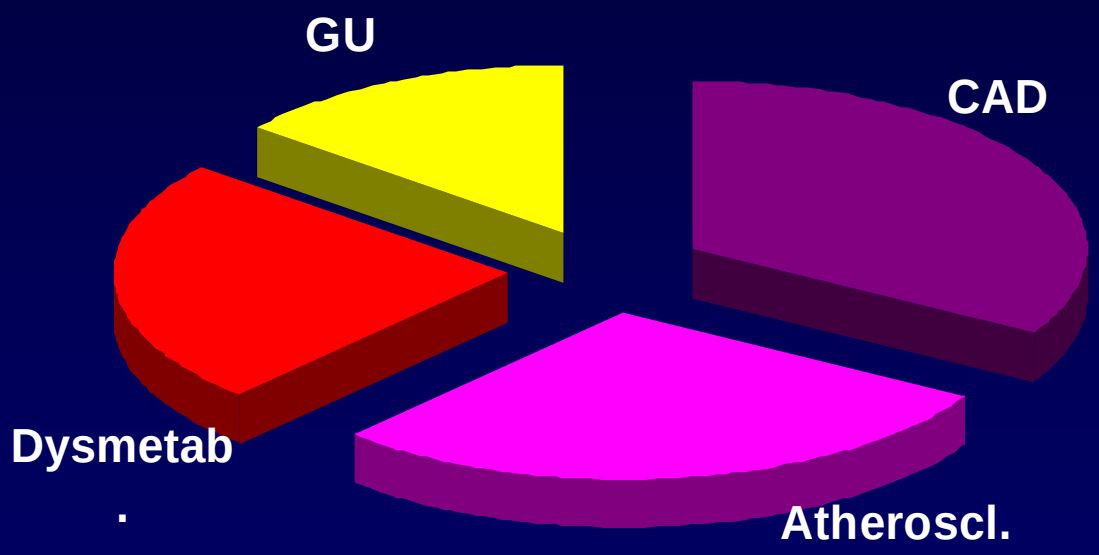
La Disfunzione Erettile Marker di Patologia Cardiovascolare

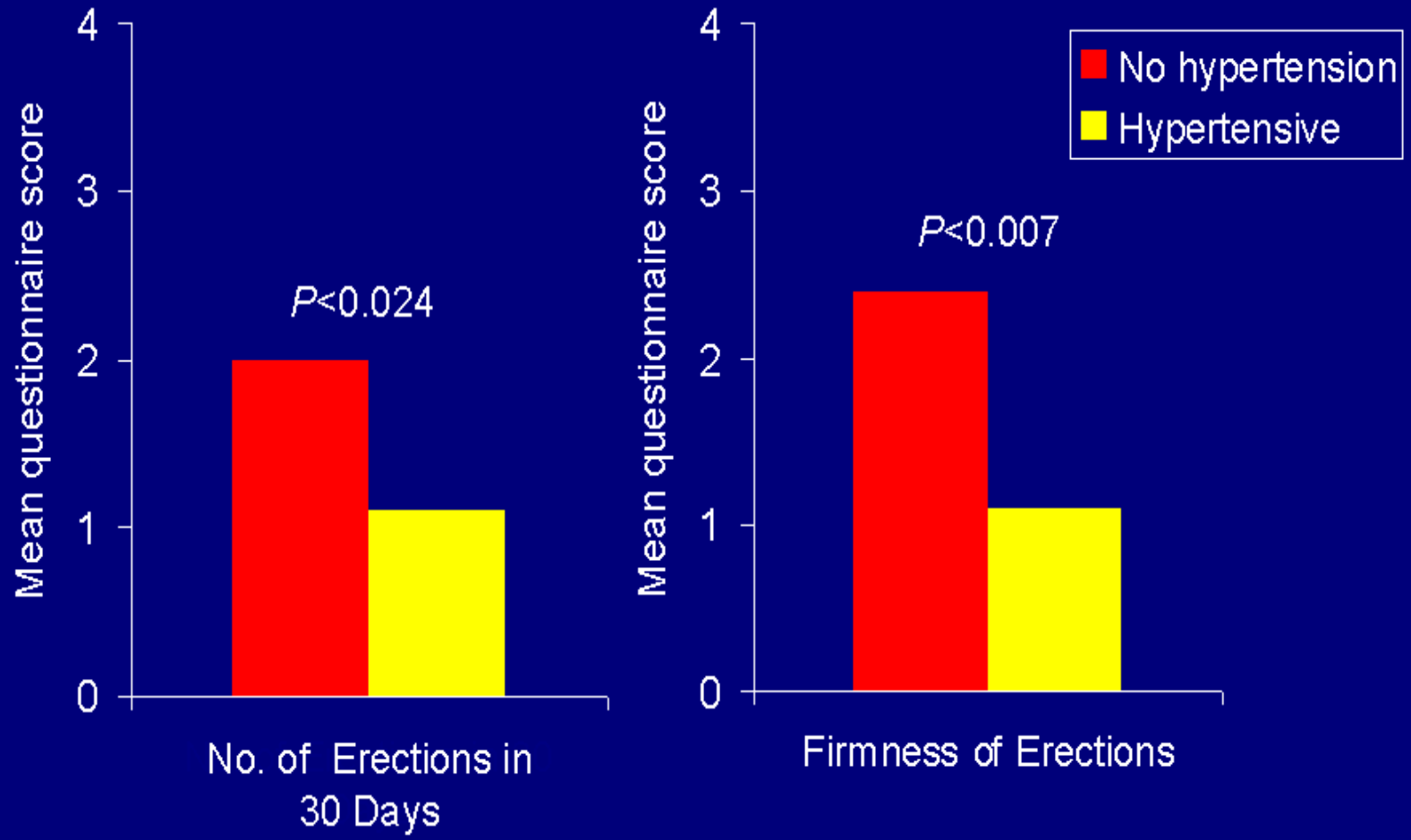
Giuseppe M.C. Rosano, MD, PhD

IRCCS San Raffaele - Roma

ED and Cardiovascular Diseases



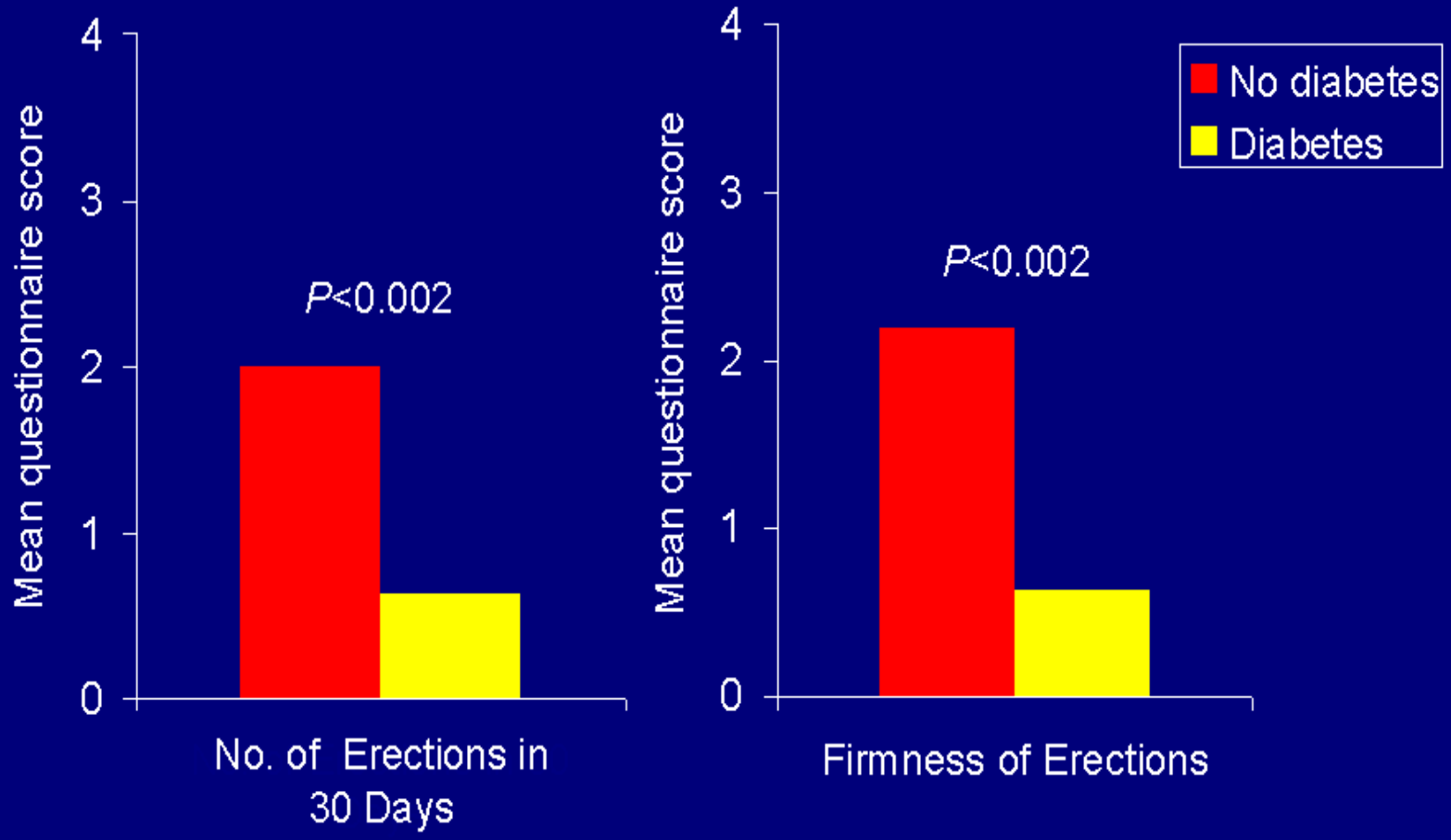
Effects of Hypertension on Erectile Function



Mean scores are based on a scale from 0 to 4 where 0=least and 4=most.

Greenstein A et al. *Int J Impot Res.* 1997;9:123-126.

