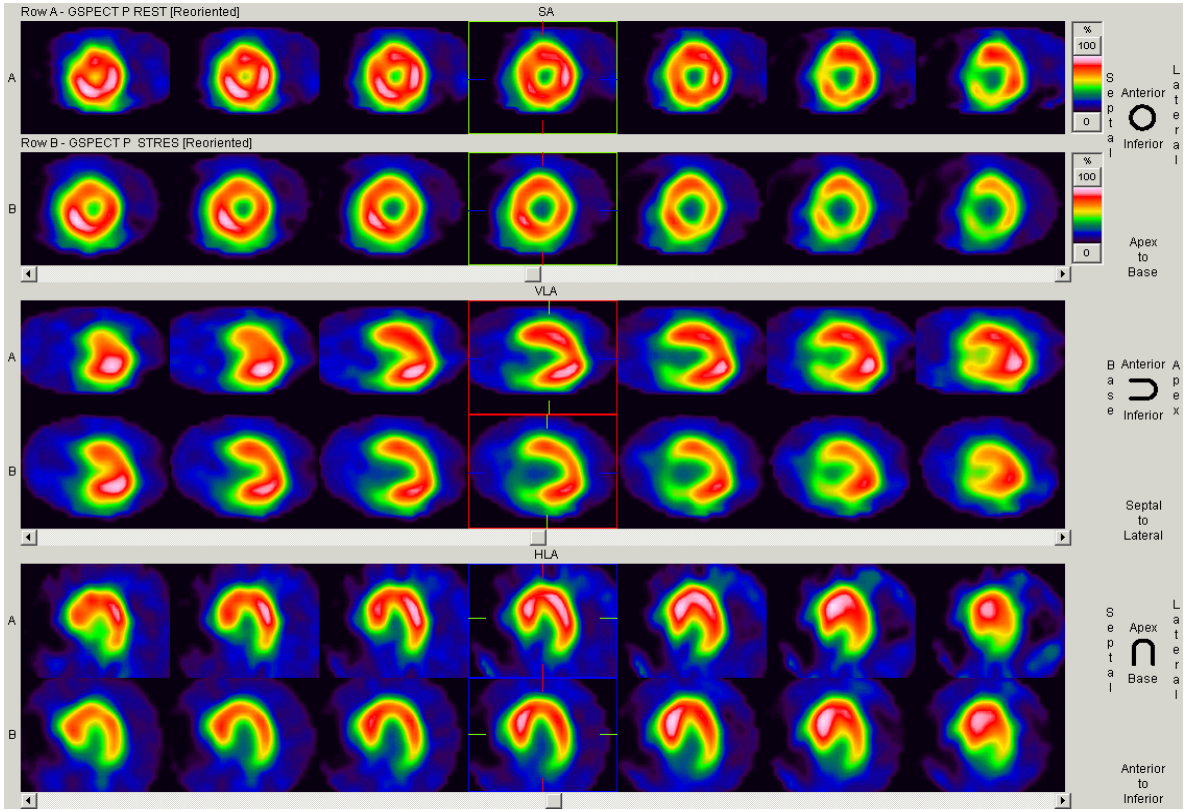
Picco esercizio



AP maschio a. 71

Il cardiologo prescrive atorvastatina 40 invece di 20 mg

Programma scintigrafia da sforzo



Referto:
piccolo difetto fisso infero-basale, FE conservata, minima ischemia anterolaterale

AP maschio a. 71

Viene associato nitrato long-acting e programmata scintigrafia di controllo a 6-8 mesi

Less Is More

How Less Health Care Can Result in Better Health

ARCH INTERN MED/VOL 170 (NO. 9), MAY 10, 2010

Deborah Grady, MD, MPH
Rita F. Redberg, MD, MSc
Editor

If some medical care is good, more care is better. Right?

Unfortunately, this is often not the case.

L’insostenibile leggerezza della angioplastica nella cardiopatia ischemica cronica

Original Investigation

How Cardiologists Present the Benefits of Percutaneous Coronary Interventions to Patients With Stable Angina
A Qualitative Analysis

Sarah L. Goff, MD; Kathleen M. Mazor, EdD; Henry H. Ting, MD, MBA; Reva Kleppel, MSW, MPH; Michael B. Rothberg, MD, MPH

JAMA Intern Med. August 25, 2014

CONCLUSIONS AND RELEVANCE Few cardiologists discussed the evidence-based benefits of angiogram and PCI for stable CAD, and some implicitly or explicitly overstated the benefits. The etiology of patient misunderstanding is likely multifactorial, but if future quantitative studies support the findings of this hypothesis-generating analysis, modifications to cardiologists' approach to describing the risks and benefits of the procedure may improve patient understanding.

REVIEW ARTICLE

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

Background: Prior meta-analyses have yielded conflicting results regarding the outcomes of treatment of stable coronary artery disease (CAD) with initial percutaneous coronary intervention (PCI) vs medical therapy. However, most of the studies in prior systematic reviews used balloon angioplasty as well as medical therapies that do not reflect current interventional or medical practices. We therefore performed a meta-analysis of all randomized clinical trials comparing initial coronary stent implantation with medical therapy to determine the effect on death, nonfatal myocardial infarction (MI), unplanned revascularization, and persistent angina.

Methods: Prospective randomized trials were identified by searches of the MEDLINE database from 1970 to September 2011. Trials in which stents were used in less than 50% of PCI procedures were excluded. Data were extracted from each study, and summary odds ratios (ORs) were obtained using a random effects model.

Results: Eight trials enrolling 7229 patients were identified. Three trials enrolled stable patients after MI, whereas 5 studies enrolled patients with stable angina and/or ischemia on stress testing. Mean weighted follow-up was 4.3 years. The respective event rates for death with stent implantation and medical therapy were 8.9% and 9.1% (OR, 0.98; 95% CI, 0.84-1.16); for nonfatal MI, 8.9% and 8.1% (OR, 1.12; 95% CI, 0.93-1.34); for unplanned revascularization, 21.4% and 30.7% (OR, 0.78; 95% CI, 0.57-1.06); and for persistent angina, 29% and 33% (OR, 0.80; 95% CI, 0.60-1.05).

Conclusion: Initial stent implantation for stable CAD shows no evidence of benefit compared with initial medical therapy for prevention of death, nonfatal MI, unplanned revascularization, or angina.

Arch Intern Med. 2012;172(4):312-319

UCSF Medical Center

The NEW ENGLAND JOURNAL of MEDICINE

September 2014

Sham Controls in Medical Device Trials

«PCI, a widely used procedure for treating stable coronary artery disease, has never been investigated in a blinded trial. Some nonblinded RCTs have shown that PCI has a beneficial effect on anginal symptoms, but ***there appears to be no difference between PCI and medical therapy in rates of the objective end points of nonfatal myocardial infarction and death due to cardiac causes. It is possible, therefore, that the perceived symptomatic benefit is actually a placebo effect and not attributable to PCI.»***

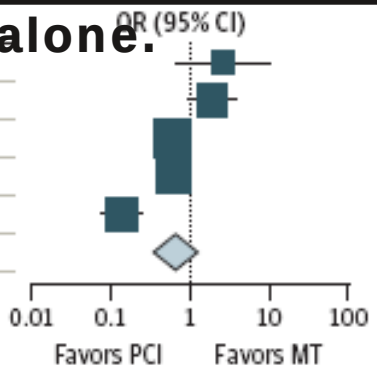
Metanalisi effetto PCI in pazienti con CAD stabile e documentazione ischemia

Stergiopoulos et al. JAMA Intern Med 2014;174:232-40

Morte

A

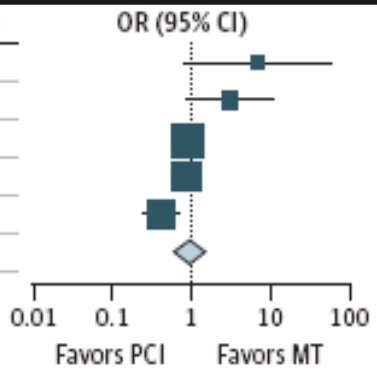
Source	OR (95% CI)	P Value
Hambrecht[15]	1.02 (0.02-52.43)	.99
Hambrecht[15]	2.60 (0.63-10.71)	.18
MASS II[13]	1.84 (0.91-3.73)	.09
COURAGE[17]	0.60 (0.48-0.74)	<.001
BARI 2D[14]	0.61 (0.46-0.80)	<.001
FAME 2[16]	0.13 (0.07-0.24)	<.001
Overall	0.64 (0.35-1.17)	.14



IMA non fatale

B

Source	OR (95% CI)	P Value
Hambrecht[15]	3.12 (0.12-78.45)	.49
Hambrecht[15]	6.82 (0.79-58.85)	.08
MASS II[13]	3.06 (0.83-11.29)	.09
COURAGE[17]	0.91 (0.74-1.10)	.33
BARI 2D[14]	0.87 (0.59-1.28)	.47
FAME 2[16]	0.42 (0.25-0.72)	<.001
Overall	0.90 (0.57-1.44)	.67

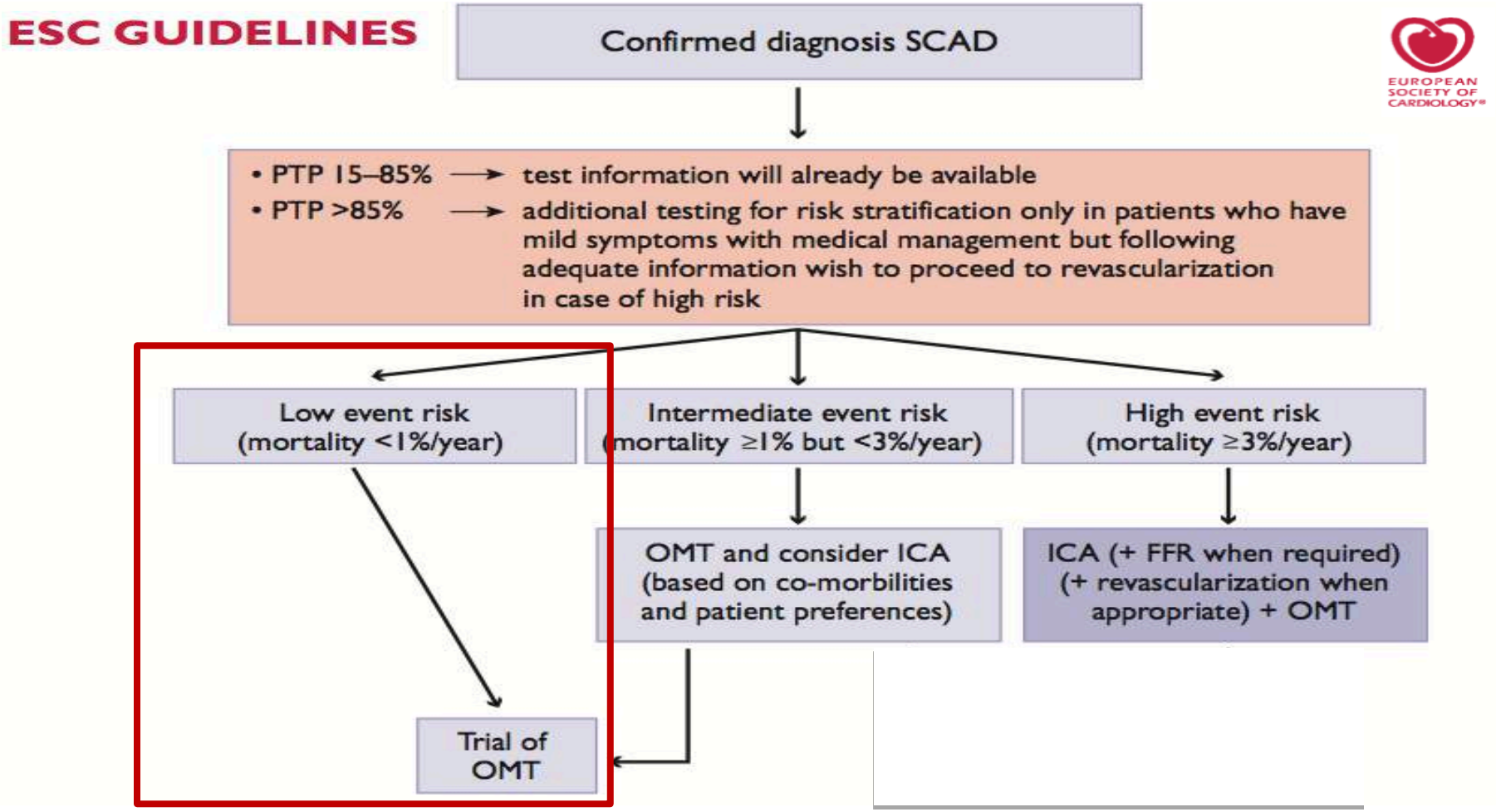


CONCLUSIONS AND RELEVANCE:

