

BOLOGNA , 16-17 giugno 2017

Diagnosi di cardiopatia ischemica nel paziente diabetico



UNIVERSITÀ
DEGLI STUDI
DI PADOVA



SIPREC
società italiana
per la prevenzione
cardiovascolare

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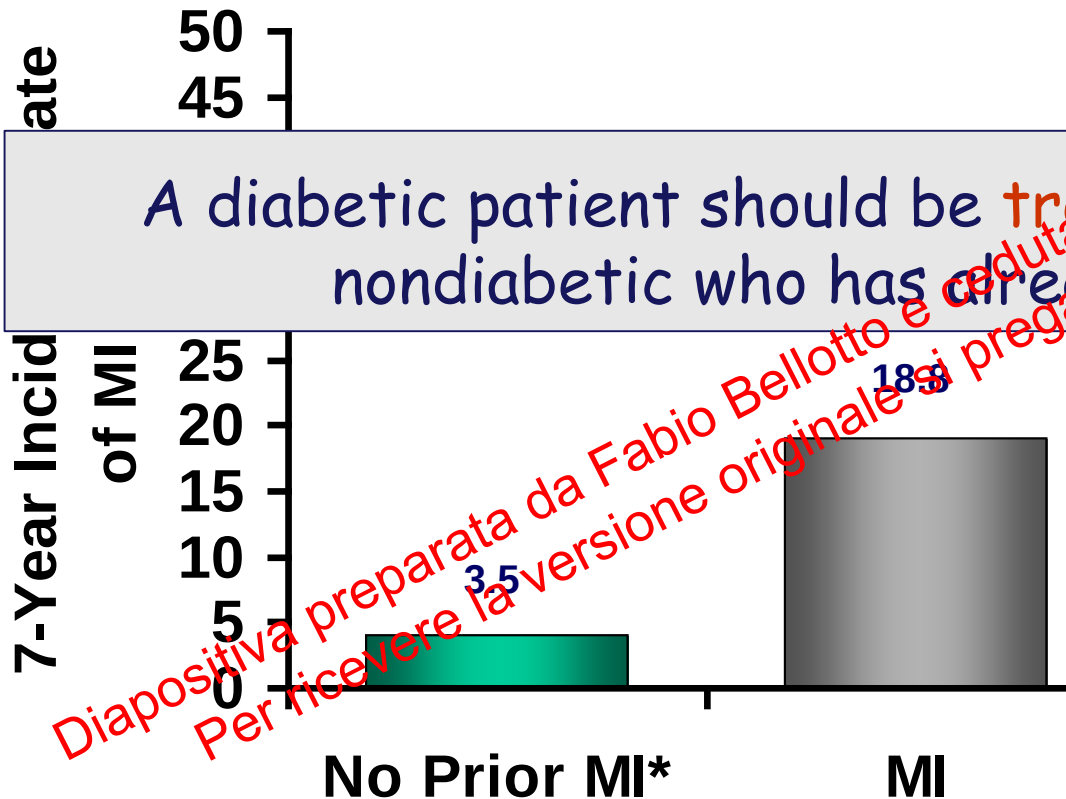
www.ilQuore.it

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Type 2 Diabetes and CHD: 7-Year Incidence of Fatal/Nonfatal MI (East West Study)

Haffner SM et al. *N Engl J Med.* 1998;339:1229-234

Nondiabetic n = 1373



CHD = coronary heart disease; MI = myocardial infarction. *These patients had no prior MI at baseline.

Principles for diagnosis and management

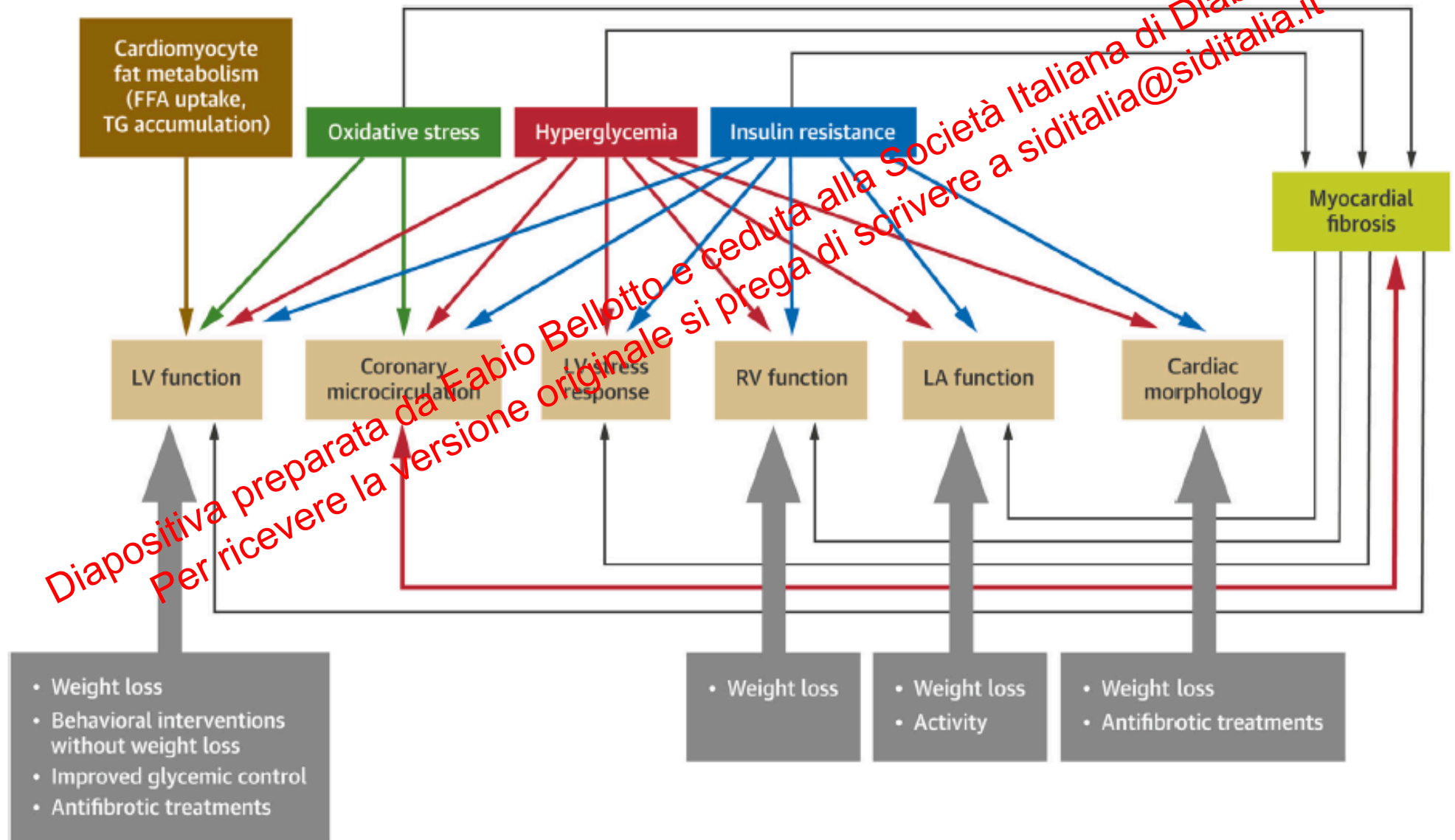
Cardiovascular disease (CVD) and
Diabetes mellitus (DM)

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Subclinical Myocardial Impairment in Metabolic Diseases

Kosmala W, Sanders P, Marwick TH. *J Am Coll Cardiol Img* 2017;10:692–703

Pathophysiological Mechanisms, Cardiac Abnormalities, and Therapeutic Interventions in Metabolic Heart Disease



Type 2 diabetes mellitus (T2DM) and obesity are the principal causes of functional and structural myocardial disease that are independent of coronary, congenital, or valvular heart disease (1.2.)

1. Elliott P, Andersson B, Arbustini E, et al. Classification of the cardiomyopathies: a position statement from the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J 2008;29:270–6.

2. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol 2004;49:565–71.

T2DM has been reported by the Framingham Heart Study to be responsible for a 2- to 5-fold increase in HF risk, with an even higher frequency in the elderly (3).

3. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure. Am J Cardiol 1974;34:382–384.

The same cohort indicate an increase in HF risk of 5% in men and 7% in women for every unit increase in BMI, after adjustment for traditional cardiovascular risk factors, and a 9% to 14% increment of risk associated purely with weight excess (4).

4. Kenchaiah S, Evans JC, Levy D, et al. Obesity and the risk of heart failure. N Engl J Med 2002; 347:305–13.

The presence of subclinical disease confers an increased cardiovascular risk, with the risk of total mortality increased 2.9-fold for men and 1.7-fold for women (5).

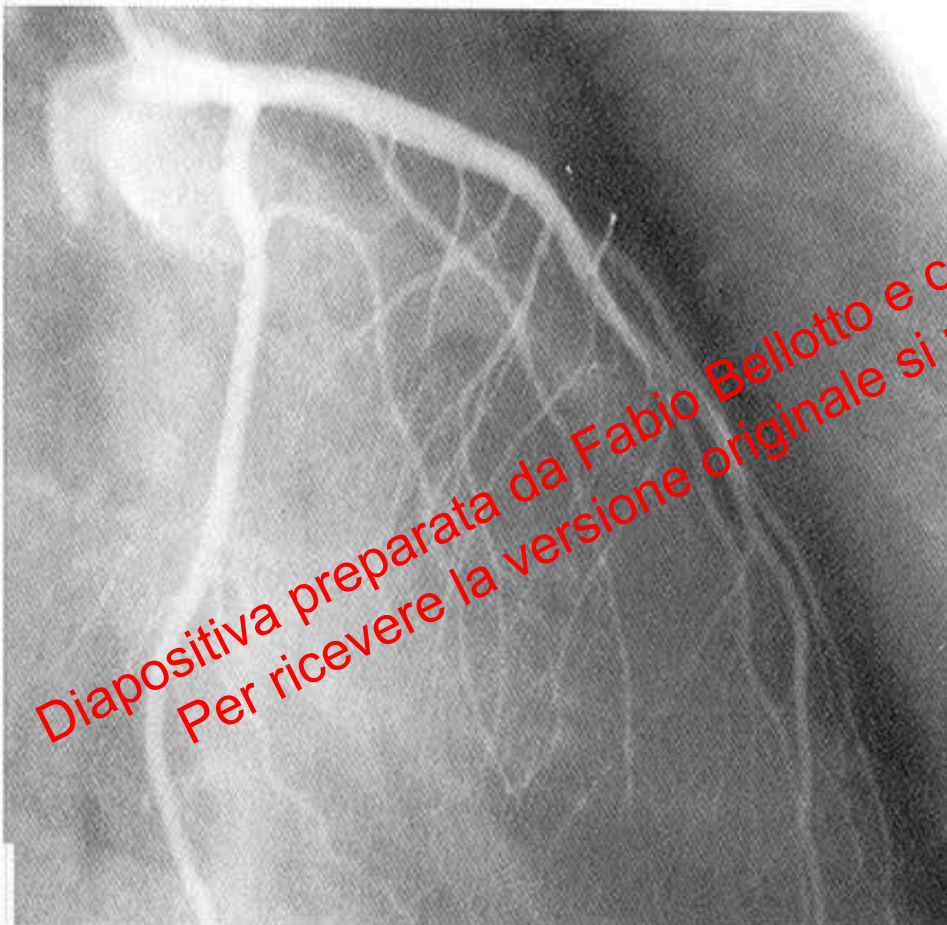
5. Kuller LH, Shemanski L, Psaty BM, et al. Subclinical disease as an independent risk factor for cardiovascular disease. Circulation 1995;92:720–6.

Several pop studies have also provided evidence of a strong and dose-dependent association of obesity and risk of AF with a 29% increase in AF risk per 5-unit increase in BMI (6).

6. Wong CX ST, Sun MT, et al. Obesity and the risk of incident, post-operative, and post-ablation AF: a meta-analysis of 626,603 individuals in 51 studies. J Am Coll Cardiol EP 2015;1: 139–52.

Tratto da GOOGLE immagini

MALATTIA CORONARICA (CHD)



soggetto normale



paziente diabetico

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Prima domanda:



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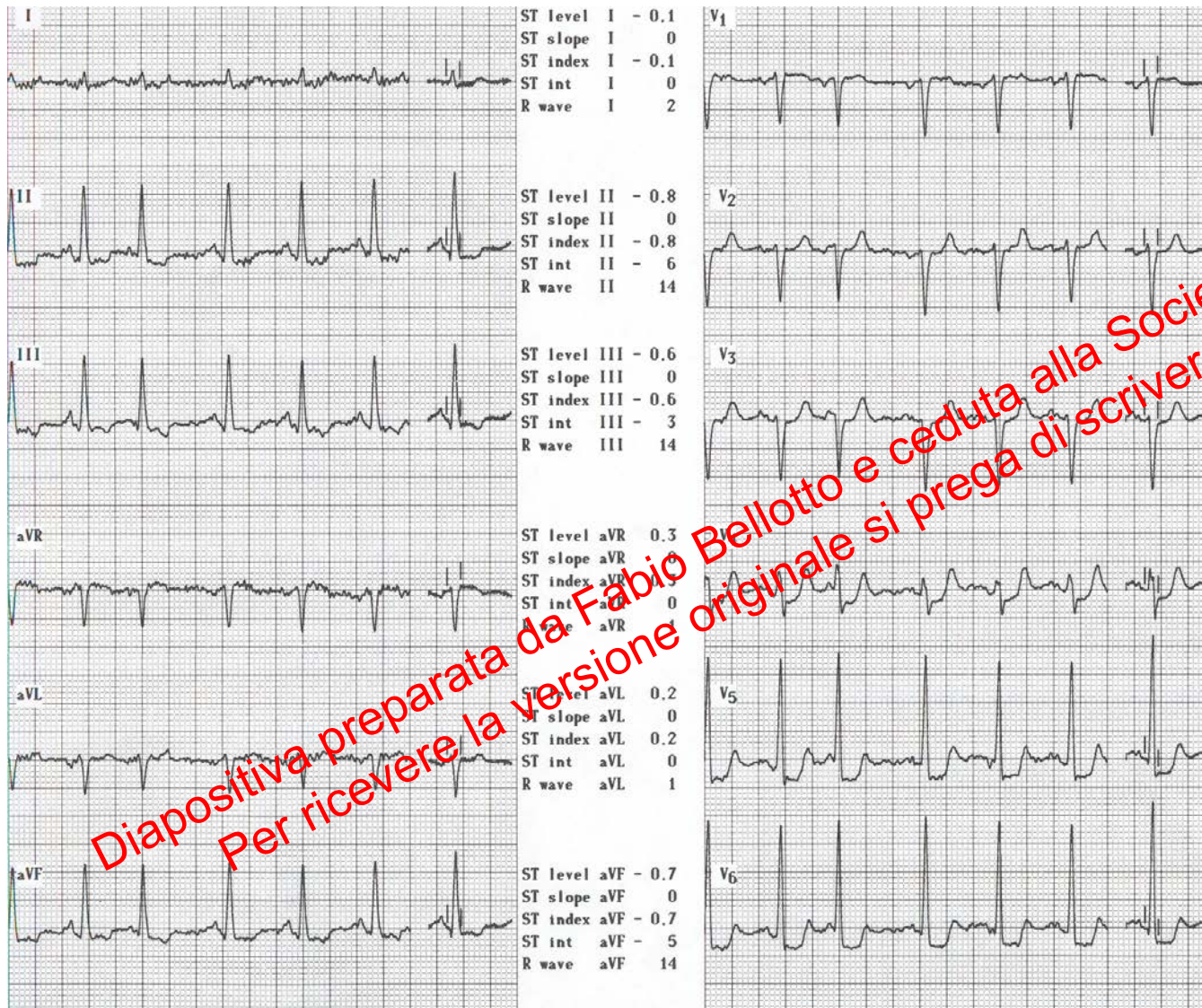
Una diagnostica cardiologica più approfondita può migliorare la prognosi nel Paziente con disturbi del metabolismo?

Test diagnostici non invasivi per la cardiopatia ischemica

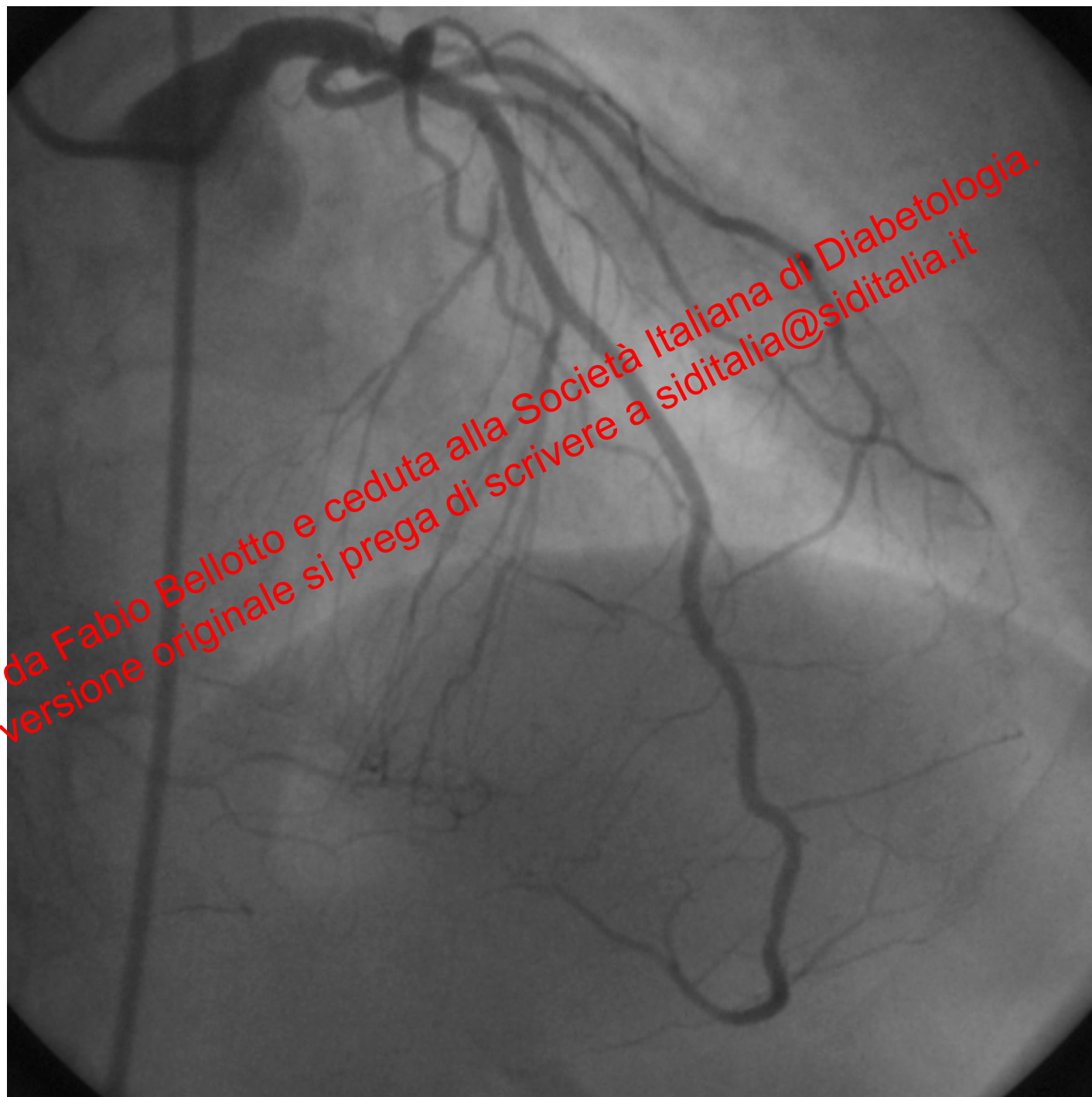
	Sensibilità %	Specificità %
ECG da sforzo	68	77
ECO da sforzo	80 - 85	84 - 86
Scintigrafia perfus. da sforzo	85 - 90	70 - 75
ECO - dobutamina	40 - 100	62 - 100
ECO - dipyridamolo	56 - 92	87 - 100
Scintigrafia perfus. con vasodilatatori	83 - 94	64 - 90

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E' utile eseguire un test ergometrico a tutti i pazienti in quanto diabetici? Anche in assenza di sintomi guida?

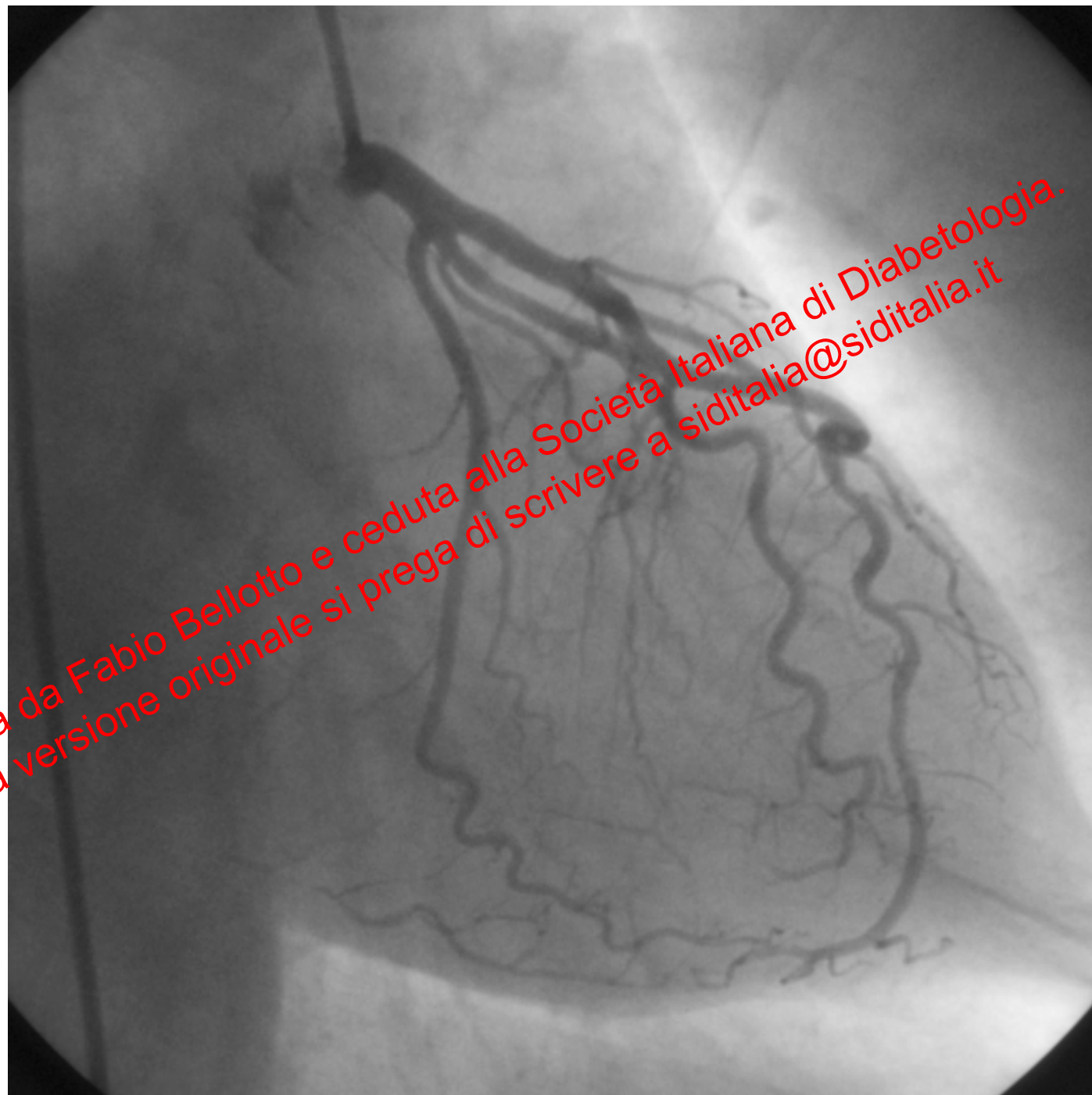


Test ergometrico interrotto a 50 w per sotto- slivellamento ST V3-V6, in assenza di sintomatologia anginoso.



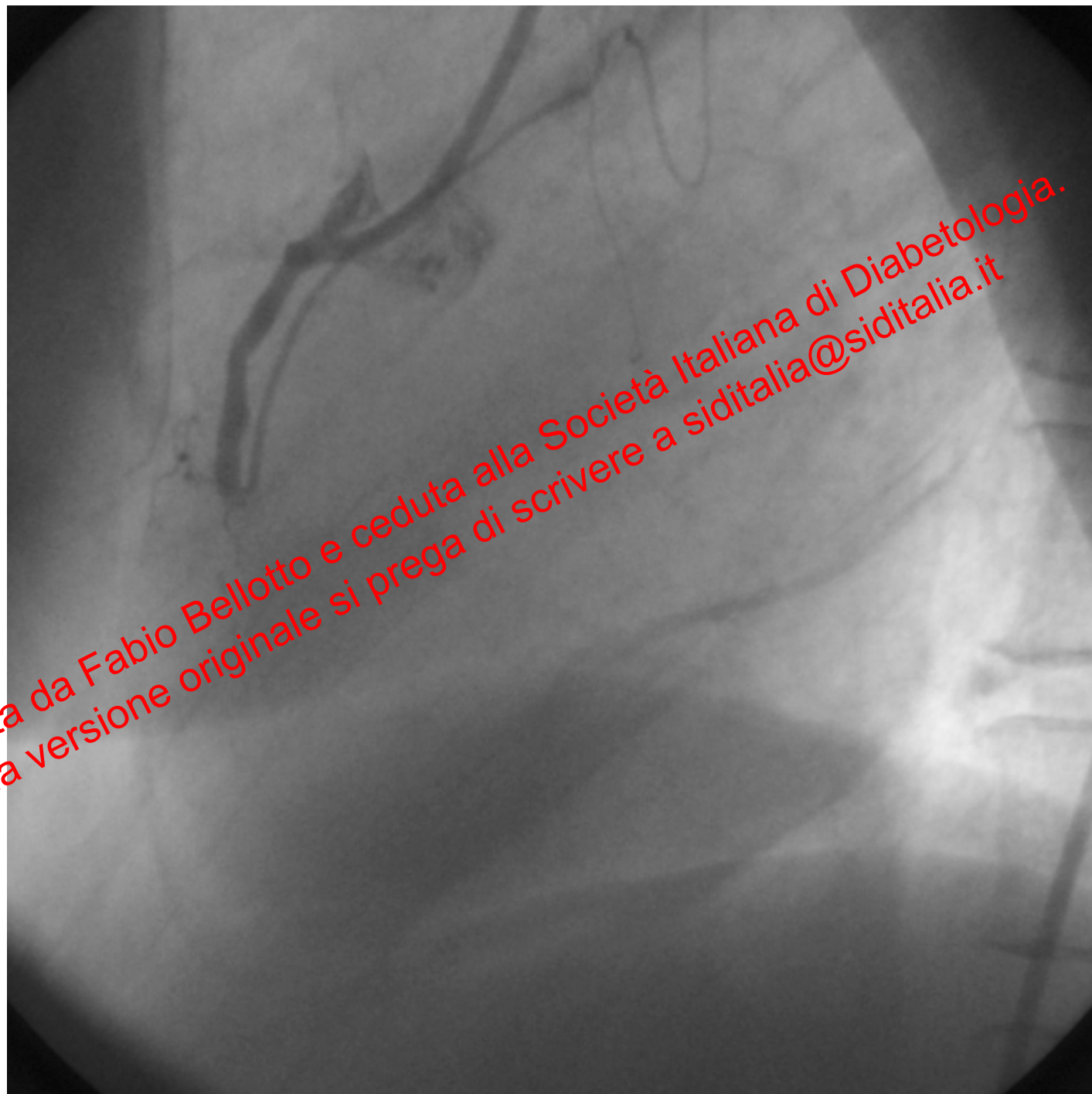
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L.G. aa 59, F



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L.G. aa 59, F



L.G. aa 59, F

lesioni "eccentriche" e "concentriche"

Glagov S et al. NEJM 1987;316:1371

Test ergometrico verosimilmente **POSITIVO**



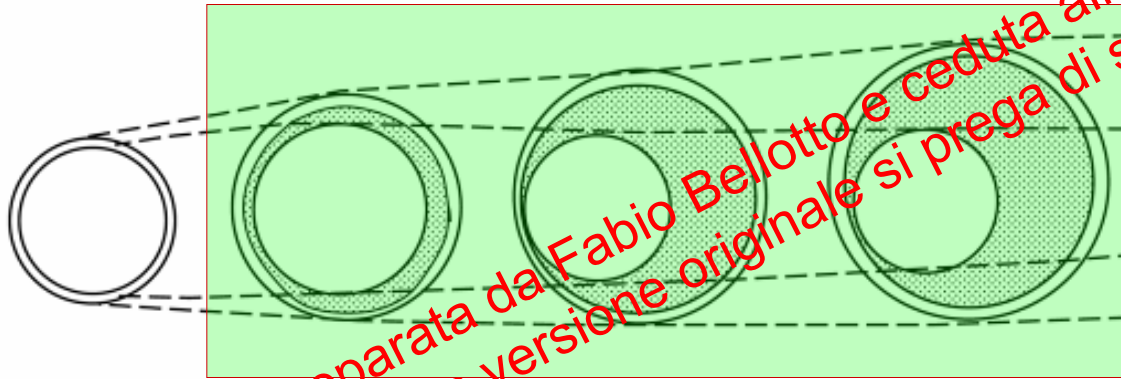
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OUTWARD (POSITIVE) REMODELING

lesioni "eccentriche" e "concentriche"

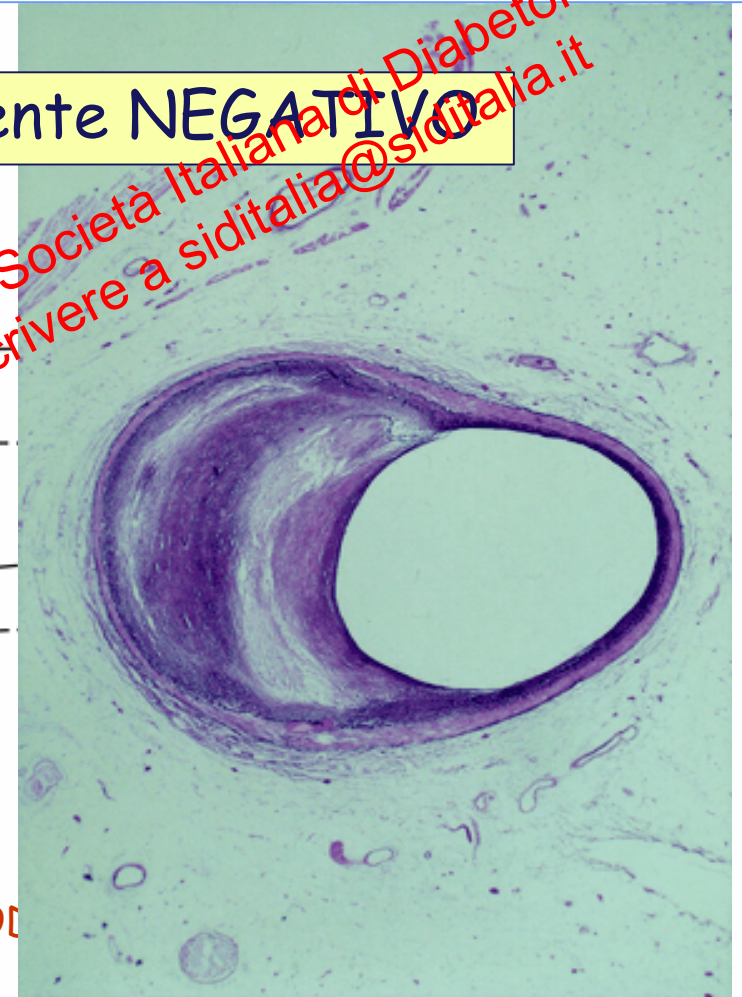
Glagov S et al. NEJM 1987;316:1371

Test ergometrico verosimilmente **NEGATIVO**



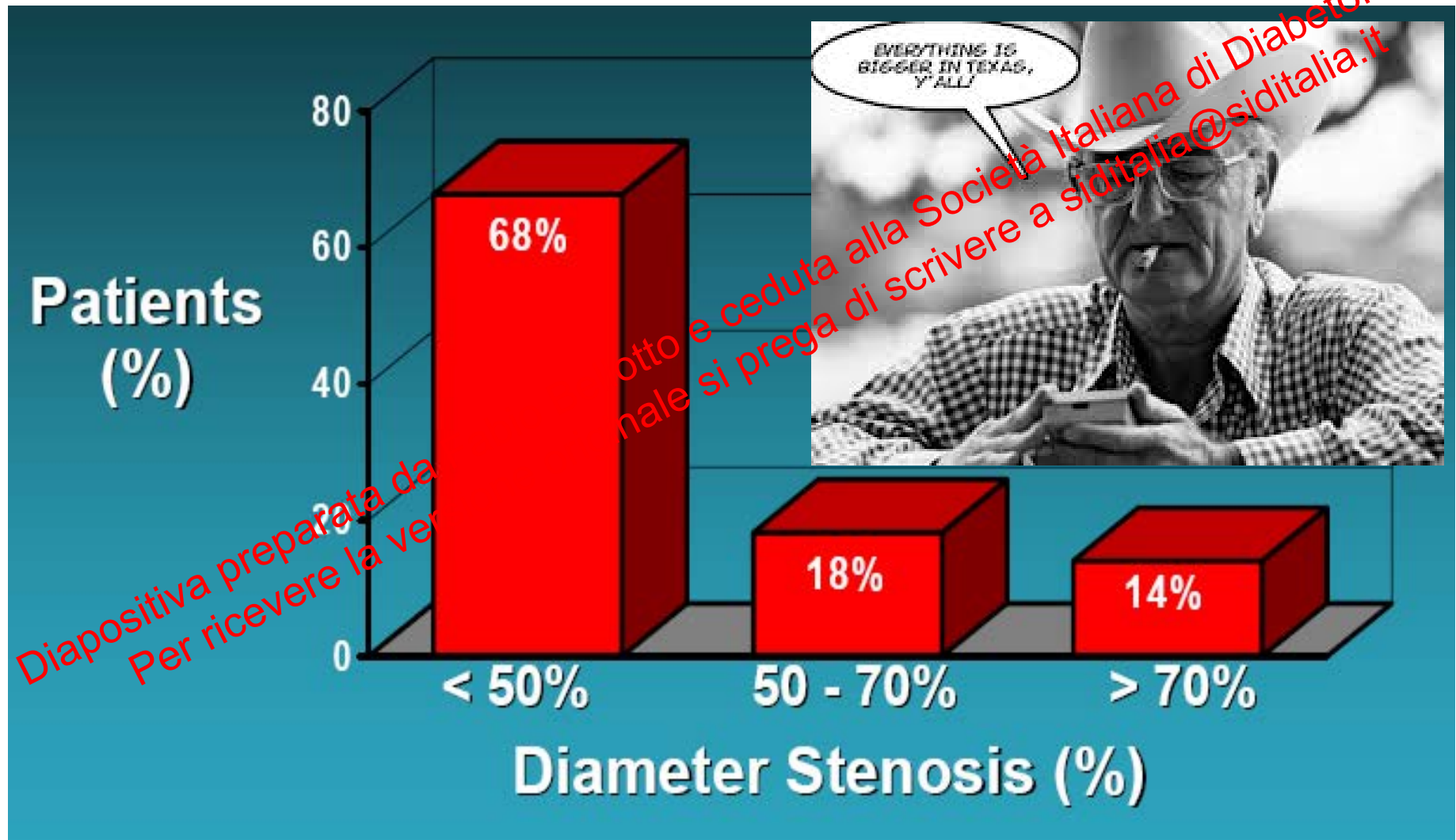
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OUTWARD (POSITIVE) REMOD



Severity of coronary artery stenosis before AMI

Falk et al. *Circulation* 1995;92:657-71



Data of retrospective angiographic studies suggest that, in more than two-thirds of patients, AMI evolves from mild to moderate (<70%) stenoses

- Diapositiva preparata da Fabio Bellotto e ceduta alla Societa Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it
1. Little WC, et al. Can coronary angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate coronary artery disease? *Circulation* 1988;78:1157–66.
 2. Ambrose JA, et al. Angiographic progression of coronary artery disease and the development of myocardial infarction. *J Am Coll Cardiol* 1988;12:56–62.
 3. Dacanay S, et al. Morphological and quantitative angiographic analyses of progression of coronary stenoses. A comparison of Q-wave and non-Q-wave myocardial infarction. *Circulation* 1994;90:1739–46.