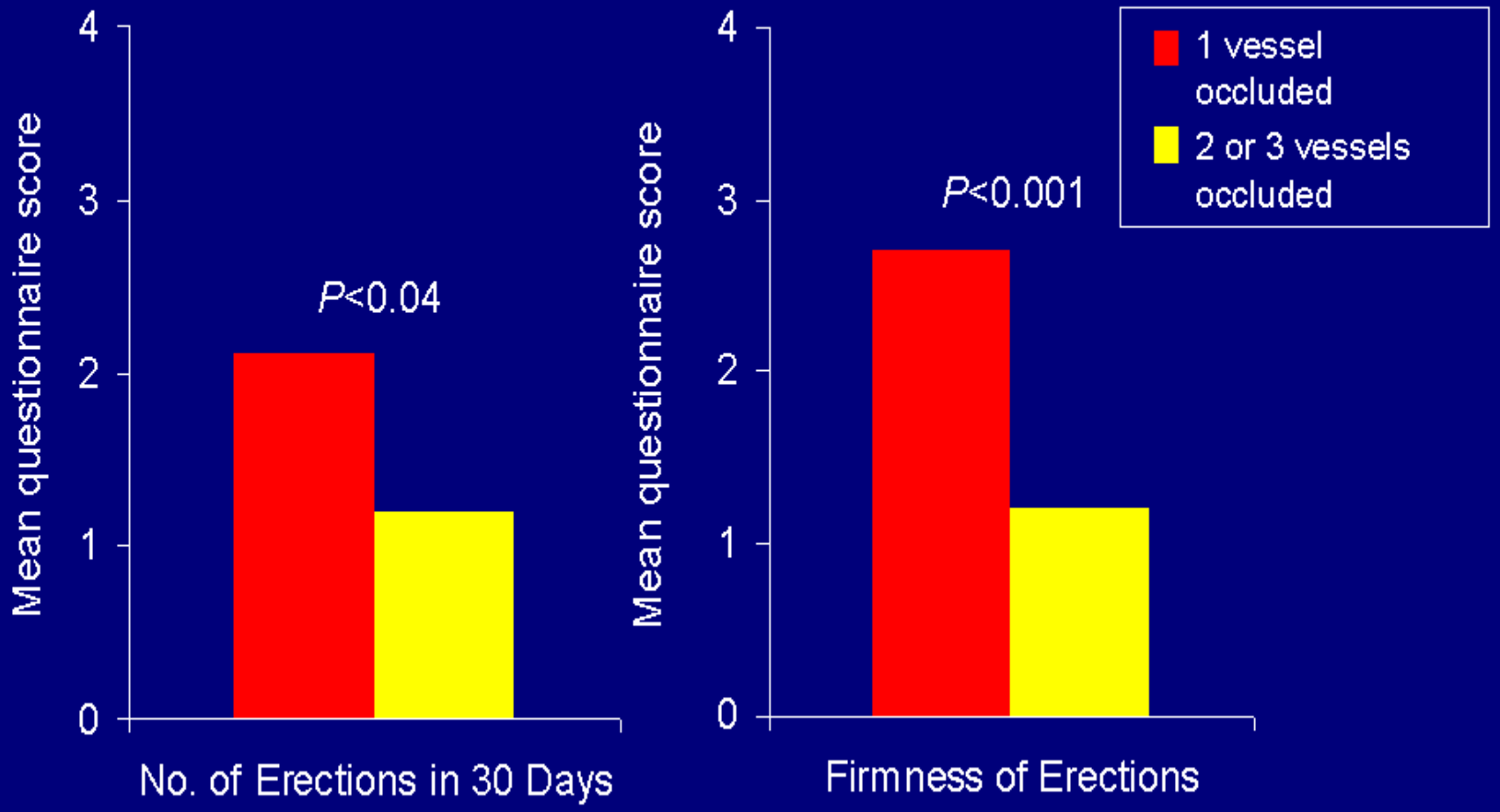
Effects of Diabetes on Erectile Function



Mean scores are based on a scale from 0 to 4 where 0=least and 4=most.

Greenstein A et al. *Int J Impot Res*. 1997;9:123-126.

Effects of Severity of Coronary Artery Disease on Erectile Function



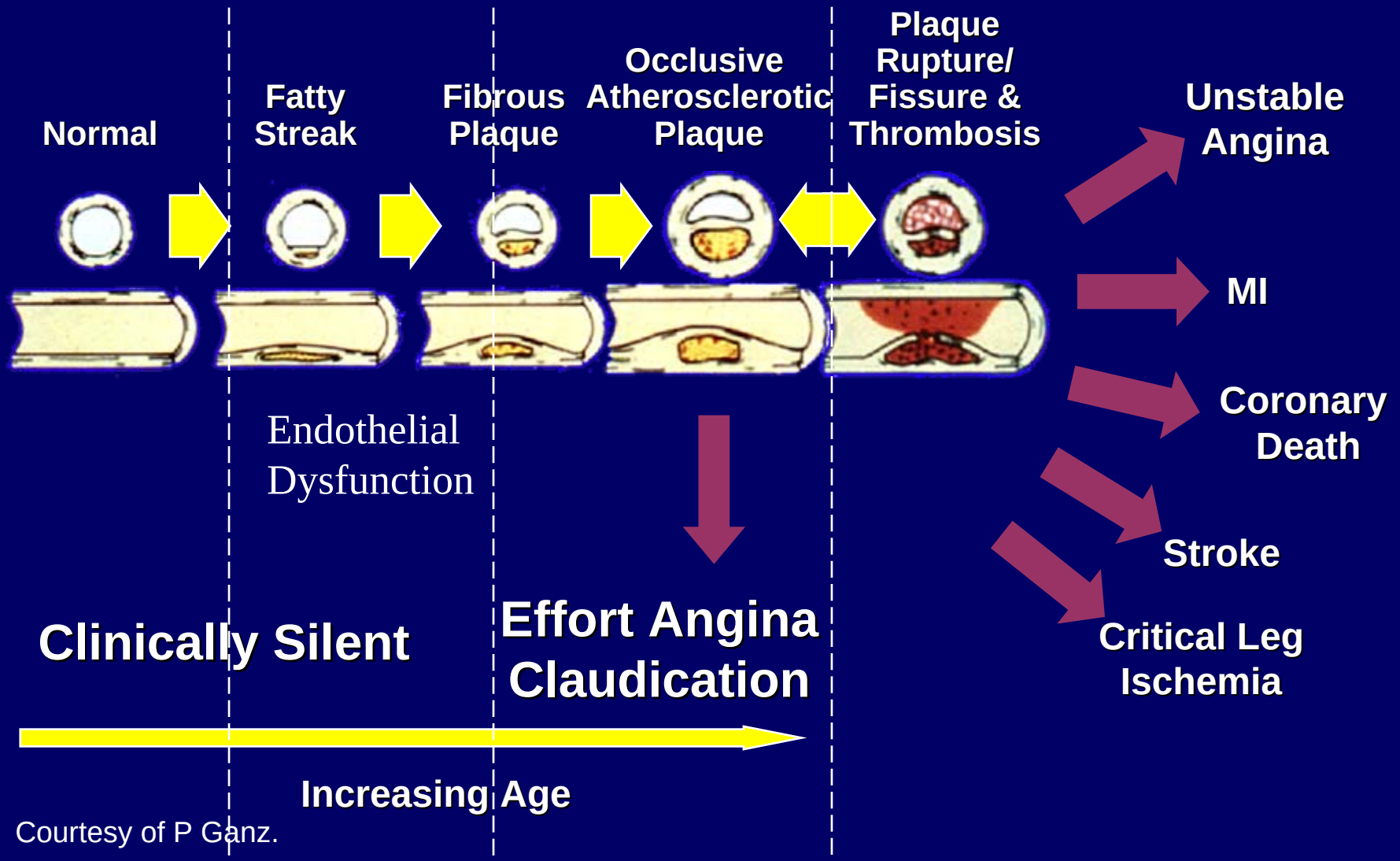
Mean scores are based on a scale from 0 to 4 where 0=least and 4=most.

Greenstein A et al. *Int J Impot Res*. 1997;9:123-126.

ED and Cardiovascular Disease

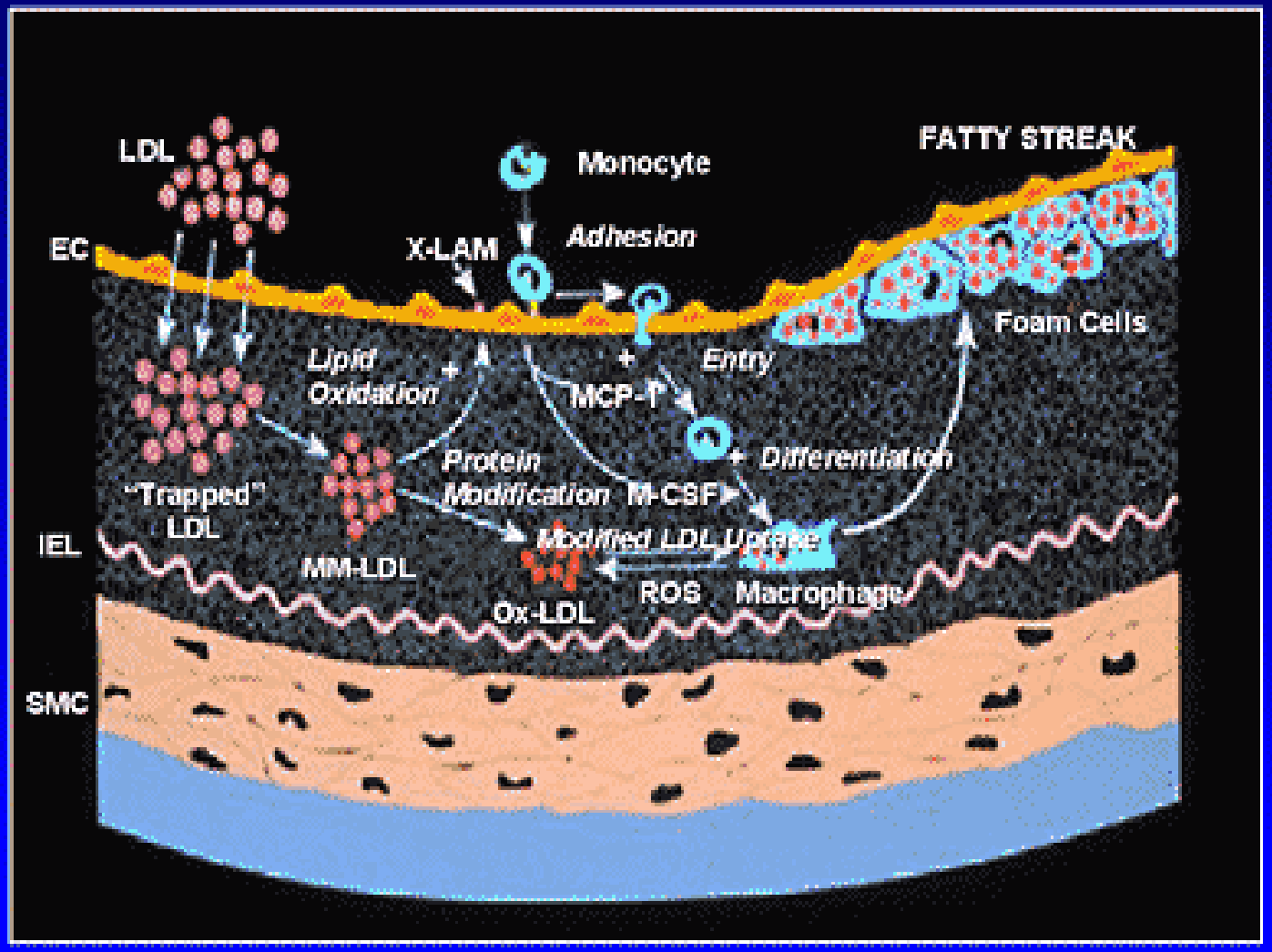
- Changes in arterial wall
- Diffuse atherosclerosis and blood flow obstruction
- Production of EDRF
- Vasoactive peptides
- Metabolic syndrome
- Medical therapy
- Psycogen