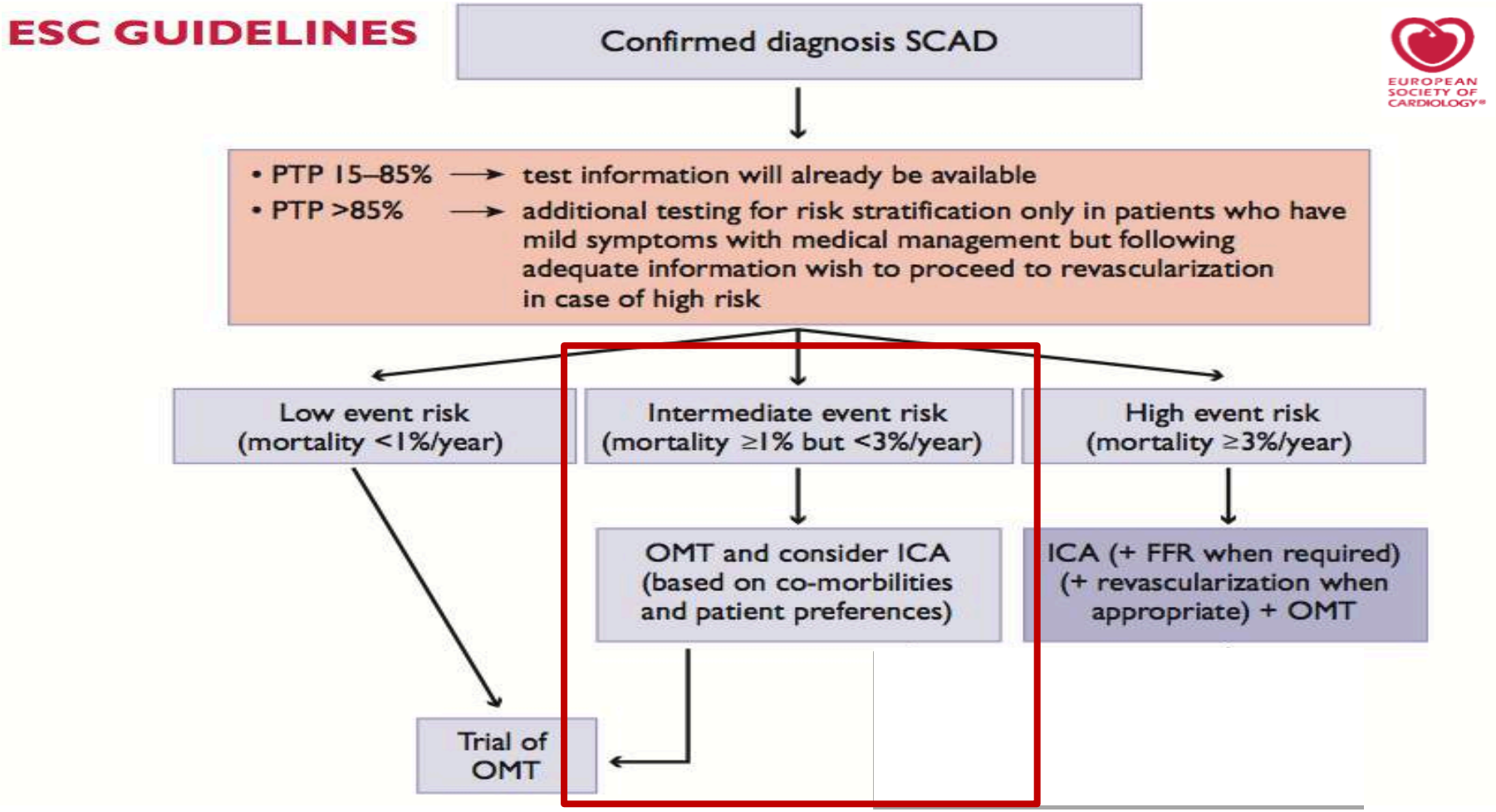
In patients with stable CAD and objectively documented myocardial ischemia, PCI with OMT was not associated with a reduction in death, nonfatal MI, unplanned revascularization, or angina compared with OMT alone.

Il ruolo irrinunciabile della terapia medica ottimale nell'angina stabile

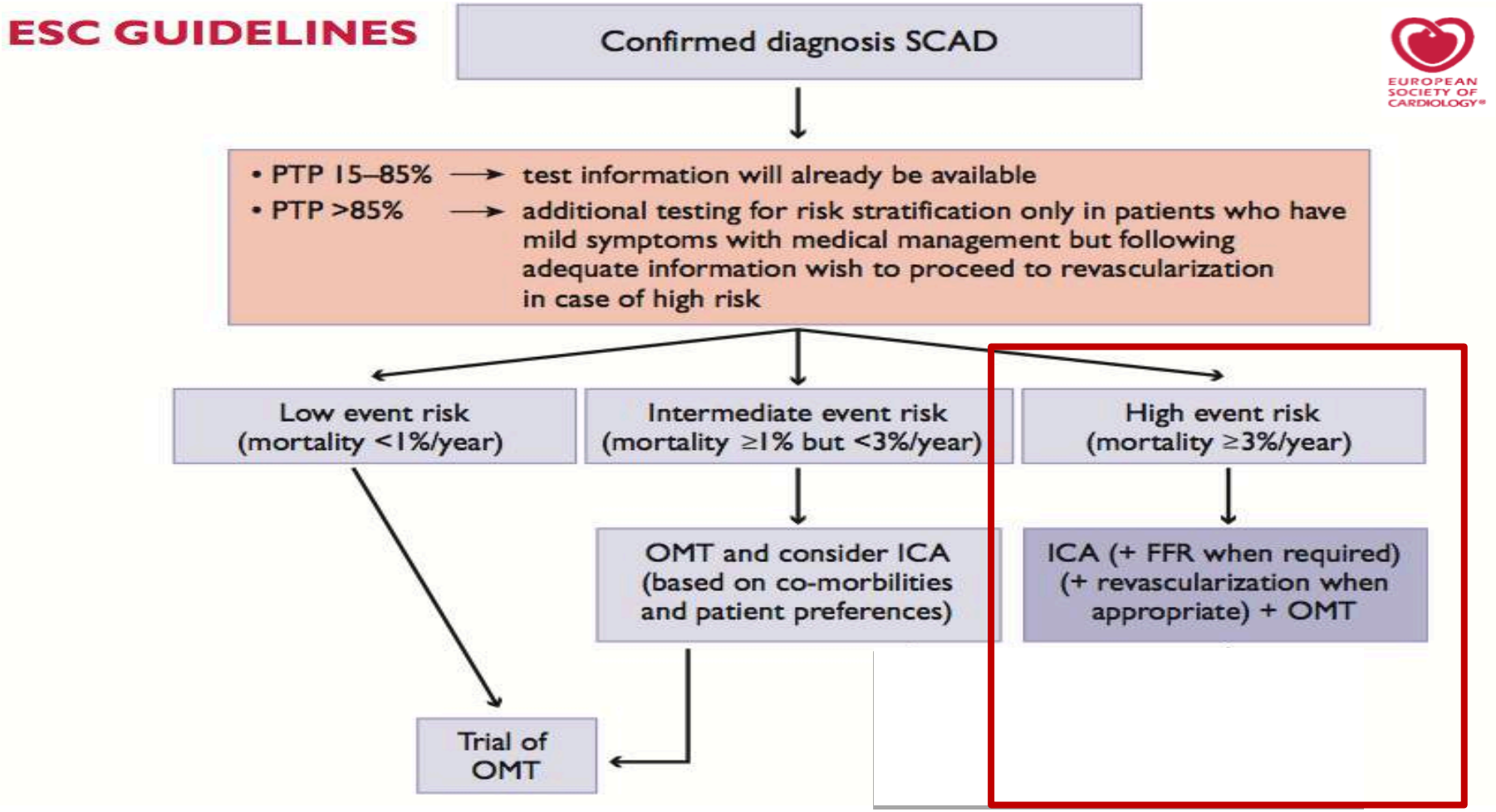
Gestione terapeutica della cardiopatia ischemica cronica sintomatica



Gestione terapeutica della cardiopatia ischemica cronica sintomatica



Gestione terapeutica della cardiopatia ischemica cronica sintomatica



Patterns and Intensity of Medical Therapy in Patients Undergoing Percutaneous Coronary Intervention

William B. Borden, MD
Rita F. Redberg, MD, MSc
Alvin I. Mushlin, MD, ScM
David Dai, PhD
Lisa A. Kaltenbach, MS
John A. Spertus, MD, MPH

ALTHOUGH PERCUTANEOUS coronary intervention (PCI) may improve outcomes for patients with acute coronary syndrome, optimal medical therapy (OMT) results in similar rates of cardiovascular events when compared with PCI in patients with stable coronary artery disease (CAD).[1,2] In fact, a meta-analysis of 11 trials[2] concluded that there was no benefit of PCI in preventing myocardial infarction or death in patients with stable CAD. The most definitive randomized trial comparing the effectiveness of OMT vs OMT plus PCI in patients with stable CAD was the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study.[3] In the COURAGE trial, patients with stable CAD underwent diagnostic coronary angiography to define their coronary anatomy and received aggressive secondary prevention therapy,[4] with half

Context The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study, which provided optimal medical therapy (OMT) to all patients and demonstrated no incremental advantage of percutaneous coronary intervention (PCI) on outcomes other than angina-related quality of life in stable coronary artery disease (CAD), suggests that a trial of OMT is warranted before PCI. It is unknown to what degree OMT is applied before PCI in routine practice or whether its use increased after the COURAGE trial.

Objective To examine the use of OMT in patients with stable angina undergoing PCI before and after the publication of the COURAGE trial.

Design, Setting, and Participants An observational study of patients with stable CAD undergoing PCI in the National Cardiovascular Data Registry between September 1, 2005, and June 30, 2009. Analysis compared use of OMT, both before PCI and at the time of discharge, before and after the publication of the COURAGE trial. Optimal medical therapy was defined as either being prescribed or having a documented contraindication to all medicines (antiplatelet agent, β-blocker, and statin).

Main Outcome Measures Rates of OMT before PCI and at discharge (following PCI) between the 2 study periods.