Distribuzione e sovrapposizione delle patologie vascolari nei pazienti con aterotrombosi

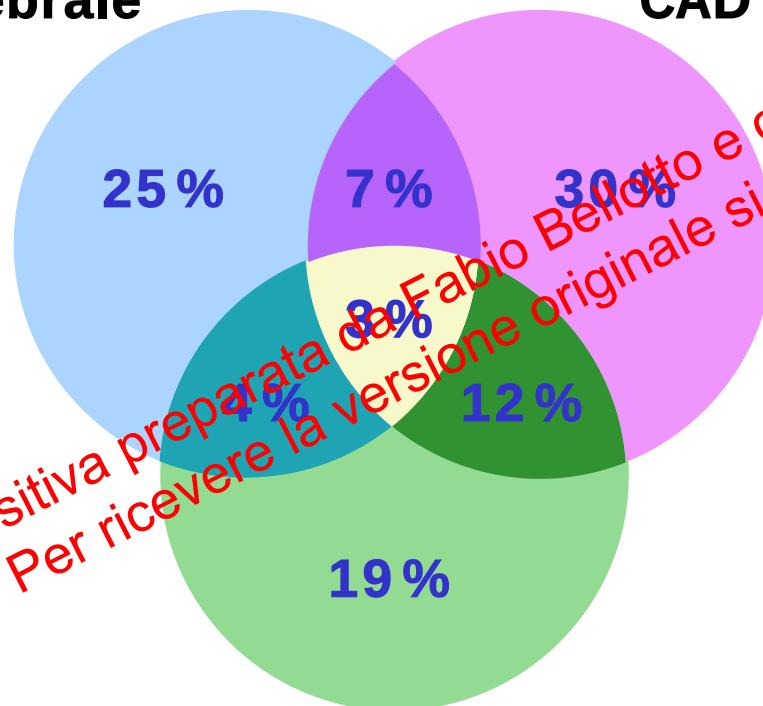
Adapted from TransAtlantic Inter-Society Consensus Group. J Vasc Surg 2000; 32:S16

CAPRIE

Aronow & Altmann

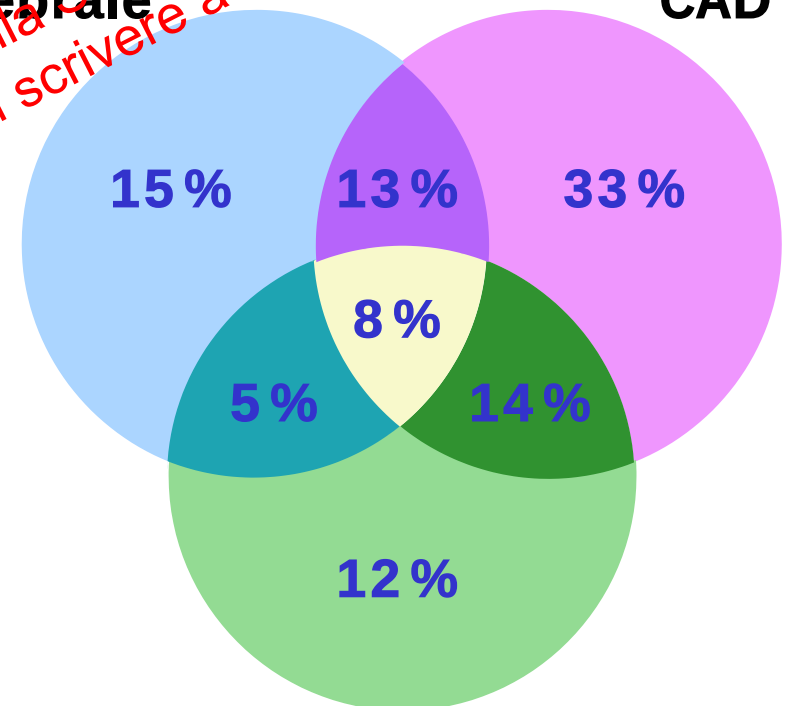
**Ischemia
cerebrale**

CAD



**Ischemia
cerebrale**

CAD



PAD

PAD

PAD = peripheral artery disease; **CAD** = coronary artery disease

Eco-Doppler carotideo

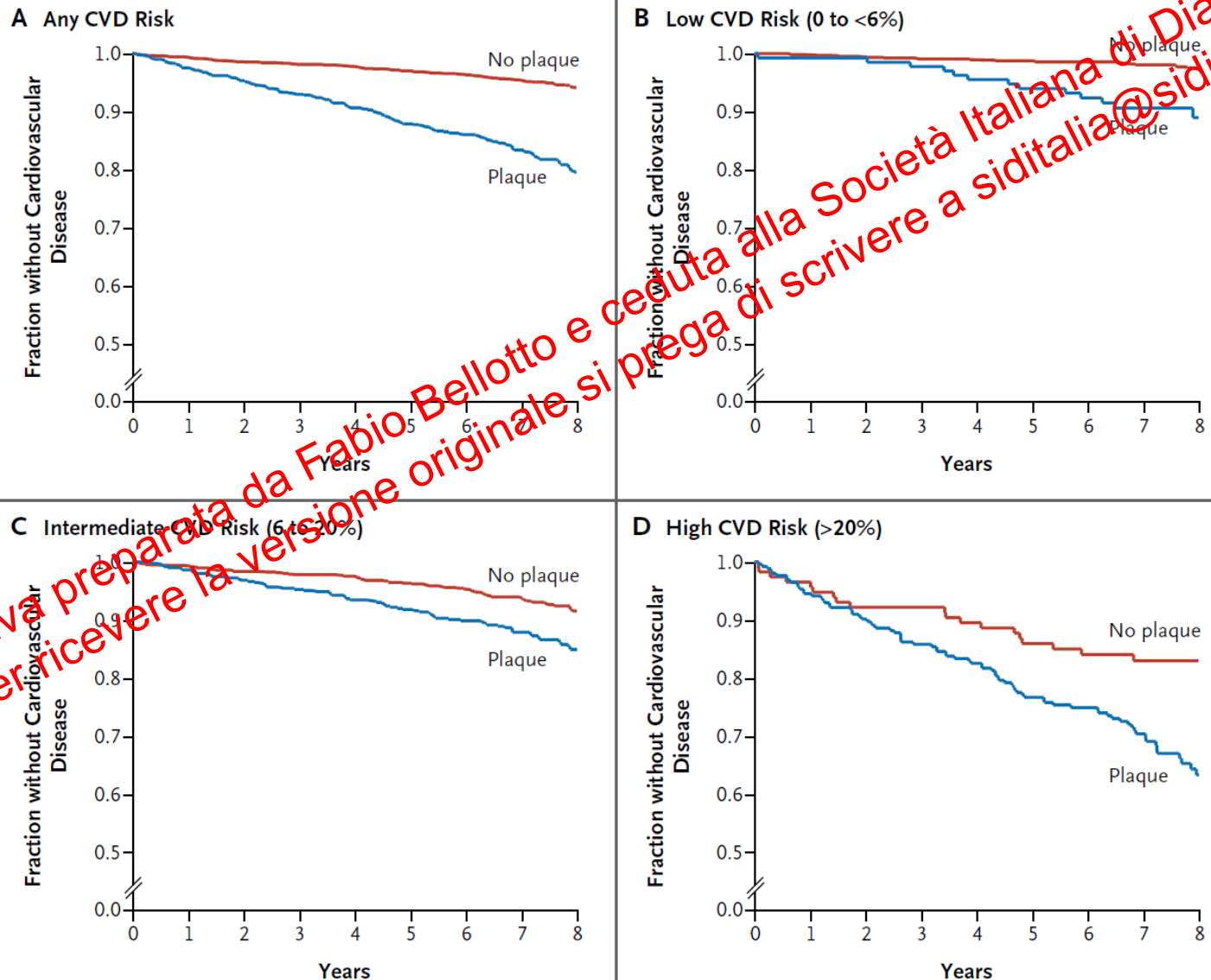


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Carotid-Wall Intima-Media Thickness and Cardiovascular Events

Polak F, et al. *N Engl J Med* 2011;365:213-21.

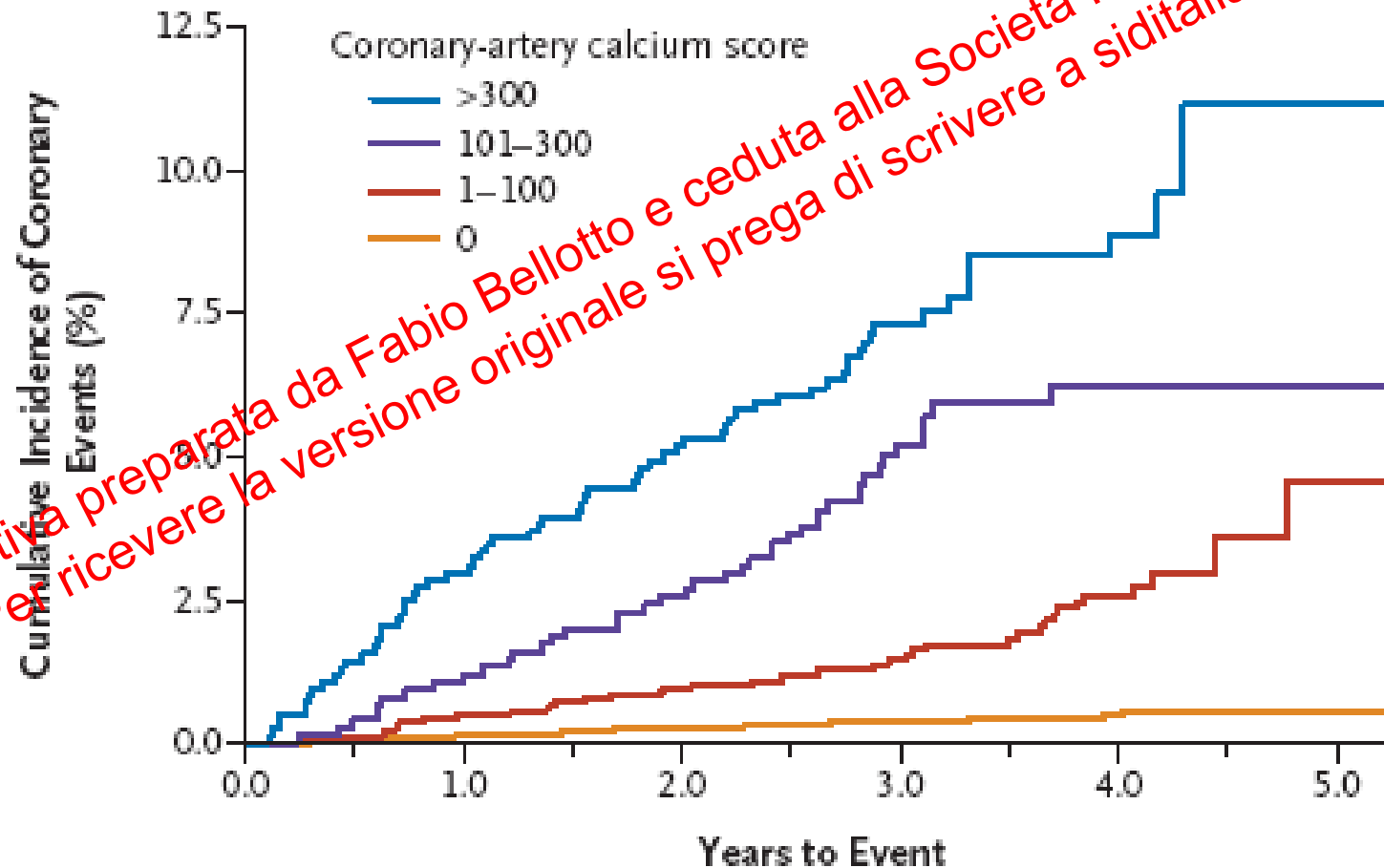
Kaplan-Meier Estimates of the Probability of New-Onset Cardiovascular Disease (CVD).



Coronary Calcium as a Predictor of Coronary Events in 4 Racial Ethnic Groups

Detrano R et al, *N Engl J Med* 2008; 358:1336-45.

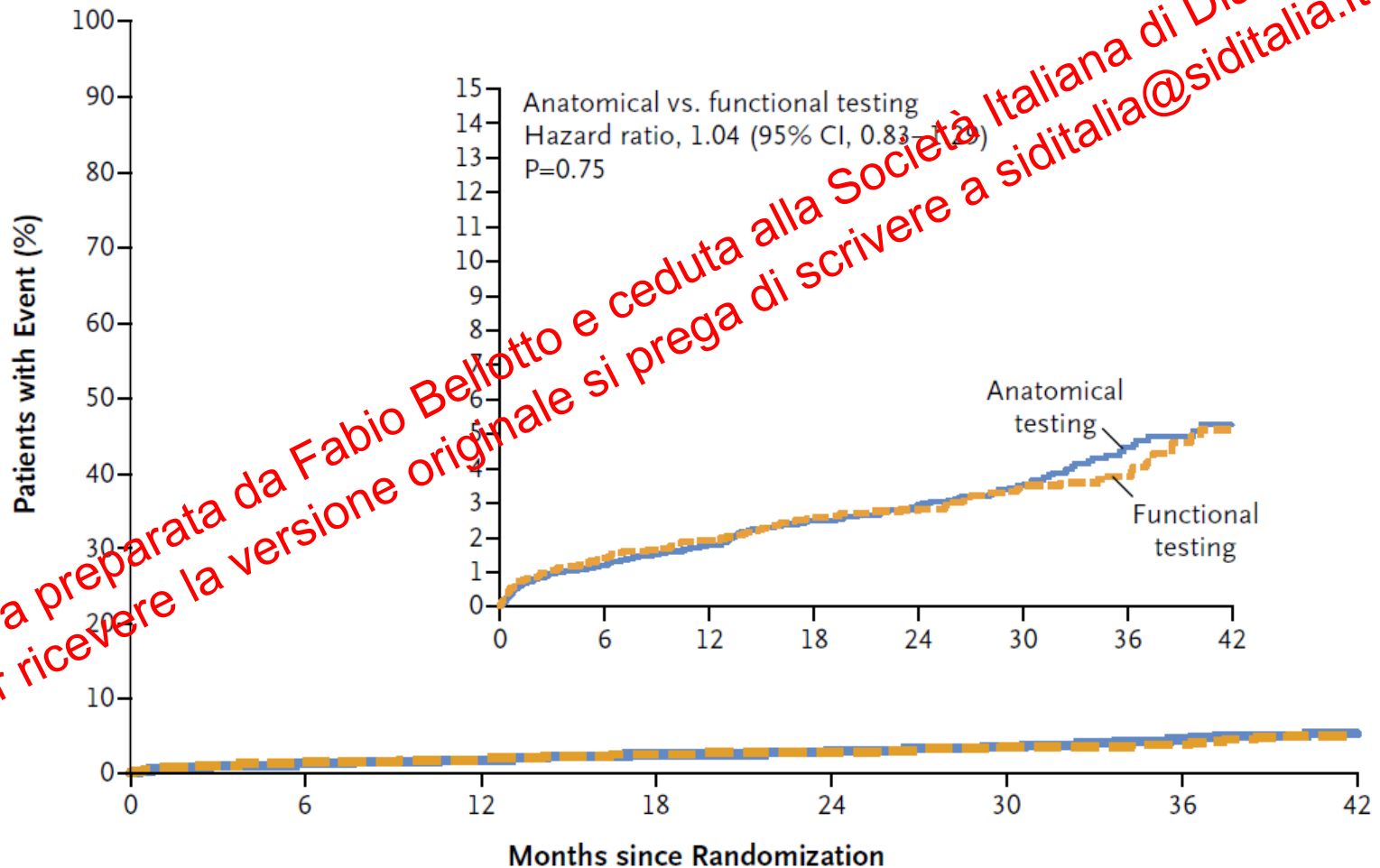
Rates for any coronary event



Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease

Douglas PS, et al for the PROMISE Investigators. March 14, 2015, at NEJM.org

Kaplan-Meier Estimates of the Composite Primary End Point as a Function of Time after Randomization



No. at Risk

Anatomical testing	4996	4703	4362	3551	2652	1705	902	269
Functional testing	5007	4536	4115	3331	2388	1518	832	258

- Il Doppler dei tronchi sovra-aortici ed il calcium score alla TAC possono aiutare a definire il livello di "rischio CV"
- Una coronaria angiograficamente sana alla coronarografia potrebbe, in realtà, essere già profondamente malata
- Una coronaria con stenosi lievi, comunque non critiche (<50-70%), si associa (solitamente) a test ergometrico negativo ma è comunque a rischio di complicarsi con trombosi e SCA
- il test ergometrico dovrebbe essere eseguito in presenza di sintomi che indirizzano verso la diagnosi di angina da sforzo o quando il paziente - anche asintomatico - intende sottoporsi ad un ciclo di ricondizionamento basato sull'esercizio

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Seconda domanda:



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La conoscenza dell'anatomia coronarica (evidenza di stenosi "critiche") ci consente **scelte terapeutiche** differenziate?

Back to coronary arteries

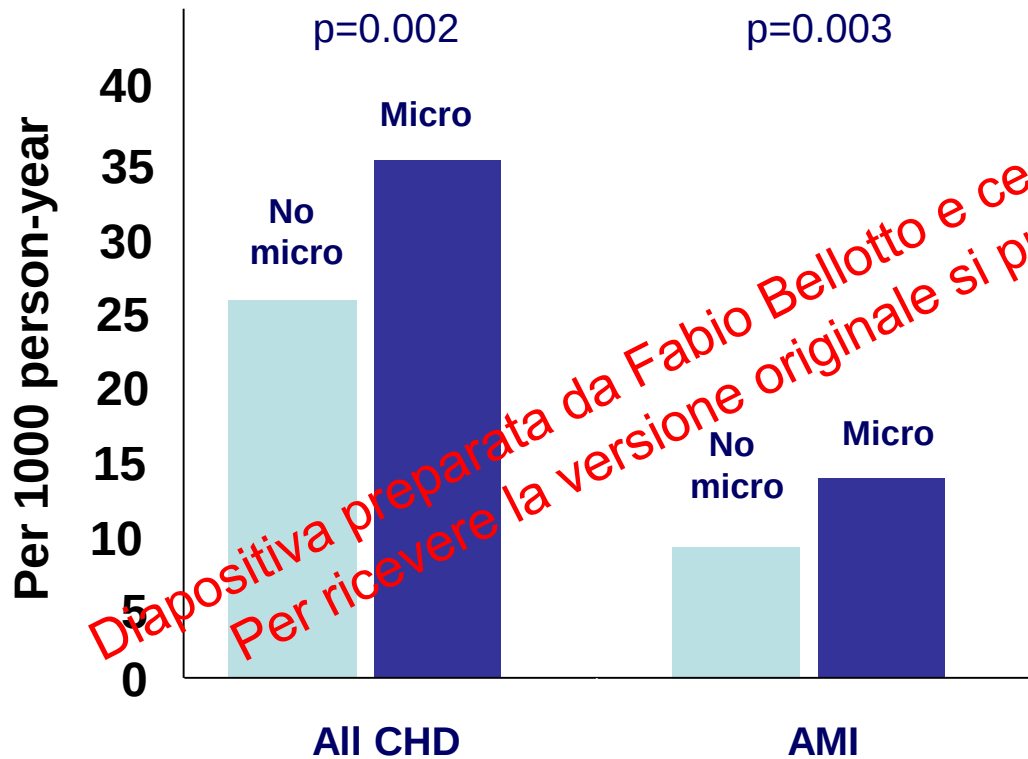


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Incidence Rate of CHD Events: The role of microvascular complications

Avogaro A, et al. 2007

Males

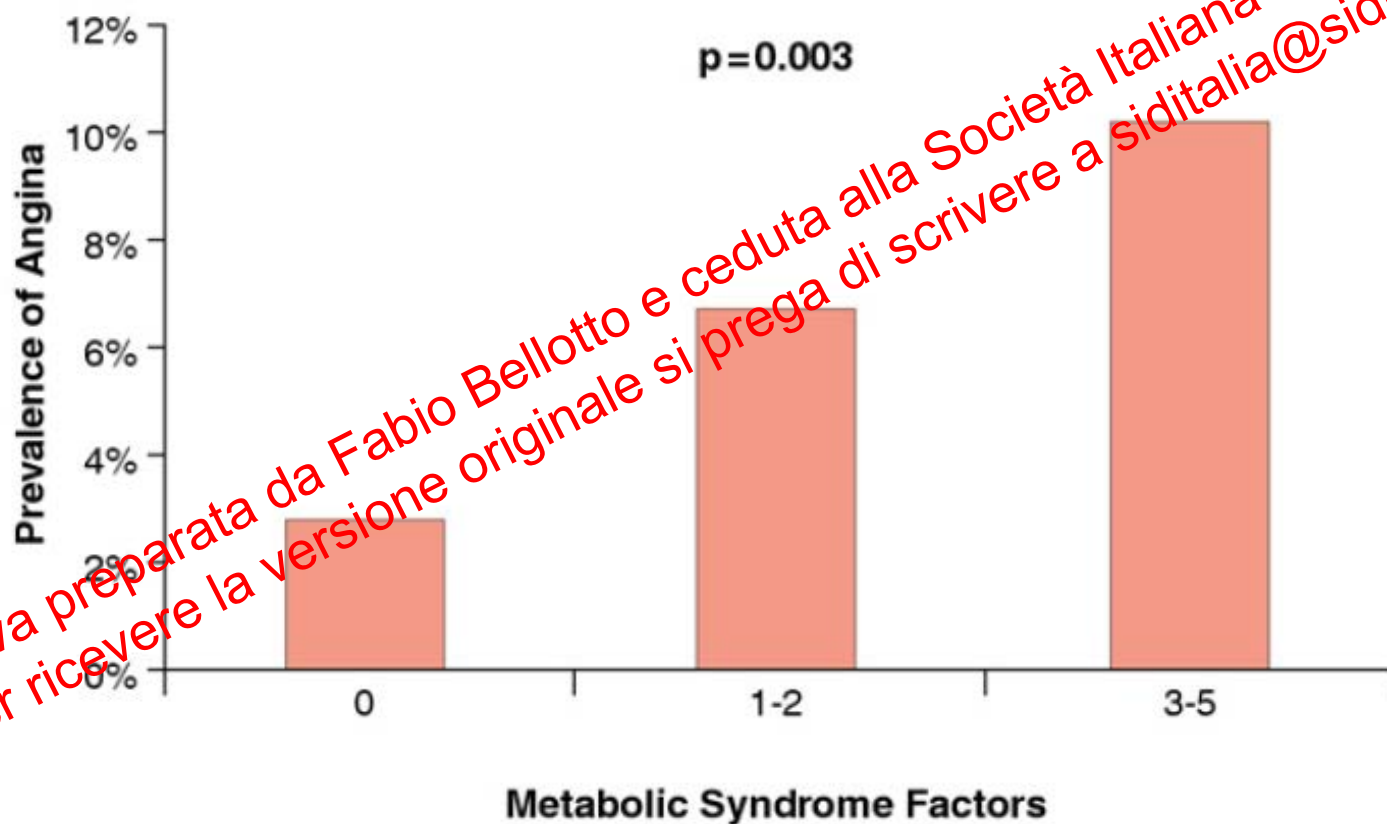


Clinical characteristics, vascular function, and inflammation in women with angina in the absence of coronary atherosclerosis

The Dallas Heart Study

Banks K et al. *J Am Coll Cardiol Img* 2011;4:65–73.