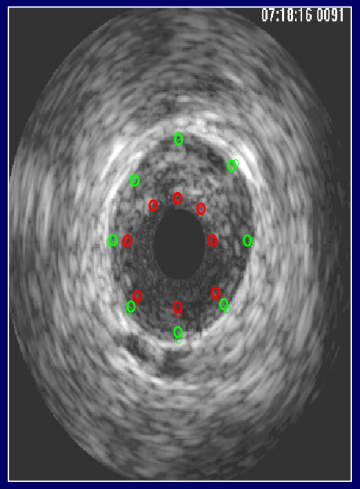
Atherosclerosis: A Progressive Process



Courtesy of P Ganz.

Early Events in Atherosclerosis

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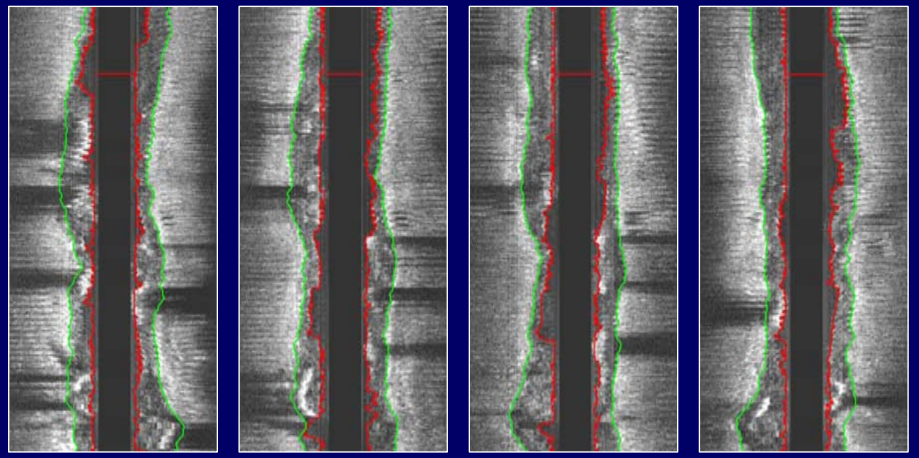
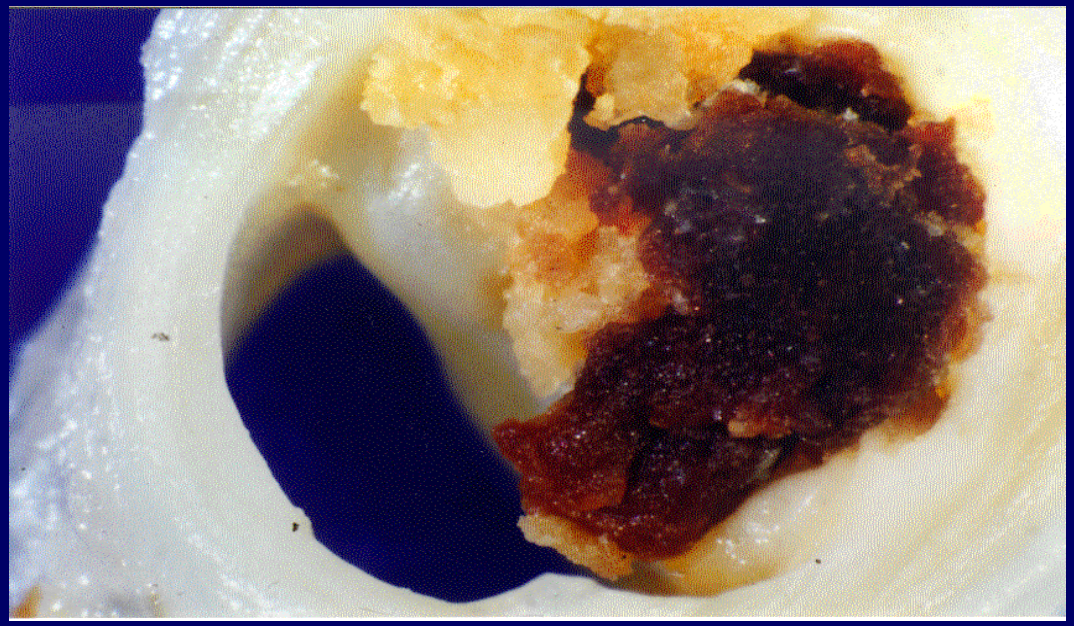
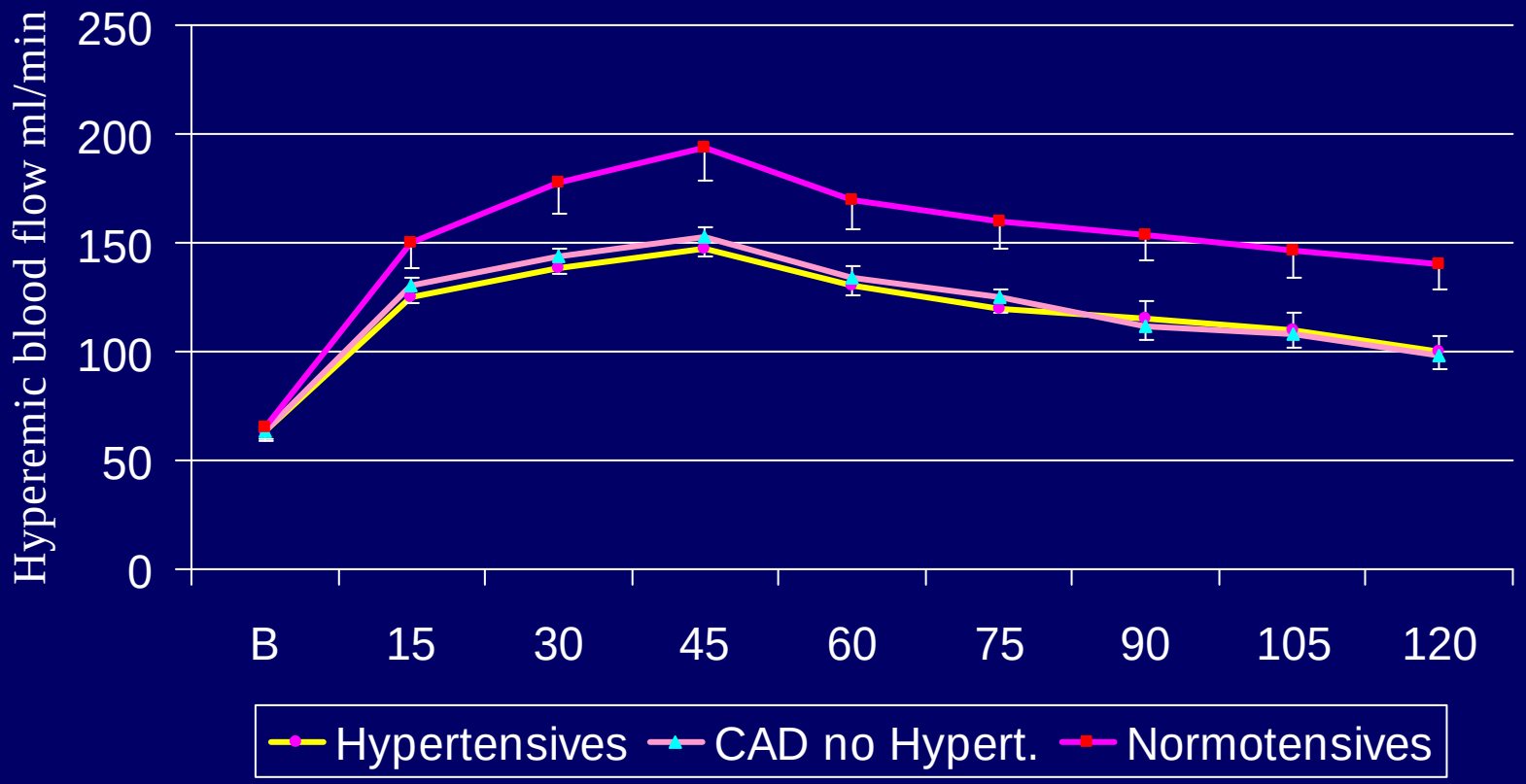




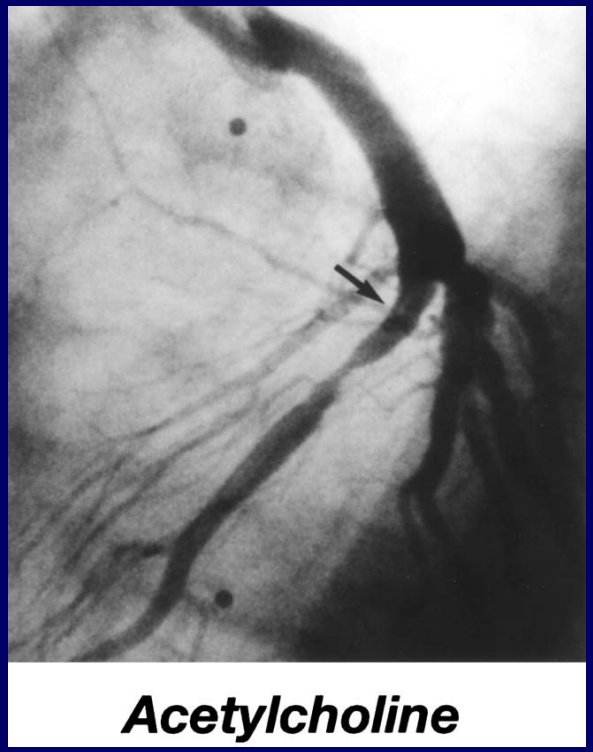
Cardiovascular disease is associated with endothelial dysfunction