Results Among all 467 211 patients (173 416 before [37.1%] and 293 795 after [62.9%] the COURAGE trial) meeting study criteria, OMT was used in 206 569 patients (44.2%; 95% confidence interval [CI], 44.1%-44.4%) before PCI and in 303 864 patients (65.0%; 95% CI, 64.9%-65.2%) at discharge following PCI ($P<.001$). Before PCI, OMT was applied in 75 381 patients (43.5%; 95% CI, 43.2%-43.7%) before the COURAGE trial and in 131 188 patients (44.7%; 95% CI, 44.5%-44.8%) after the COURAGE trial ($P<.001$). The use of OMT at discharge following PCI before and after the COURAGE trial was 63.5% (95% CI, 63.3%-63.7%) and 66.0% (95% CI, 65.8%-66.1%), respectively ($P<.001$).

Conclusion Among patients with stable CAD undergoing PCI, less than half were receiving OMT before PCI and approximately two-thirds were receiving OMT at discharge following PCI, with relatively little change in these practice patterns after publication of the COURAGE trial.

JAMA. 2011;305(18):1882-1889 www.jama.com

…undergoing PCI, less than half were receiving OMT ….

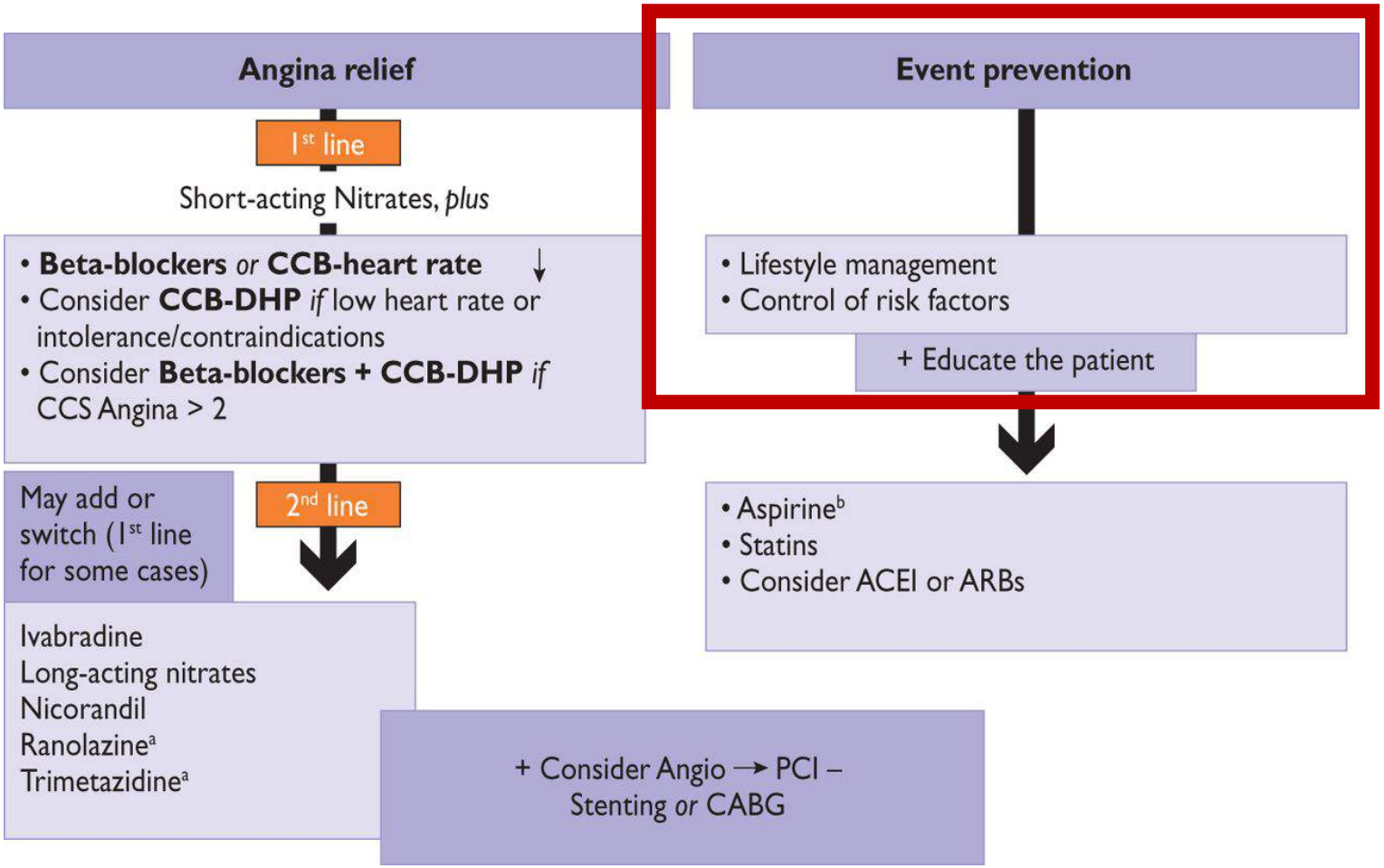
Qual'è la terapia ottimale nell'angina stabile secondo le Linee Guida?

NHS
National Institute for
Health and Clinical Excellence

➢ Key points

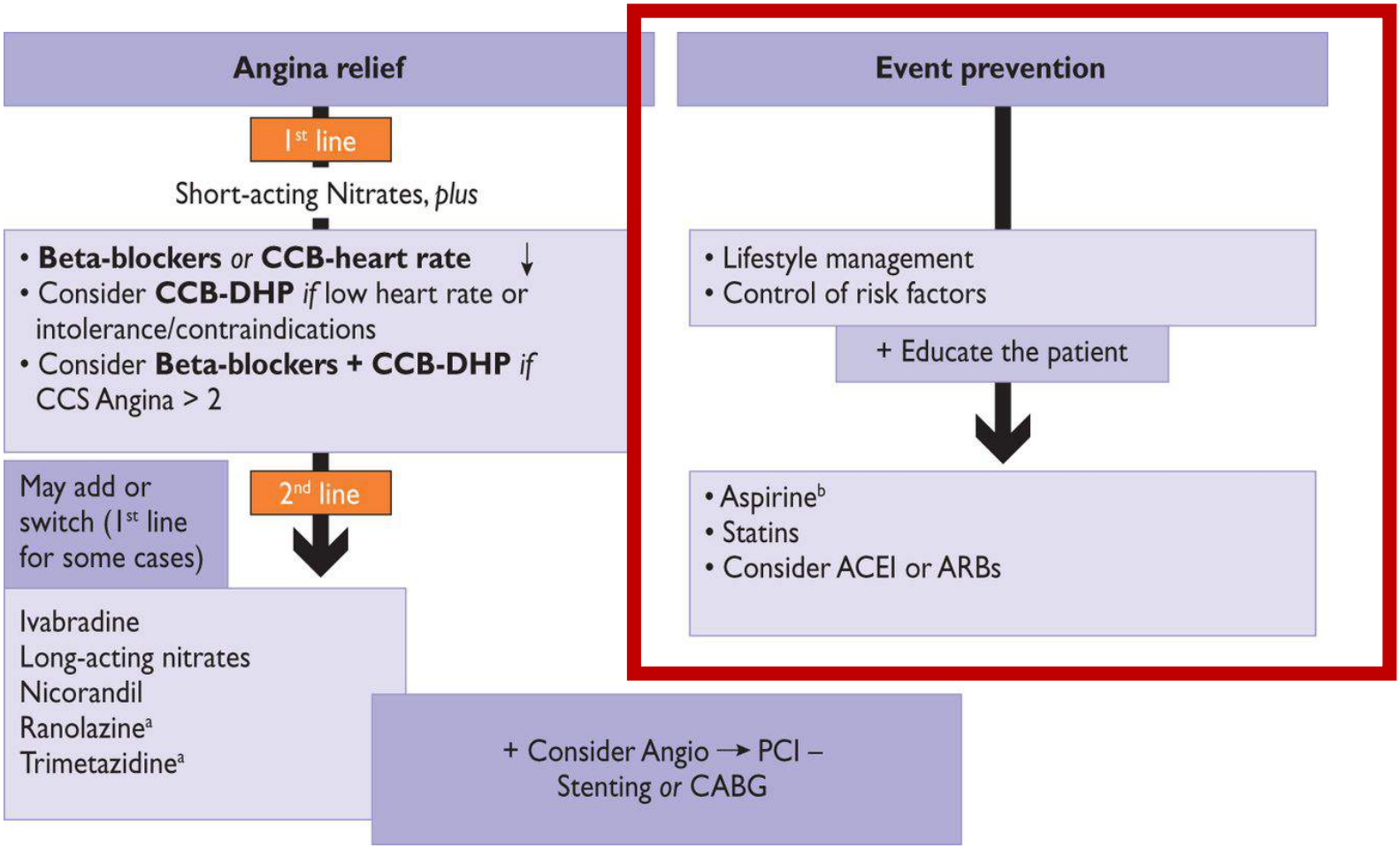
- **Lifestyle changes are vital in the management of stable angina, including smoking cessation, healthy diet, weight loss and control of lipid levels**
- Associated conditions, such as hypertension and diabetes, should be treated according to relevant guidance
- Anti-anginal drugs should be titrated to the optimal licensed dose to control symptoms
- Revascularisation should be considered in selected patients

Medical management of patients with stable coronary artery disease



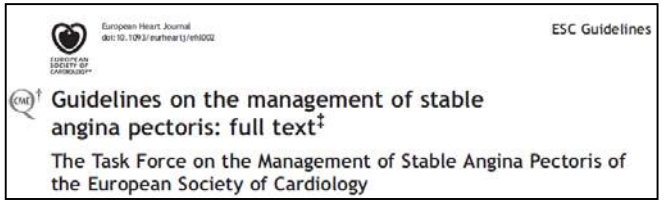
ESC Guidelines. Eur Heart J 2013; 34: 2949-3003

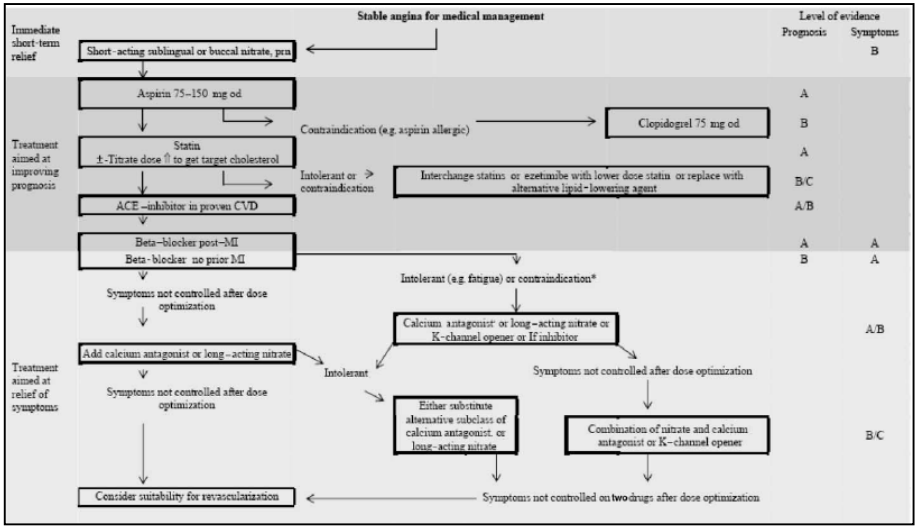
Medical management of patients with stable coronary artery disease