Relationship between angina and number of Metabolic Syndrome factors

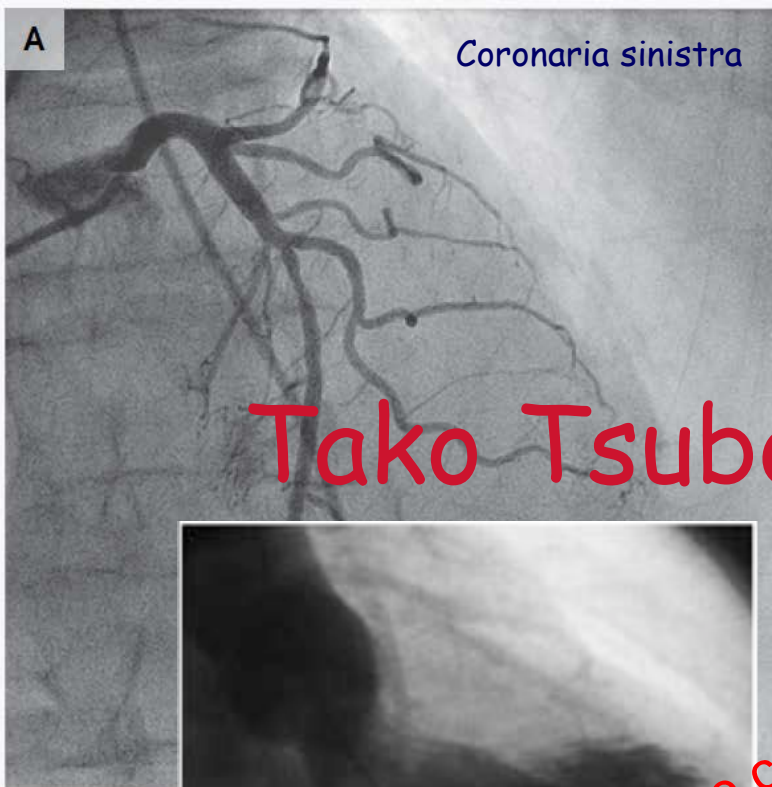


Metabolic syndrome factors:

waist circumference **35** inches, triglycerides **150** mg/dl, HDL cholesterol **50** mg/dl, BP **130/85** mm Hg, and fasting glucose **100** mg/dl

A

Coronaria sinistra



B

Coronaria destra



Tako Tsubo syndrome

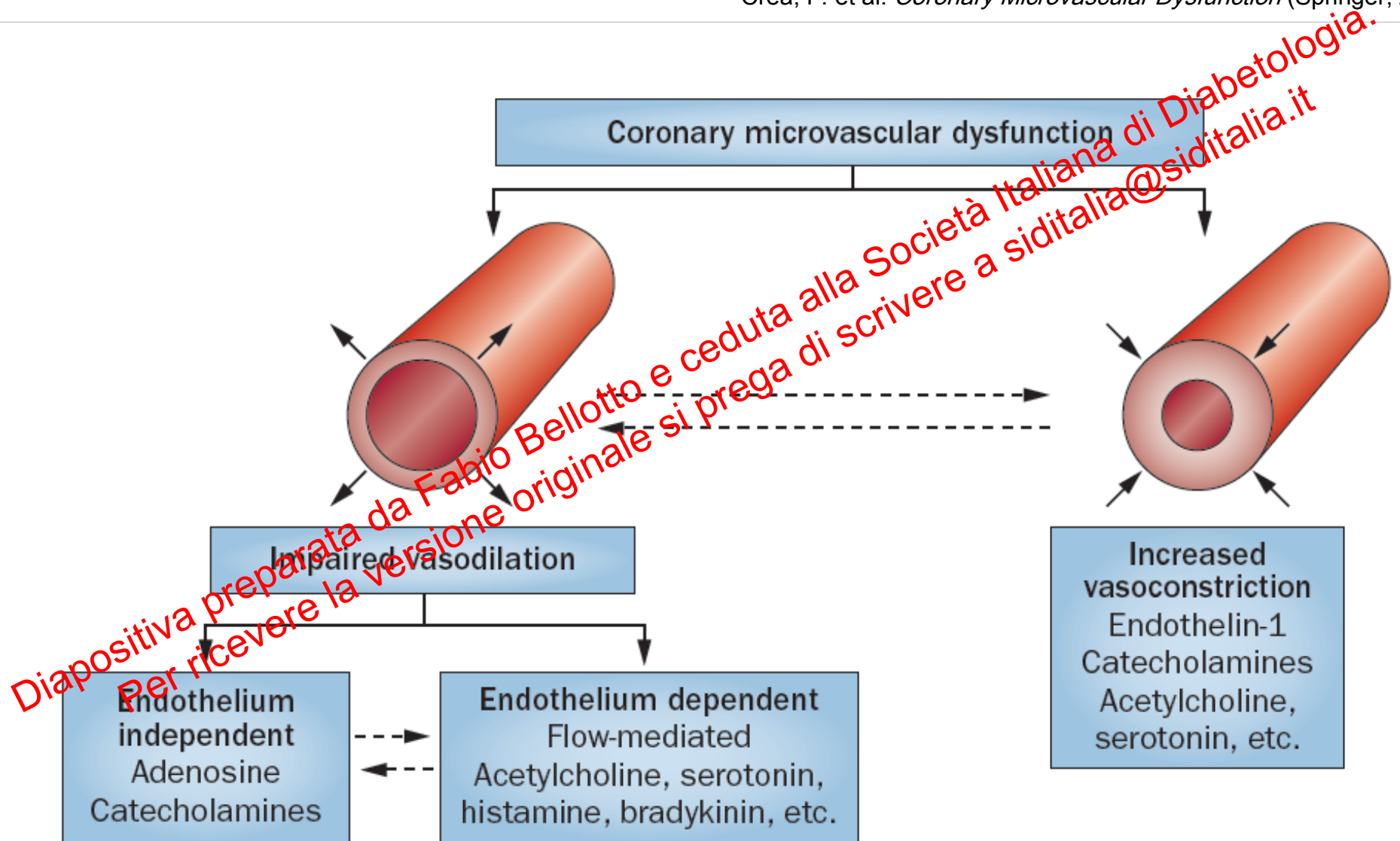
C



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Coronary microvascular dysfunction: mechanisms and functional assessment

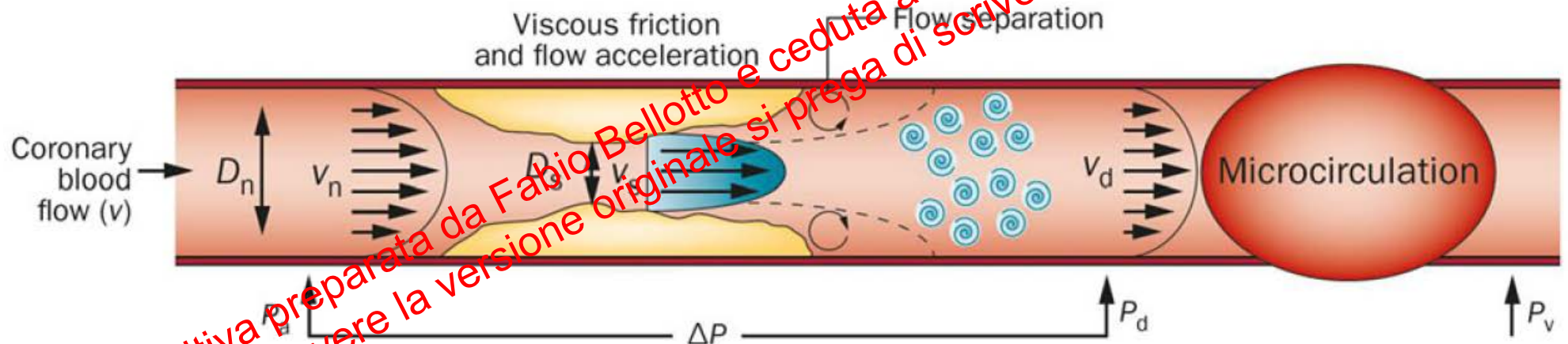
Crea, F. et al. *Coronary Microvascular Dysfunction* (Springer, 2014)



Fundamentals in clinical coronary physiology: why coronary flow is more important than coronary pressure

van de Hoef TP, et al. Eur Heart J 36(47):3312-19;2015

Diagram of stenosis flow field

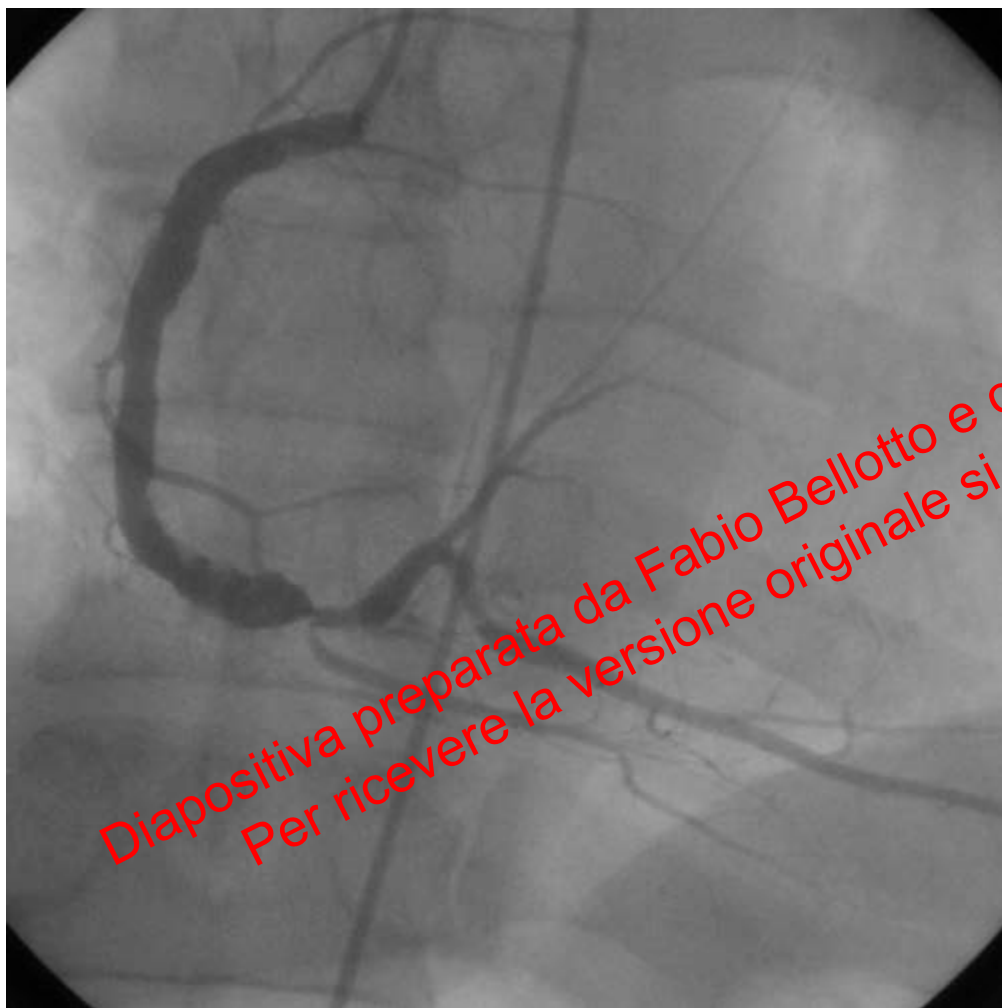


Coronarografia

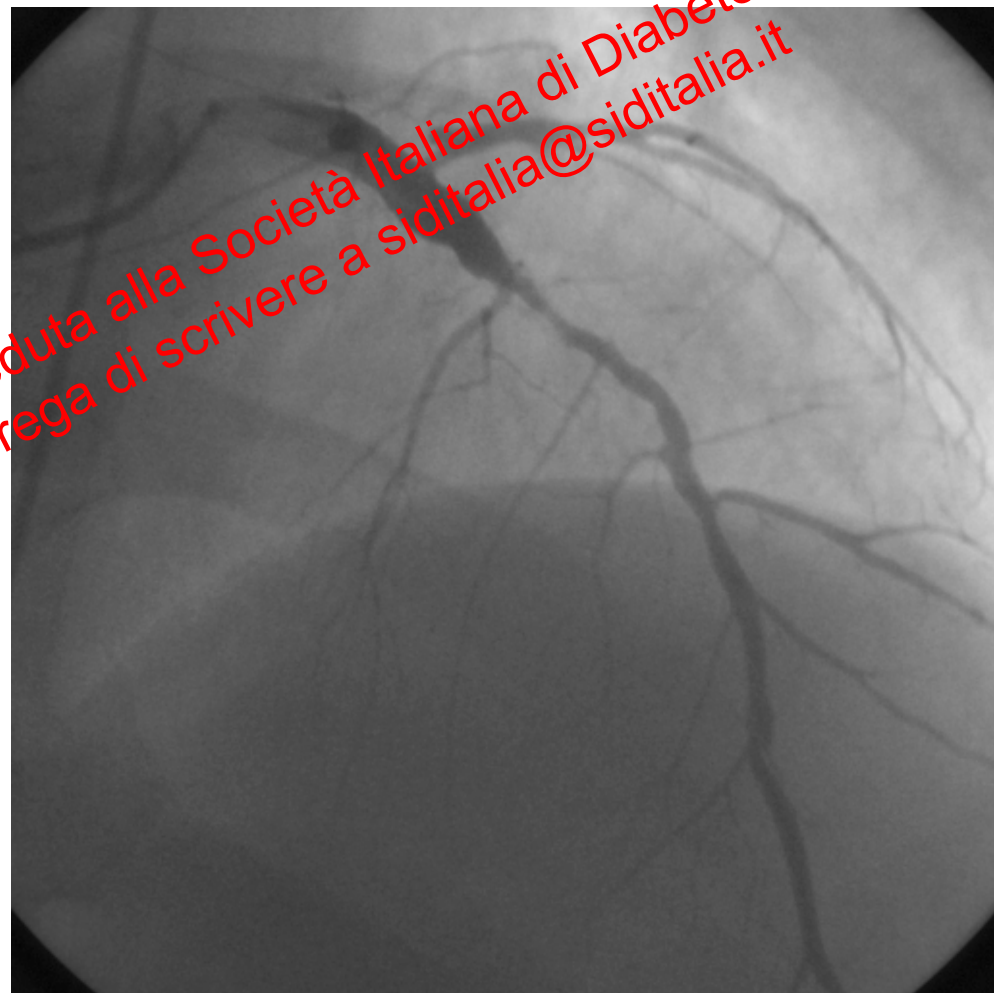


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Back to coronary arteries



Coronaria destra



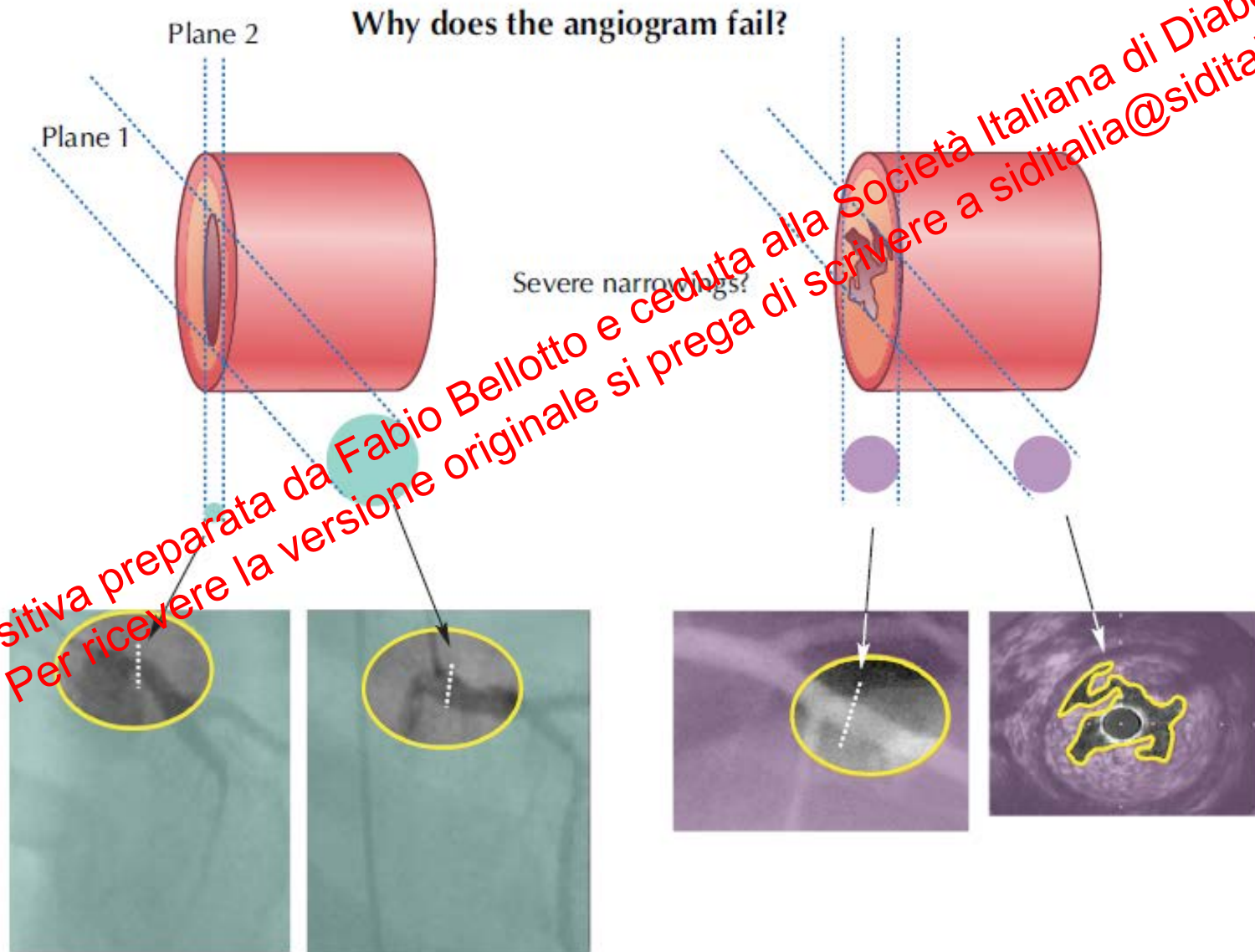
Coronaria sinistra

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Current Concepts of Integrated Coronary Physiology in the Catheterization Laboratory

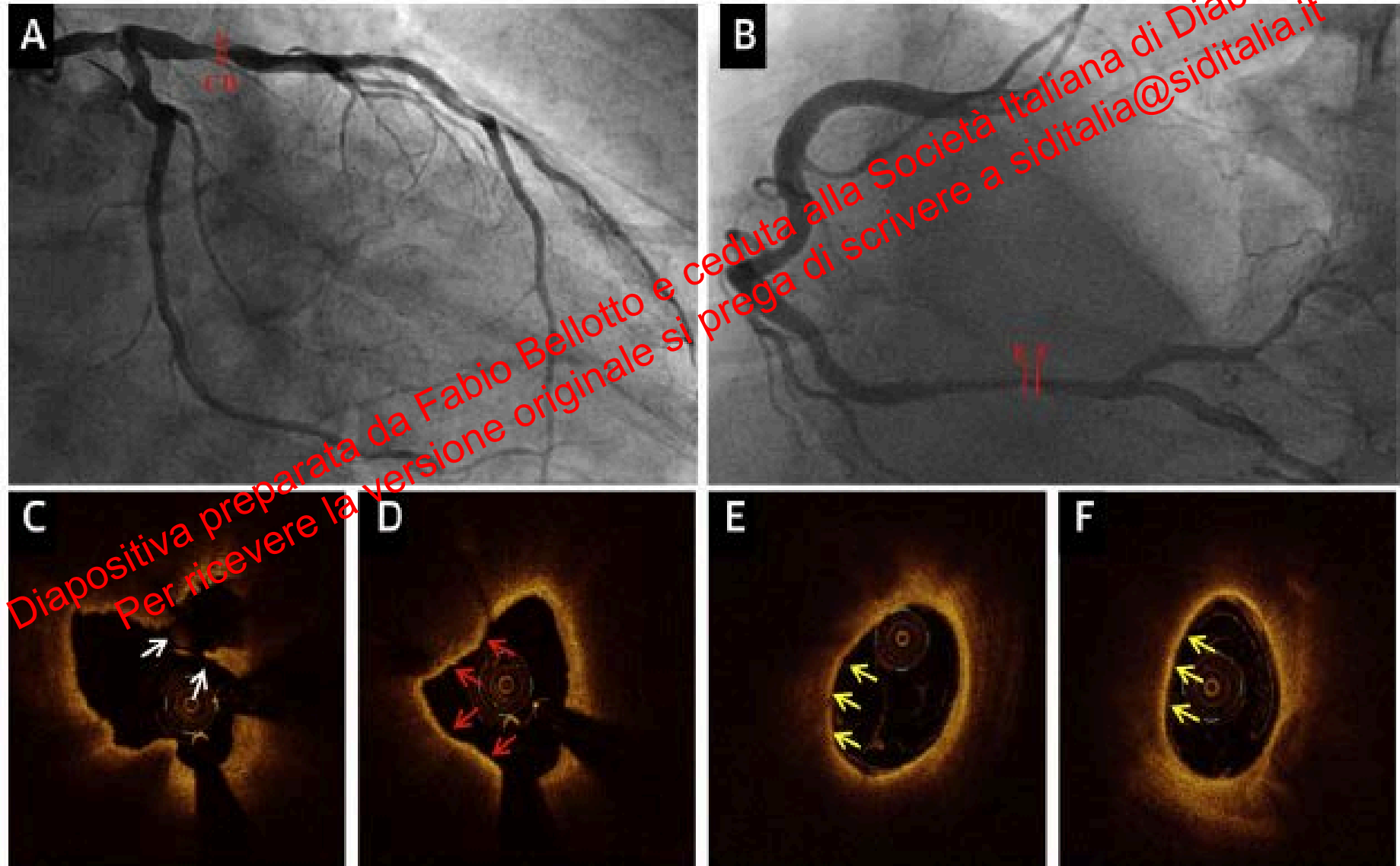
STATE-OF-THE-ART PAPER

Kern and Samady. *J Am Coll Cardiol* 2010;55,3:173-85



Prevalence and Characteristics of TCFA and Degree of Coronary Artery Stenosis An OCT, IVUS, and Angiographic Study

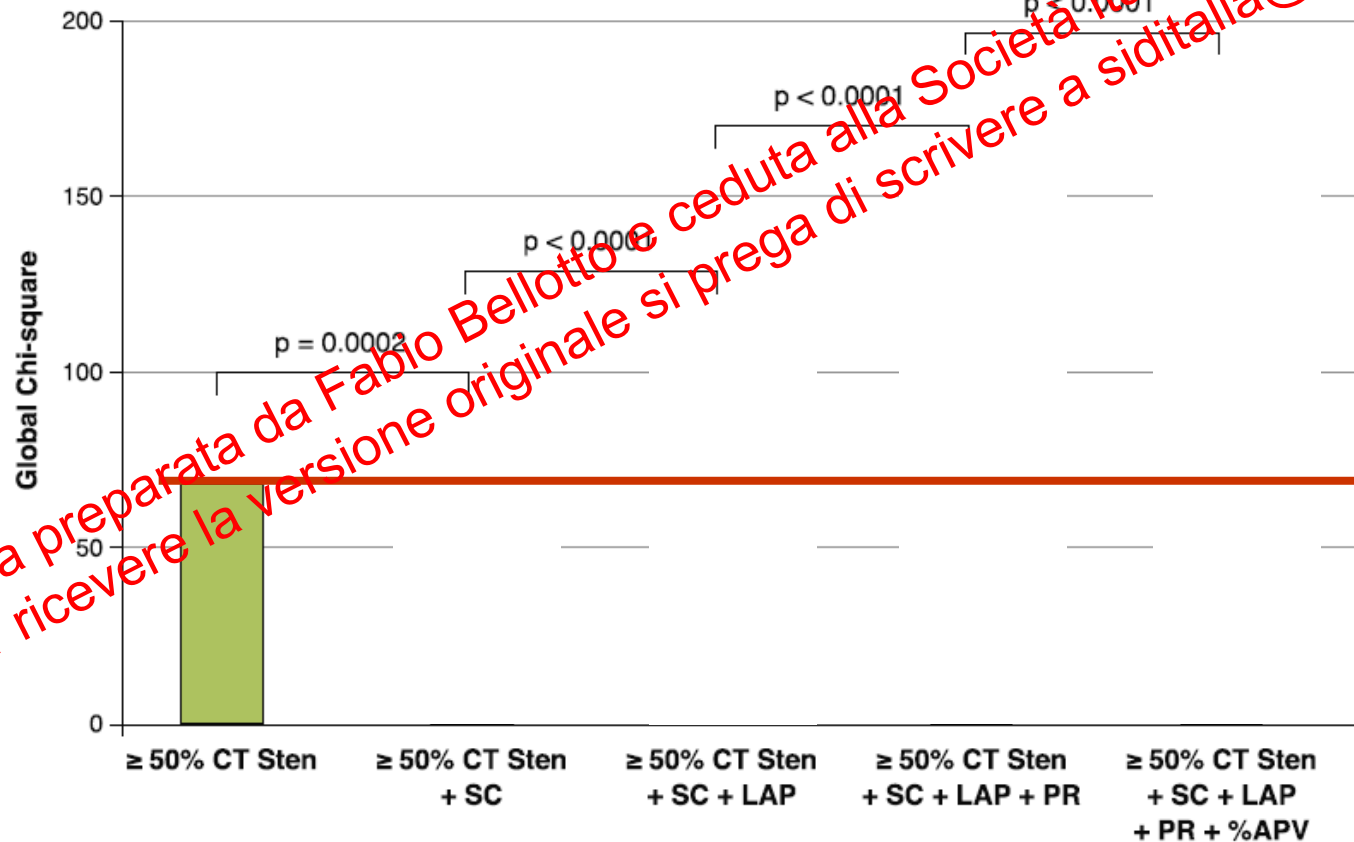
Tian J, et al. *J Am Coll Cardiol* 2014;64:672–80



Atherosclerotic Plaque Characteristics by CT Angiography Identify Coronary Lesions That Cause Ischemia

Park HB, et al. *JAmCollCardiol Img* 2012;8:1–10

Incremental risk prediction beyond computed tomographic



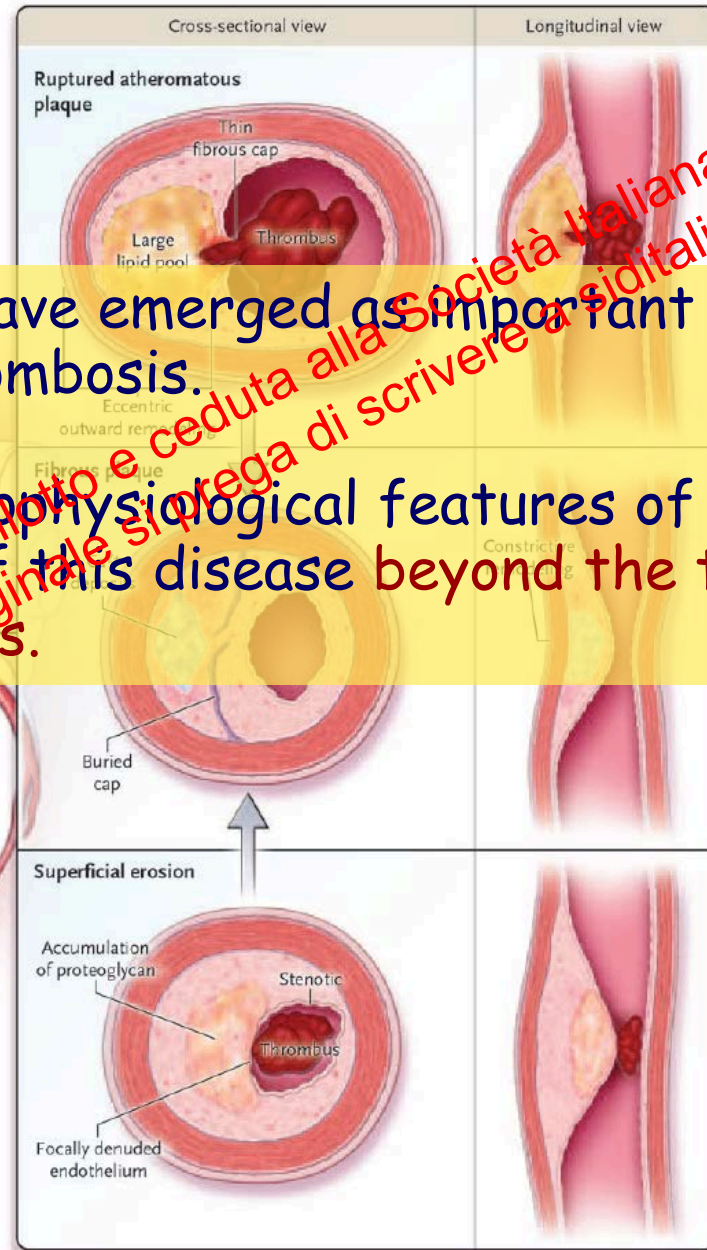
CT: computed tomographic; **SC**: spotty calcification; **LAP**: low attenuation plaque; **PR**: positive arterial remodeling; **%APV**: percent aggregate plaque volume

Mechanisms of Acute Coronary Syndromes and Their Implications for Therapy

Peter Libby. *N Engl J Med* 2013;368:2004-13

Inflammatory pathways have emerged as important drivers of plaque disruption and thrombosis.

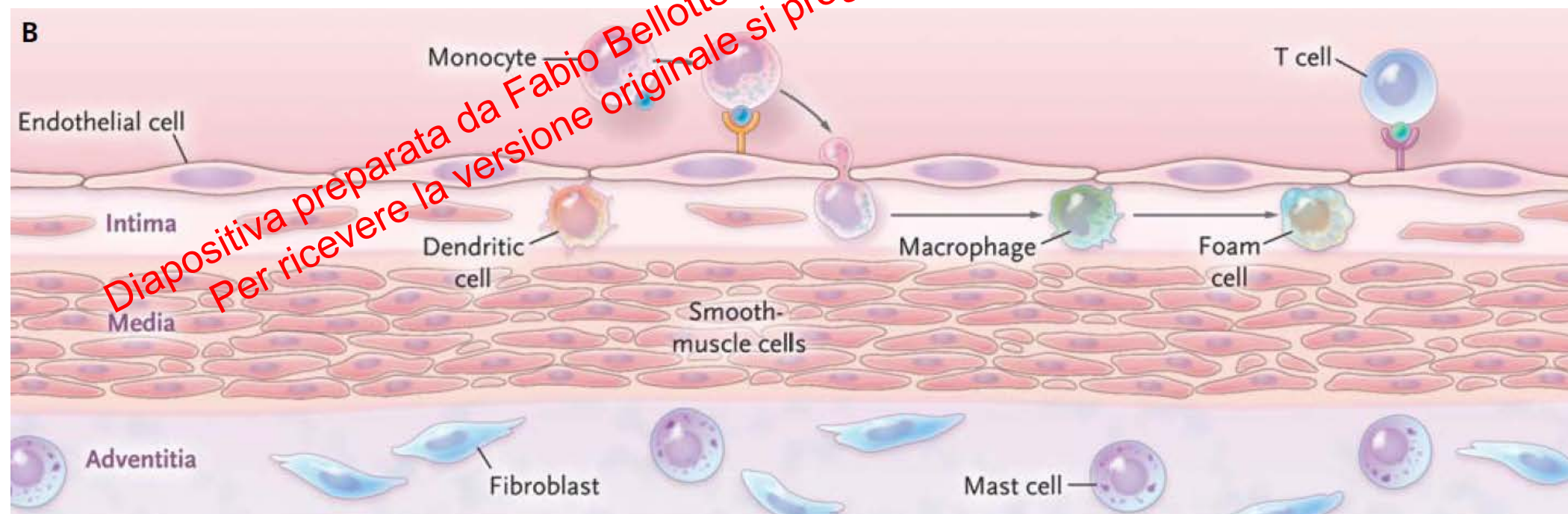
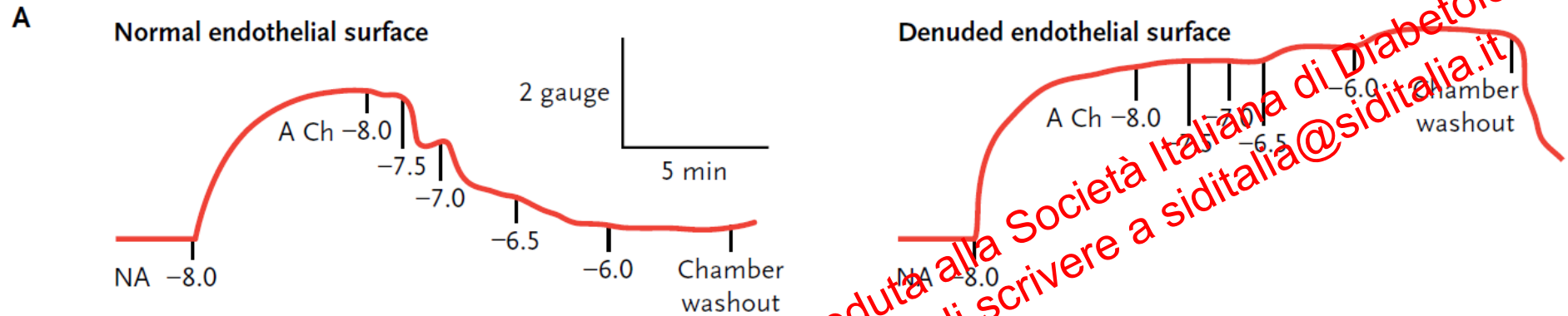
This insight into the pathophysiological features of ACS expands the scope of treatment of this disease beyond the traditional focus on reducing stenoses.