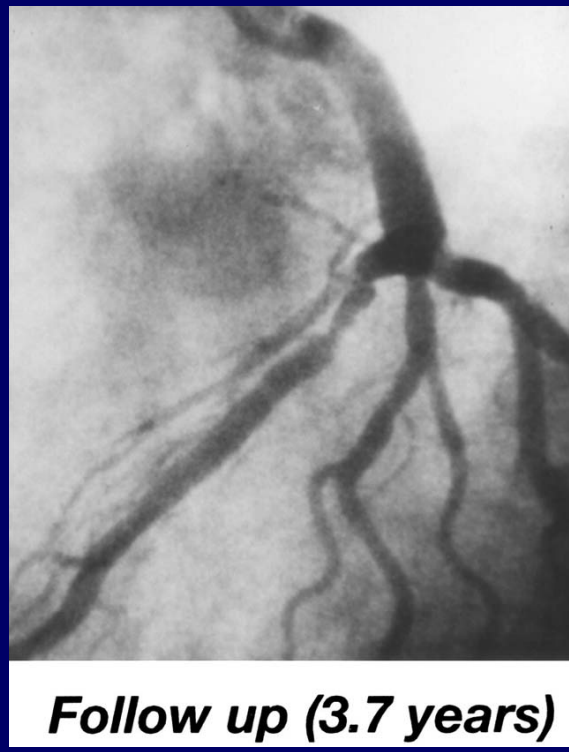
Adapted from Taddei S. et al. Hypertension 1996; 28: 576-82

Prognostic Impact of Atherosclerosis and Vasodilator Dysfunction on Long-Term Outcome of CAD

Baseline



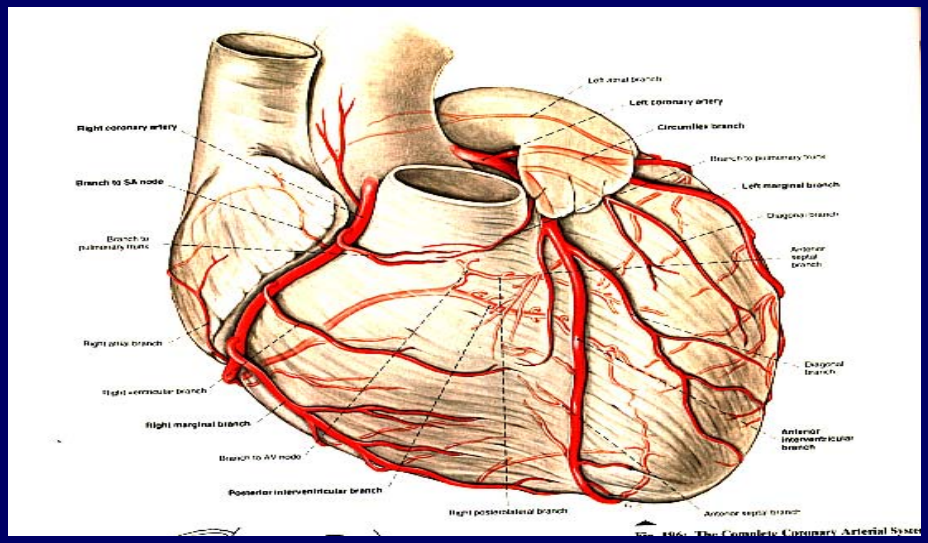
Acetylcholine

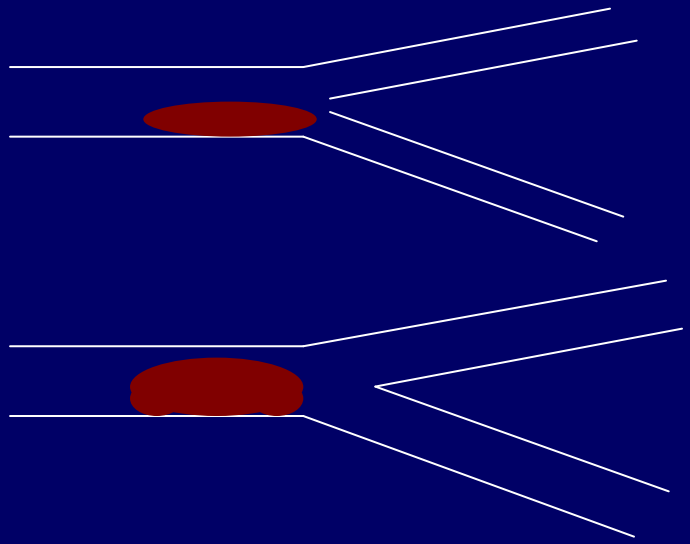


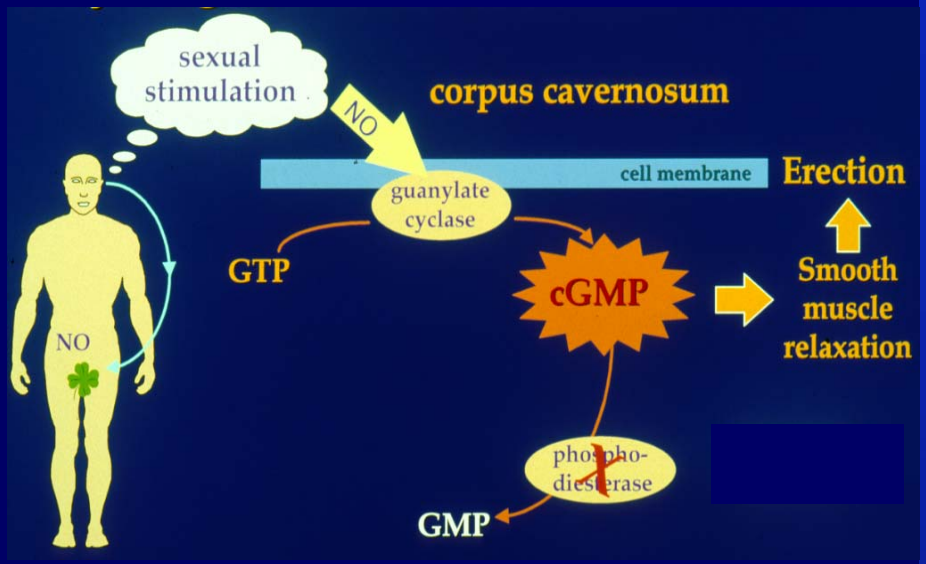
Follow up (3.7 years)

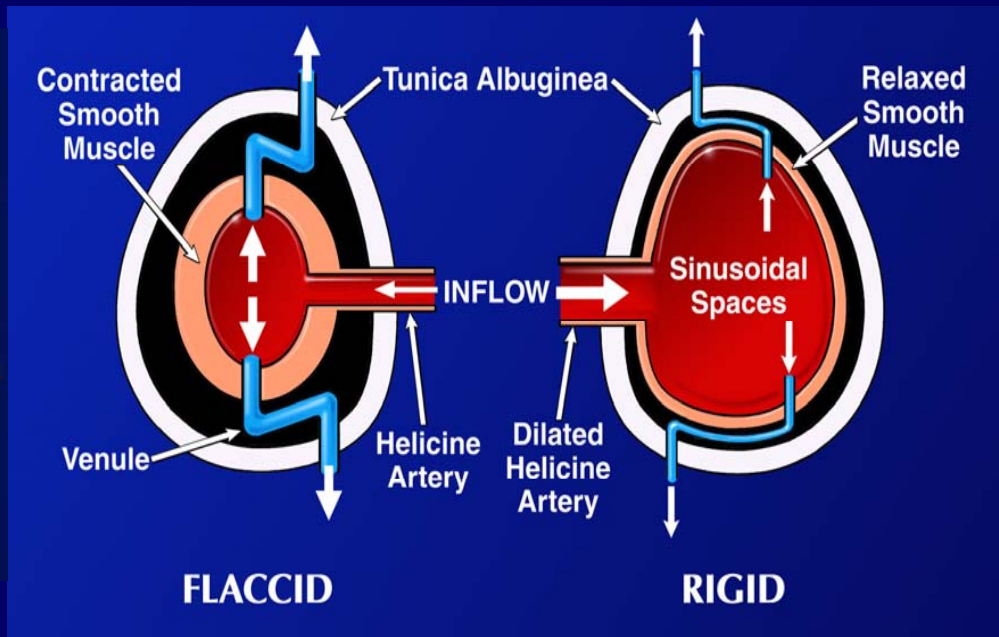
Schachinger et al. 2000. Circulation 101: 1899

Different Control of Blood Flow in Different Vascular Districts









Incidence of Cardiovascular Disease in Patients Referred for ED

Study Objective

- Evaluate cardiovascular risk and incidence of cardiovascular disease in cardiac asymptomatic patients with ED

Study esign

- Indication of exercise ECG and eventually to coronary angiography to 50 cardiac asymptomatic patients with suspected vasculogenic ED