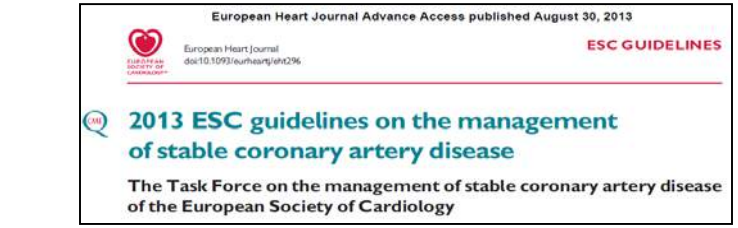


ESC Guidelines. Eur Heart J 2013; 34: 2949-3003

β-bloccanti nella angina stabile: confronto L.G. ESC 2006 vs 2013







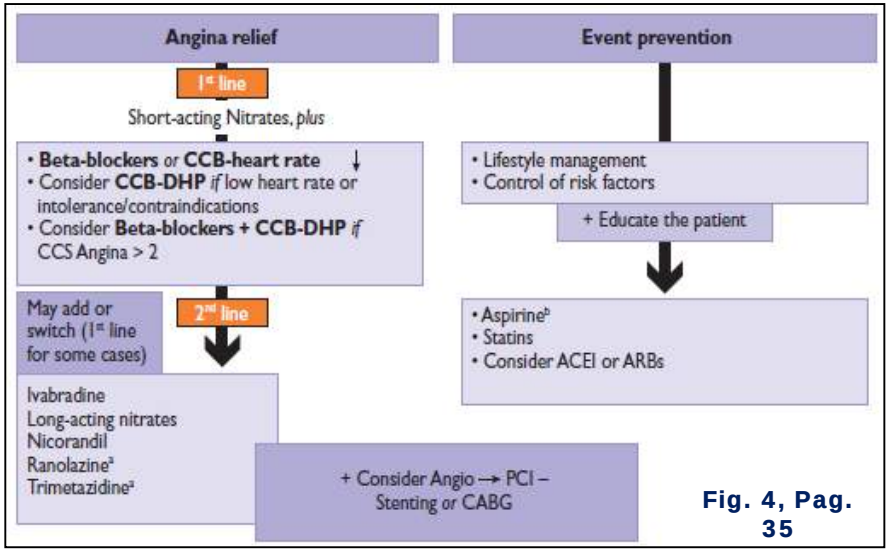


Fig. 4, Pag. 35

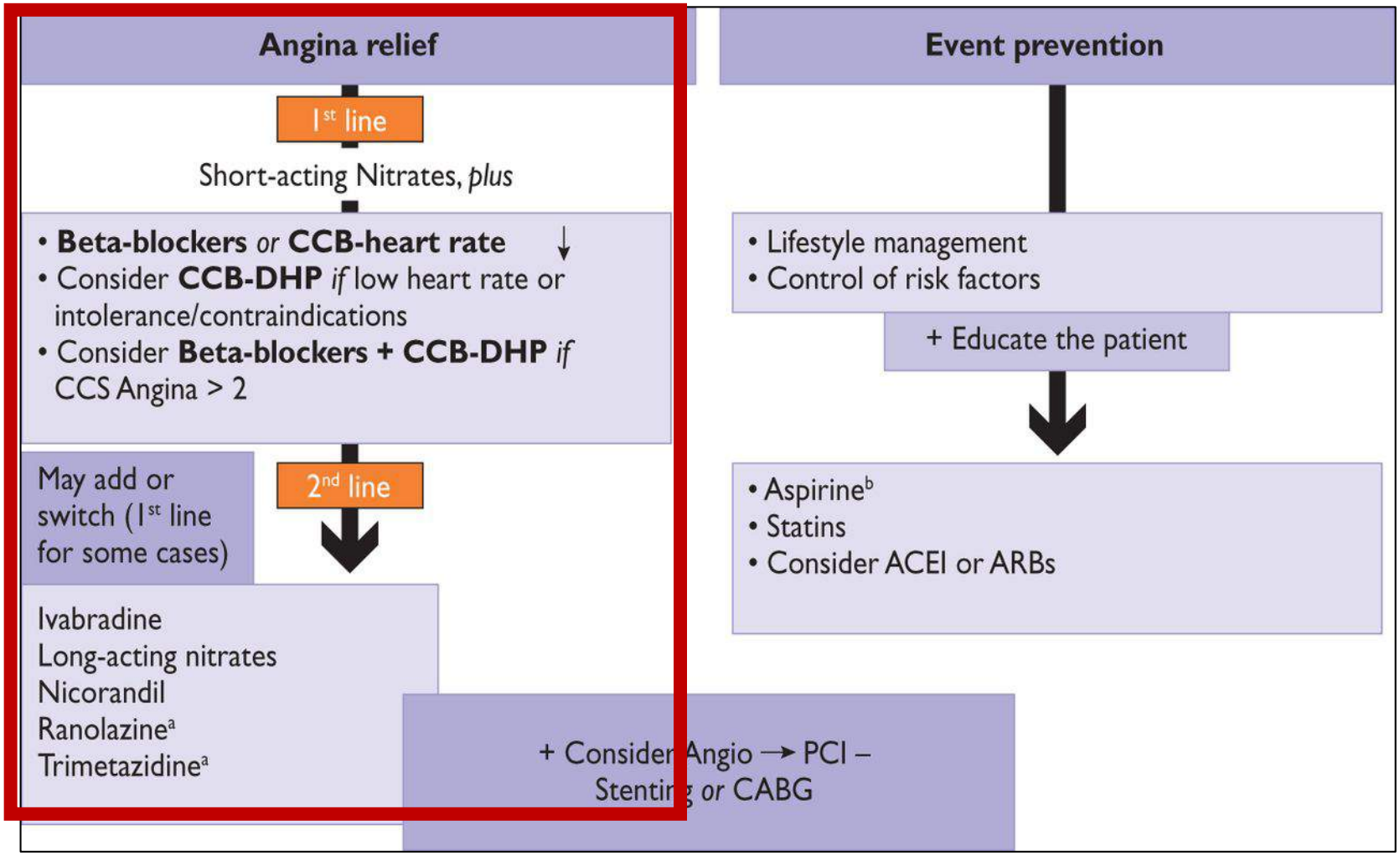
Raccomandazioni dei BB (2006)

Sintomi	Prognosi
1 A	1 A angina e post-IM 1 B angina senza IM

Raccomandazioni dei BB (2013)