Diapositiva preparata da Fabio Benfante e ceduta alla Società Italiana di Diabetologia. Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

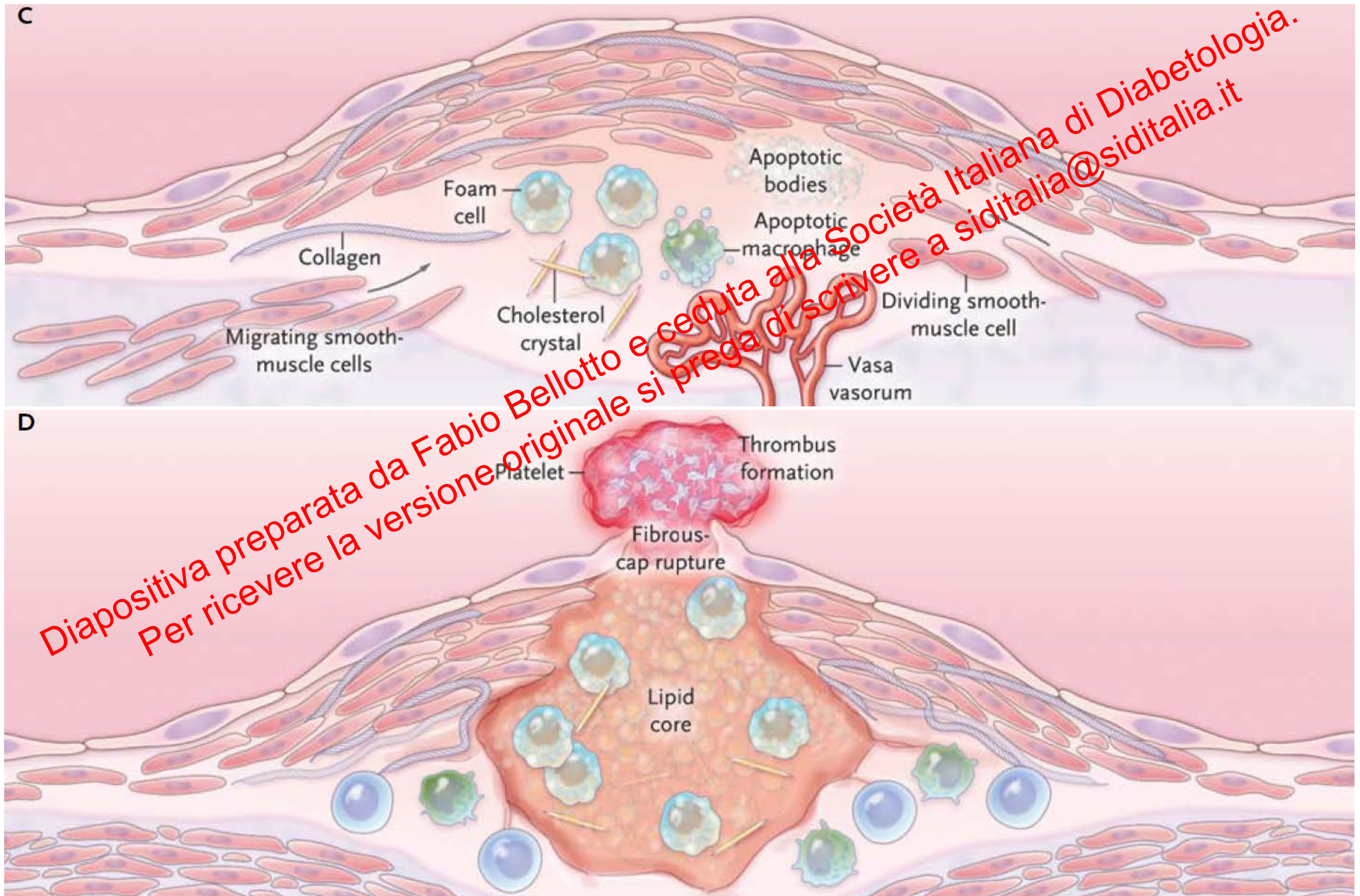
A Tale of Coronary Artery Disease and Myocardial Infarction

Nabel EG and Braunwald E. *N Engl J Med* 2012;366:54-63



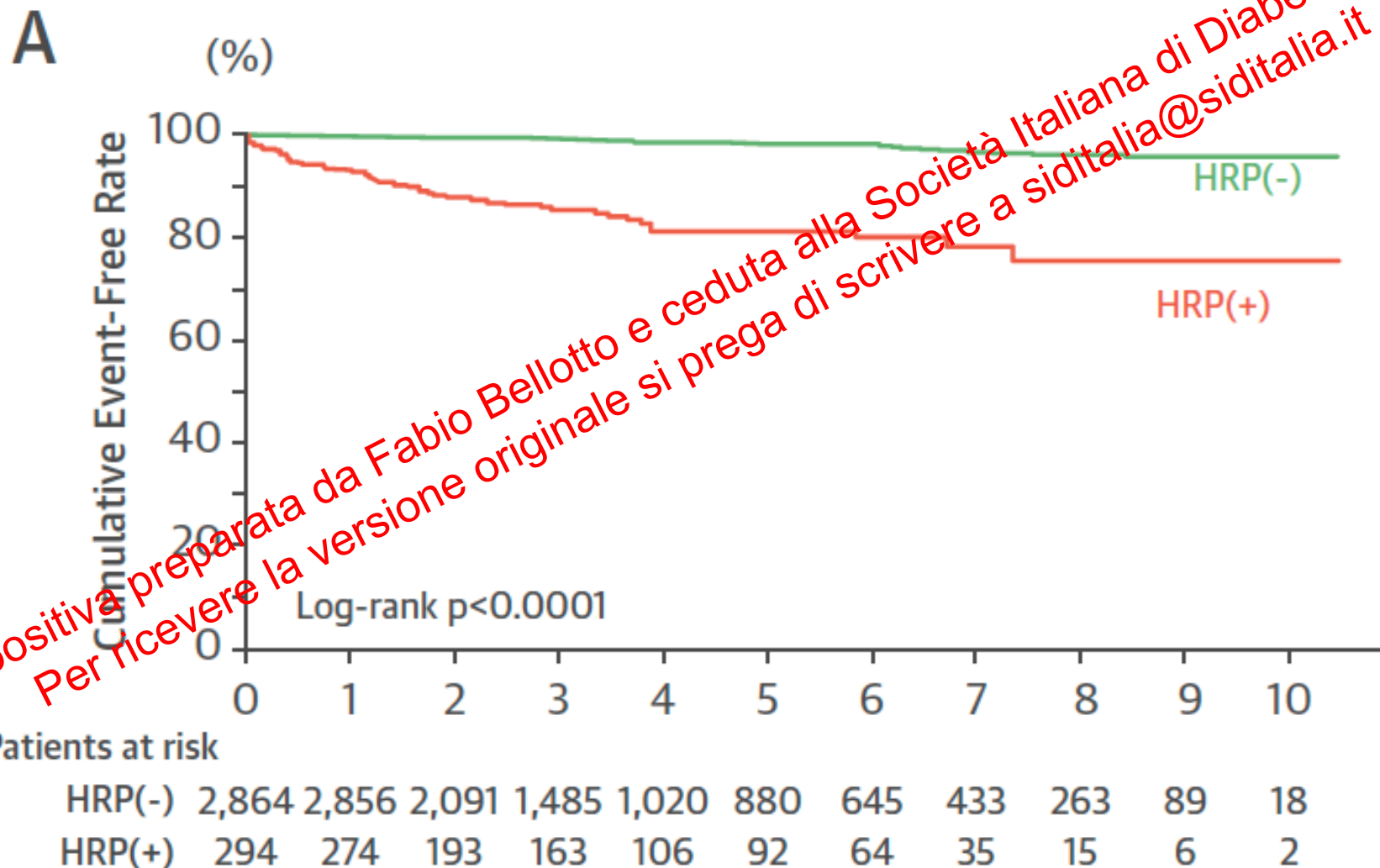
A Tale of Coronary Artery Disease and Myocardial Infarction

Nabel EG and Braunwald E. *N Engl J Med* 2012;366:54-63



Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up

Motoyama S, et al. *J Am Coll Cardiol* 2015;66:337–46



HRP: high-risk plaque (low attenuation plaque & positive remodeling)

Pathology of the vulnerable plaque

Virmani R, Burke AP, Farb A, Kolodgie FD. *J Am Coll Cardiol* 2006;47

- plaque burden,
- thin-cap fibroatheroma,
- positive arterial remodeling,
- necrotic cores,
- spotty calcifications,
- macrophage infiltration.

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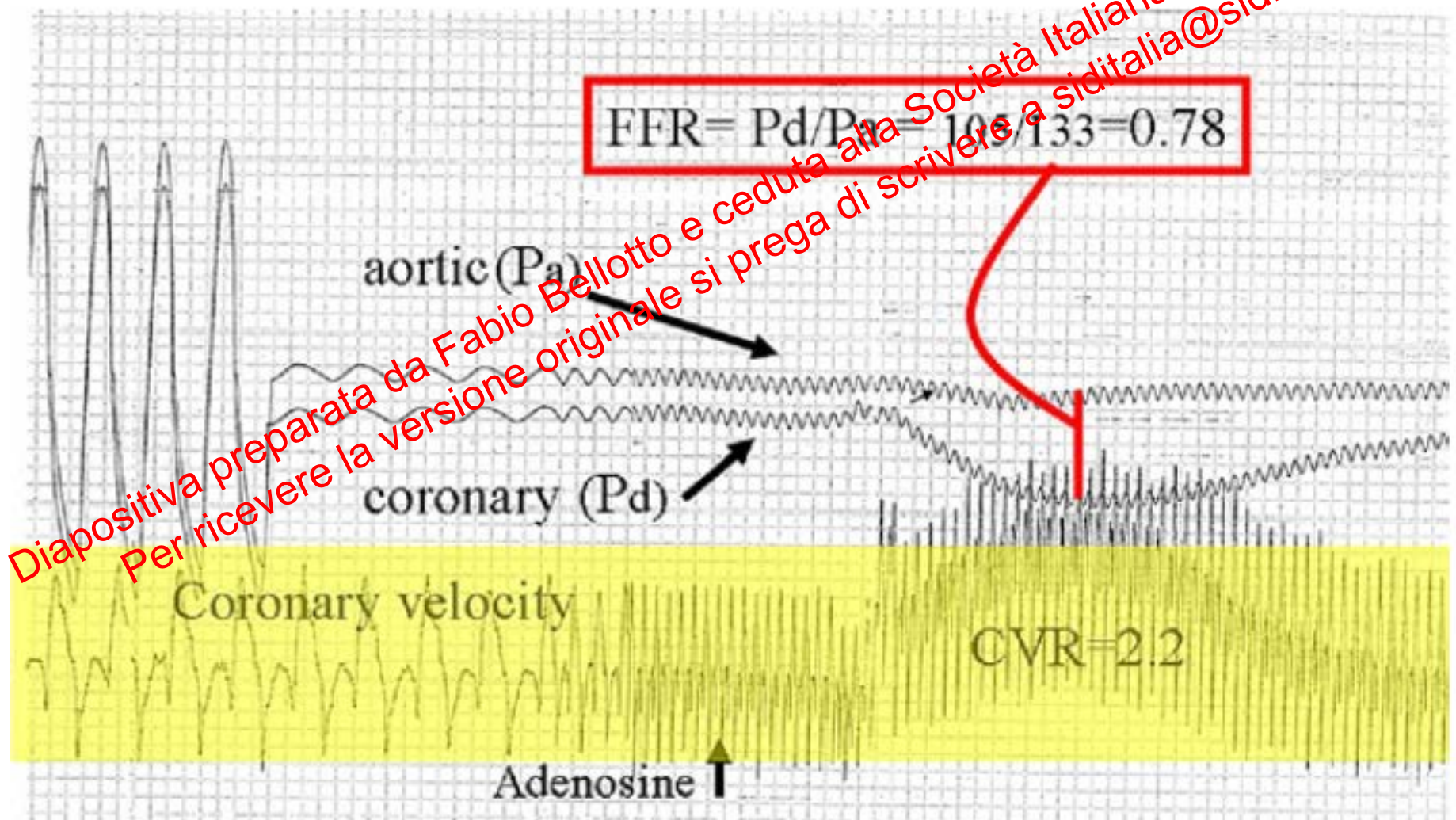


Current Concepts of Integrated Coronary Physiology in the Catheterization Laboratory

STATE-OF-THE-ART PAPER

Kern and Samady. *J Am Coll Cardiol* 2010; 55:173-85

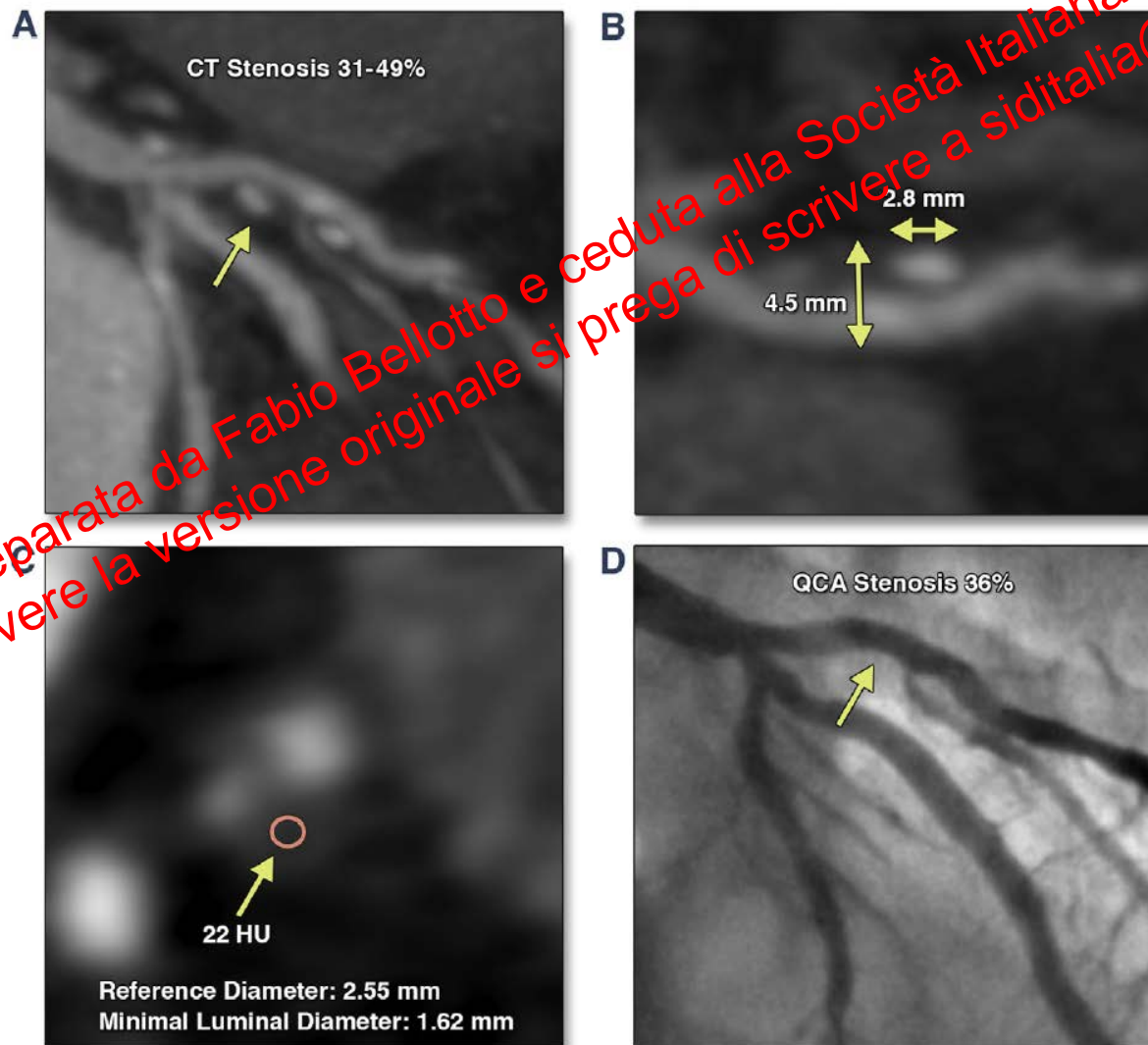
FRACTIONAL FLOW RESERVE (FFR)



Atherosclerotic Plaque Characteristics by CT Angiography Identify Coronary Lesions That Cause Ischemia

Park HB, et al. *JAmCollCardiol Img* 2015;8:1–10

Nonobstructive Coronary Stenosis Causing Ischemia

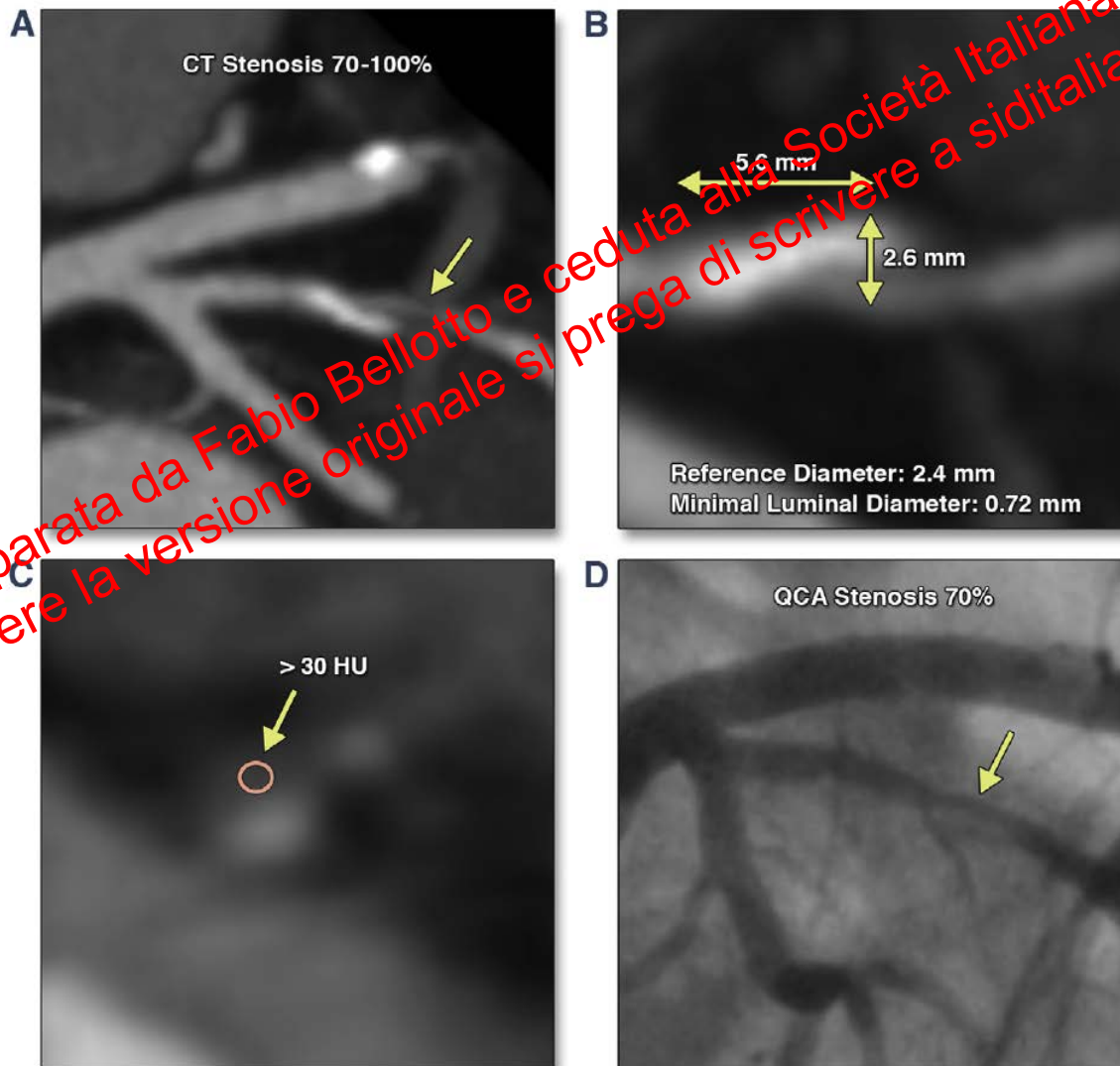


The FFR value
was 0.76

Atherosclerotic Plaque Characteristics by CT Angiography Identify Coronary Lesions That Cause Ischemia

Park HB, et al. *JAmCollCardiol Img* 2015;8:1–10

Obstructive Coronary Stenosis Does Not Cause Ischemia



The FFR value
was 0.89

- La "qualità" della placca molto più che la sua entità (% di stenosi) è in grado di influenzare la prognosi
- L'"infiammazione" associata agli altri agenti patogeni determina l'instabilità della placca ed i fenomeni trombotici successivi
- La coronaropatia diabetica presenta delle peculiarità (diffusione e distalità delle lesioni, maggior presenza di infiammazione e di disfunzione endoteliale, etc) che si ripercuotono sulla prognosi, sulla diagnostica e sulla terapia

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Terza domanda:



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La **riperfusion** (PTCA, CABG) di una stenosi critica
migliora la prognosi *quoad vitam* nella **cardiopat**
ischemica stabile ?

The history of Myocardial Revascularization

- 1958: coronary endarterectomy
- 1962: patch-graft reconstruction
- 1964: transaortic endarterectomy
- 1967: carotid sinus stimulation
- 1970: coronary artery bypass grafting
- 1979: balloon angioplasty
- 1993: atherectomy
- 1994: coronary stents
- 1999: transmyocardial laser revascularization
- 2001: intracoronary gamma radiation
- 2013: thrombus aspiration

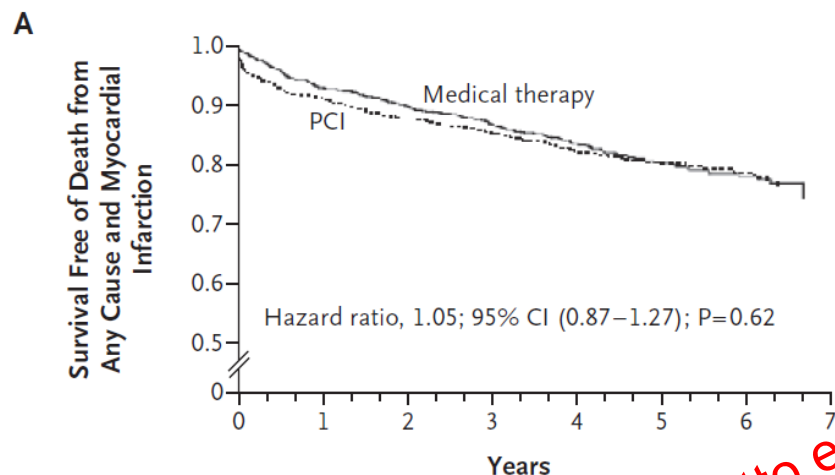
Diapositiva preparata da Fabio Bellotto e ceduta alla Società Italiana di Diabetologia.
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Optimal Medical Therapy with or without PCI for Stable Coronary Disease

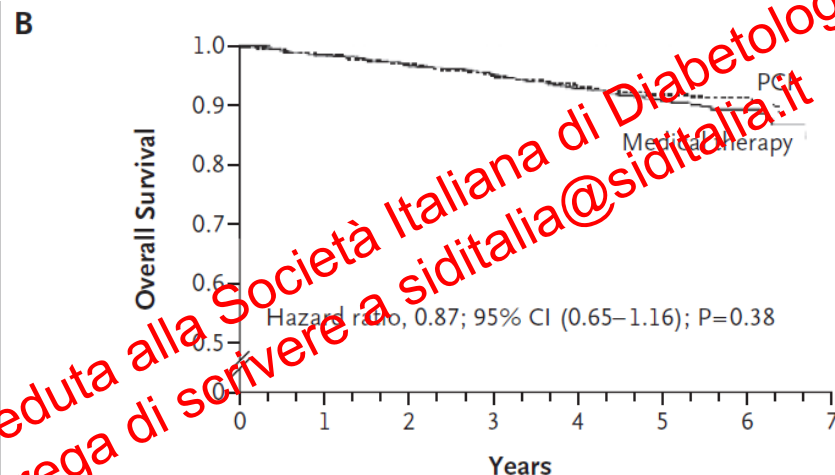
the COURAGE Trial Research Group

Boden WE, et al. N Engl J Med 2007;356:1503-16

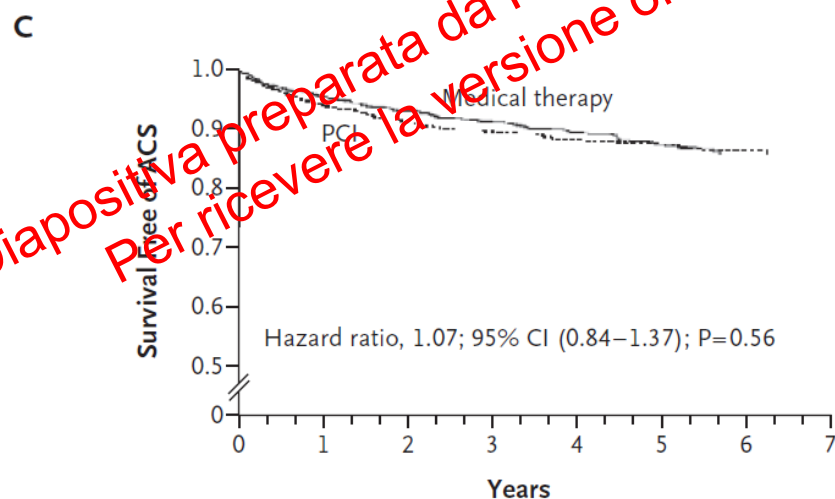
Kaplan-Meier Survival Curves



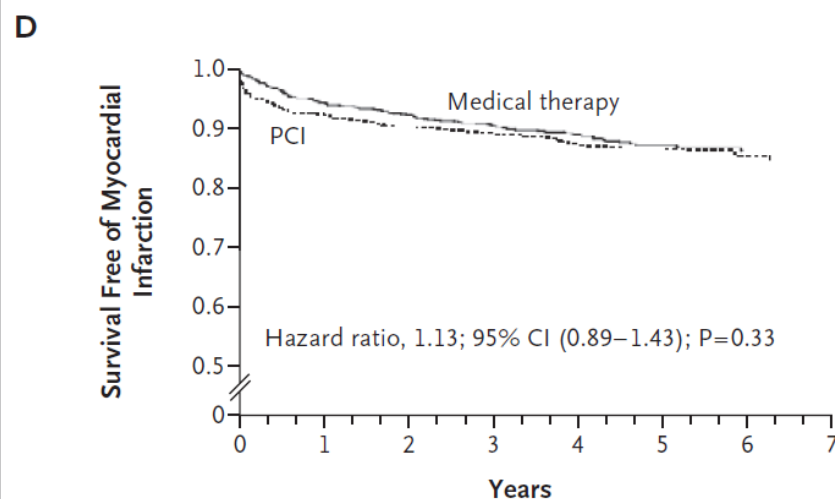
No. at Risk								
Medical therapy	1138	1017	959	834	638	408	192	30
PCI	1149	1013	952	833	638	417	200	35



No. at Risk								
Medical therapy	1138	1073	1029	917	717	468	302	38
PCI	1149	1094	1051	929	733	488	312	44



No. at Risk								
Medical therapy	1138	1025	956	833	662	418	236	127
PCI	1149	1027	957	835	667	431	246	134



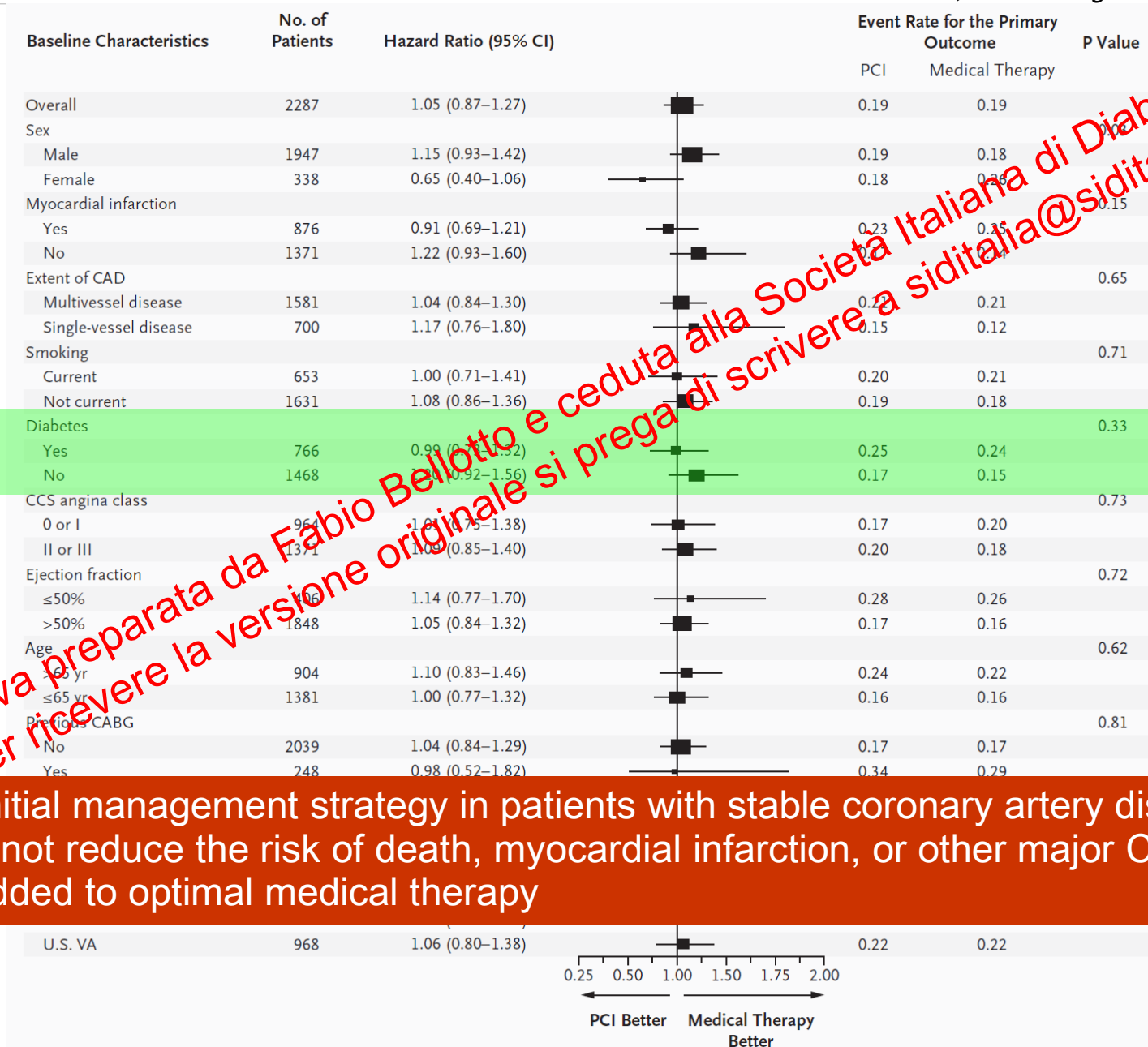
No. at Risk								
Medical therapy	1138	1019	962	834	638	409	192	120
PCI	1149	1015	954	833	637	418	200	134

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Optimal Medical Therapy with or without PCI for Stable Coronary Disease

the COURAGE Trial Research Group

Boden WE, et al. N Engl J Med 2007;356:1503-16



As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major CV events when added to optimal medical therapy

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La popolazione del COURAGE non è rappresentativa del mondo reale

- 35,539 pz valutati, 2287 arruolati (6.4%)
- 10% degli arruolati persi in entrambi i gruppi
- randomizzazione eseguita solo dopo la coronarografia
- probabile esclusione di pz ad alto rischio
- ottimale aderenza alla prevenzione e alla correzione dei FRCV (LDL = a 5 da: PCI 71 ± 13.3 vs MT 72 ± 1.21)
- STENT non d'ultima generazione

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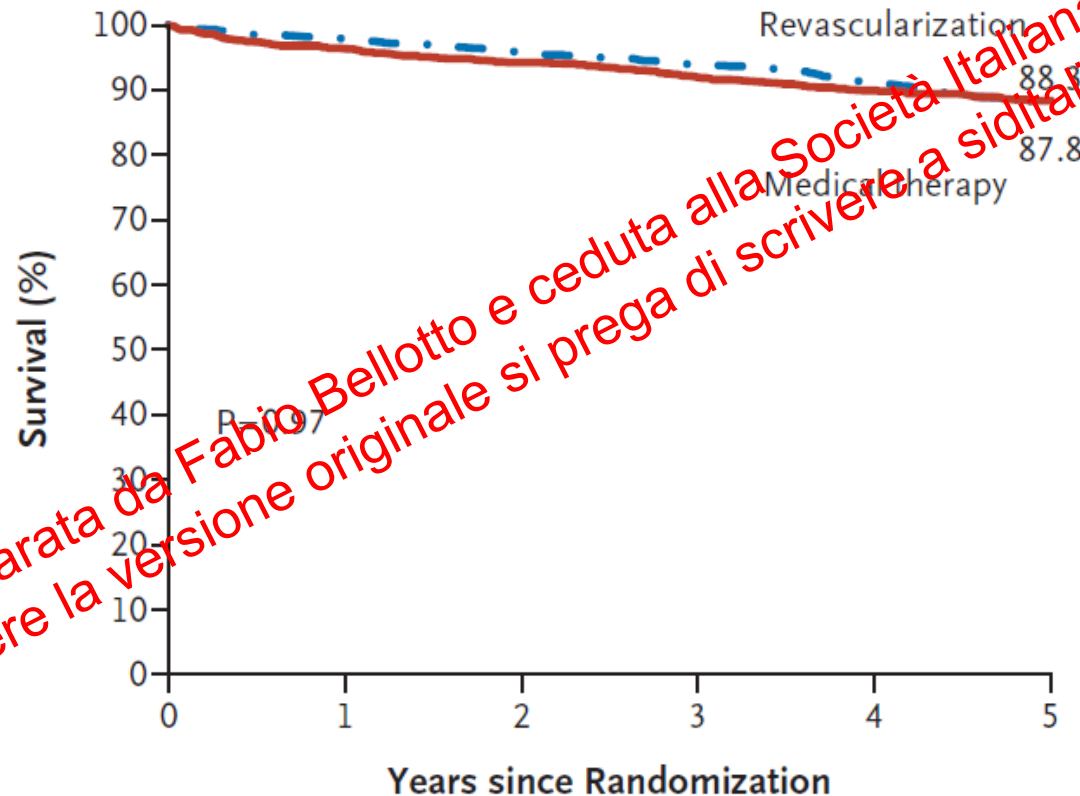
A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group