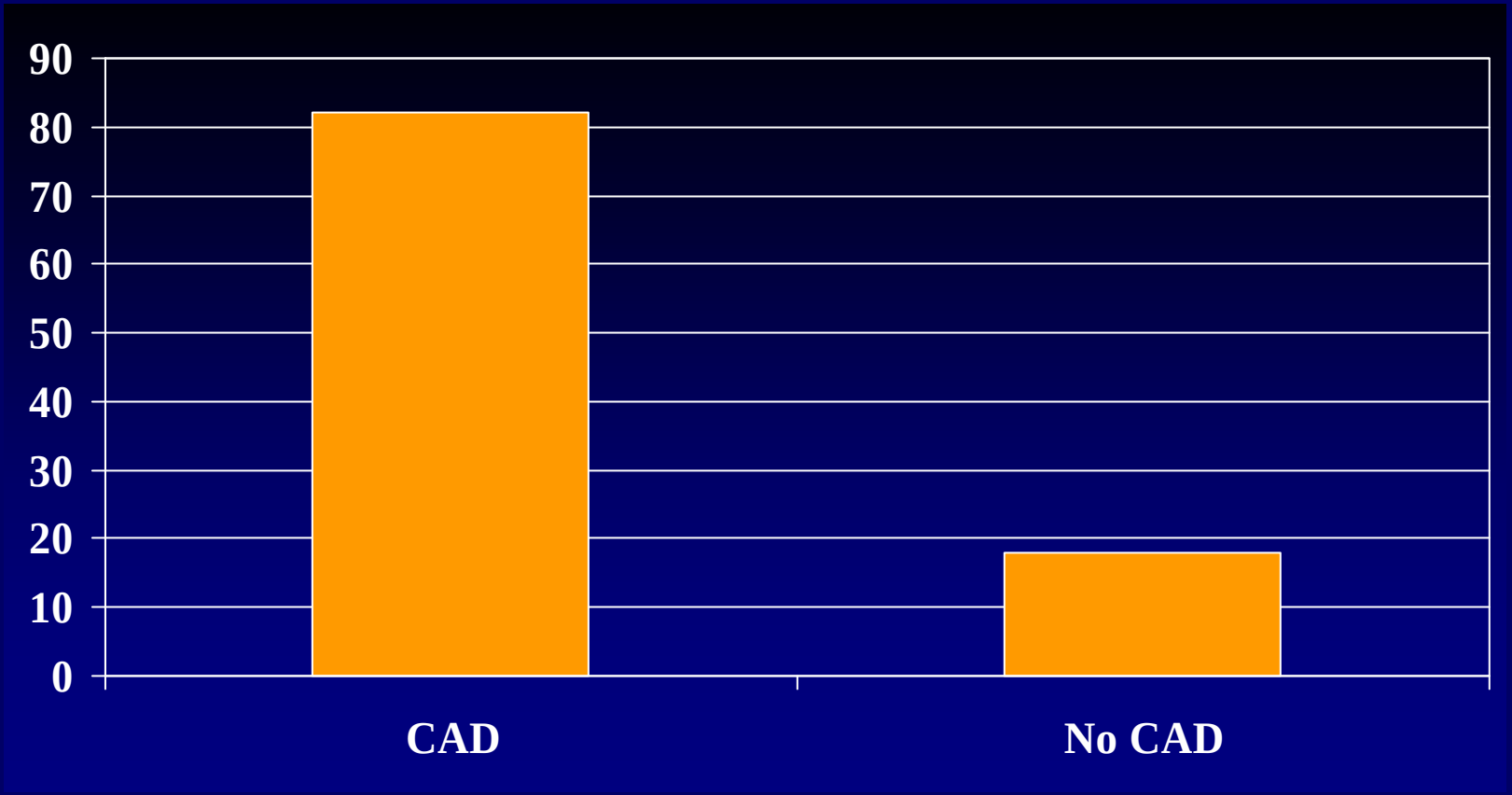
Pritzker MR. *Circulation*. 1999; 100 (suppl 1): I-711. Abstract 3751

Cardiovascular Disease in Patients with ED

- In 40 patients out of 50 (80%) there was presence of multiple risk factors for CAD
  - Family history (n=32)
  - cigarette smoking (n=40)
  - total cholesterol >200 mg/dl (n=35)
  - HDL-c <40 mg/dl (n=18)
  - Hypertension (n=24)
  - Sedentary life style (n=38)
  - diabetes (n=10)
- Exercise ECG was positivein 28/50 pazients
- Coronary angiography was performed in 20 patients and showed
  - proximal LAD or 3vd in 6 pts
  - 2 vd in 7
  - Single vessel disease in 7 pts

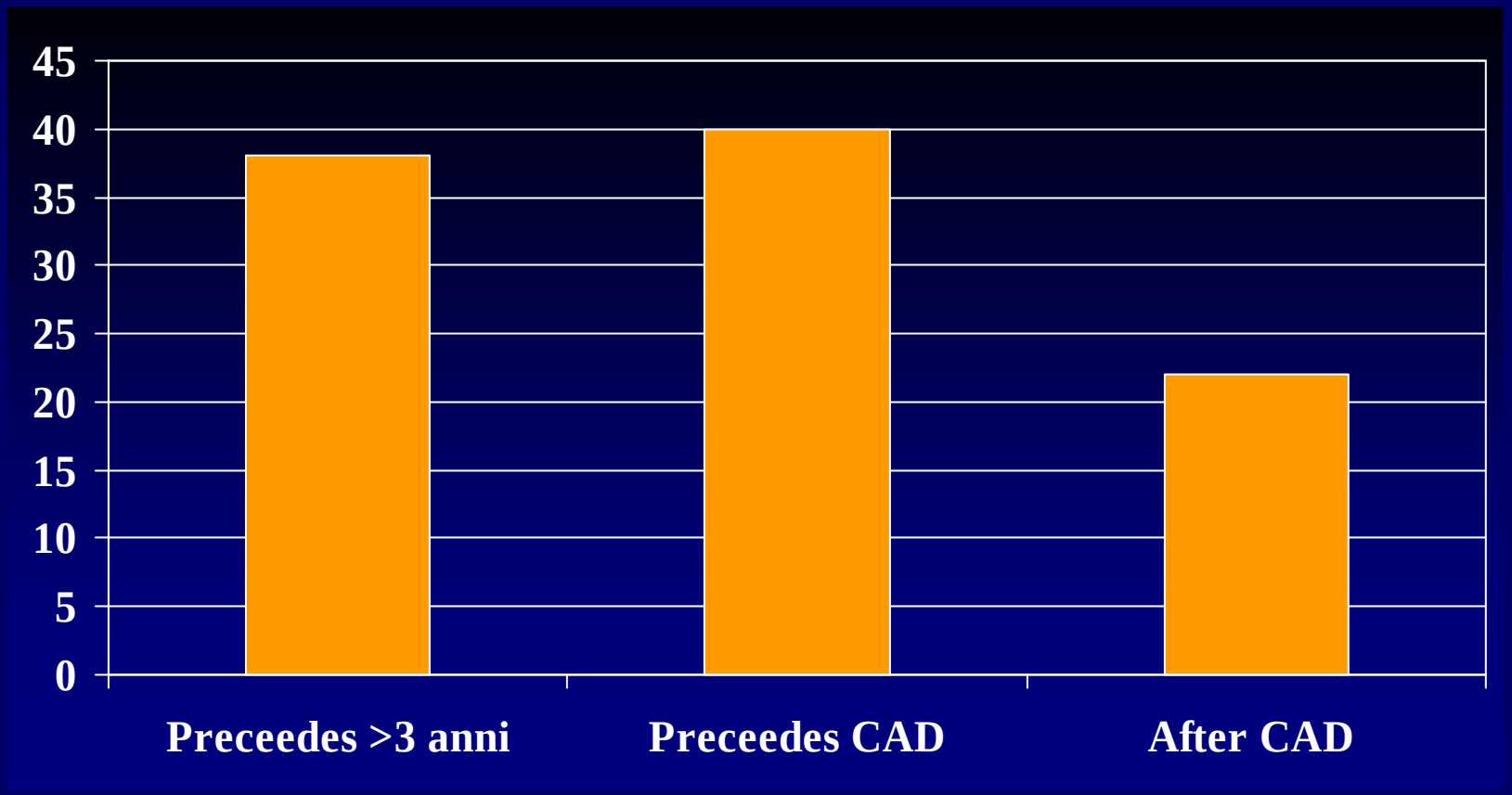
Pritzker MR. *Circulation*. 1999; 100 (suppl 1): I-711. Abstract 3751