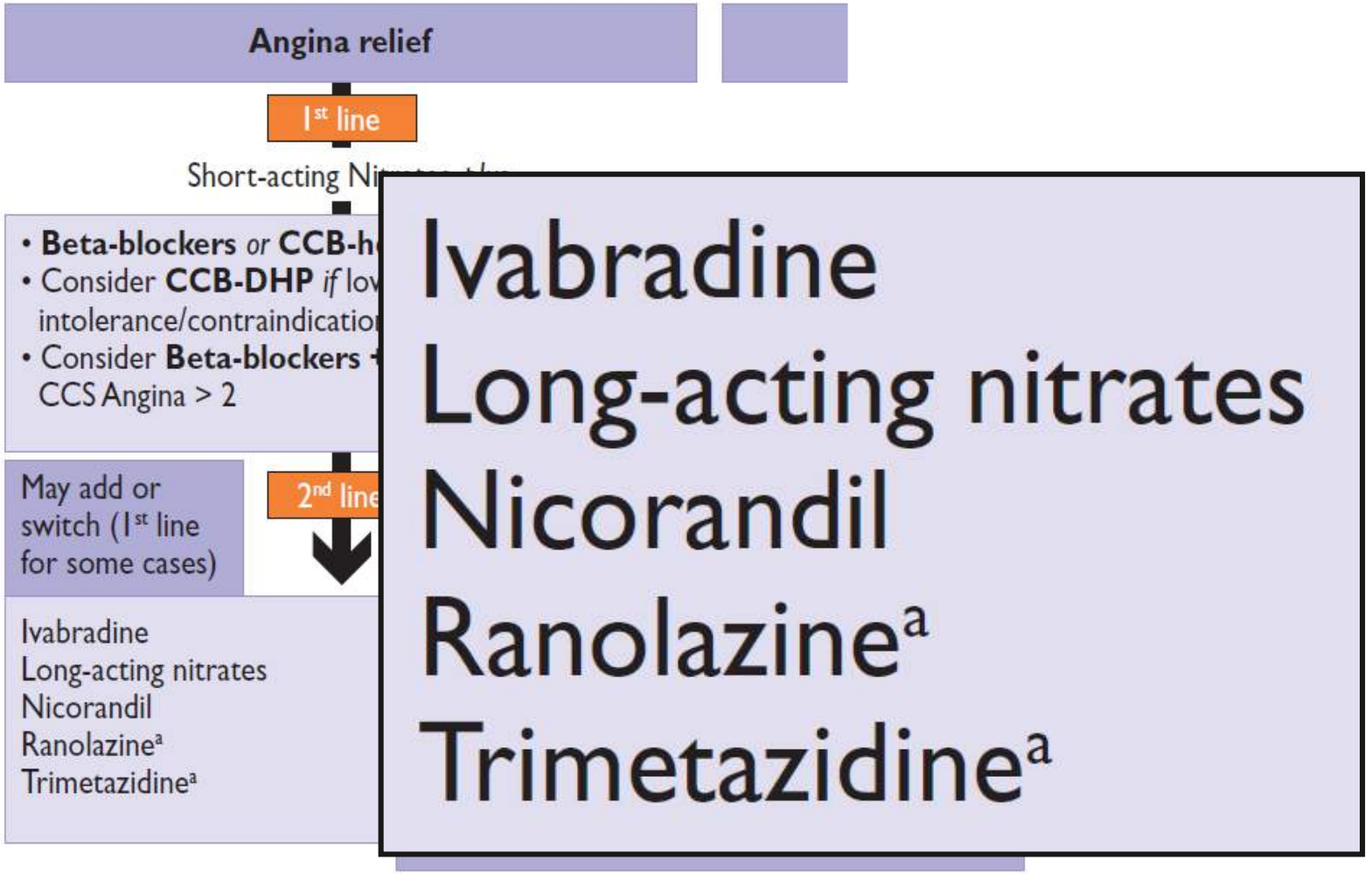
Sintomi	Prognosi
1 A	

Medical management of patients with stable coronary artery disease

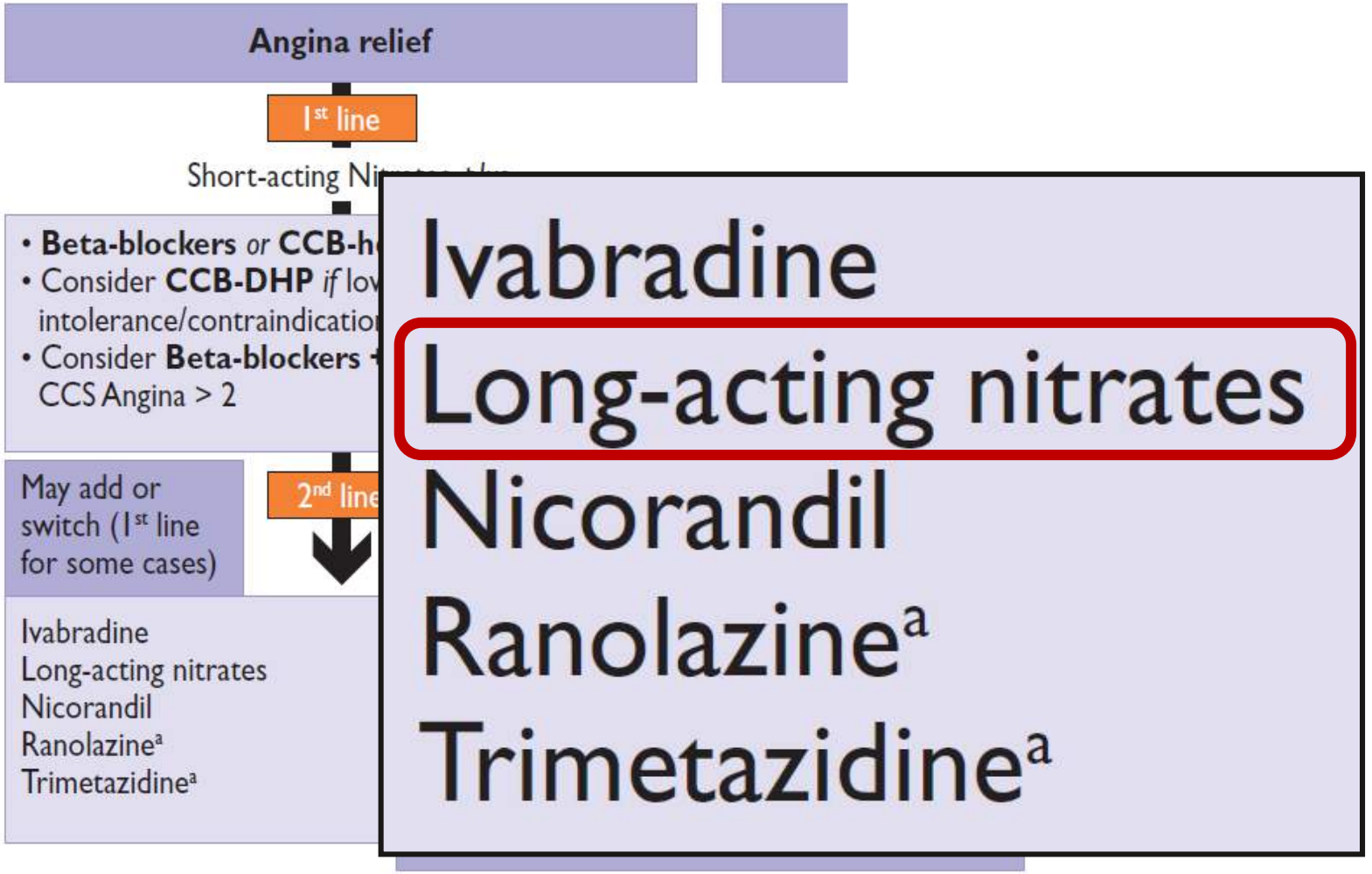


ESC Guidelines. Eur Heart J 2013; 34: 2949-3003

2013 ESC guidelines on the management of stable coronary artery disease



2013 ESC guidelines on the management of stable coronary artery disease



I livello ATC/ Sottogruppi	Spesa pro capite	DDD/1000 ab die	Δ% 2015-2014			
			spesa	DDD	prezzi	mix
Italia	**133,7**	**1.041,1**	**-0,6**	**0,5**	**-1,7**	**0,6**
C-Sistema cardiovascolare	**41,8**	**467,4**	**-1,4**	**-0,4**	**-1,9**	**0,9**
Inibitori della HMG CoA reduttasi	7,9	67,6	-1,0	2,7	-0,2	-3,4
Antagonisti dell'angiotensina II e diuretici	4,6	38,7	-8,4	-2,4	-7,2	1,1
Antagonisti dell'angiotensina II, non associati	4,5	55,6	0,5	-0,2	-0,2	0,9
Derivati diidropiridinici	3,4	51,6	-4,8	-2,7	-2,1	<0,05
Inibitori dell'enzima di conversione dell'angiotensina (ace), non associati	3,3	87,6	-2,9	-1,6	-0,2	-1,1
Betabloccanti, selettivi	2,9	35,9	4,0	1,6	-0,6	3,0
Inibitori dell'enzima di conversione dell'angiotensina (ace) e diuretici	2,6	23,9	-4,2	-4,4	-0,1	0,3
Altri ipocolesterolemizzanti ed ipotrigliceridemizzanti	2,2	5,4	-3,2	11,8	-11,6	-2,0
Inibitori HMG CoA reduttasi c/altri modificatori dei lipidi	2,0	3,6	3,1	1,2	-0,1	2,0
Inibitori dell'enzima di conversione dell'angiotensina (ace) e calcioantagonisti	1,1	7,8	20,1	20,9	<0,05	-0,7
Nitrati organici	1,0	12,6	-12,1	-10,7	-1,5	0,1
Bloccanti dei recettori alfa adrenergici	0,9	7,5	-1,3	-1,4	-0,1	0,2
Antagonisti dell'angiotensina II associati a calcio-antagonisti	0,9	3,6	33,4	34,9	-1,1	0,1
Antiaritmici, classe IC	0,7	4,6	3,1	-0,2	-0,2	3,6
Sulfonamidi, non associate	0,7	25,9	1,6	2,1	<0,05	-0,5
Bloccanti dei recettori alfa e beta adrenergici	0,5	3,8	-5,3	-5,0	<0,05	-0,3
Betabloccanti selettivi e tiazidi	0,4	4,3	17,5	15,6	0,7	0,9
Antagonisti dell'aldosterone	0,4	3,8	-2,0	-0,1	-3,7	1,9
Fibrati	0,3	2,5	-0,3	0,8	<0,05	-1,2
Agonisti dei recettori dell'imidazolina	0,2	1,9	-4,5	-4,6	<0,05	0,2
Antiaritmici, classe III	0,2	3,0	-2,1	-0,9	<0,05	-1,1
Derivati benzotiazepinici	0,2	1,5	-16,8	-8,0	-9,2	-0,4
Altri preparati cardiaci	0,2	0,2	-8,2	0,8	-5,0	-4,0
Derivati fenilalchilaminici	0,1	1,7	-9,4	-8,6	<0,05	-0,8
Betabloccanti selettivi ed altri diuretici	0,1	2,4	-5,4	-5,5	<0,05	0,2
Diuretici ad azione diuretica minore e farmaci risparmiatori di potassio	0,1	3,0	-6,2	-6,2	<0,05	<0,05
Betabloccanti, non selettivi	0,1	1,6	-2,8	-2,9	-0,8	0,8

EUROPEAN SOCIETY OF CARDIOLOGY®

2013 ESC guidelines on the management of stable coronary artery disease

Long-acting nitrates for angina prophylaxis

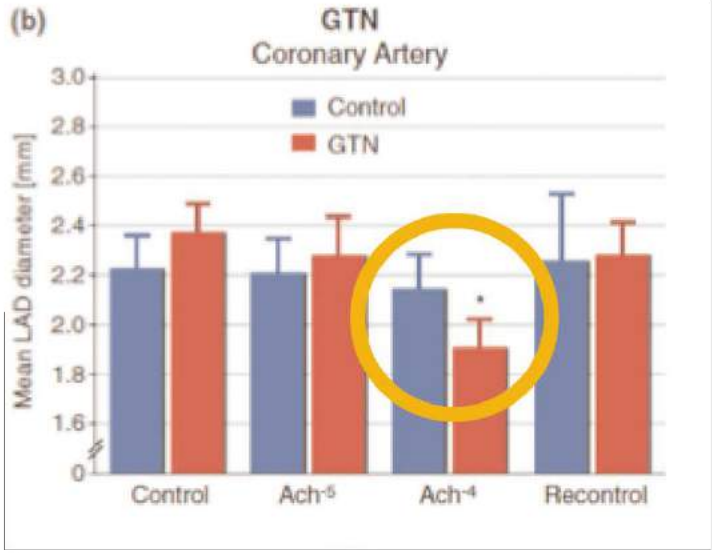
Thus prolonged therapy with isosorbide dinitrate is not evidence-based

Nitrati «long-acting» e funzione endoteliale

Current Opinion in Pharmacology
2013; 13:251-259

Nitrate therapy and nitrate tolerance in patients with coronary artery disease

Thomas Münzel and Tommaso Gori



Prolonged exposure to organic nitrates induces tolerance, sympathetic activation, and endothelial dysfunction in patients with cardiovascular disease

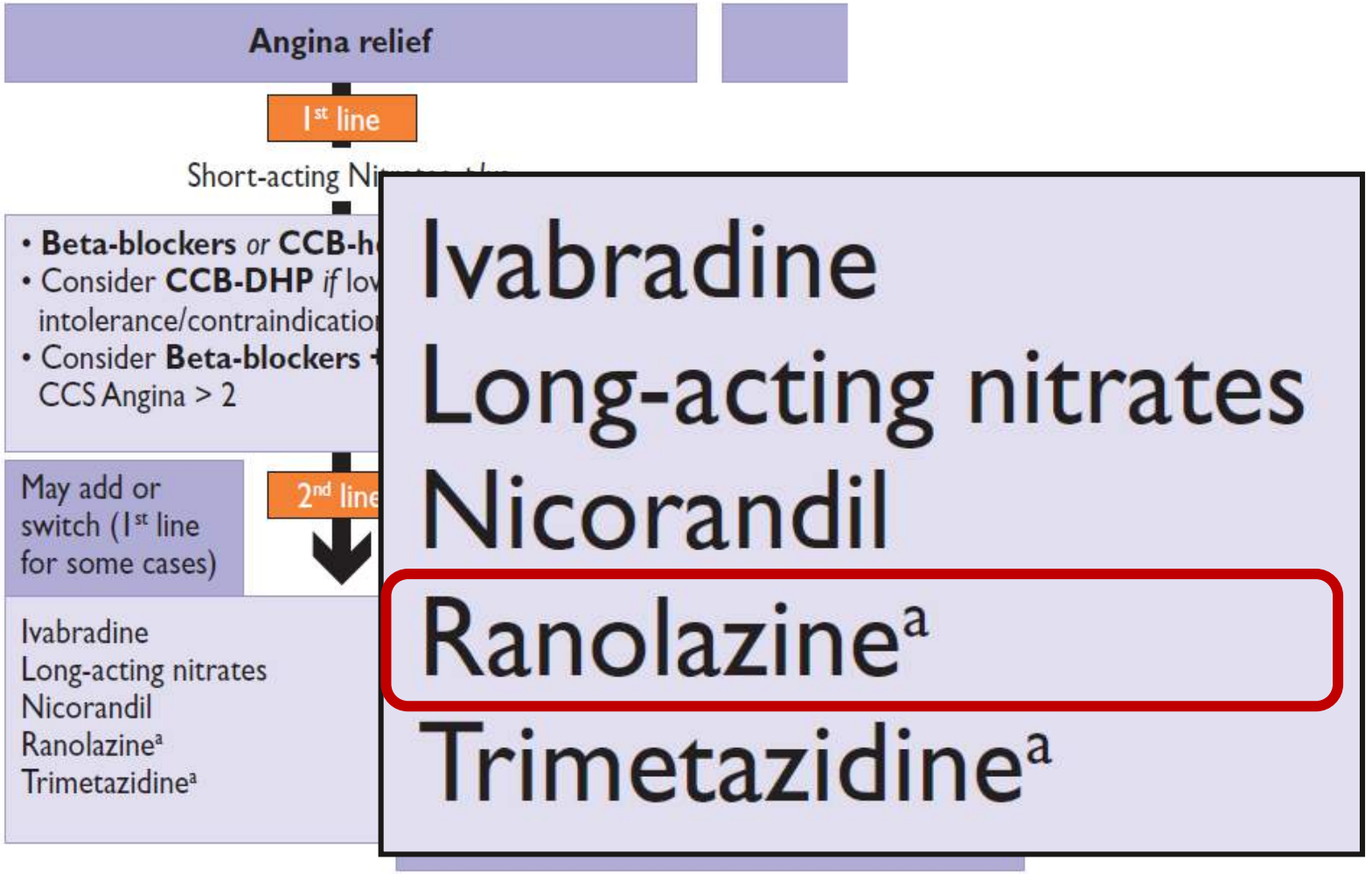
Nitrate-induced endothelial disfunction, human studies

Isosorbide-5-mononitrate and endothelial function: a wolf in sheep's clothing

Rassaf, Eur Heart J 2013

Taken together, the seminal findings reported by Oelze *et al*. and emerging data from preclinical studies using PKC, NADPH oxidase inhibitors, and inorganic nitrates may lead to a rethink and re-evaluation of our current therapeutic strategies in using various types of NO donors and oxidative stress-modulating substances in patients with vascular dysfunction and diseases.