N Engl J Med 2009;360:2503-15

Rates of Survival

A Survival, Revascularization vs. Medical Therapy



No. at Risk 2368 2296 2247 2197 1892 1196



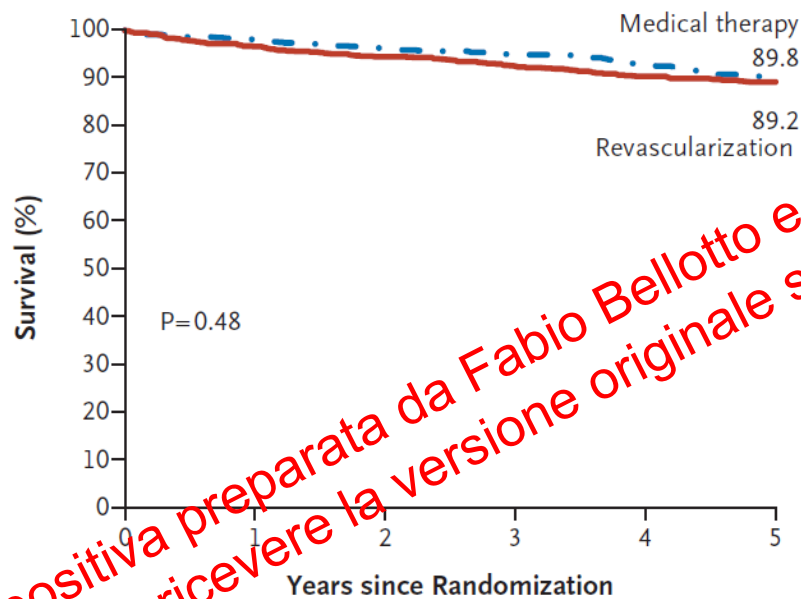
A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group

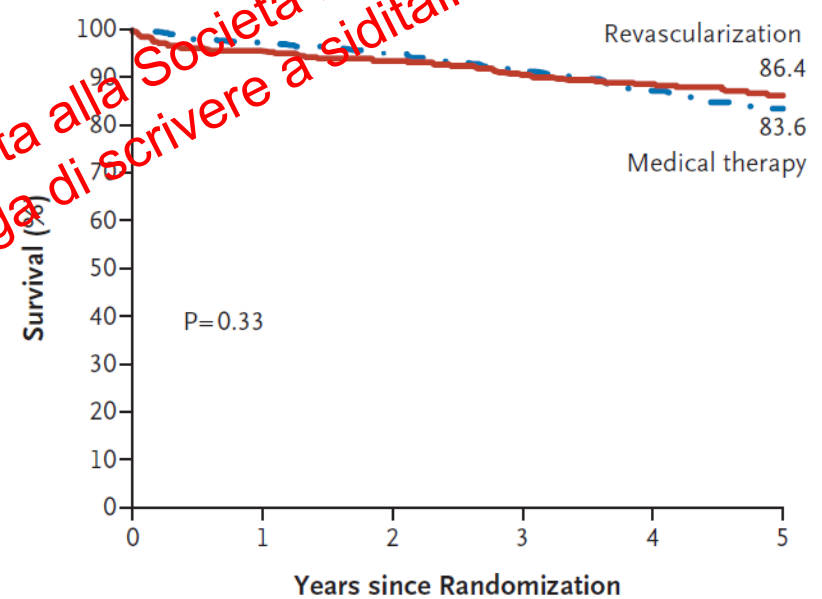
N Engl J Med 2009;360:2503-15

Rates of Survival

A Survival in PCI Stratum



B Survival in CABG Stratum



No. at Risk 1605 1562 1529 1505 1306 863

No. at Risk 763 734 718 692 586 333

— Revascularization
• • • • • Medical therapy

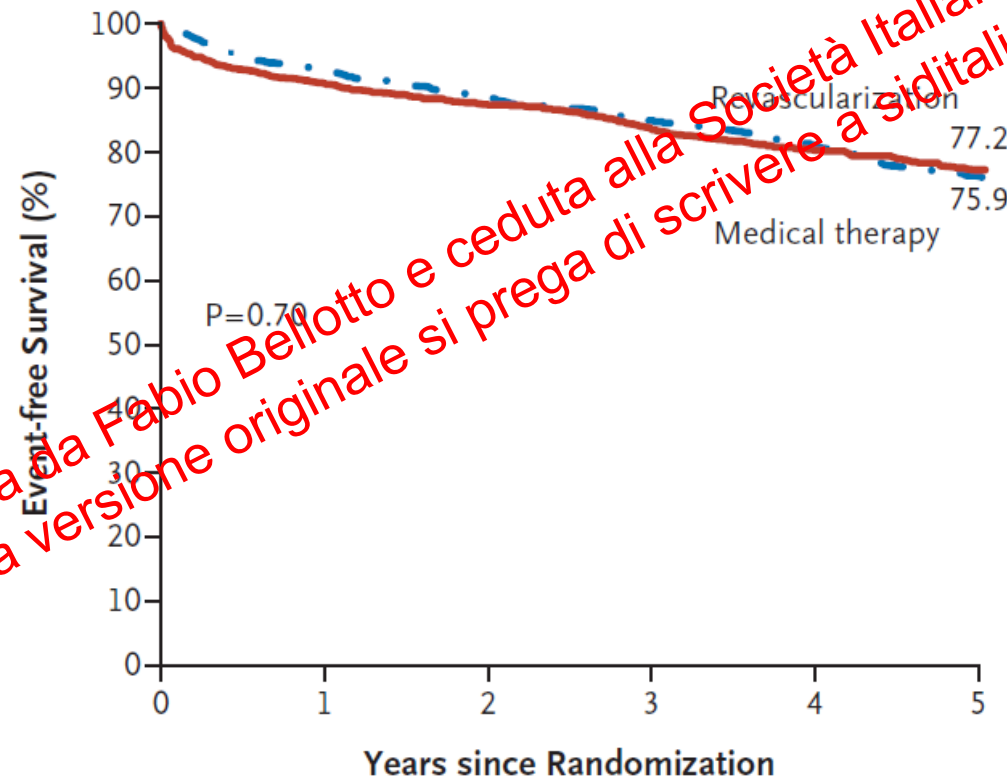
A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group

N Engl J Med 2009;360:2503-15

Rates of Freedom from Major Cardiovascular Events

C Freedom from Major Cardiovascular Events, Revascularization vs. Medical Therapy



No. at Risk 2368 2094 1984 1807 1459 823



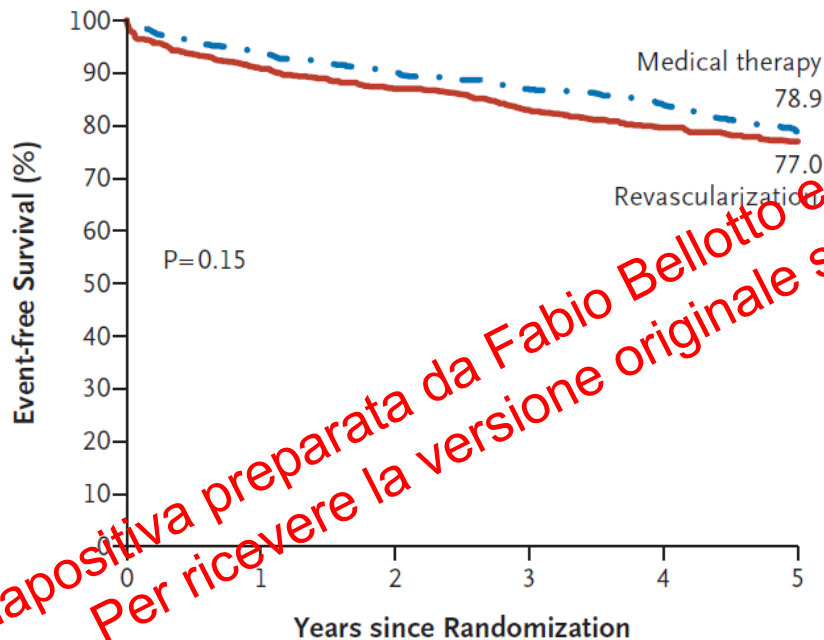
A Randomized Trial of Therapies for Type 2 Diabetes and Coronary Artery Disease

The BARI 2D Study Group

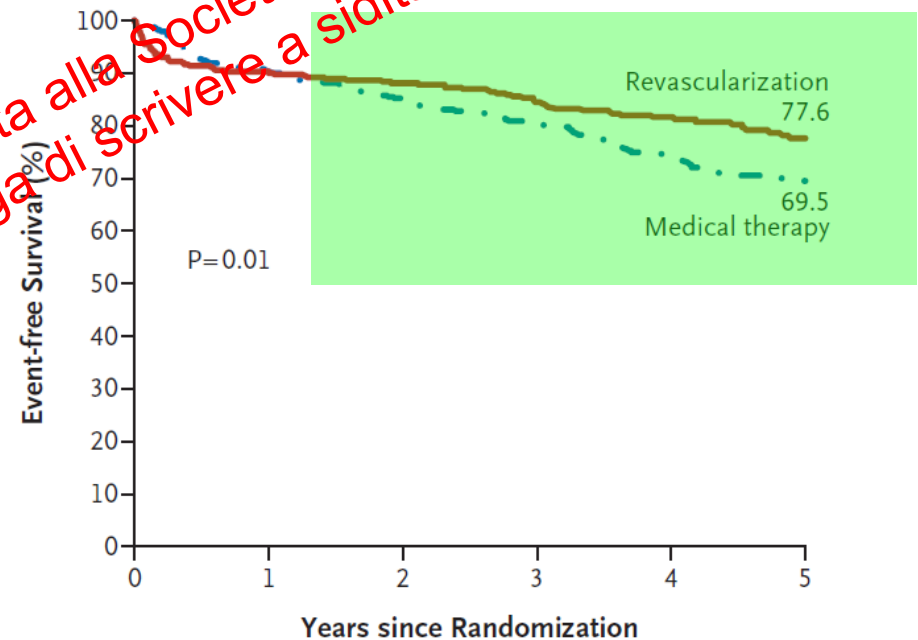
N Engl J Med 2009;360:2503-15

Rates of Freedom from Major Cardiovascular Events, According to PCI and CABG Strata

C Freedom from Major Cardiovascular Events in PCI Stratum



D Freedom from Major Cardiovascular Events in CABG Stratum



Overall, there was no significant difference in the rates of death and major CV events between patients undergoing prompt revascularization and those undergoing medical therapy

— Revascularization
- - - Medical therapy

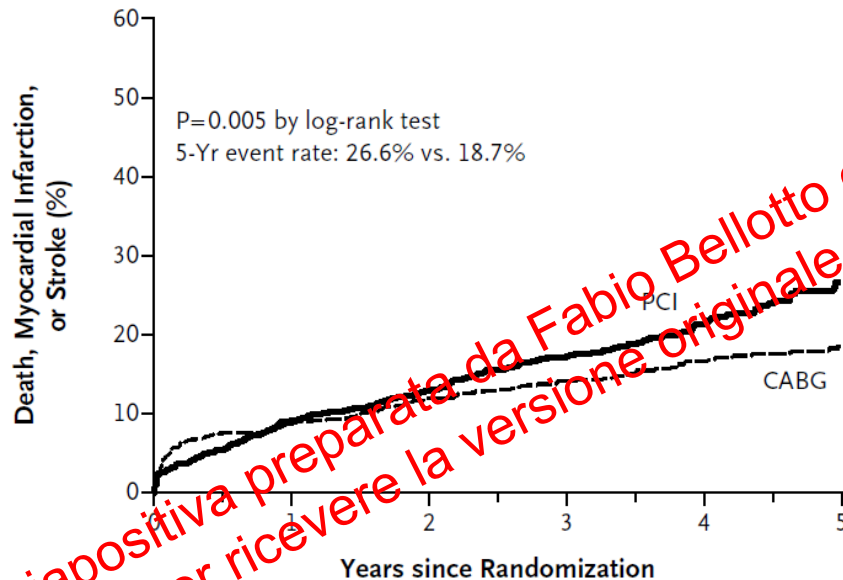
Strategies for Multivessel Revascularization in Patients with Diabetes

The FREEDOM trial

Farkouh ME, et al. *N Engl J Med* 2012;367:2375-84

Kaplan–Meier Estimates of the Composite Primary Outcome and Death

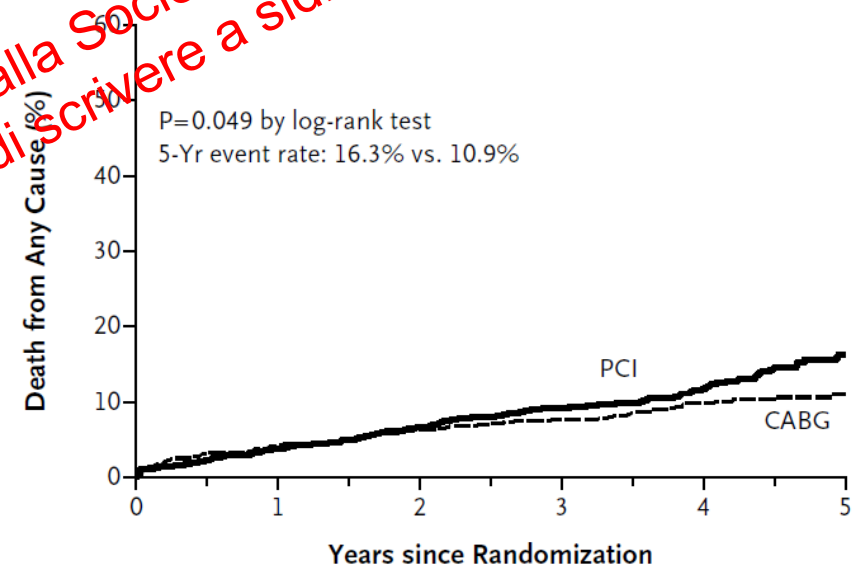
A Primary Outcome



No. at Risk

PCI	953	848	788	625	416	219
CABG	947	814	758	613	422	221

B Death



No. at Risk

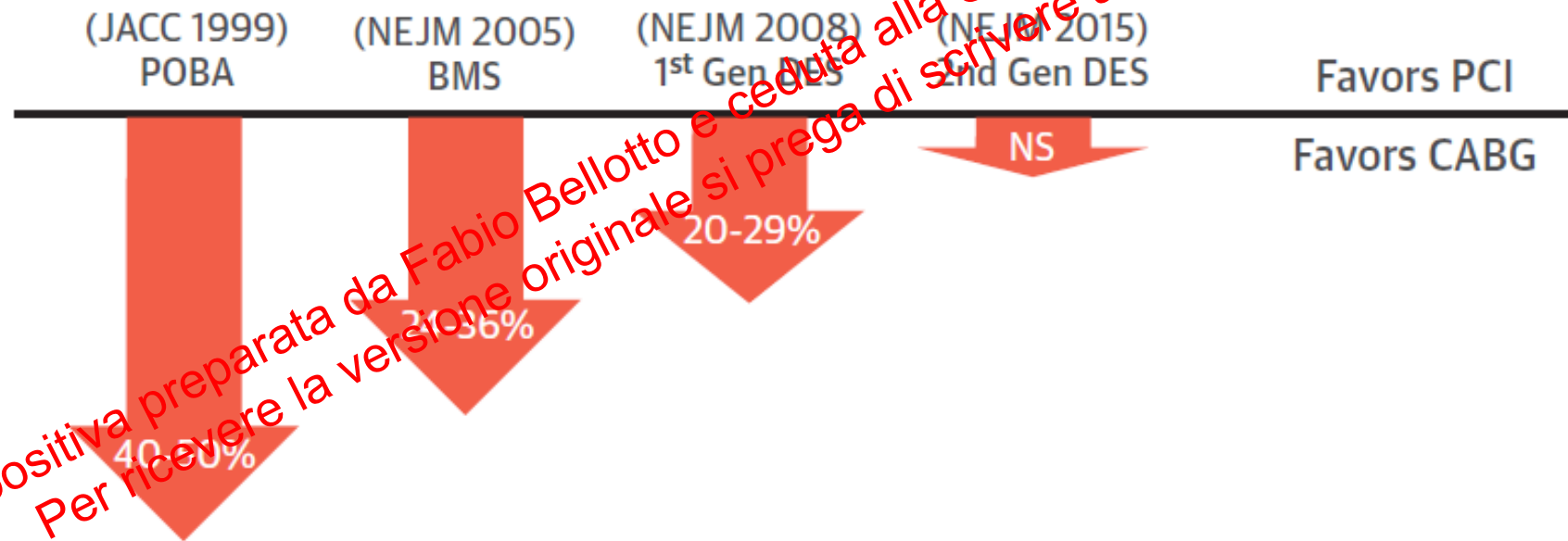
PCI	953	897	845	685	466	243
CABG	947	855	806	655	449	238

For patients with diabetes and advanced coronary artery disease, CABG was superior to PCI in that it significantly reduced rates of death and MI, with a higher rate of stroke.

EDITORIAL

Applicability of the COURAGE, BARI 2D, and FREEDOM Trials to Contemporary Practice

Bangalore S. *JACC* 68:10:996-8;2016

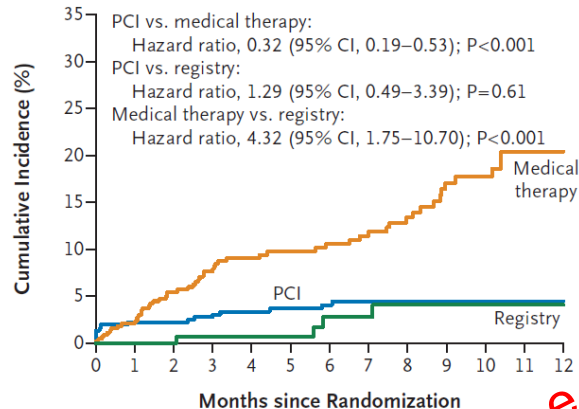


POBA: plain old balloon angioplasty; DES: drug-eluting stents; BMS: bare-metal stent

Fractional Flow Reserve-Guided PCI versus Medical Therapy in Stable Coronary Disease

De Bruyne B, et al. *N Engl J Med* 2012;367:991-1001

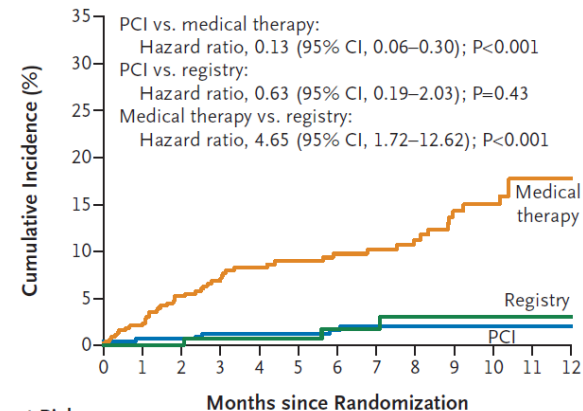
A Primary End Point



No. at Risk

Medical therapy	441	414	370	322	283	253	220	192	163	144	100	70	37
PCI	447	414	388	351	308	277	246	212	175	155	121	82	53
Registry	166	156	145	133	117	100	83	74	64	53	41	25	13

D Urgent Revascularization



No. at Risk

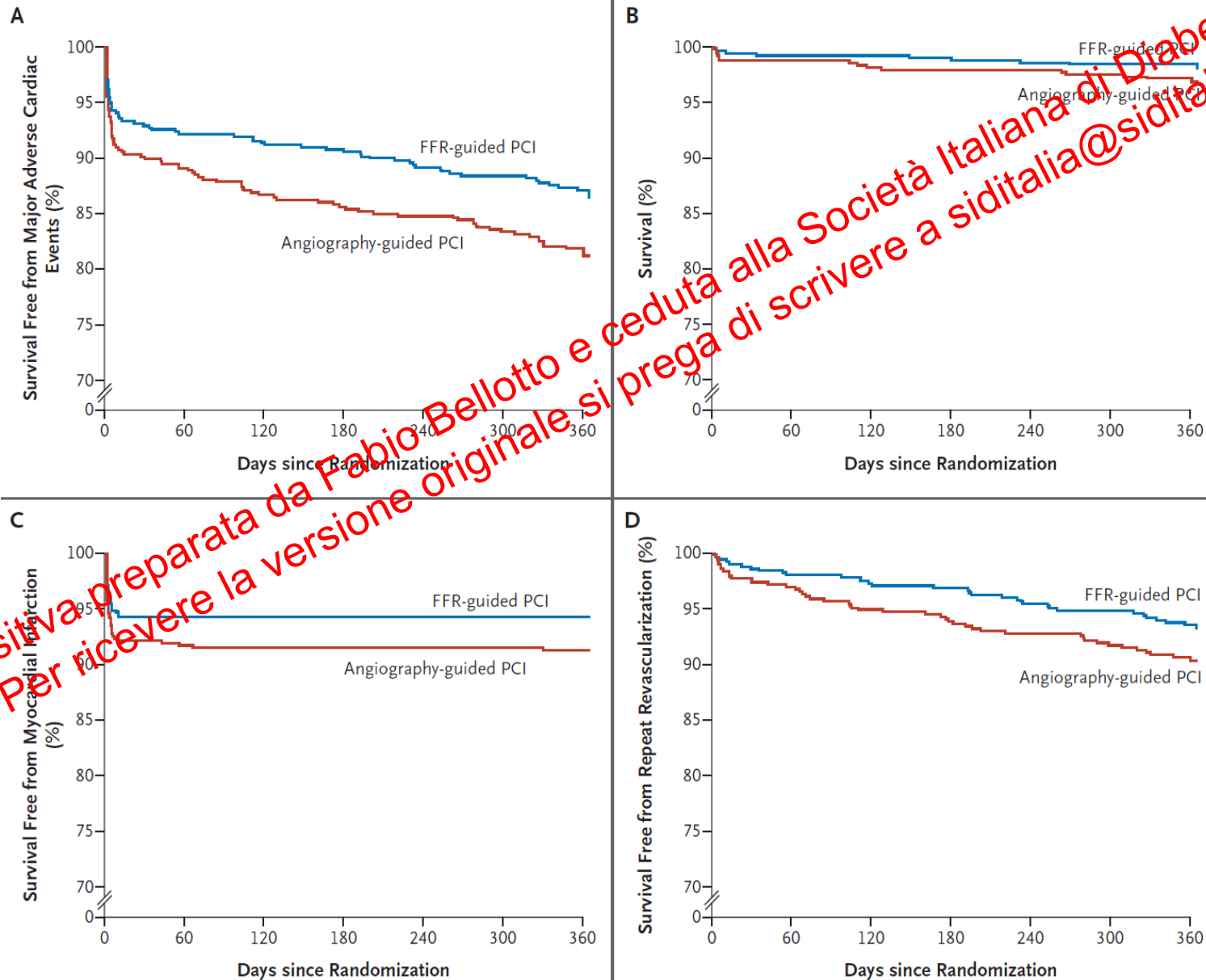
Medical therapy	441	414	371	325	286	256	223	195	164	129	101	71	38
PCI	447	421	395	356	315	285	248	217	180	160	119	93	53
Registry	166	156	145	133	117	106	94	75	65	53	42	26	13

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Fractional Flow Reserve versus Angiography for Guiding Percutaneous Coronary Intervention

the FAME Trial Investigators

Tonino P, et al. *N Engl J Med* 2009;360:213-24

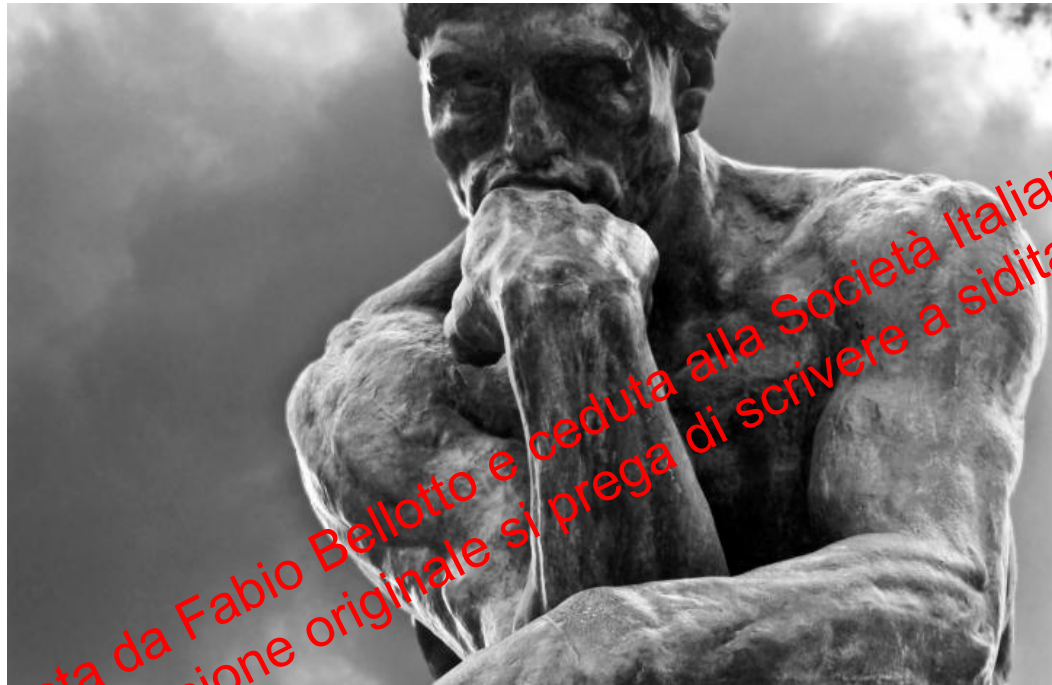


- L'accertamento usuale (CRG) della presenza/assenza di lesioni anatomicamente significative è di **scarsa utilità** in prevenzione primaria perché - **nel DM** - l'approccio farmacologico e comportamentale deve comunque essere attuato
- La correzione delle "**stenosi critiche**" nel diabetico (per il momento meglio CABG che PTCA) influisce sulla sintomatologia ma molto meno sulla prognosi **rispetto alla terapia medica ottimale** ed al controllo puntuale di tutti i fattori di rischio
- E' possibile che lo studio della **FFR**, in un prossimo futuro, venga utilizzata per appurare la reale "**criticità clinica**" modificando le attuali indicazioni a PTCA e CABG

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Quarta domanda:



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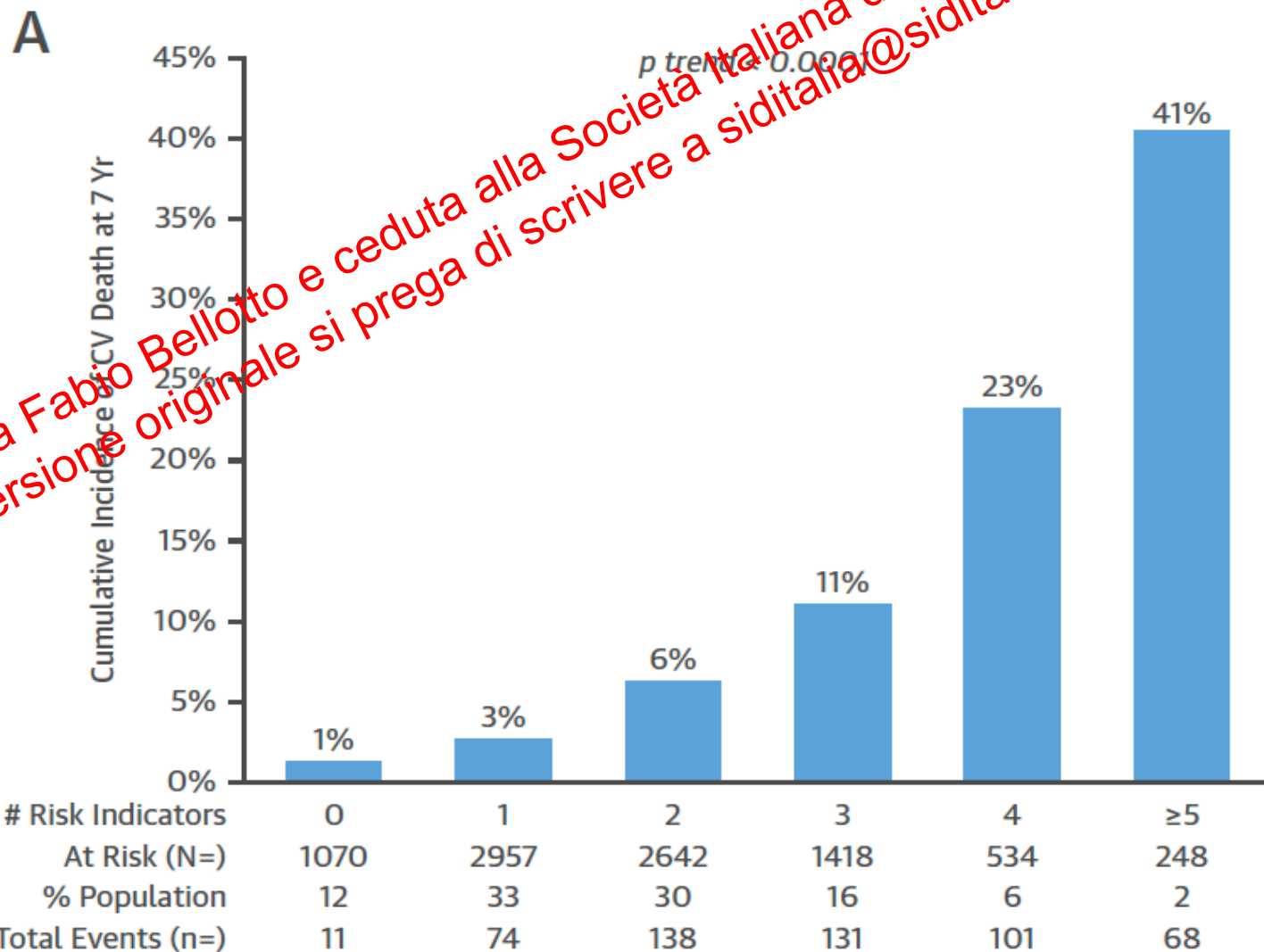
Come possiamo migliorare la prognosi cardiologica nel
Paziente diabetico?