Prevalence of ED in Patients Undergoing Coronary Angiography



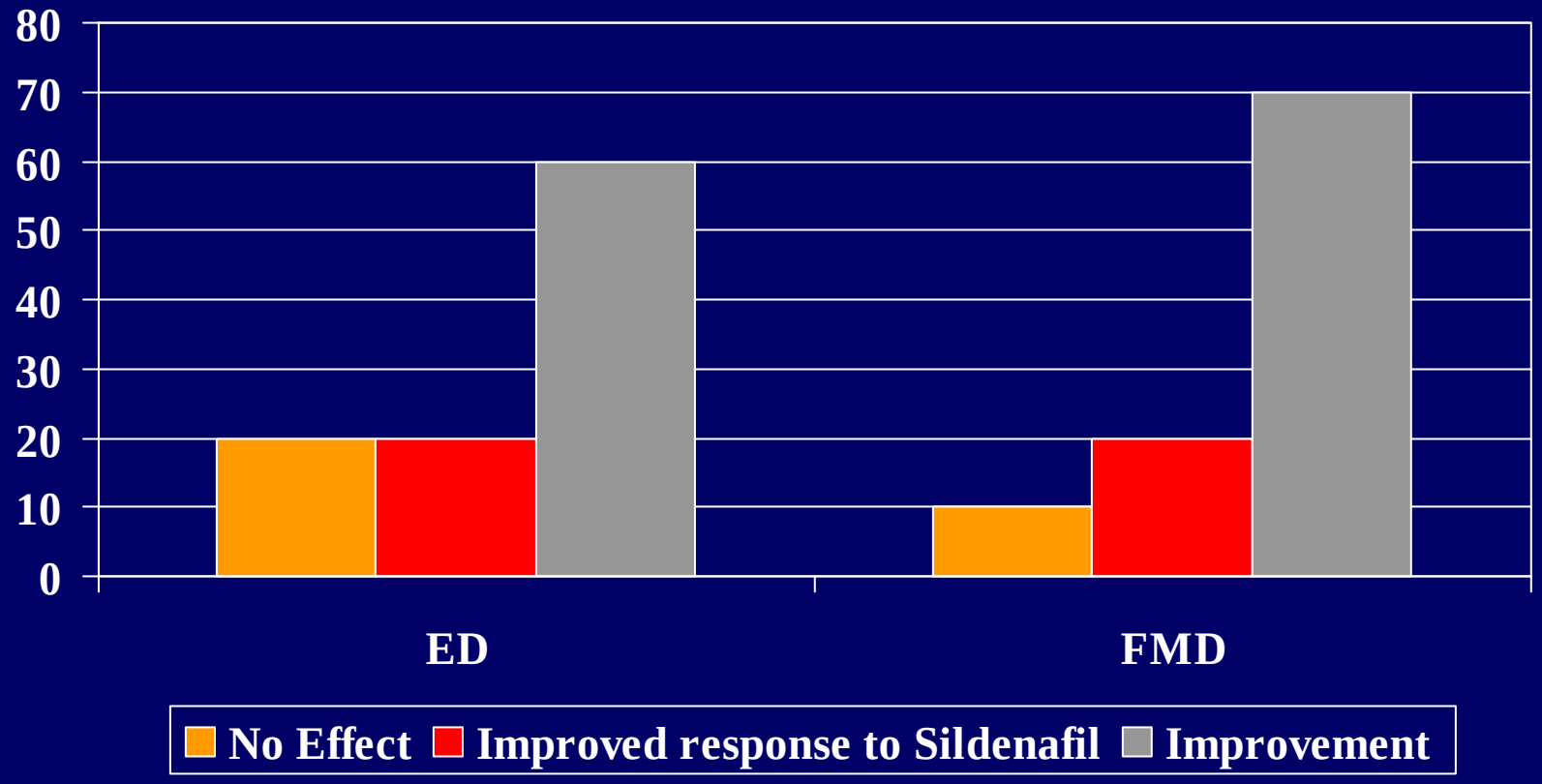
Montorsi F. et al. *Eur Urol 2003*

Incidence of ED in Patients with CAD



Cerquetani E. et al. 2003

Cardiac Rehabilitation and ED



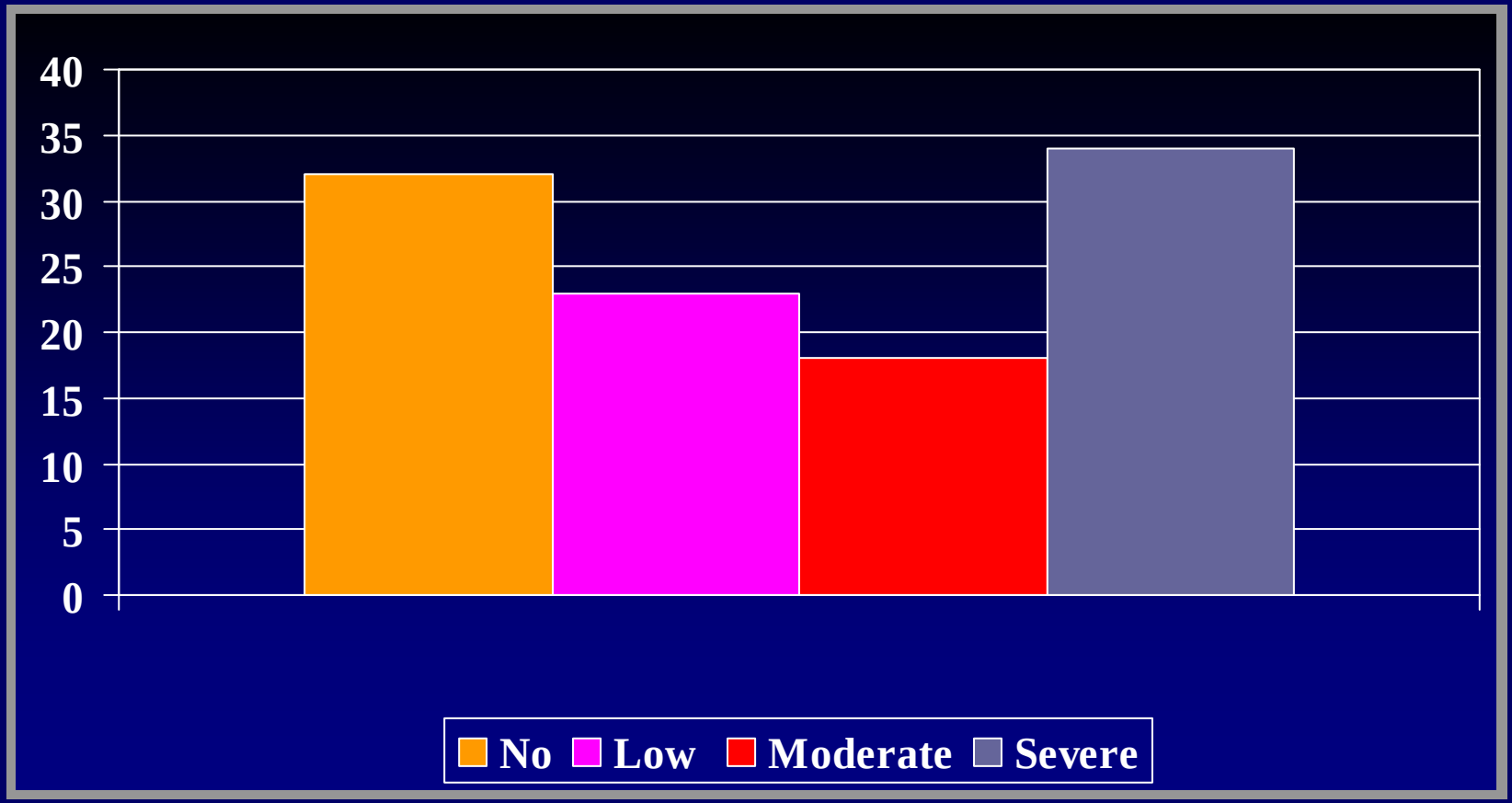
Cerquetani E. et al. 2003

Cardiobluenet Project

- 168 patients
- Mean age 58 years
- 67% arterial hypertension
- 46% previous MI
- 39% heart failure
- 86% CAD

Incidence of ED in Patients Admitted in Cardiac Rehabilitation

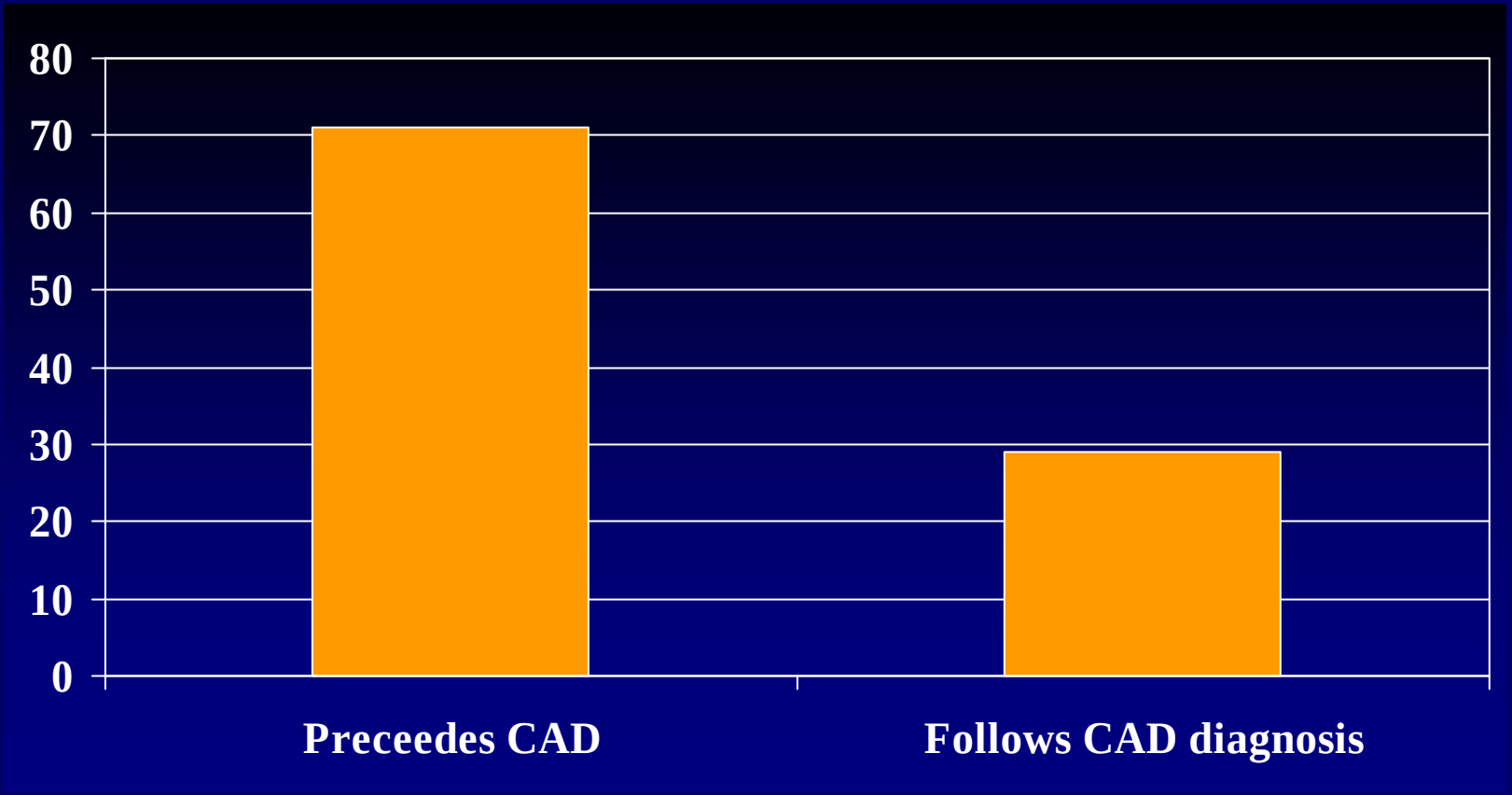
1589 pts



Rosano G, Volterrani M for Cardiobluenet Project

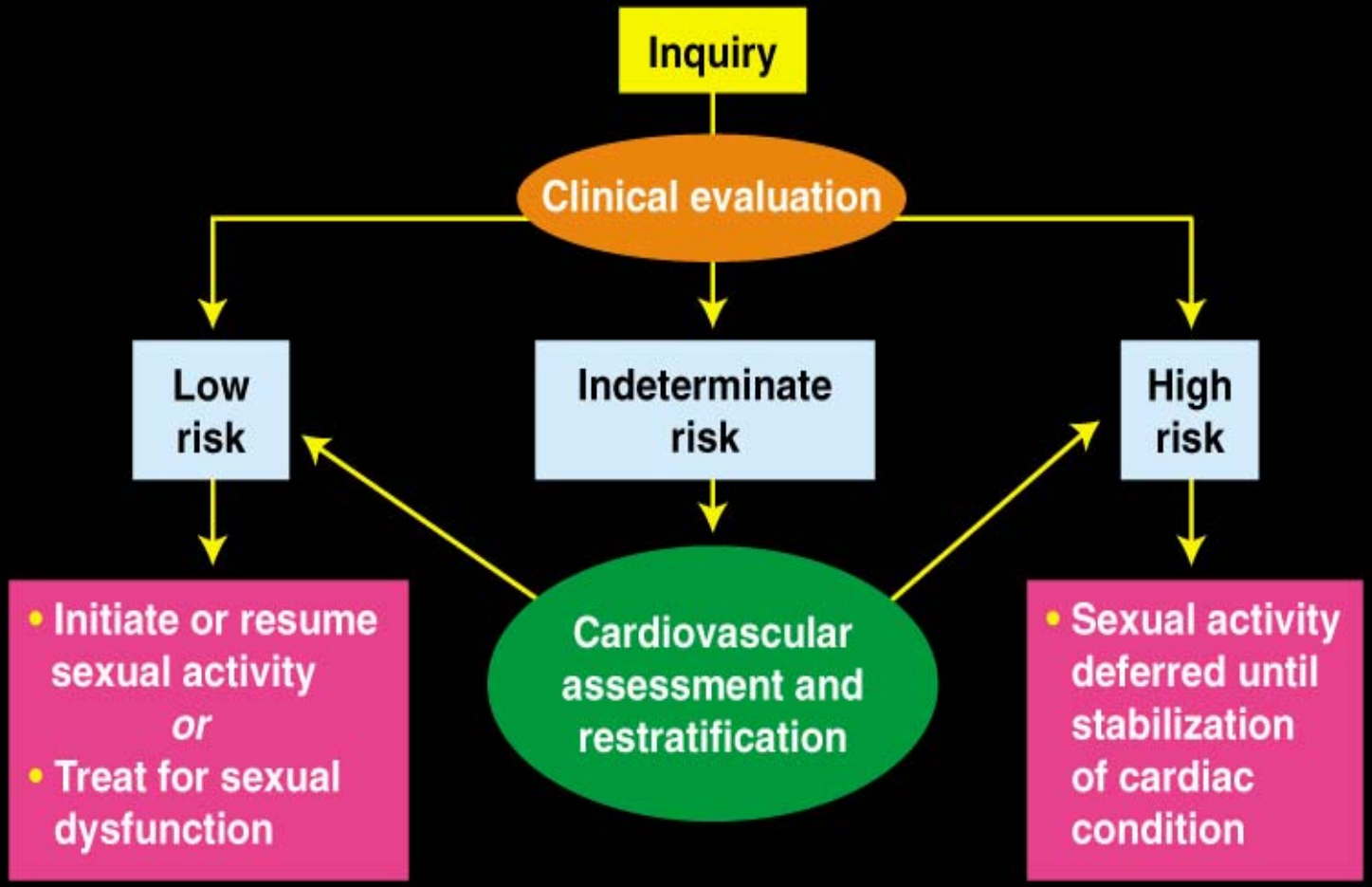
Incidence of ED in Patients Admitted in Cardiac Rehabilitation