2013 ESC guidelines on the management of stable coronary artery disease



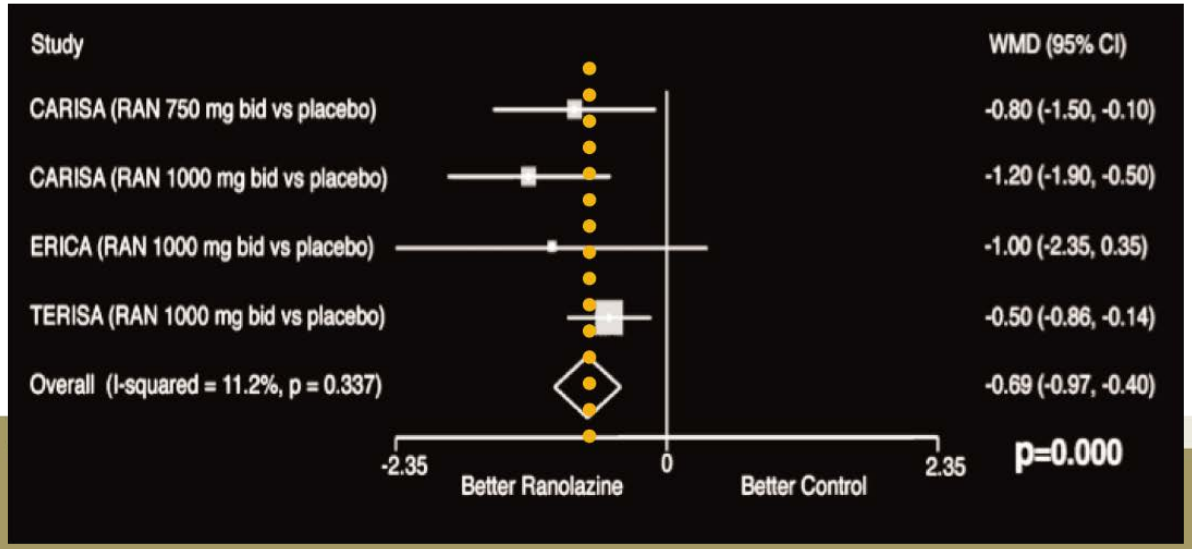
Effects of ranolazine in symptomatic patients with stable coronary artery disease. A systematic review and meta analysis

Savarese, Int. J Cardiol 2013

Gianluigi Savarese[a], Giuseppe Rosano[b], Carmen D'Amore[a], Francesca Musella[a], Giuseppe Luca Della Ratta[a], Angela Maria Pellegrino[a], Tiziana Formisano[a], Alice Vitagliano[a], Annapaola Cirillo[a], Gennaro Cice[c], Luigi Fimiani[a], Luca del Guercio[d], Bruno Trimarco[a], Pasquale Perrone-Filardi[a]*

[a] Department of Advanced Biomedical Science, Federico II University, Naples, Italy / [b] Clinical and Experimental Research Center, IRCCS San Raffaele, Rome, Italy
[c] Division of Cardiology , Second University of Naples, Naples, Italy / [d] Department of vascular and Endovascular Surgery, Federico II University, Naples, Italy

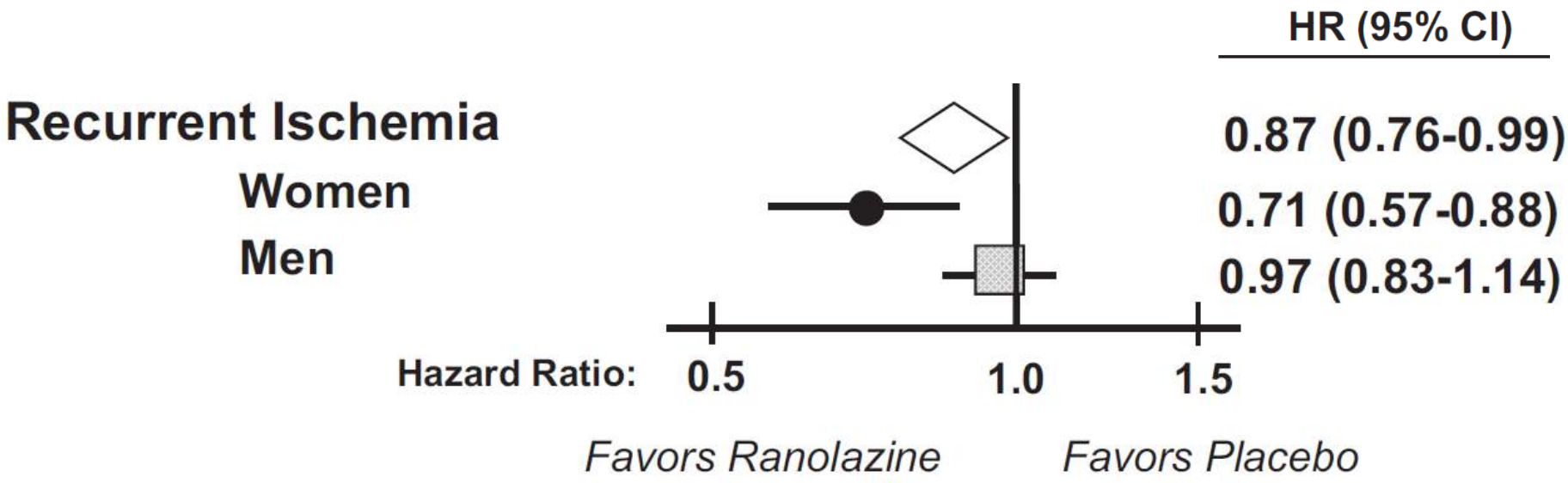
Mean difference estimate of weekly angina onset in Ranolazine versus control study groups



Clinical Features and Outcomes of Women With Unstable Ischemic Heart Disease

Observations From Metabolic Efficiency With Ranolazine for Less Ischemia in Non–ST-Elevation Acute Coronary Syndromes–Thrombolysis in Myocardial Infarction 36 (MERLIN-TIMI 36)

Mega J, Circulation 2010



JACC: CARDIOVASCULAR IMAGING
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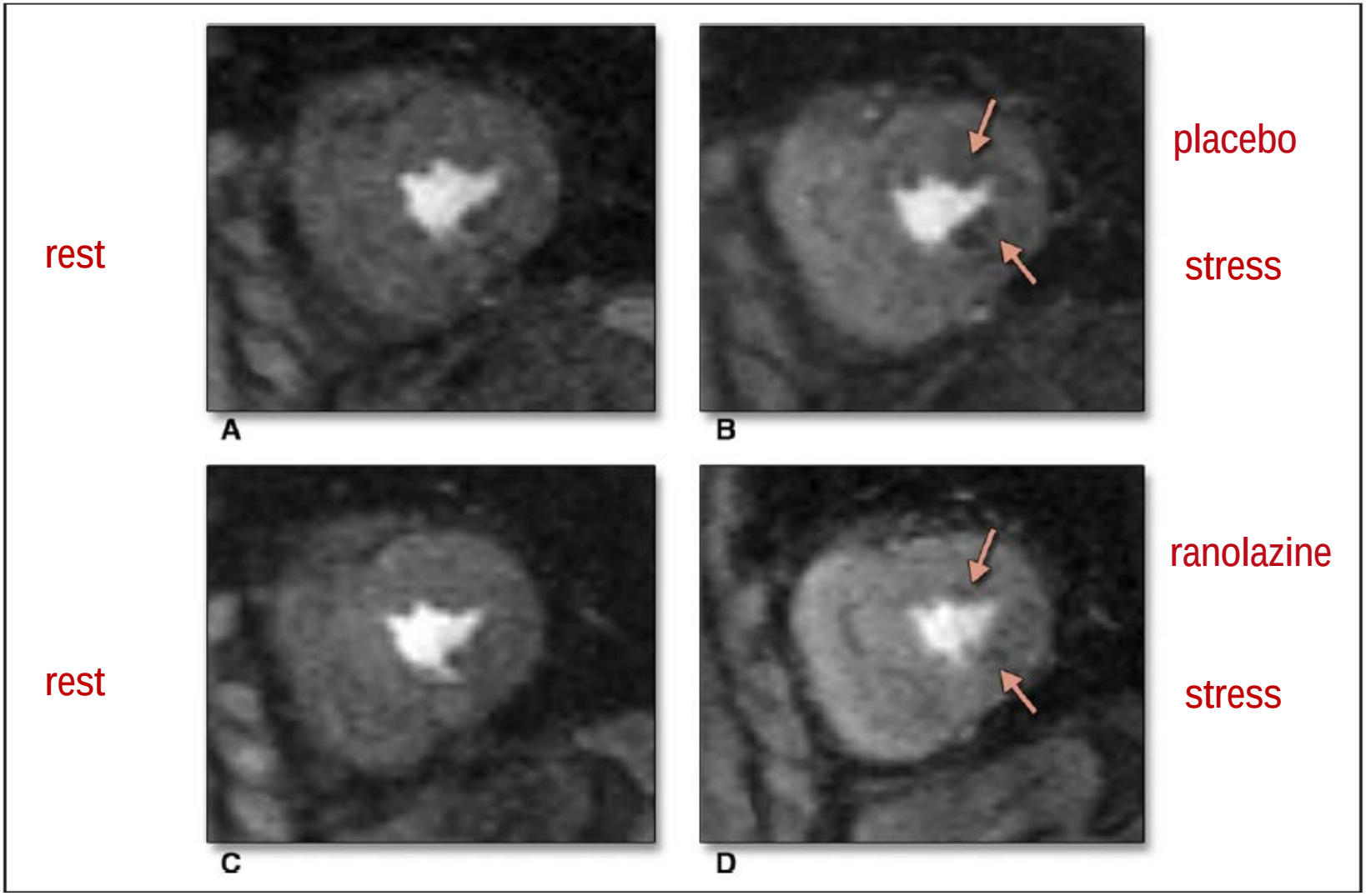
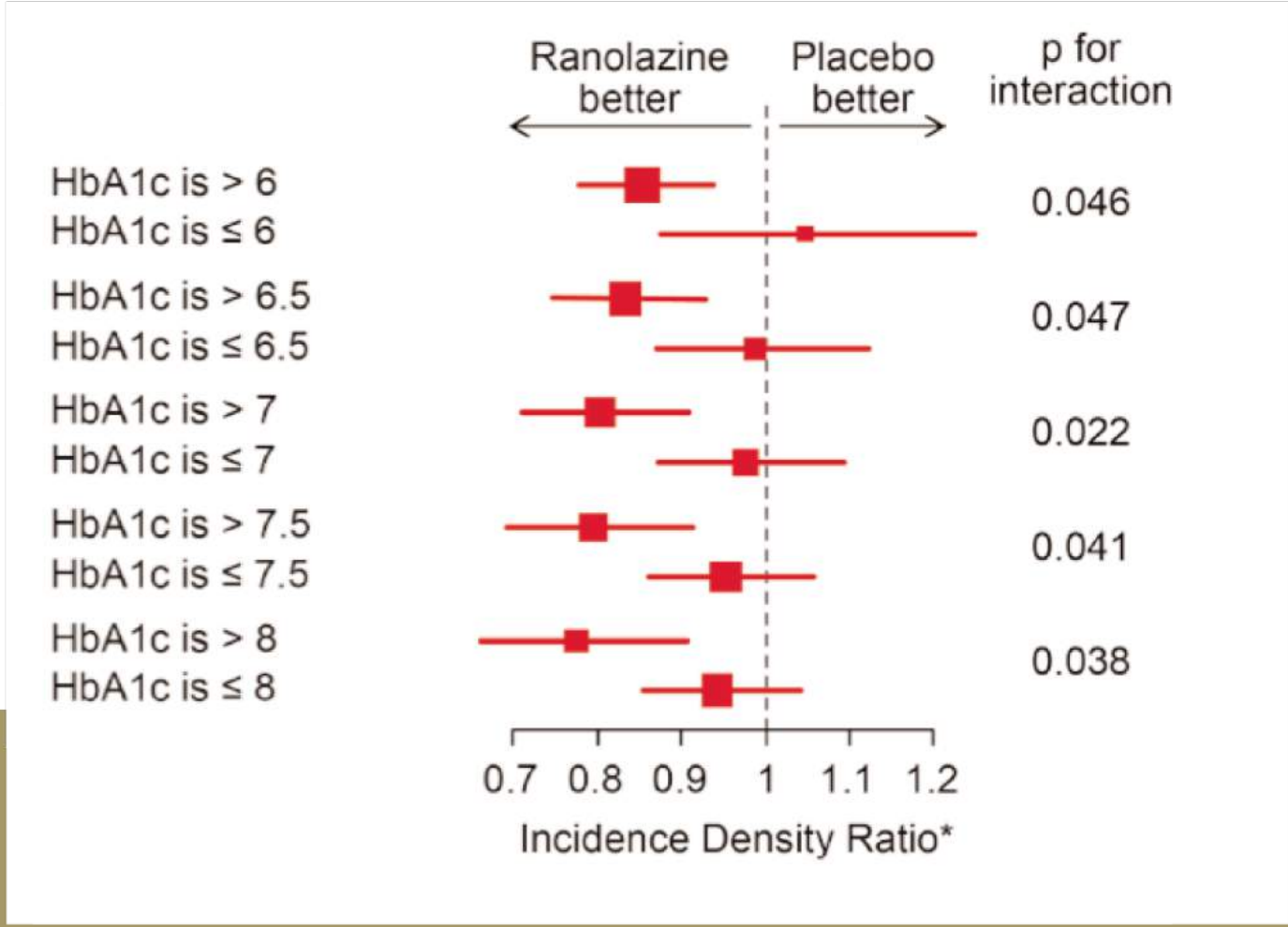
ISSN 1936-878X/$36.00
DOI:10.1016/j.jcmg.2011.03.007