Atherothrombotic Risk Stratification and Ezetimibe for Secondary Prevention

Bohula EA, et al. *J Am Coll Cardiol* 2017;69:911–21

Risk stratification of individual endpoints in the control arm

TRS 2°P Risk Indicators	Points
CHF	1
HTN	1
Age ≥75	1
DM	1
Prior Stroke	1
Prior CABG	1
PAD	1
eGFR <60	1
Smoking	1
Maximum Possible	9



Adherence to Healthy Lifestyle and Cardiovascular Diseases in the Chinese Population

Lv J, et al. *J Am Coll Cardiol* 2017;69:1116–25

461,211 participants 30 to 79 years, NO CVD, cancer, or DM

Low-risk lifestyle factors:

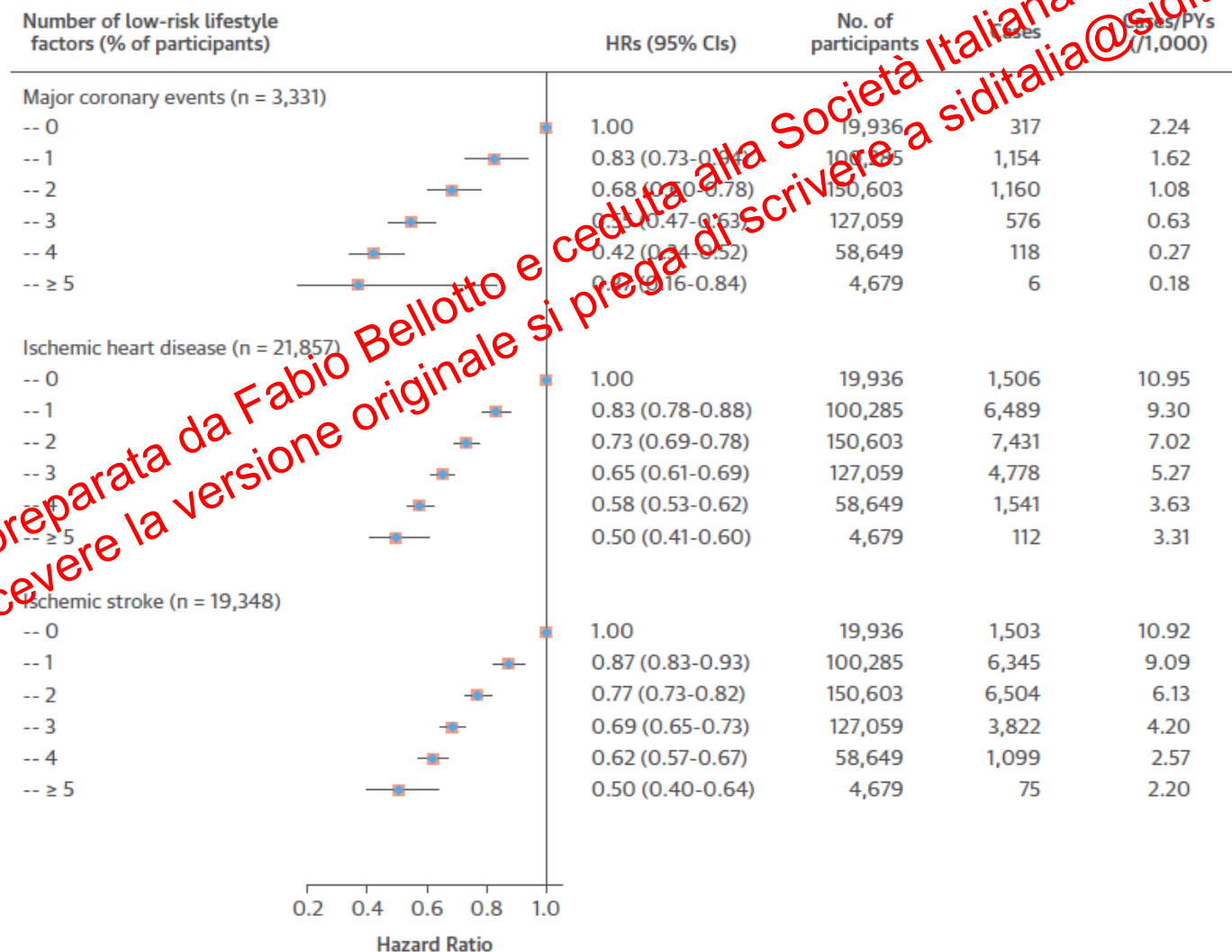
1. nonsmoking status or having stopped smoking
2. alcohol consumption of <30 g/day
3. a median or higher level of physical activity,
4. a diet rich in vegetables and fruits ,
5. BMI of 18.5 to 23.9 kg/m²,
6. a waist-to-hip ratio <0.90 for men and <0.85 for women.

3 lifestyle factors indicating smoking, physical activity, and dietary pattern; 4 factors including the first 3 factors and body mass index (BMI); 5 factors including the first 4 factors and waist-to-hip ratio (WHR); 6 factors including the first 5 factors and alcohol consumption. Multivariable model was adjusted for age, sex, education, marital status, family histories of heart attack or stroke, and prevalent hypertension at baseline. All 6 lifestyle factors were included simultaneously in the same model.

Adherence to Healthy Lifestyle and Cardiovascular Diseases in the Chinese Population

Lv J, et al. *J Am Coll Cardiol* 2017;69:1116–25

Multivariable-Adjusted HRs (95% CIs) for Incident Ischemic CD by Number of Low-Risk Lifestyle Factors among 461,211 Participants

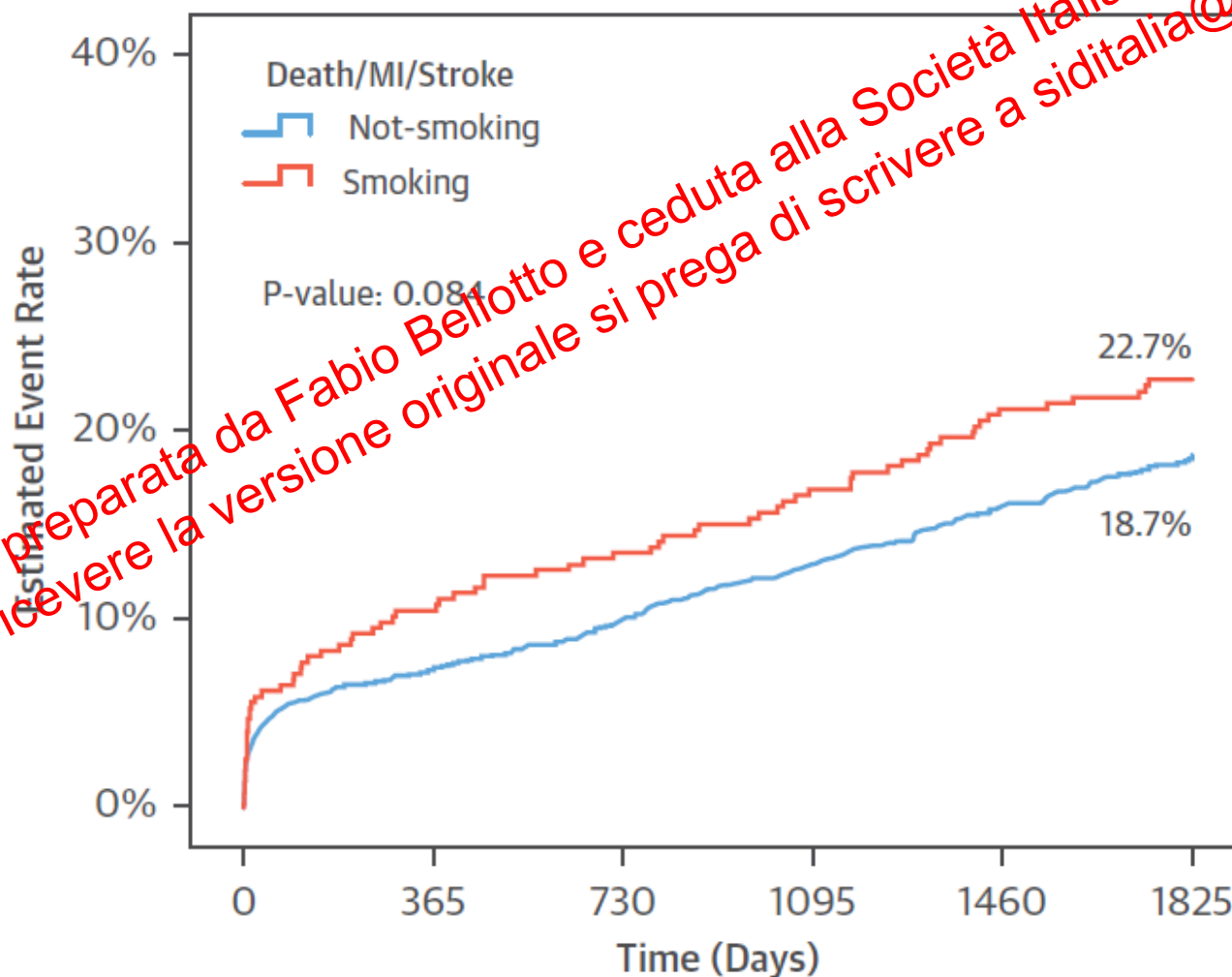


Smoking Is Associated With Adverse Clinical Outcomes in Patients Undergoing Revascularization With PCI or CABG

The SYNTAX Trial at 5-Year Follow-Up

Zhang YJ, et al. *J Am Coll Cardiol* 2015;65:1107–15

Kaplan-Meier Cumulative Events for Primary Endpoint and MACE

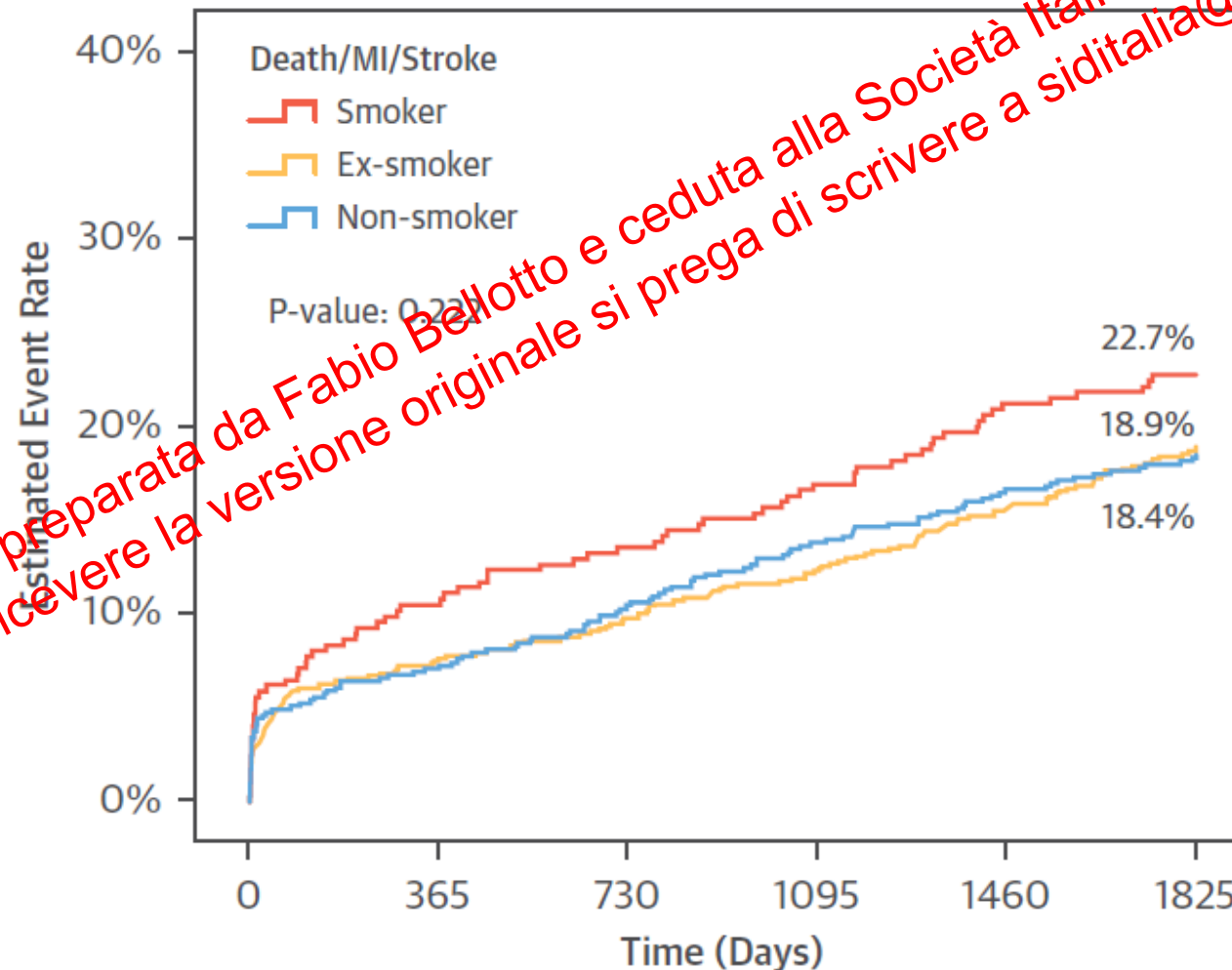


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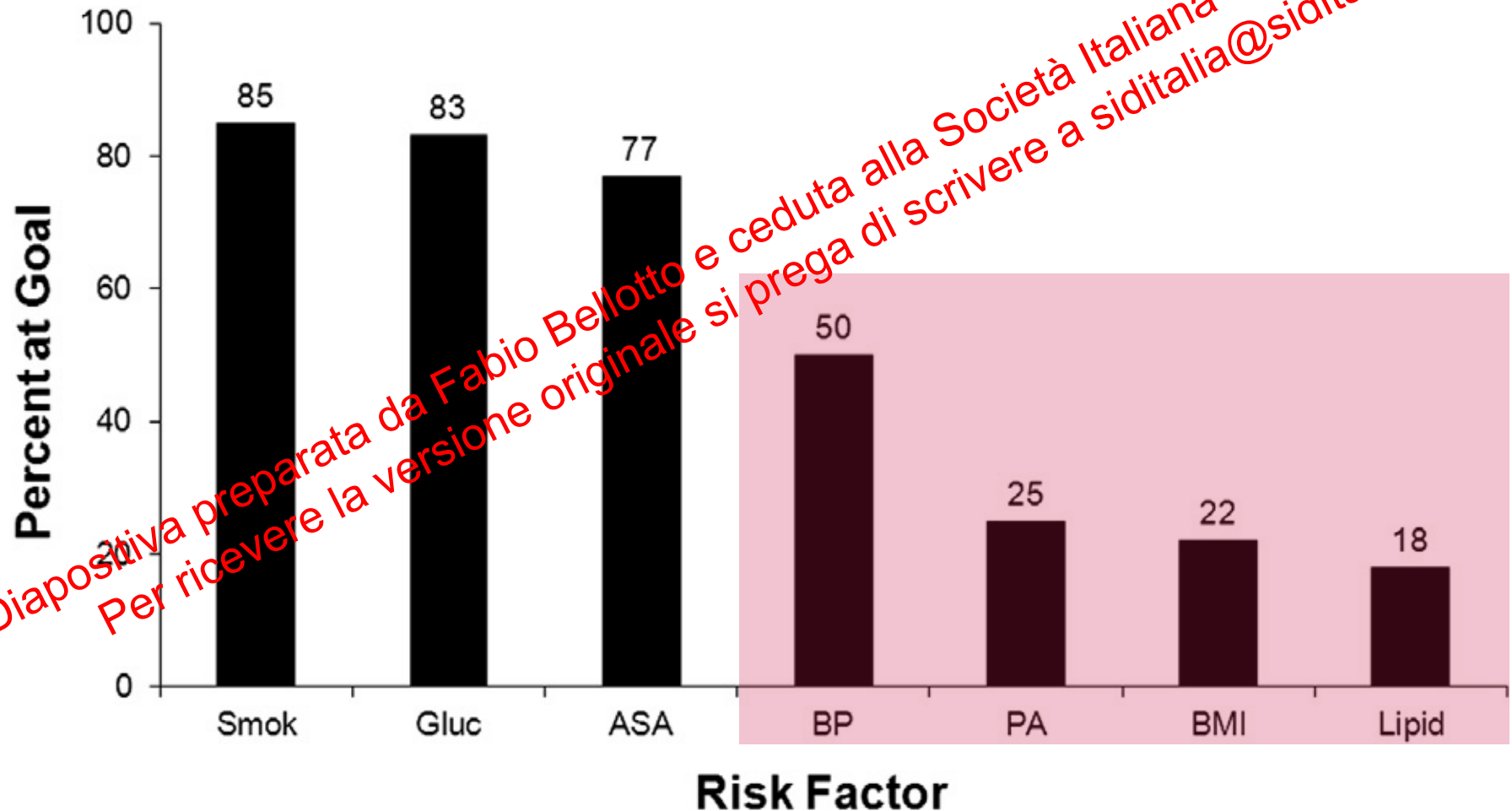
Kaplan-Meier Cumulative Events for Primary Endpoint and MACE



Achievement of Optimal Medical Therapy Goals for U.S. Adults With Coronary Artery Disease

Results From the REGARDS Study

Brown TM, et al. *J Am Coll Cardiol* 2014;63:1626-33



REVIEW TOPIC OF THE WEEK

Cardiac Rehabilitation and Risk Reduction Time to “Rebrand and Reinvigorate”

Sandesara PB, et al. *J Am Coll Cardiol*. 2015;65,4:389-95

Potential Cardioprotective Effects of Increased Lifestyle Activity, Structured Exercise, and/or Improved Cardiorespiratory Fitness

Anti-inflammatory

Reduced plasma level of C-reactive protein, which is a biomarker of inflammation (10)

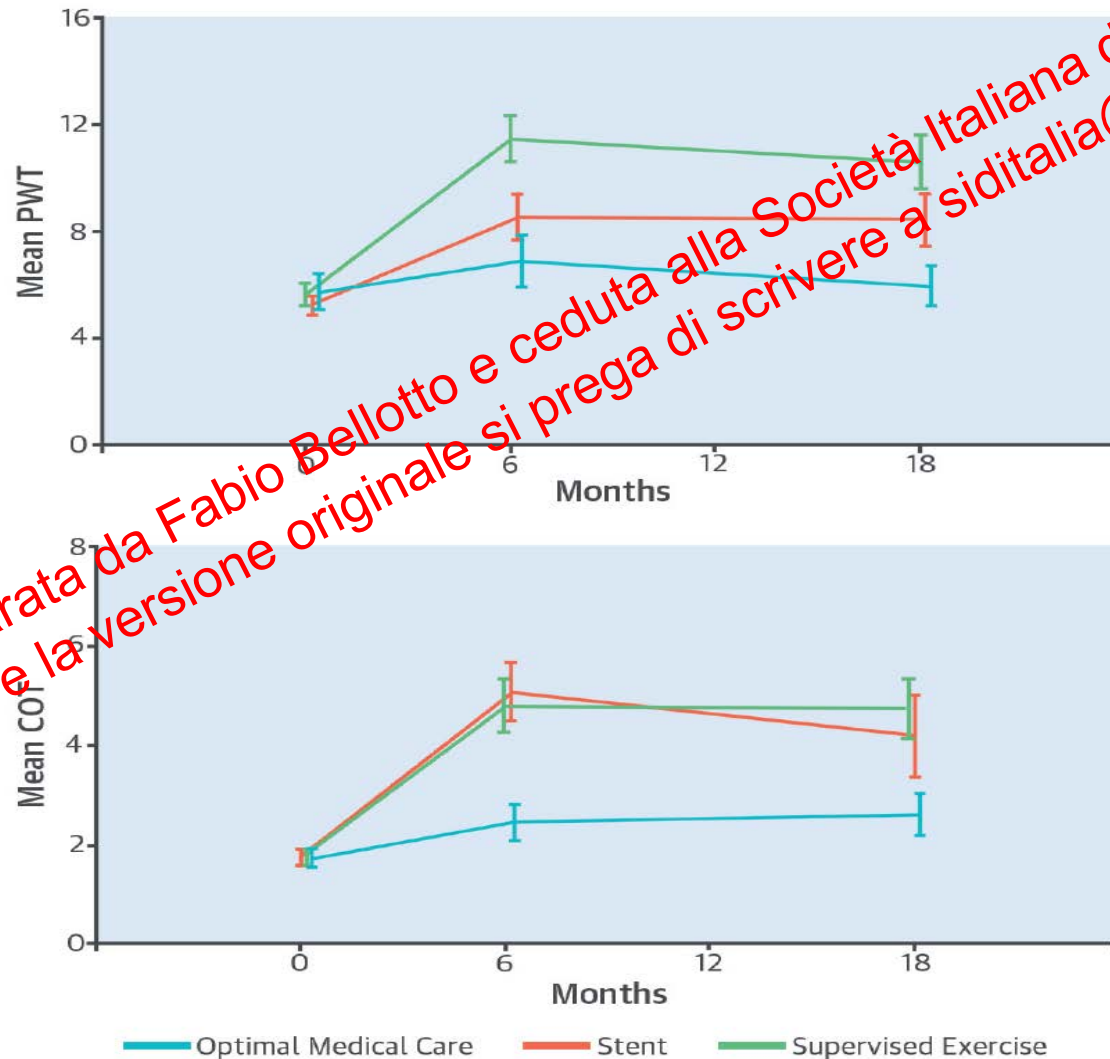
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Supervised Exercise, Stent Revascularization, or Medical Therapy for Claudication Due to Aortoiliac Peripheral Artery Disease.

The CLEVER Study

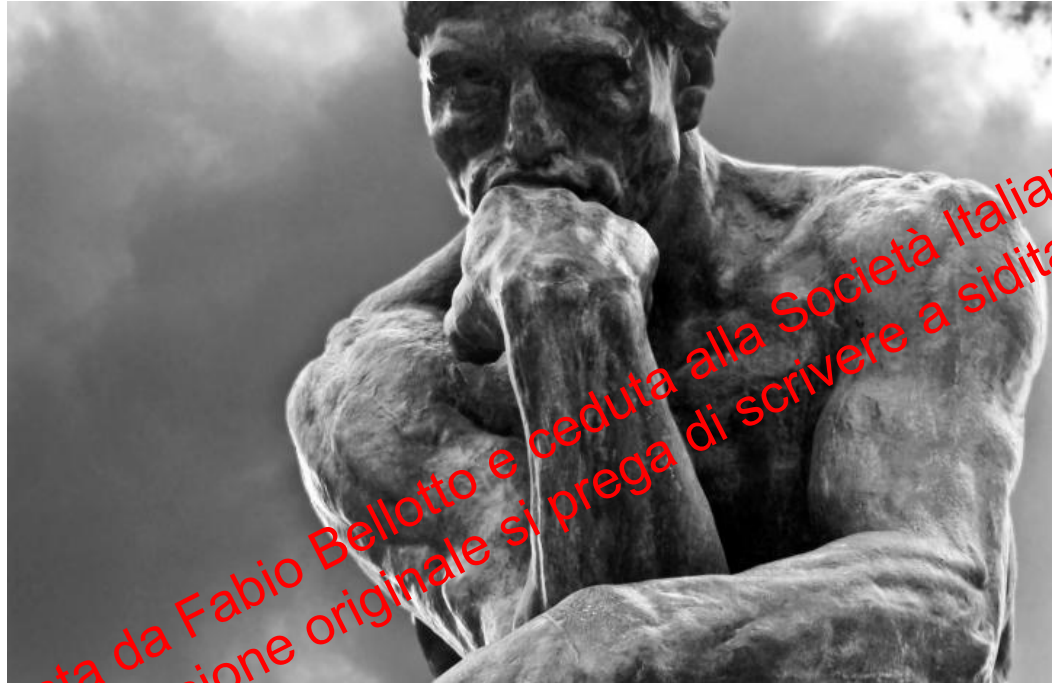
Murphy TP, et al. *J Am Coll Cardiol* 2015;65:999–1009

Exercise or Intervention for Claudication Due to Aortoiliac PAD



COT: claudication onset time on a graded treadmill test; **PWT:** peak walking time

Quinta domanda:



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Come possiamo migliorare la prognosi nella cardiopatia ischemica, in particolare nel pos-infarto?

The management of AMI in the cardiological intensive care units in Italy: the 'BLITZ 4 Qualità' campaign for performance measurement and quality improvement

Olivari Z, et al. *European Heart Journal* 2012

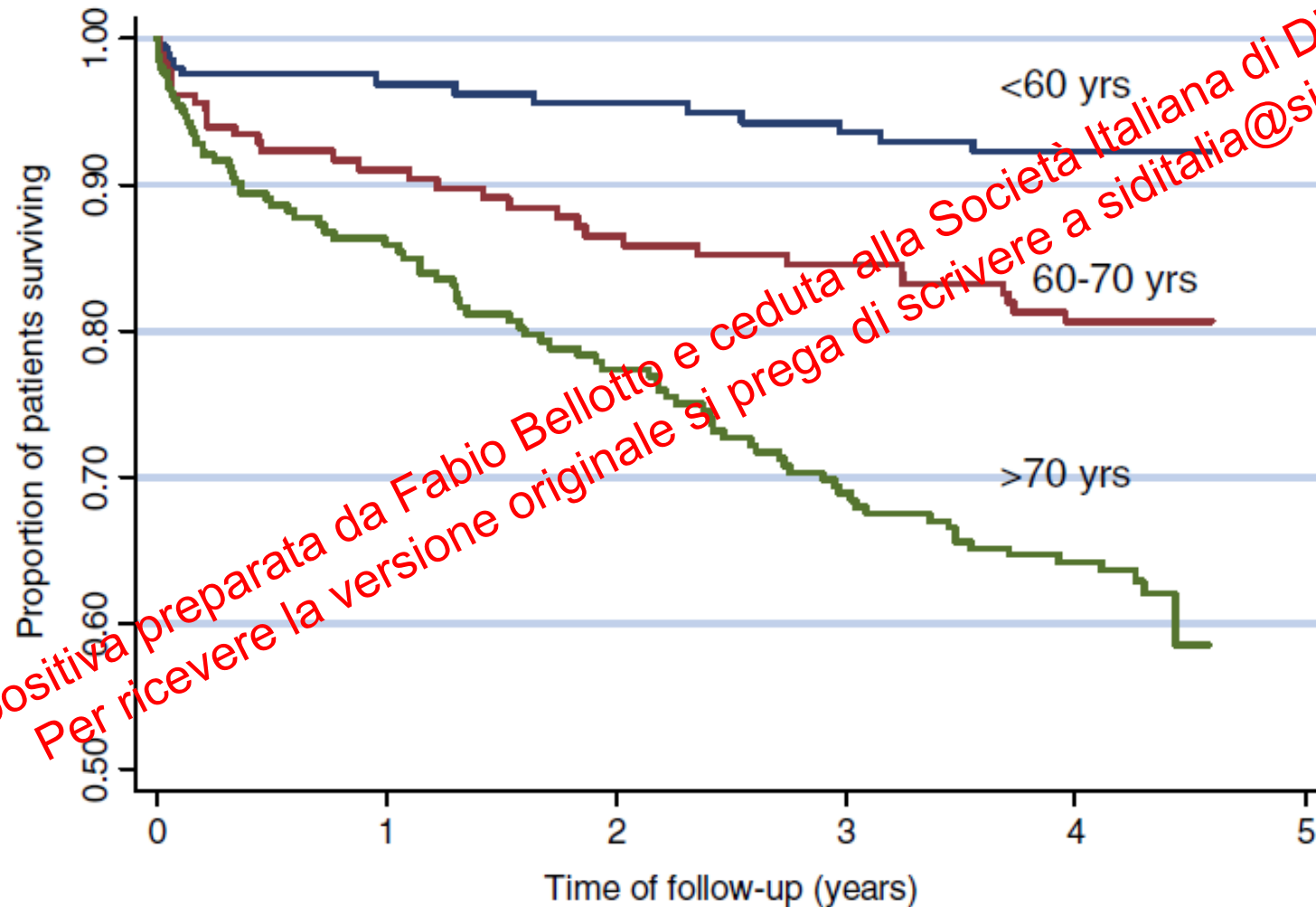
Clinical outcomes in CCU or cardiology ward and at 30 days

Outcome	STEMI (n=5854)		NSTEMI (n=5852)	
	In CCU/ward	At 30 days	In CCU/ward	At 30 days
Death	237 (4.1)	315 (5.4)	122 (2.1)	189 (3.4)
Reinfarction	62 (1.1)	72 (1.4)	57 (1)	66 (1.3)
Stroke	43 (0.7)	52 (1.0)	34 (0.6)	42 (0.8)
Haemorrhagic complications	224 (3.8)	230 (4.4)	225 (3.8)	227 (4.4)
Blood transfusions	75 (1.3)	NA	111 (1.9)	NA
Congestive heart failure	629 (10.7)	646 (12.2)	671 (11.5)	683 (13.1)
Recurrence of angina	147 (2.5)	161 (3.1)	299 (5.1)	310 (6.0)

Values are n (%). Event rates at 30 days refers to the population with available data: mortality in 11,163 patients, reinfarction in 10,321, stroke in 10,314, haemorrhagic complications in 10,377, congestive heart failure in 10,498, and recurrence of angina in 10,350. NA, not assessed. CCU, cardiological intensive care unit.