1589 pts



Rosano G, Volterrani M. for Cardiobluenet Project

Suggested algorithm for management of erectile dysfunction in patients at risk for CV events

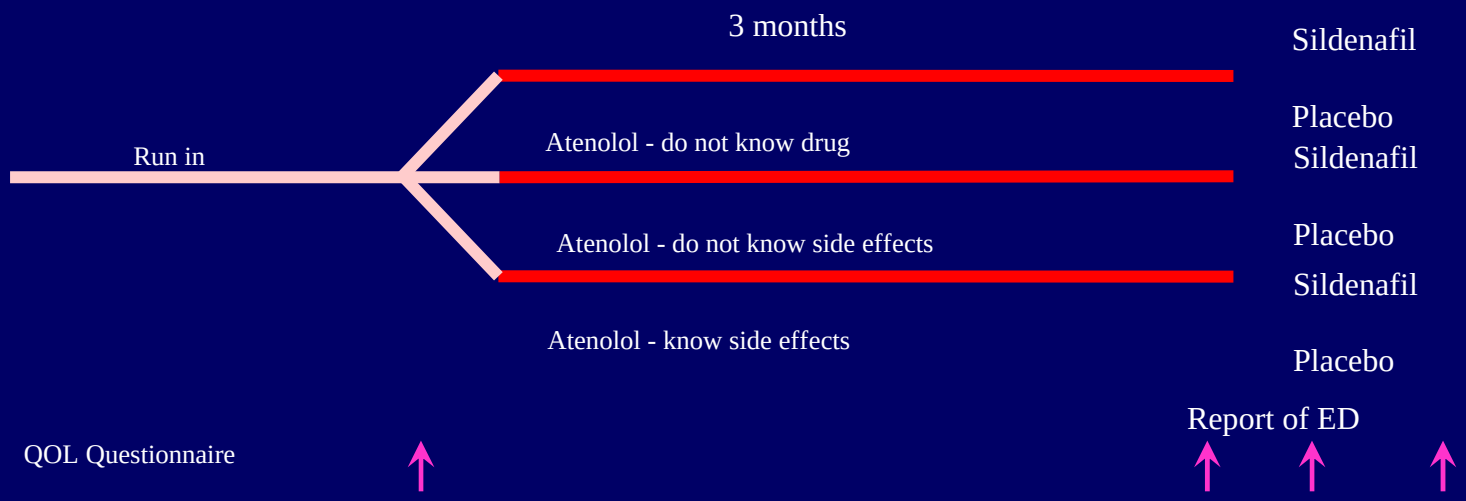


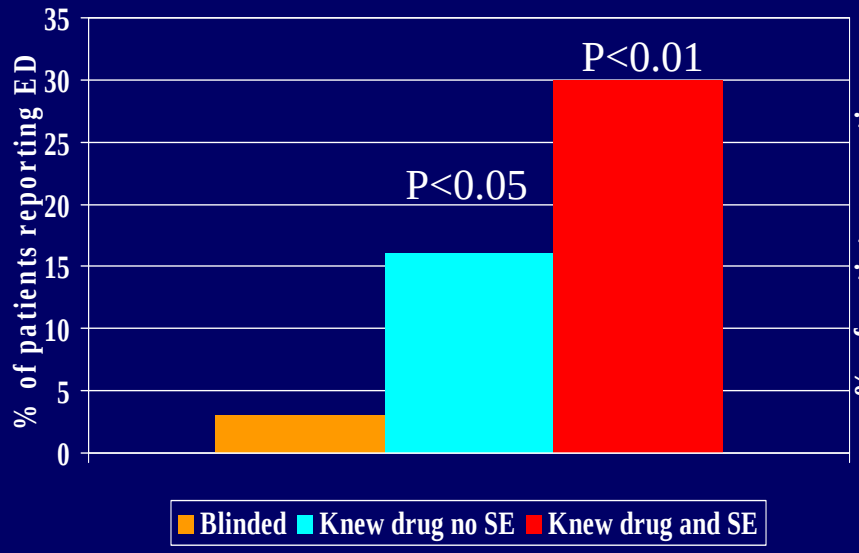
DeBusk RF, et al. *Am J Cardiol.* 2000;86:175-181.

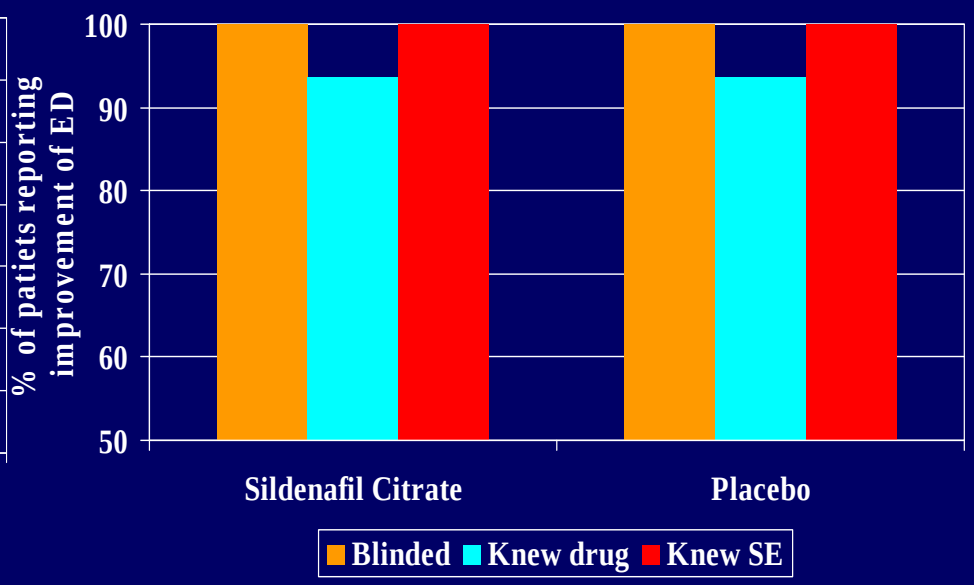
Cardiovascular Disease and ED

• Diuretics	Frequent
• Beta-blockers	Frequent
• Ca- antagonists	
Verapamil	Frequent
Diltiazem	Frequent
Amlodipine	Frequent
• ACE-Inhibitors	Frequent
• ATII blockers	Rare
• Alfa-blockers	Improvement of erection