Ranolazine Improves Angina in Women



Evaluation of Ranolazine in Patients with Type 2 Diabetes Mellitus and Chronic Stable Angina. Results from the TERISA randomized clinical trial

Kosiborod MJ Am Coll Cardiol 2013



Documento ANMCO/GICR-IACPR/GISE L'organizzazione dell'assistenza nella fase post-acuta delle sindromi coronariche

Commissione ANMCO/GICR-IACPR/GISE

Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO)
Società Italiana di Cardiologia Riabilitativa e Preventiva (GICR-IACPR)
Società Italiana di Cardiologia Invasiva (GISE)

Cesare Greco, Francesco M. Bovenzi, Sergio Berti, Maurizio Abrignani, Francesco Bedogni, Roberto Ceravolo, Furio Colivicchi, Leonardo De Luca, Pompilio Faggiano, Francesco Fattirolli, Giuseppe Favretto, Pantaleo Giannuzzi, Gian Francesco Mureddu, Giuseppe Musumeci, Zoran Olivari, Carmine Riccio, Roberta Rossini, Pier Luigi Temporelli

con l'endorsement di:

ARCA (Associazioni Regionali Cardiologi Ambulatoriali)
ANCE (Cardiologia Italiana del Territorio)
SIMG (Società Italiana di Medicina Generale)

realizzato con il contributo scientifico di:

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Volume 15 — Suppl. 1 al n. 1
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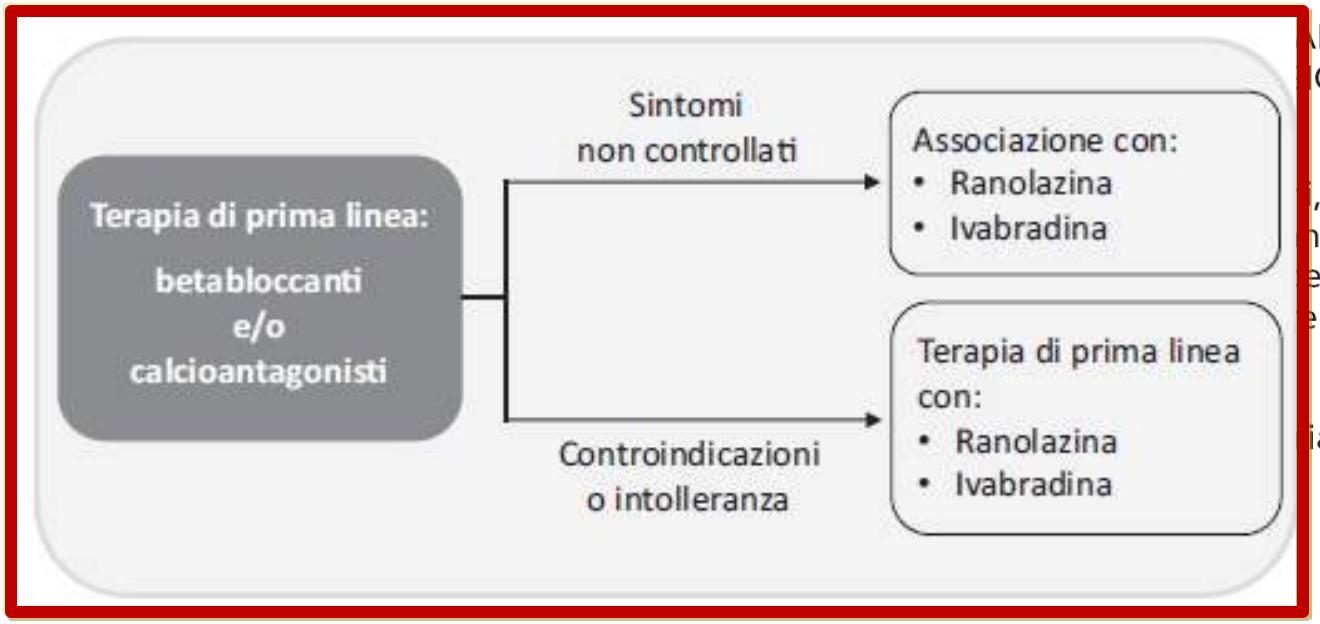
Commissione ANMCO/GICR-IACPR/GISE



NMCO)
CR-IACPR)

, Francesco Bedogni,
no, Francesco Fattirolli,
e Musumeci, Zoran Olivari,
elli

iali)

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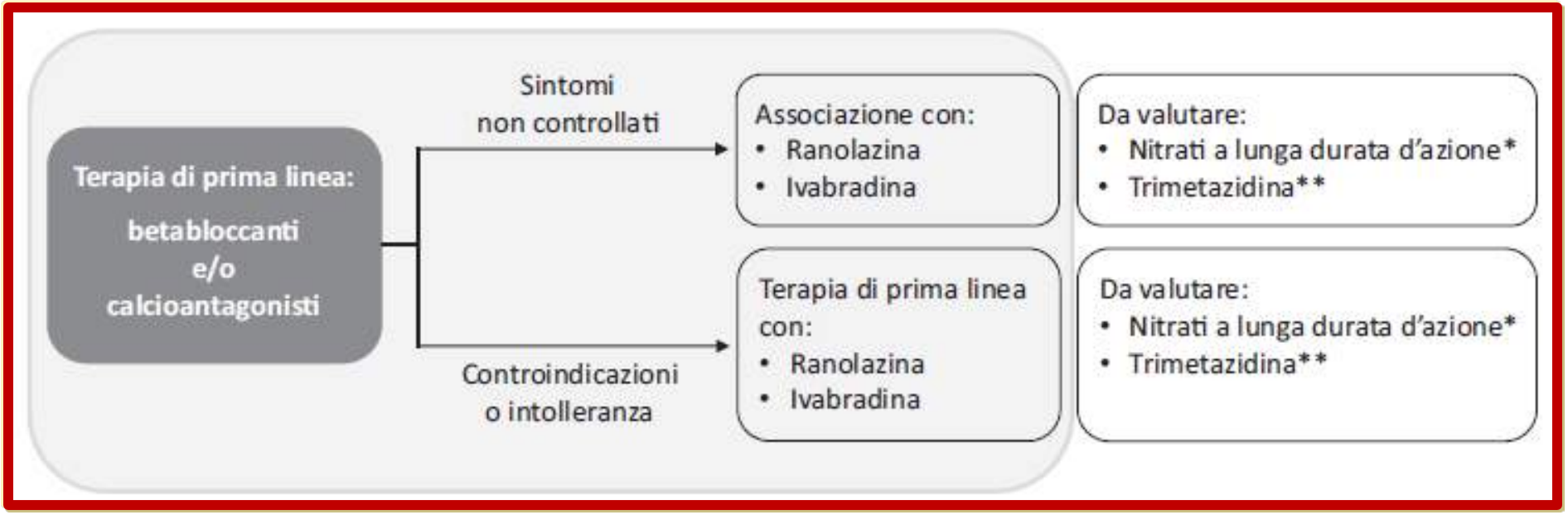