Mortality following non-ST elevation acute coronary syndrome: 4 years follow-up of the PRAIS UK registry

Taneja AK et al. *European Heart Journal* 2004; 25, 2013–2018



AHA Statistical Update

Heart Disease and Stroke Statistics—2009 Update

A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee

Lloyd-Jones D, et al. *Circulation* 2009;119:e21-e181

On the basis of pooled data from the FHS, ARIC,
and CHS studies of the NHLBI

within 1 year after a first MI will die:

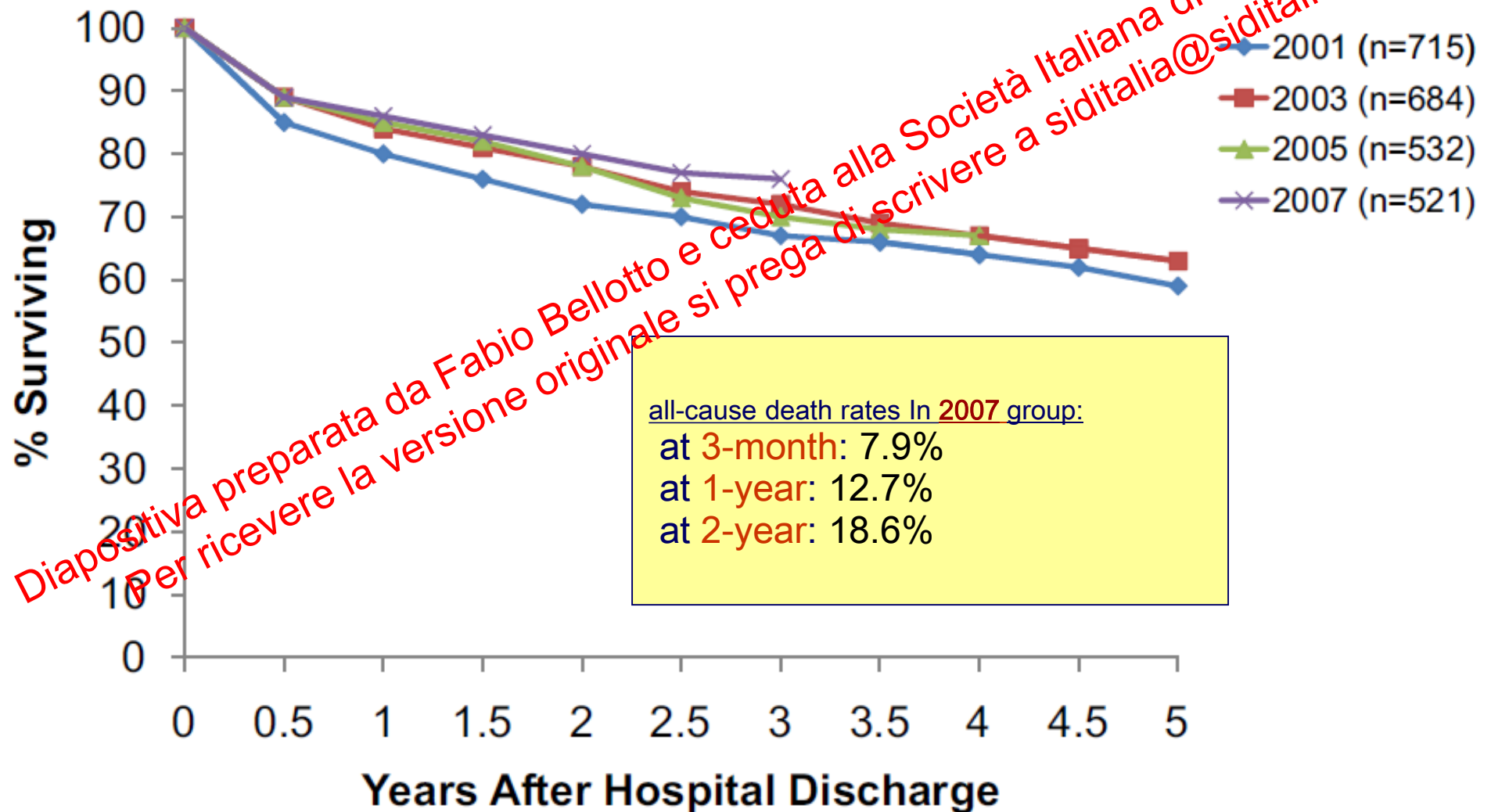
— At 40 to 69 years of age, 8% of white men, 12% of white women, 14% of black men, and 11% of black women

— At 70 years of age, 27% of white men, 32% of white women, 26% of black men, and 28% of black women

Recent Trends in Post-Discharge Mortality Among Patients With an Initial Acute Myocardial Infarction

Coles AH, et al *Am J Cardiol* 2012, september

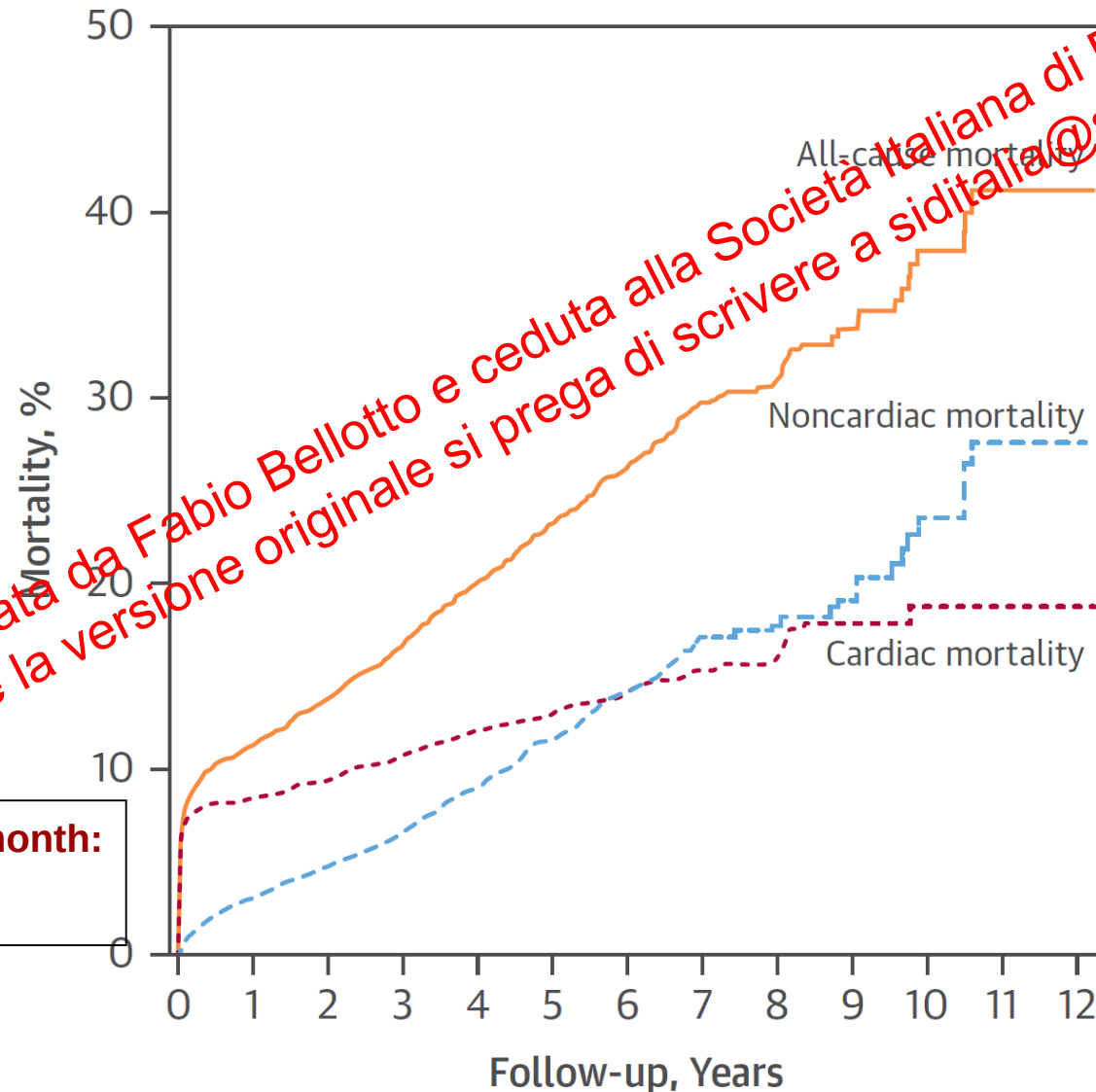
Post-hospital discharge survival for patients with initial AMIs.



Short- and Long-Term Cause of Death in Patients Treated With Primary PCI for STEMI

Pedersen F, et al. *J Am Coll Cardiol* 2014;64:2101–8

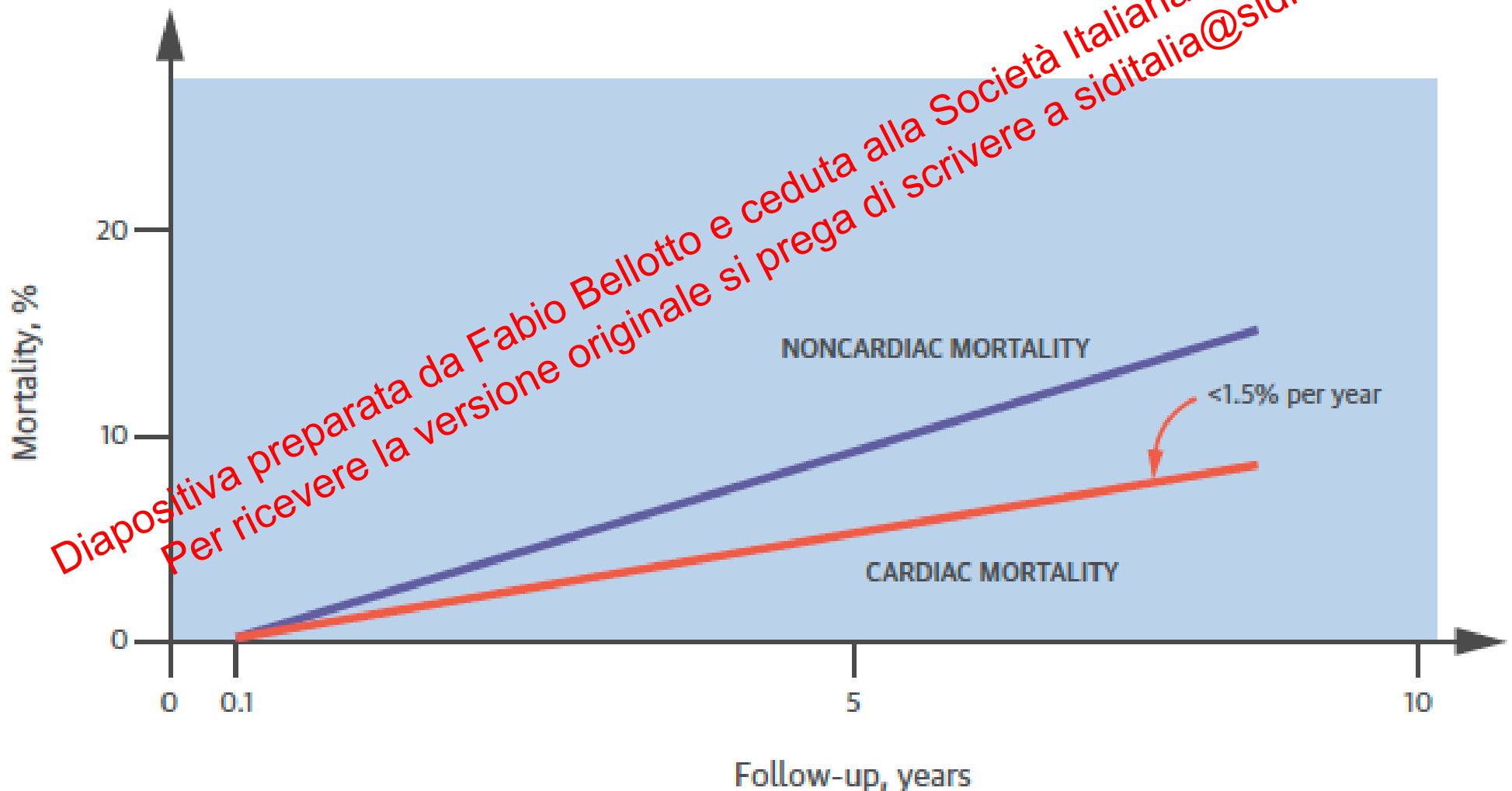
Long-Term Mortality of Patients With ST-Segment Elevation MI After Primary PCI



Short- and Long-Term Cause of Death in Patients Treated With Primary PCI for STEMI

Pedersen F, et al. *J Am Coll Cardiol* 2014;64:2101–8

Cardiac and Noncardiac Mortality From 30 Days Onward After Treatment With Primary PCI in Patients With STEMI



Incident MI and Very Late Stent Thrombosis in Outpatients With Stable Coronary Artery Disease

Lemesle G, et al. *J Am Coll Cardiol* 2017;69:2149–56

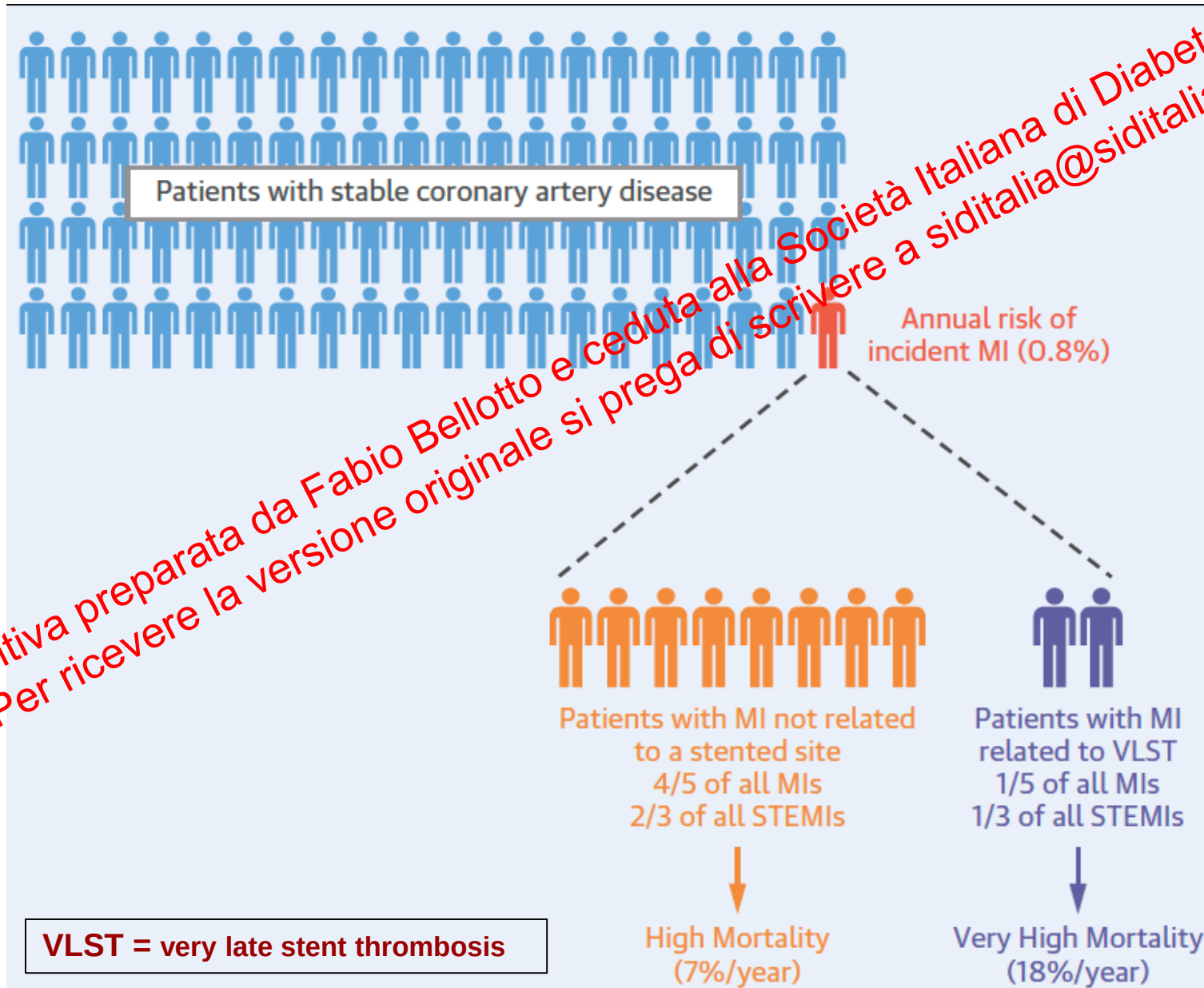
4,184 consecutive outpatients with stable CAD between February 2010 and April 2011 with at least 1 of the following criteria:

1. previous MI (>1 year ago),
2. previous coronary vascularization (>1 year ago),
3. obstruction >50% of the luminal diameter of at least 1 native vessel on coronary angiography.

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Incident MI and Very Late Stent Thrombosis in Outpatients With Stable Coronary Artery Disease

Lemesle G, et al. *J Am Coll Cardiol* 2017;69:2149–56



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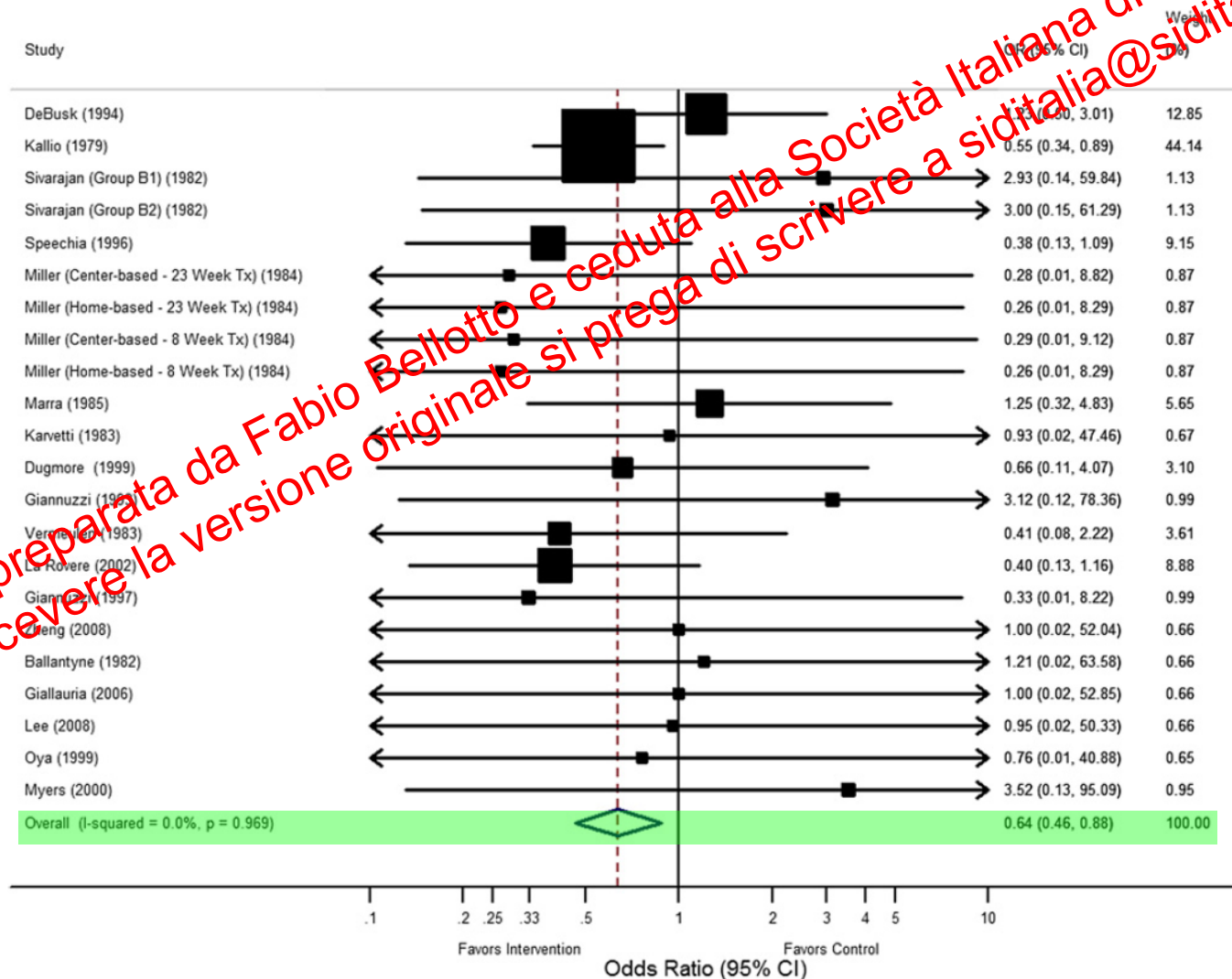
Stabilizzazione clinica
Monitorizzazione
Adeguamento della terapia
Counselling
Pianific. & Inizio dell'
Attività Fisica
Etc,



Efficacy of exercise-based cardiac rehabilitation post-MI: A systematic review and meta-analysis of randomized controlled trials

Lawler PR, et al. *Am Heart J* 2011;162:571-584

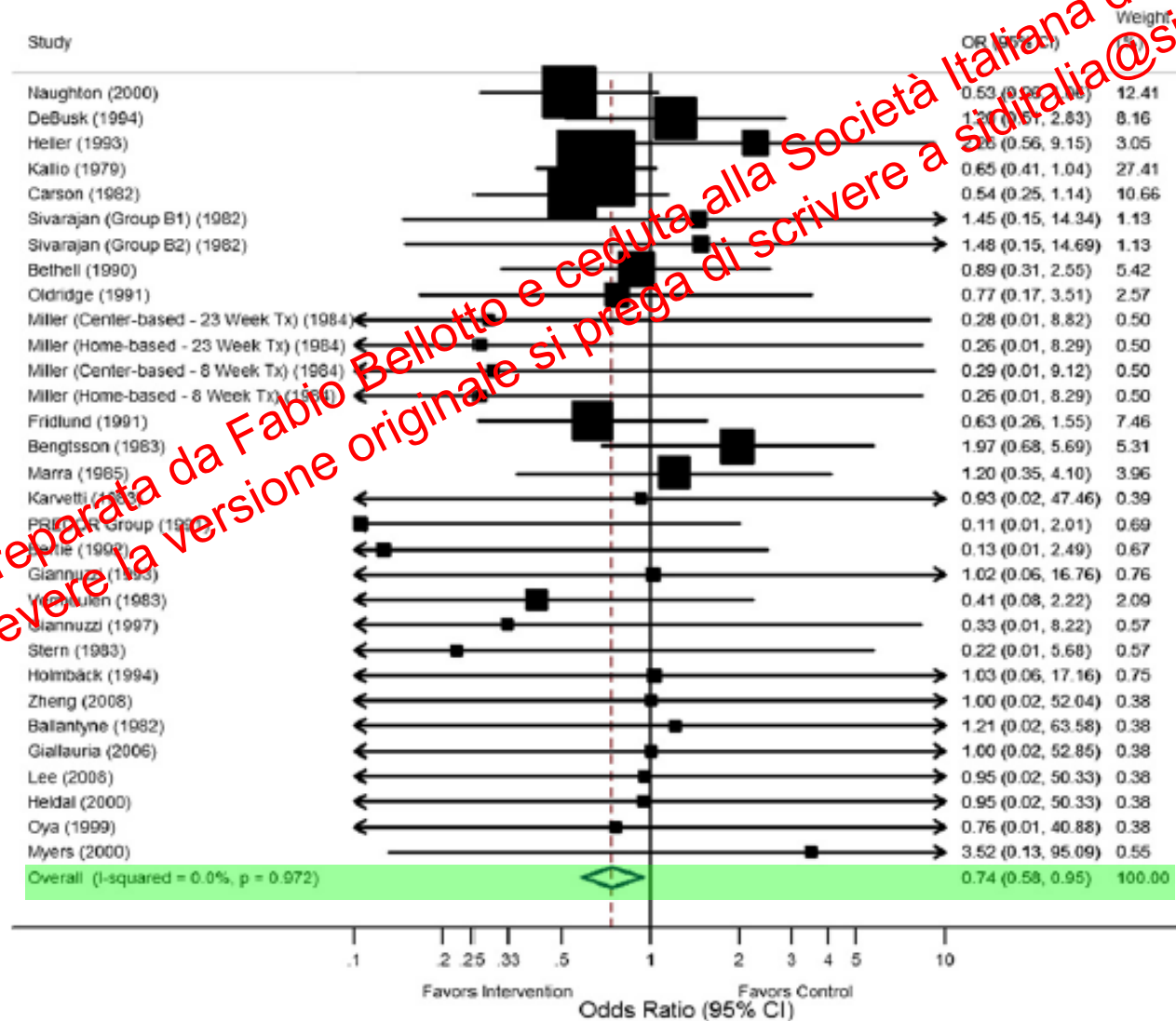
Forest plot of effect of exercise-based CR on cardiac mortality



Efficacy of exercise-based cardiac rehabilitation post-MI: A systematic review and meta-analysis of randomized controlled trials

Lawler PR, et al. *Am Heart J* 2011;162:571-584

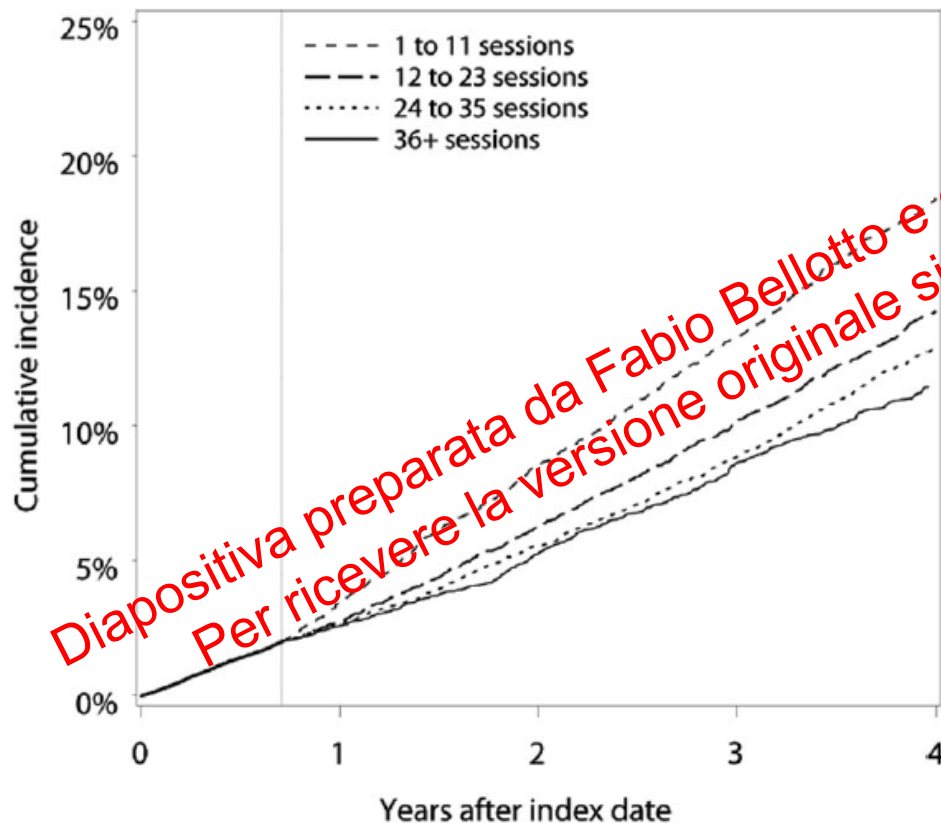
Forest plot of effect of exercise-based CR on all-cause mortality



Relationship between Cardiac Rehabilitation and long-term risks of death and MI among elderly medicare beneficiaries

Hammill BG et al. *Circulation*. 2010;121:63-70

Cumulative incidence of **death** by number of cardiac rehabilitation sessions attended.



Characteristic Patients: n 30,161 Age, median (interquartile range), y 74.0 (70.0–78.0)
Male sex, n 19,229 (63.8%)

Considerazioni

- La storia naturale dopo l'infarto non e' tanto condizionata dal **numero** ne' dall'**entita'** delle stenosi coronariche quanto dal **controllo dei fattori di rischio CV** e dall'aderenza alle terapie;
- Il controllo del maggior numero di fattori di rischio CV determina un documentato miglioramento della prognosi attraverso la "**stabilizzazione**" delle placche coronariche;
- L'**'attivita'** fisica (aerobica, leggera, regolare e continuativa) determina un miglioramento sia della **qualita'** che della **durata** della vita dopo l'infarto;
- La **riabilitazione CV**, favorendo un miglior controllo dei fattori di rischio CV, una maggior aderenza alle terapie ed un documentato, piu' rapido e piu' completo recupero delle condizioni psico-fisiche e' altamente raccomandata dopo l'infarto.

Important
Message

www.ilQuore.it

fabio.bellotto@unipd.it

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Conclusioni e risposte per il test ECM

- Nel DM la sintomatologia dell'angina è spesso più subdola e può essere del tutto assente; la coronaropatia è più diffusa ed interessa in particolare i piccoli vasi e vi è un più spiccato interessamento della microcircolazione con possibilità di angina anche in assenza di stenosi critiche.
- La mortalità per IMA è molto diminuita negli ultimi anni nella fase acuta ma rimane ancora inaccettabilmente elevata nella fase post acuta.
- La condizione che influisce maggiormente sulla prognosi nel post-infarto non è l'entità né il numero delle stenosi coronariche residue, bensì il mancato controllo dei fattori di rischio CV.
- La sola correzione (con bypass o angioplastica) di una stenosi critica nel paziente con angina da sforzo stabile influisce favorevolmente sulla qualità ma non sulla durata della vita.
- In base alle attuali conoscenze e alla disponibilità di risorse, il test ergometrico dovrebbe essere eseguito nel diabetico in presenza di sintomi che indirizzino verso la diagnosi di angina da sforzo o quando il paziente - anche asintomatico - intende sottoporsi ad un ciclo di ricondizionamento fisico basato sull'esercizio.



Conclusioni (1° di 3)

- L'attività fisica aerobica "strutturata" (adattata alle condizioni del paziente) migliora la prognosi soprattutto nei pazienti diabetici, migliorandone il profilo glicemico ed intervenendo favorevolmente sugli altri fattori di rischio CV: ipertensione, dislipidemia, obesità, fumo, etc.
- L'attività fisica non strutturata comporta però dei potenziali rischi per il soggetto non abituato ad essa

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Conclusioni (2° di 3)

- La sola anatomia coronarica separata dalla clinica e dai test induttivi di ischemia può trarre a conclusioni e scelte terapeutiche sbagliate in quanto non predice la possibilità di sindrome coronarica acuta (SCA).
- Test di screenig prima di iniziare l'attività fisica sono pertanto consigliati, in particolare quelli "funzionali" in grado di valutare la possibilità di indurre ischemia piuttosto che la sola anatomia dei vasi coronari.

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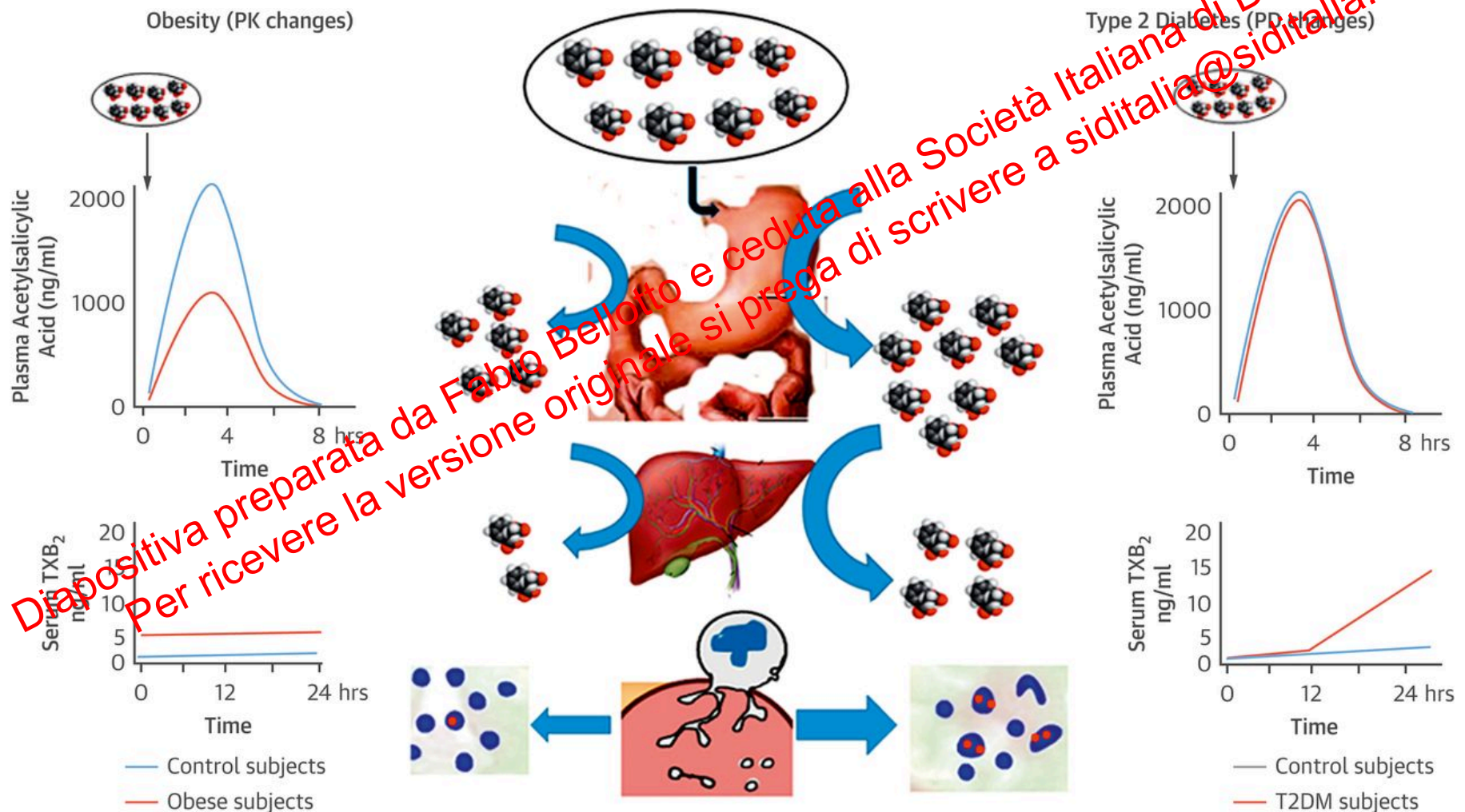
Conclusioni (3° di 3)

- Anche in prevenzione secondaria l'attività fisica è sicura e migliora la qualità e la durata della vita.
- La pianificazione mirata dell'esercizio fisico ottenibile grazie al test cardio-polmonare ne ottimizza i vantaggi.
- La riabilitazione cardio-vascolare basata sull'esercizio deve essere estesa a tutti i cardiopatici dopo un evento acuto, tanto più se anziani o se il loro rischio cardio-vascolare si presenta elevato (DMI).