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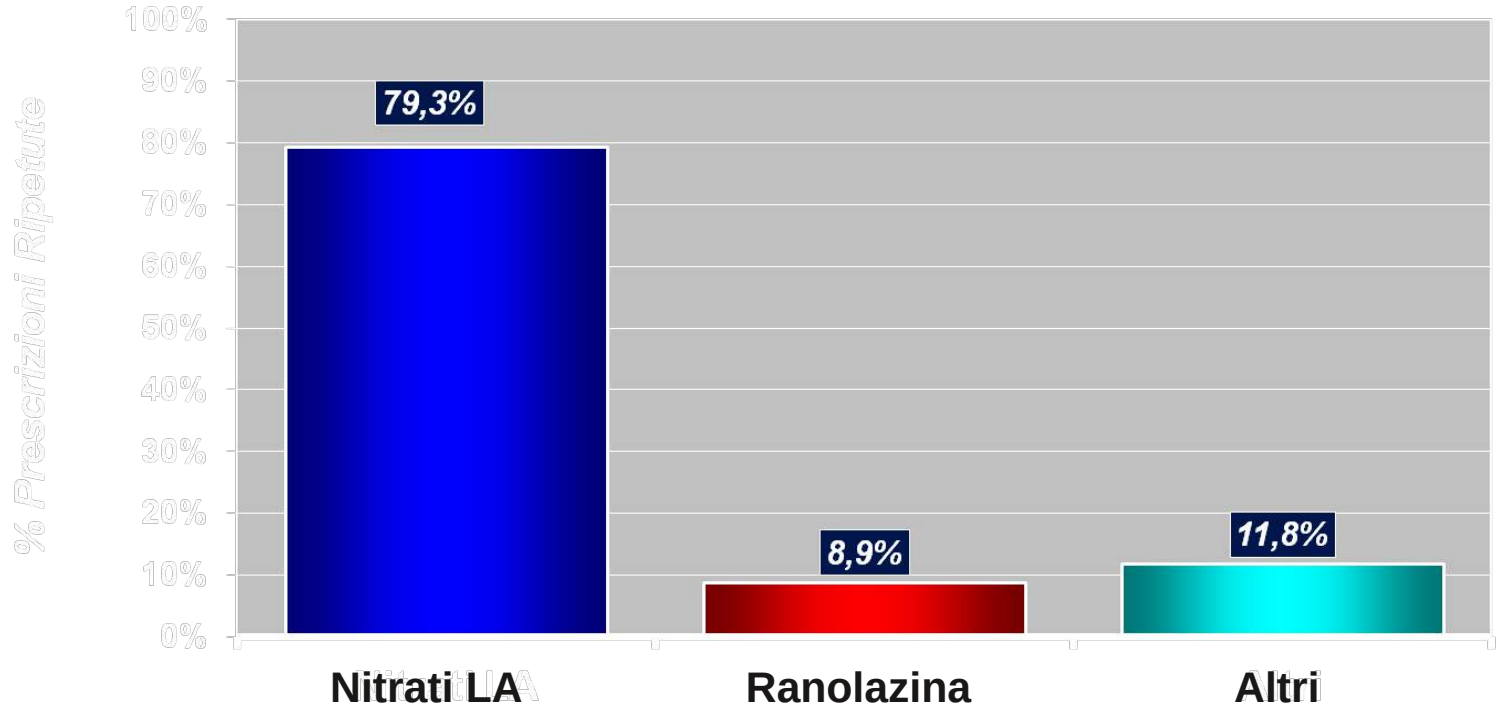
Facciamo così?

Lo specialista (CAR-GER-DIA) in quasi l'80% dei casi ripete la prescrizione di nitrati a lunga durata d'azione

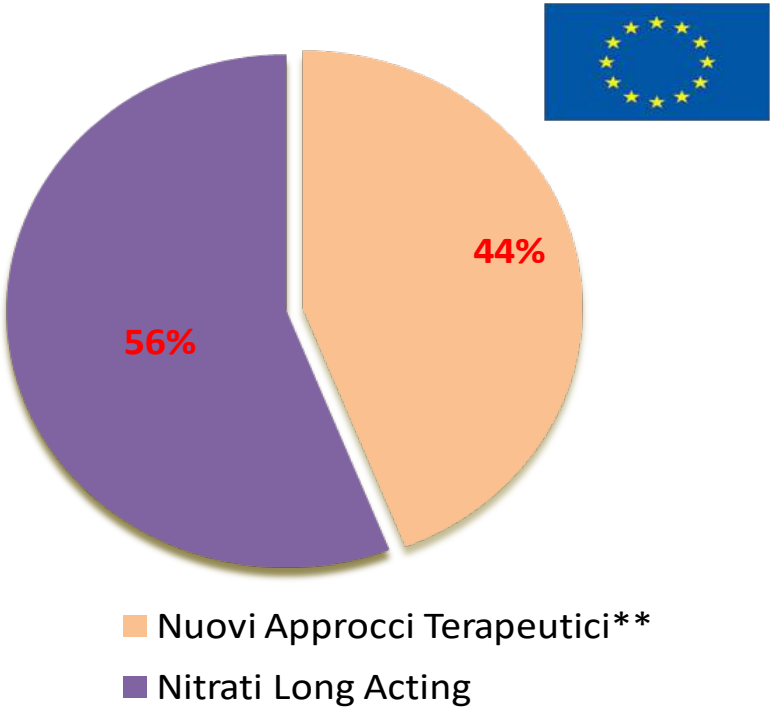
La gestione del paziente in rivalutazione



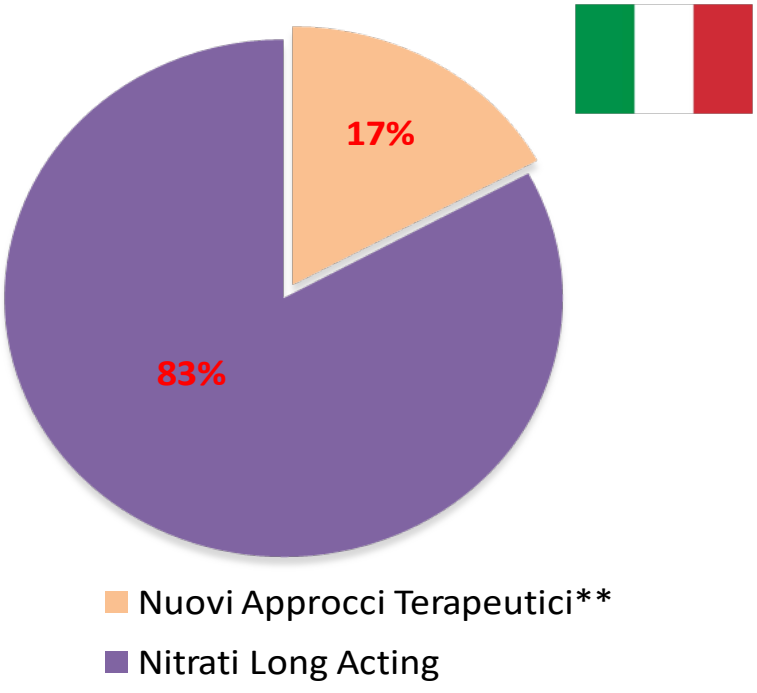
Fonte dati Medical Audit 2014

La gestione della cardiopatia ischemica cronica in Europa ed in Italia

Europa*: la gestione terapeutica del paziente con CIC



Italia: la gestione terapeutica del paziente con CIC



Limitations of Conventional Antianginal Therapies

Adapted from Gibbons RJ, et al.
ACC/AHA 2002 Guideline Update for Chronic Stable Angina

Limitations	Beta Blockers	Nitrates	Calcium Antagonists
Comorbidity Challenges	• COPD • Bradycardia • A-V conduction problems • Peripheral Vascular Disease • Sick Sinus Syndrome	• Left ventricular outflow tract obstruction	• **Bradycardia** • **Heart failure** • **Left ventricular dysfunction** • **Sick sinus syndrome** • **A-V conduction problems**
Side Effects	• Sexual dysfunction • Fatigue • Depression • Hypotension • Syncope	• Headache • Syncope • Tolerance • Hypotension	• **Flushing** • **Dizziness** • **Hypotension** • **Edema** • **Fatigue**

E’ tempo di cambiare paradigma !

Documento di consenso ANMCO/GICR-IACPR/SICI-GISE: La gestione clinica del paziente con cardiopatia ischemica cronica

Carmine Riccio[1] (Coordinatore), Michele Massimo Gulizia[2] (Coordinatore), Furio Colivicchi[3] (Coordinatore), Andrea Di Lenarda[4] (Coordinatore), Giuseppe Musumeci[5], Pompilio Massimo Faggiano[6], Maurizio Giuseppe Abrignani[7], Roberta Rossini[5], Francesco Fattirolli[8], Serafina Valente[9], Gian Francesco Mureddu[10], Pier Luigi Temporelli[11], Zoran Olivari[12], Antonio Francesco Amico[13], Giancarlo Casolo[14], Claudio Fresco[15], Alberto Menozzi[16], Federico Nardi[17]

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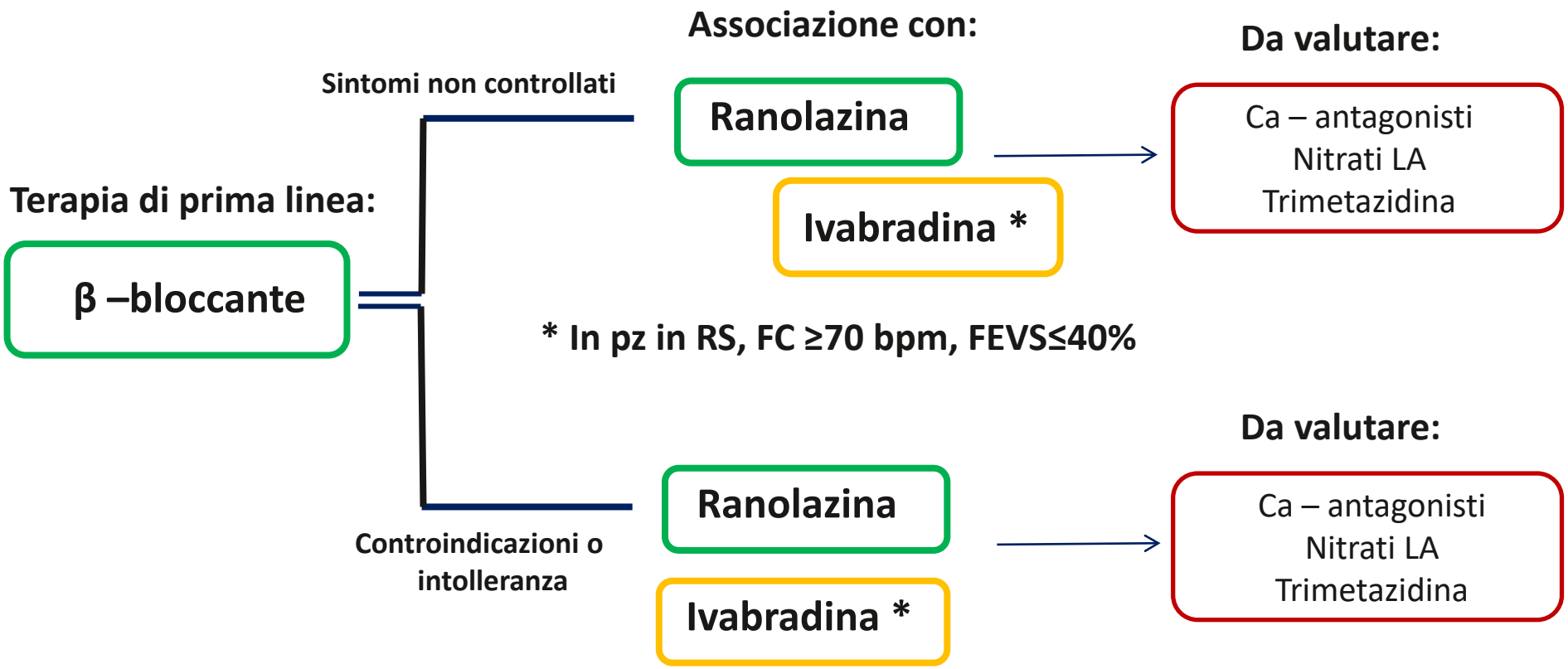
G Ital Cardiol 2016;17

Revisori del Documento
Roberto Caporale, Marco Malvezzi Caracciolo, Giovanna Geraci, Alfredo Marchese, Roberto Pedretti, Guerrino Zuin

Algoritmo per l'ottimale gestione del trattamento sintomatico del paziente con cardiopatia ischemica cronica stabile



Take Home Message

✓Alla luce delle evidenze cliniche la terapia medica ottimale dovrebbe essere il fondamento nella gestione del paziente con angina stabile

✓Terapia medica ottimale non vuol dire assenza di rivascolarizzazione a priori, piuttosto la presenza di un *intensivo approccio farmacologico e non farmacologico*

✓Nell'ambito di un ottimale approccio farmacologico secondo le recenti Linee Guida internazionali e documenti di consenso nazionali *la ranolazina occupa un ruolo di rilievo*