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Type 2 Diabetes, Obesity, and Aspirin Responsiveness

Patrono C, and Rocca B *JACC* 2017;69:613-615



BELLOTTI, NICOLÒ

Patient ID: 10246

12.05.2017 Male

10:13:00am 45yrs Caucasian

Meds:

Test Reason:

Medical History:

Ref. MD: Ordering MD:

Technician: Test Type:

Comment:

BRUCE: Total Exercise Time 12:45

Max HR: 179 bpm 102% of max predicted 175 bpm HR at rest: 63

Max BP: 158/85 mmHg BP at rest: 108/71 Max RPP: 25280 mmHg*bpm

Maximum Workload: 16.20 METS

Max ST: -1.40 mm, 0.00 mV/s in I; EXERCISE STAGE 4 11:29

Arrhythmia: A:190, PVC:3, PSVC:11, PAU1:1

Reasons for Termination: Fatigue

Summary: Resting ECG: normal. Functional Capacity: normal. HR Response to

Exercise: appropriate. BP Response to Exercise: normal resting BP - appropriate

response. Chest Pain: none. Arrhythmias: none. ST Changes: none. Overall

impression: Normal stress test.

Location Number: * 0 *

Phase Name	Stage Name	Time in Stage	Speed (mph)	Grade (%)	Workload (METS)	HR (bpm)	BP (mmHg)	RPP (mmHg*bpm)	VE (l/min)	ST Level (l mm)	Comment
PRETEST	SUPINE	01:09	0.00	0.00	1.0	67	108/71	7236	0	0.90	
	SITTING	02:10	0.20	0.00	1.1	81			1	0.90	
EXERCISE	STAGE 1	03:00	1.70	10.00	4.6	90	129/75	11610	0	0.90	
	STAGE 2	03:00	2.50	12.00	7.0	110	149/77	16390	0	0.50	
	STAGE 3	03:00	3.40	14.00	10.1	130	147/75	19170	0	0.00	
	STAGE 4	03:00	4.20	16.00	13.4	166			0	-1.10	
	STAGE 5	00:46	5.00	18.00	16.2	153			0	0.60	
RECOVERY		04:16	0.00	0.00	1.0	94	136/84	12784	0	0.30	

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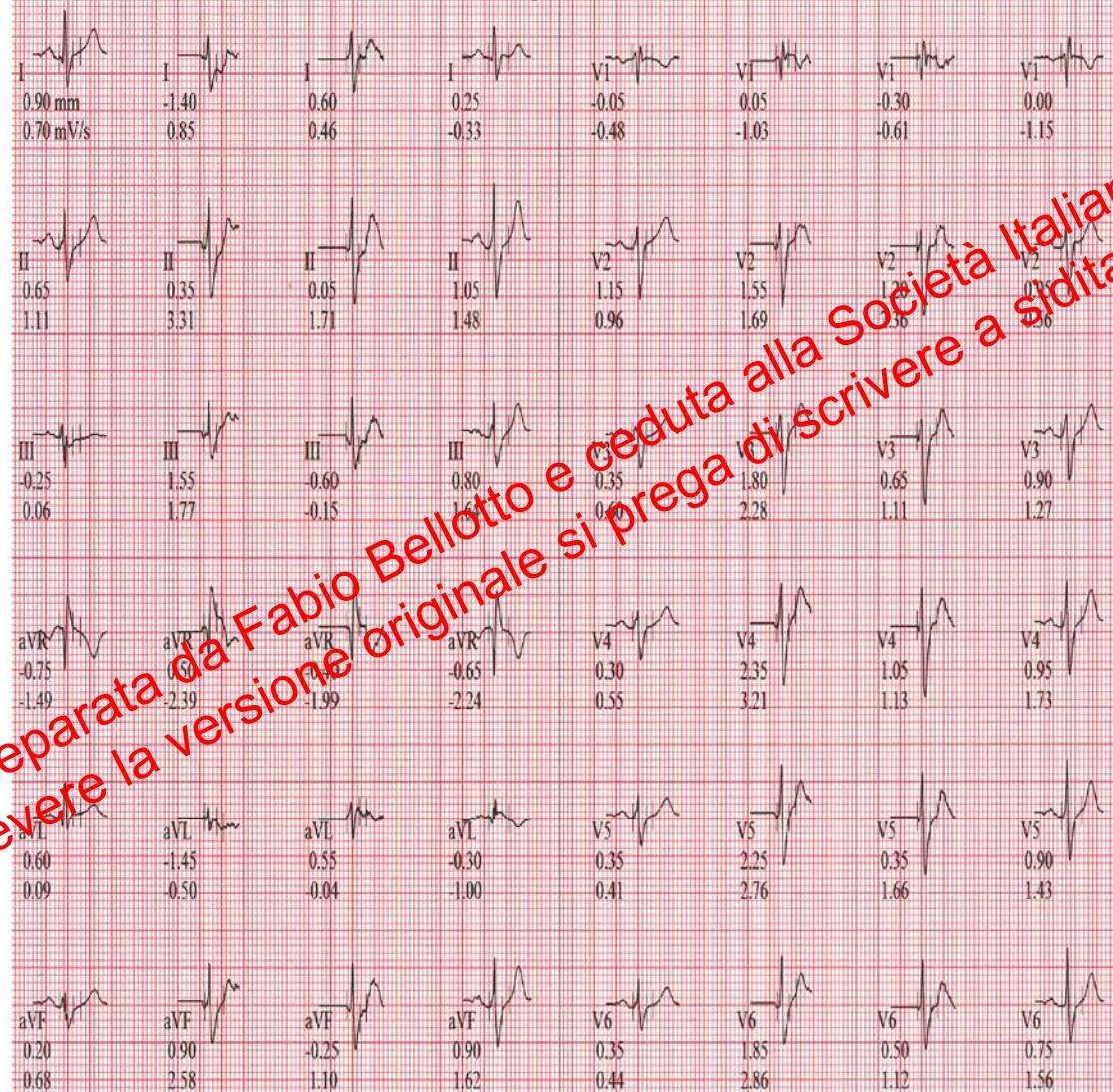
BELLOTTO, NICOLÒ

Patient ID: 10246

12.05.2017

10:13:00am

BASLINE	MAX. ST	PEAK EXERCISE	TEST END	BASLINE	MAX. ST	PEAK EXERCISE	TEST END
EXERCISE	EXERCISE	EXERCISE	RECOVERY	EXERCISE	EXERCISE	EXERCISE	RECOVERY
0:00	11:29	12:46	4:14	0:00	11:29	12:46	4:14
80 bpm	164 bpm	157 bpm	95 bpm	80 bpm	164 bpm	157 bpm	95 bpm
			136/84 mmHg				136/84 mmHg



GE CASE V6.73 (0)

10mm mV 60Hz 0.01Hz FRF+ HEART V5.4

Unconfirmed

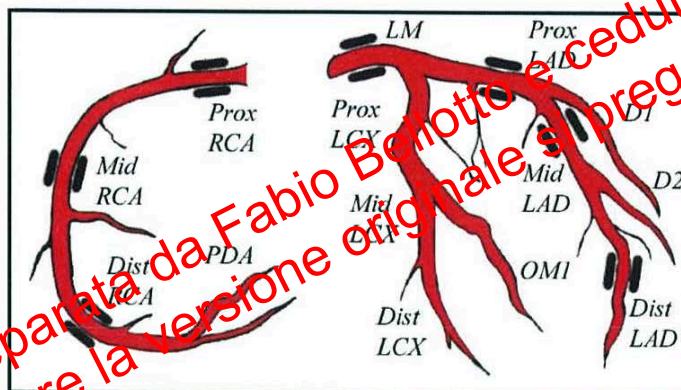
Attending MD: Dr Carl Fung

Page 2

Patient Name:	BELLOTTO, NICOLO		
Patient Age:	45	Referring MD:	DR. CARL FUNG
Patient Gender:	M	Scan Date:	05/15/2017
Date of Birth:	10/29/1971	Patient ID:	334558

Procedure:

High-resolution Computed Tomographic imaging of the chest was performed on 05/15/2017, with particular attention paid to the coronary arteries. Images from the examination were analyzed for the presence and extent of coronary artery calcification, using coronary calcium quantification software. The patient tolerated the procedure well and there were no complications. The results of the coronary calcification analysis are provided below, along with representative cross-sectional images from the examination and a schematic illustration of the coronary arteries and the location of any detected calcification. The patient's score is compared with published data relating to scores for people of a similar age and the same gender.

Findings:

The diagram to the left is a schematic of the coronary artery system. The coronary arteries are segmented into Proximal, Mid, and Distal sections, which may be annotated with black markings to illustrate the **approximate location** of any **calcified** regions detected in the examination. However please note that the markings **do not imply** the presence, absence, location or extent of arterial stenosis or any other condition other than the presence of coronary calcification.

Coronary Artery	Score
Left Main (LM)	16.69
Left Anterior Descending (LAD)	68.74
Left Circumflex (LCX)	0.00
Right Coronary Artery (RCA)	25.23
Total Agatston Score	110.67

The **Agatston Score** as reported in this table provides a measure for comparison with published studies (see "Percentile Ranking" below). The **Volume Score** can be useful for comparison with follow-up examinations, and is reported here: **87.74 mm**.

The Percentile Ranking compares this score with scores for people in a group with the same gender and similar age, as reported in the literature.

A rank **below** 50% indicates a score **better** than most in that group.
A rank **above** 50% indicates a score **worse** than most in that group.

(J Hoff et al., American Journal of Cardiology, 2001 87:1335-1339).

Percentile Ranking

greater than 75%

In a published study, greater than 75% of people of the same gender and similar age had the same or lower scores.

TECHNIQUE: ECG triggered plain MDCT scans for calcium score was performed.

FINDINGS:

The calcium score is 111 compatible with moderate fibrocalcific plaque burden and high risk of cardiovascular disease.

There are no lung nodules in the scanned region of the thorax. The ascending aorta is dilated (42 mm). The aortic root and pulmonary trunk are normal in size and appearance. Thoracic spondylosis is present.

SITE	Calcium Score
Left Main	17
LAD	69
LCx	0
RCA	25
TOTAL	111

COMMENT:

- The calcium score is 111. This implies a high risk of coronary artery disease.
- Ascending aortic aneurysm.



Dr. Yau Yat-Yin
Consultant Radiologist

MBBS (QLD), FRANZCR (Australia), FHKCR, FHKAM (Radiology)

Name **Bellotto Nicolo**
Age/Gender **45Y/M** D.O.B. **October 29, 1971**
Patient No **010246 /**
Patient I.D.
Drawn **Apr 27, 2017** Time: Not Given
Received **Apr 27, 2017 1:51 PM** Reported **April 28, 2017 10:03 AM**
Lab No **17D16440**
Remarks
Specimen **All samples are blood, unless otherwise indicated.**

(C070) (C070)
CityHealth Medical Clinic
Dr. Fung Carl Pui

香港中環太子大廈1526-7室
Hong Kong

Tel 2526 1144

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Test Name 化驗項目	Result (Conv. unit) 結果	Result (S.I. unit) 結果
Alkaline Phosphatase 鹼性磷酸酶	55 U/L Up to 126	55 U/L Up to 126
Bilirubin, Total 總膽紅素	0.9 mg/dL Up to 1.5	15 umol/L Up to 26
Protein, Total 總蛋白	7.2 g/dL 6.3 - 8.2	72 g/L 63 - 82
Albumin 白蛋白	4.8 g/dL 3.5 - 5.0	48 g/L 35 - 50
Globulin 球蛋白	2.4 g/dL 2.0 - 3.5	24 g/L 20 - 35
SGOT/AST 谷草轉氨酶	24 U/L Up to 59	24 U/L Up to 59
SGPT/ALT 谷丙轉氨酶	24 U/L Up to 58	24 U/L Up to 58
Gamma GT 丙種谷氨轉移酶	25 U/L Up to 73	25 U/L Up to 73
LDH 乳酸脫氫酶	498 U/L 313 - 618	498 U/L 313 - 618
Uric Acid 尿酸	6.1 mg/dL 3.5 - 8.5	0.36 mmol/L 0.21 - 0.51
Glucose, Fasting or Random Plasma 血糖	88 mg/dL Normal fasting glucose 70 - 99 Fasting glucose 100 - 125 Diabetes mellitus (Fasting glucose) ≥ 126 Diabetes mellitus (Random glucose) ≥ 200	4.9 mmol/L 3.9 - 5.5 5.6 - 6.9 ≥ 7.0 ≥ 11.1

Reference range:
1. Fasting is based on fasting glucose cutoff values only.
2. Glucose ranges should be interpreted appropriately for either random or fasting draws.
3. Fasting is defined as no caloric intake for at least 8 hours.
4. In the absence of unequivocal hyperglycemia, the diagnosis of DM on fasting and random samples need to be confirmed by repeat testing.

Source: ADA Diabetes Care 2014:37.

Urea 尿素	30 mg/dL 19 - 43	5.1 mmol/L 3.1 - 7.2
Creatinine 肌酸酐	0.79 mg/dL 0.66 - 1.25	70 umol/L 58 - 111
Sodium 鈉	144 mmol/L 137 - 145	144 mmol/L 137 - 145
Potassium 鉀	4.8 mmol/L 3.6 - 5.4	4.8 mmol/L 3.6 - 5.4
Chloride 氯化物	103 mmol/L 98 - 107	103 mmol/L 98 - 107

NOTES	✓
DOCTOR	CT1 C2
FILE	
PATIENT INFORMED	
ACTION	71m + cms 12/5/17

Approved signatory :
Reg. M.L.T. : LEE, Fung Kuen Carmen
PathLab Medical Laboratories Ltd.

Printed : Apr 28, 2017 10:06:25
Report # A005962306



Name **Bellotto Nicolo**
Age/Gender 45Y/M D.O.B. October 29, 1971
Patient No 010246 /
Patient I.D.
Drawn Apr 27, 2017 Time : Not Given
Received Apr 27, 2017 1:51 PM Reported April 28, 2017 10:03 AM
Lab No **17D16440**
Remarks
Specimen All samples are blood, unless otherwise indicated.

(C070) (C070)

CityHealth Medical Clinic

Dr. Fung Carl Pui

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Hong Kong

Tel 2526 1144

Fax 2526 1146

Test Name 化驗項目	Result (Conv. unit) 結果	Result (S.I. unit) 結果
ECO2 碳酸氫鹽	28 mmol/L 23 - 32	28 mmol/L 23 - 32
Calcium 鈣	9.5 mg/dL 8.4 - 10.2	2.32 mmol/L 2.09 - 2.54
Phosphorus 磷	1.5 mg/dL 2.5 - 5.0	1.13 mmol/L 0.81 - 1.61
Lipid Profile, Direct 血脂組合		
Cholesterol, Total 總膽固醇	199 mg/dL	5.14 mmol/L
Desirable	< 200	< 5.18
Borderline high	200 - 239	5.18 - 6.18
High	≥ 240	≥ 6.21
HDL Cholesterol 高密度脂蛋白膽固醇	43 mg/dL	1.11 mmol/L
Low	< 40	< 1.03
High (Desirable)	> 60	> 1.55
Chol/HDL Ratio 總膽固醇及高密度脂蛋白膽固醇之比率	4.6 Up to 4.0	
LDL Cholesterol, Direct 低密度脂蛋白膽固醇, 直接	132 mg/dL	3.41 mmol/L
Optimal	< 100	< 2.59
Near or above optimal	100 - 129	2.59 - 3.34
Borderline high	130 - 159	3.35 - 4.11
High	160 - 189	4.12 - 4.89
Very High	≥ 190	≥ 4.90
VLDL Cholesterol, by Calc 非常低密度脂蛋白膽固醇	24 mg/dL	0.62 mmol/L
Desirable	Up to 62	Up to 1.60
Triglycerides 三酸甘油脂	160 mg/dL	1.8 mmol/L
Normal (Fasting)	< 150	< 1.7
Borderline High	150 - 199	1.7 - 2.3
High	200 - 499	2.3 - 5.6
Very High	≥ 500	≥ 5.6

Diapositiva preparata da Fabio Bellotto e ceduta alla Società Italiana di Diabetologia.
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Complete Blood Count 全血計數

WBC & Differential Count

WBC Count 白血球計數

Neutrophils 中性粒細胞

Lymphocytes 淋巴細胞

Monocytes 單核細胞

Eosinophils 嗜酸性細胞

Basophils 嗜鹼細胞

Result 結果	Ref. Range	Result % 結果	Ref. Range
4.9 k/uL	4.0 - 11.0		
2.2 k/uL	1.4 - 8.5	46 %	40 -
2.0 k/uL	1.0 - 4.8	45 %	20 -
0.2 k/uL	up to 1.4	4 %	up to
0.1 k/uL	up to 0.7	2 %	up to
0.0 k/uL	up to 0.5	1 %	up to

*Unless otherwise indicated an automated differential count is reported.

Automated differential counts occasionally may not add up to exact total count or 100 % due to rounding of decimals.

RBC & Morphology

RBC Count 紅血球計數

Haemoglobin 血紅蛋白

Hematocrit 紅血球壓積量

MCV 平均紅血球容積

MCH 紅細胞平均血紅蛋白量

MCHC 紅細胞平均血紅蛋白濃度

RDW 紅血球分佈比率

Result 結果	Ref. Range
5.04 M/uL	4.30 - 6.00
14.9 g/dL	13.5 - 18.0
43.9 %	40.0 - 54.0
87.1 fL	81.0 - 100.0
29.5 pg	27.0 - 34.0
33.9 g/dL	30.0 - 36.0
13.3 %	10.5 - 14.5

Platelets

Platelet Count 血小板計數

MPV 平均血小板容積

160 k/uL	130 - 440
8.9 fL	7.6 - 11.9

ESR 血沉降率檢查

Females ≤ 50 yrs
Females > 50 yrs
Males ≤ 50 yrs
Males > 50 yrs

3 mm/hr
0 - 20
0 - 30
0 - 15
0 - 20

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Subclinical Myocardial Impairment in Metabolic Diseases

Kosmala W, Sanders P, Marwick TH. *J Am Coll Cardiol Img* 2017;10:692–703

Cardiodepressant Effects of Metabolic Aberrations

Aberration	Effect
Hyperglycemia	↑ Mitochondrial superoxide production, ↓ nitric oxide and cGMP; ↓ protein kinase G activity; hypophosphorylation of titin; ↑ myocardial deposition of advanced glycation products due to nicotinamide adenine dinucleotide phosphate oxidase and inflammatory activation
↑ FFA uptake into cardiomyocytes	Mitochondrial dysfunction with uncoupling of oxidative phosphorylation; cardiomyocyte lipoapoptosis
↑ Myocardial triglyceride accumulation	Cardiomyocyte lipoapoptosis
↑ Oxidative stress	↑ Nuclear factor kappa B; ↑ cardioinhibitory and profibrotic cytokines; dysregulation of intracellular Ca^{+2} turnover (effect on Ca^{+2}-sensitive contractile proteins, $\text{Na}^{+}/\text{Ca}^{+2}$ exchanger and sarcoplasmic or endoplasmic reticulum Ca^{+2}-ATPase pump)
Insulin resistance and hyperinsulinemia	↑ Cardiomyocyte hypertrophy and intrinsic stiffness by the activation of phosphoinositide 3-kinase/protein kinase B cascade; activation of insulin-like growth factor 1 receptors, ↑ response to angiotensin II; sodium retention with intravascular volume expansion

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Subclinical Myocardial Impairment in Metabolic Diseases

Kosmala W, Sanders P, Marwick TH. *J Am Coll Cardiol Img* 2017;10:692–703

Imaging Characteristics of Metabolic Heart Disease

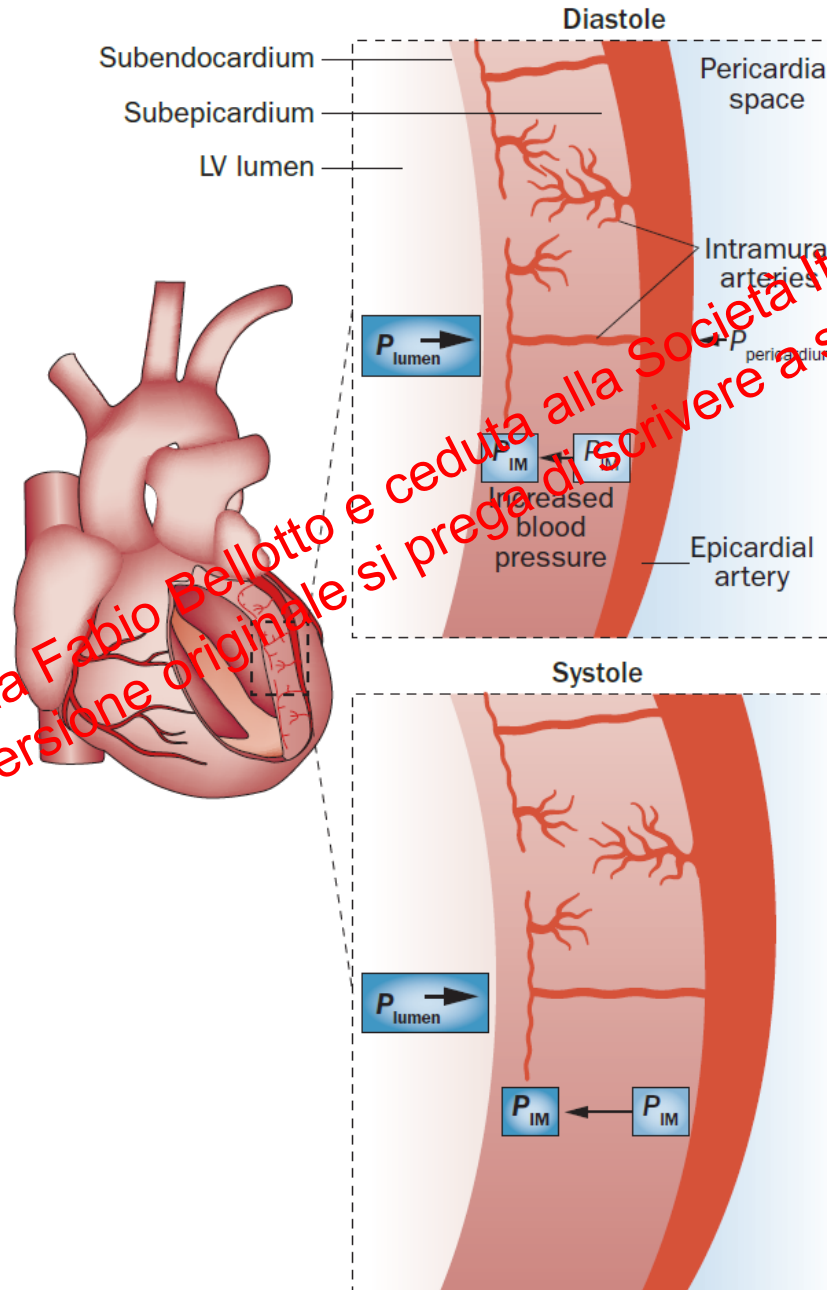
Domain	Findings
Cardiac morphology	LV concentric or eccentric hypertrophy
Myocardial tissue characterization	Higher cIB and shorter post-contrast CMR-derived T1 time, both indicative of enhanced myocardial fibrosis
LV diastolic function	Usually delayed relaxation, evidence of LV filling pressure elevation less common in preclinical phase
LV systolic function	EF and FS usually normal or even supranormal in obesity Decrease in longitudinal function (strain or myocardial systolic velocities) Circumferential and radial deformations unchanged, decreased, or increased (radial)
LV rotational function	Increased LV torsion and untwisting rate
RV function	Systolic and diastolic abnormalities evidenced by longitudinal strain and myocardial velocities
LA function	Impaired LA deformation (reduced function)
LV response to stress	Usually reduced systolic and diastolic reserve, as evidenced by tissue velocities, longitudinal strain and strain rate, E/e' ratio, EF, FS, stroke volume, and ventriculoarterial coupling
Coronary microvascular function	Reduced coronary flow reserve and diminished endothelium-dependent and independent vasodilation, as demonstrated by myocardial contrast echocardiography, distal coronary Doppler flow, and PET, usually with a vasodilating stressor agent (dipyridamole, adenosine, regadenoson) or with dobutamine

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REVIEW

Coronary microvascular dysfunction: mechanisms and functional assessment

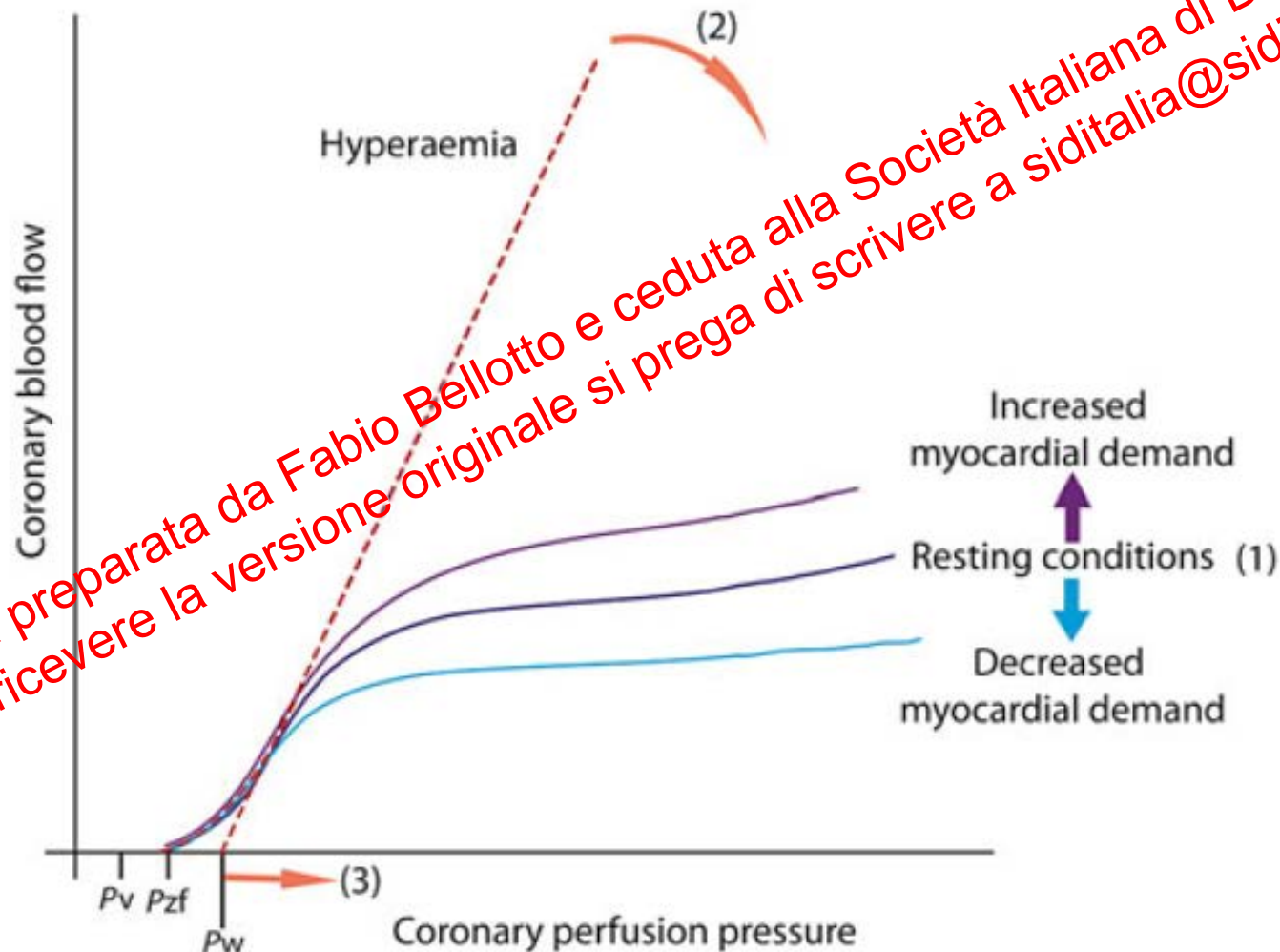
Camici PG, d'Amati G, and Rimoldi O. *Nat. Rev. Cardiol.* 12, 48–62 (2015)



Fundamentals in clinical coronary physiology: why coronary flow is more important than coronary pressure

van de Hoef TP, et al. Eur Heart J 36(47):3312-19;2015

The coronary pressure–flow relationship



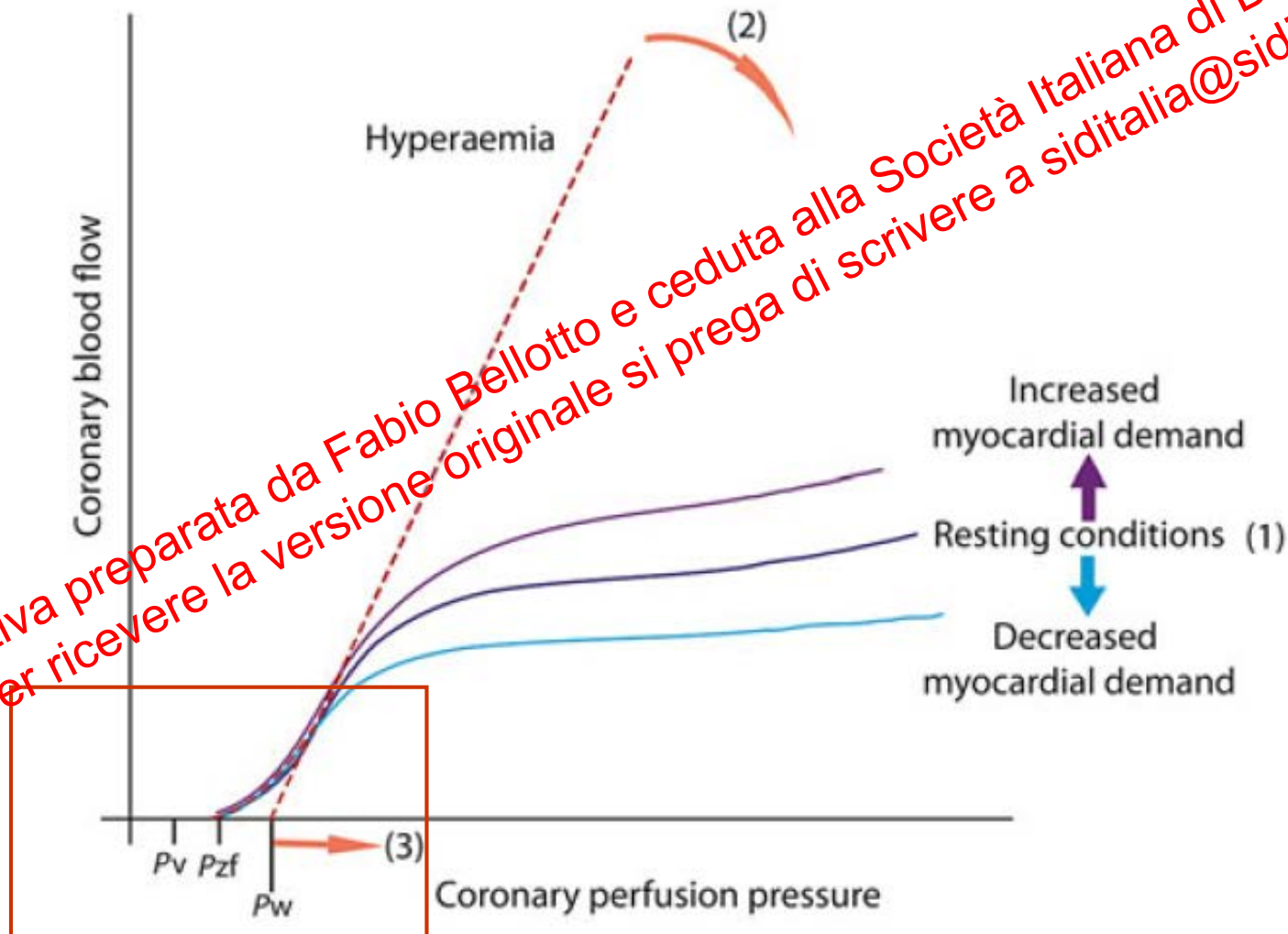
Diapositiva preparata da Fabio Bellotto e ceduta alla Società Italiana di Diabetologia.
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P_{zf} : The zero-flow intercept on the pressure axis P_v : venous pressure P_w : coronary wedge pressure

Fundamentals in clinical coronary physiology: why coronary flow is more important than coronary pressure

van de Hoef TP, et al. Eur Heart J 36(47):3312-19;2015

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