Beta-blockers and ED

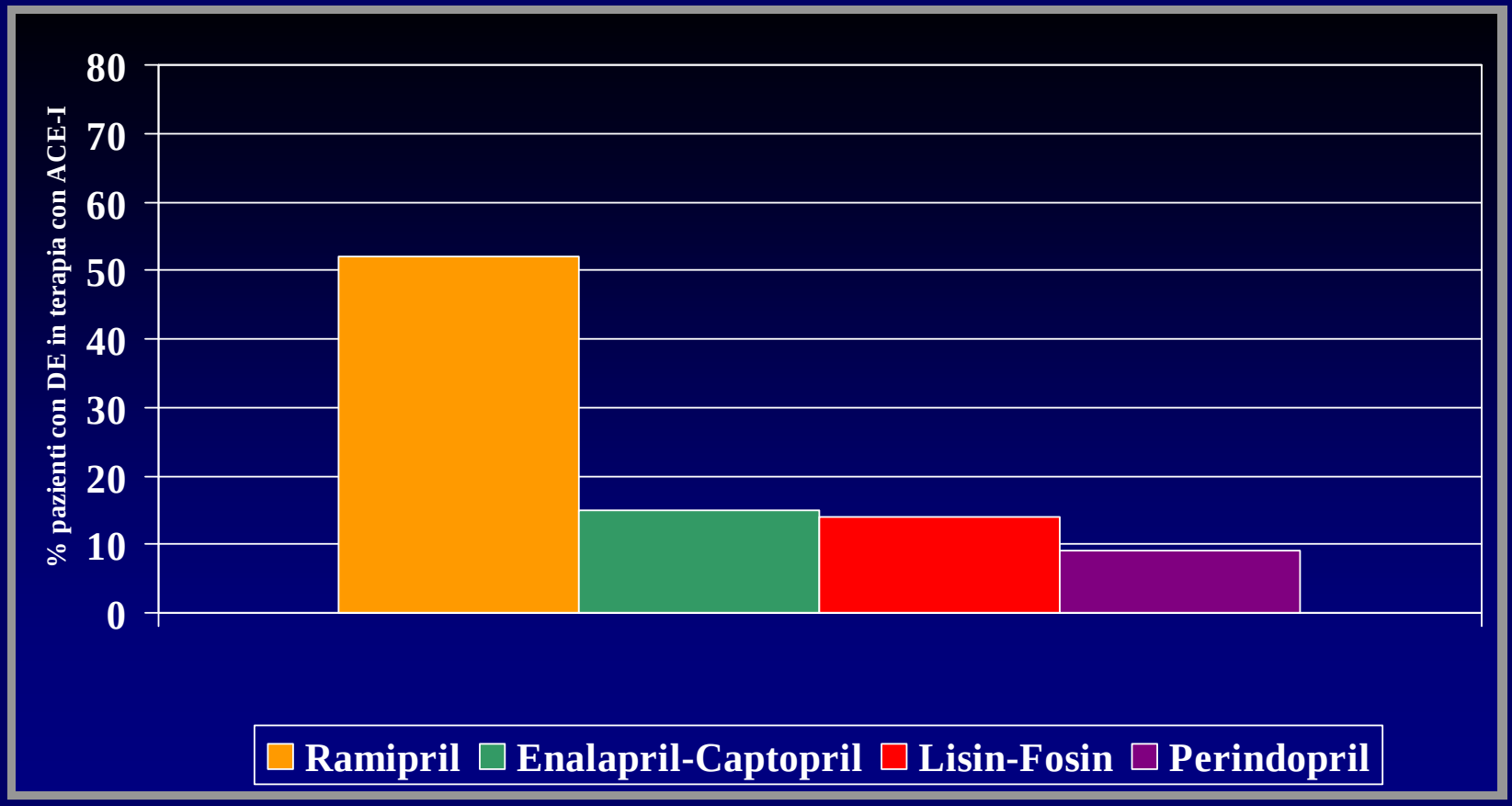






Silvestri et al. Eur Heart J 2003

ED and ACE-Inhibitors



Rosano G, Volterrani M for Cardiobluenet Project

ED – An Early Marker of Atherosclerosis

- ED is a marker of impaired endothelial function and therefore of subclinical atherosclerosis
- Asymptomatic patients with vasculogenic ED have a high incidence of CAD that is often undiagnosed
- The evaluation of cardiovascular risk in patients with ED may help to identify those patients with an increased risk of cardiovascular events
- The onset of ED in patients taking anti-hypertensives may be related to an haemodynamic effect but may also related to a direct drug effect
- An aggressive treatment of cardiovascular risk factors coupled with regular physical activity improves endothelial function and ED

6th AME National Meeting – 3rd Joint Meeting with AACE

Erectile Dysfunctions (ED) in Internal Medicine

Diabetes and ED: how to manage?

Antonio Aversa MD, PhD

Cattedra di Medicina Interna

DFM ROMA

Università di Roma "La Sapienza"

VERONA, 28 ottobre 2006

ED and diabetes: Epidemiology

- Men affected by DM are at higher risk (3-fold) of ED compared with normal controls
- ED prevalence in diabetic population is between 35% and 75% (mean 50%), which is significantly higher than the general population (15%)
- ED onset in diabetic population is about 10-15 ys before than general population, and it is related to the duration of diabetes

Comparison of main results from epidemiological studies on prevalence of ED in type-I and type-II diabetic subjects

Type of DM	**Authors (year)**	**Subjects No**	**Age**	**%ED**
Type I	McCulloch et al. (1980), Diabetologia	318	20-59	36
	Fedele et al. (2000), Int J Epidemiol	1253	20-59	22
	Brunner et al. (1995), Wien Med W	59	18-67	49
	Klein et al. (1996), Diabetes Care	359	21-76	20
	Klein (1996), Diabetes Care	200	≥43	47
	Fedele et al. (2000), Int J Epidemiol	585	≥43	46
	Fedele et al. (2000), Int J Epidemiol	1383	20-70	51
Type II	McCulloch et al. (1980), Diabetologia	221	20-59	35
	Fedele et al. (2000), Int J Epidemiol	4402	20-59	31
	Nathan et al. (1986), Am J Med	125	55-74	71
	Fedele et al. (2000), Int J Epidemiol	5814	55-70	43
	Fedele et al. (2000), Int J Epidemiol	8373	20-70	37

Prevalence of Risk Factors According to Age in 18,000 Italian Men with ED Referring to a Free-call Service

Table 3 - *Prevalence of various risk factors for erectile dysfunction according to age group (%).*

	<20	20-29	30-39	40-49	50-59	60-69	70-79	>80
Hypertension	1.19	0.69	4.79	16.90	29.94	41.11	40.89	34.90
Diabetes Mellitus	0.00	0.60	1.50	7.69	14.83	17.84	19.46	10.48
Dyslipidemia	0.00	0.10	2.04	5.13	7.15	6.85	6.83	4.03
Depression	0.00	2.58	4.39	5.16	4.36	3.28	2.90	2.42
Endocrine disorders	0.00	0.50	0.90	1.26	1.26	1.03	0.83	0.81
Liver diseases	0.00	0.20	0.80	1.05	1.79	1.61	0.52	0.81
Renal disease	0.00	2.38	0.20	0.43	0.67	0.68	1.24	0.81
Anxiety – Stress	2.38	4.37	8.42	7.19	5.81	4.28	2.90	1.61
Traumatic injuries of the CNS	0.00	0.00	0.35	0.29	0.08	0.18	0.00	0.00
Prostate Surgery	0.00	0.00	0.05	0.29	1.84	6.28	11.70	12.10
Prostatitis	0.00	1.39	3.09	3.11	2.63	2.78	2.38	2.42
BPH	0.00	0.00	0.45	1.48	5.73	12.92	16.15	22.58
Tumors	0.00	0.10	0.20	0.18	0.50	1.25	1.66	0.00
Neurological diseases	0.00	0.40	1.30	0.90	2.09	2.25	1.66	0.81
Heart diseases	0.00	0.40	0.55	2.06	6.51	12.85	20.08	29.03
Smokers	34.52	30.95	27.87	27.19	25.59	15.49	9.73	4.84
Alcohol abuse	2.38	3.67	3.54	3.39	3.91	2.93	3.00	0.81
Drug's addiction	2.38	1.98	0.75	0.11	0.00	0.00	0.10	0.00
Ex-smokers	0.00	1.88	3.39	6.03	10.95	13.13	13.56	11.29

CNS: central nervous system; BPH: benign prostatic hipertrophy.

Aversa A et al. JEI 27: 548-556 (2004)

Incidence of erectile dysfunction stratified by type, duration and control of diabetes, and body mass index

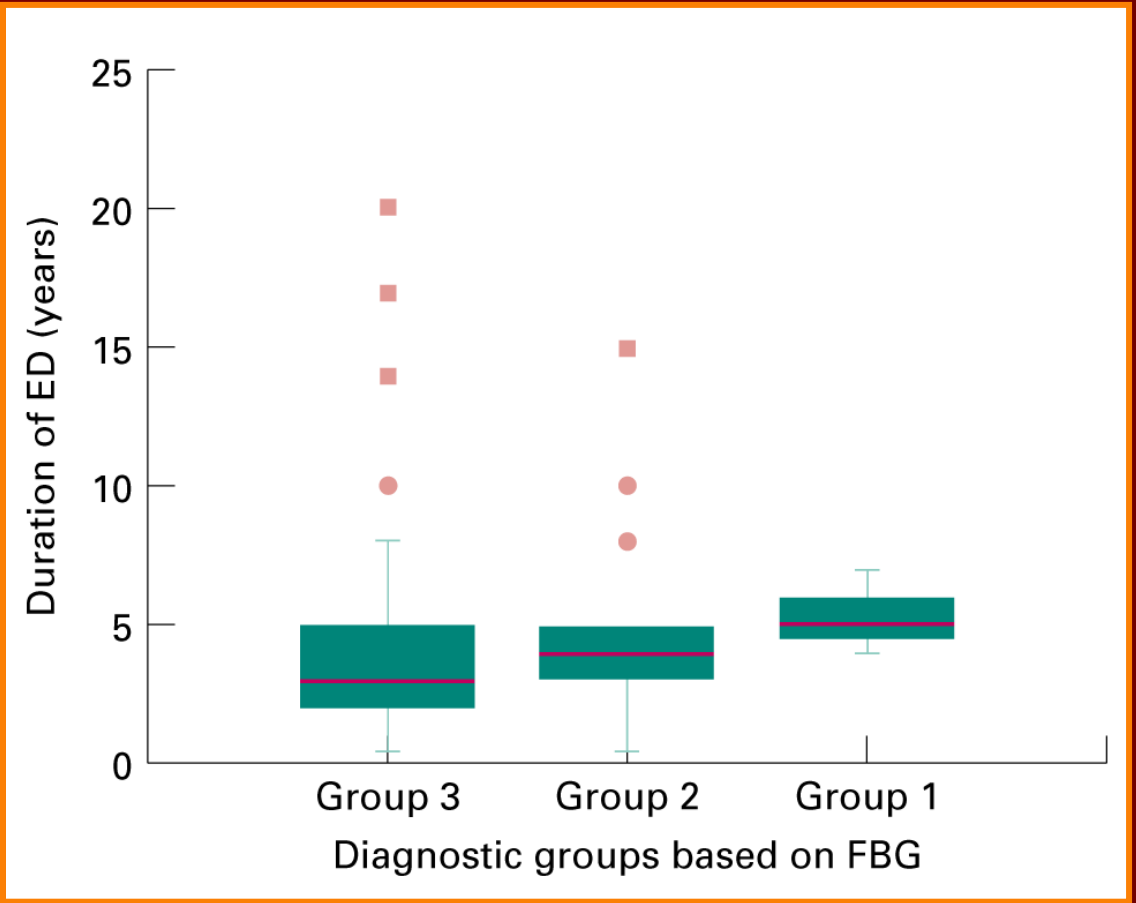
	Incidence/1,000 Pts. (95% CI)
Diabetes type:	
1	45 (28–62)
2	74 (63–84)
Diabetes duration (yrs.):	
1–5	47 (19–75)
6–10	55 (40–70)
11 or Greater	77 (65–91)
Metabolic control (% hemoglobin A1c):	
Good (less than 7.5)	52 (40–64)
Fair (7.5 to less than 9)	77 (61–93)
Poor (greater than 9)	90 (61–119)
Body mass index:*	
Normal (18.5–24.9)	51 (36–64)
Pre-obese (25.0–29.9)	70 (56–84)
Obese (greater than 30)	92 (68–116)

* No participant was underweight.

D. Fedele et al., J Urol 2001

Prevalence of undiagnosed diabetes mellitus in male erectile dysfunction (ED)

Prevalence of undiagnosed DM (FBG>7.0 mmol/L) and IFG (FBG>6.1 <7.0 mmol/L) in an unselected population (n=129) of men from Southern England presenting with ED was **4.7+3.7=9.4%**

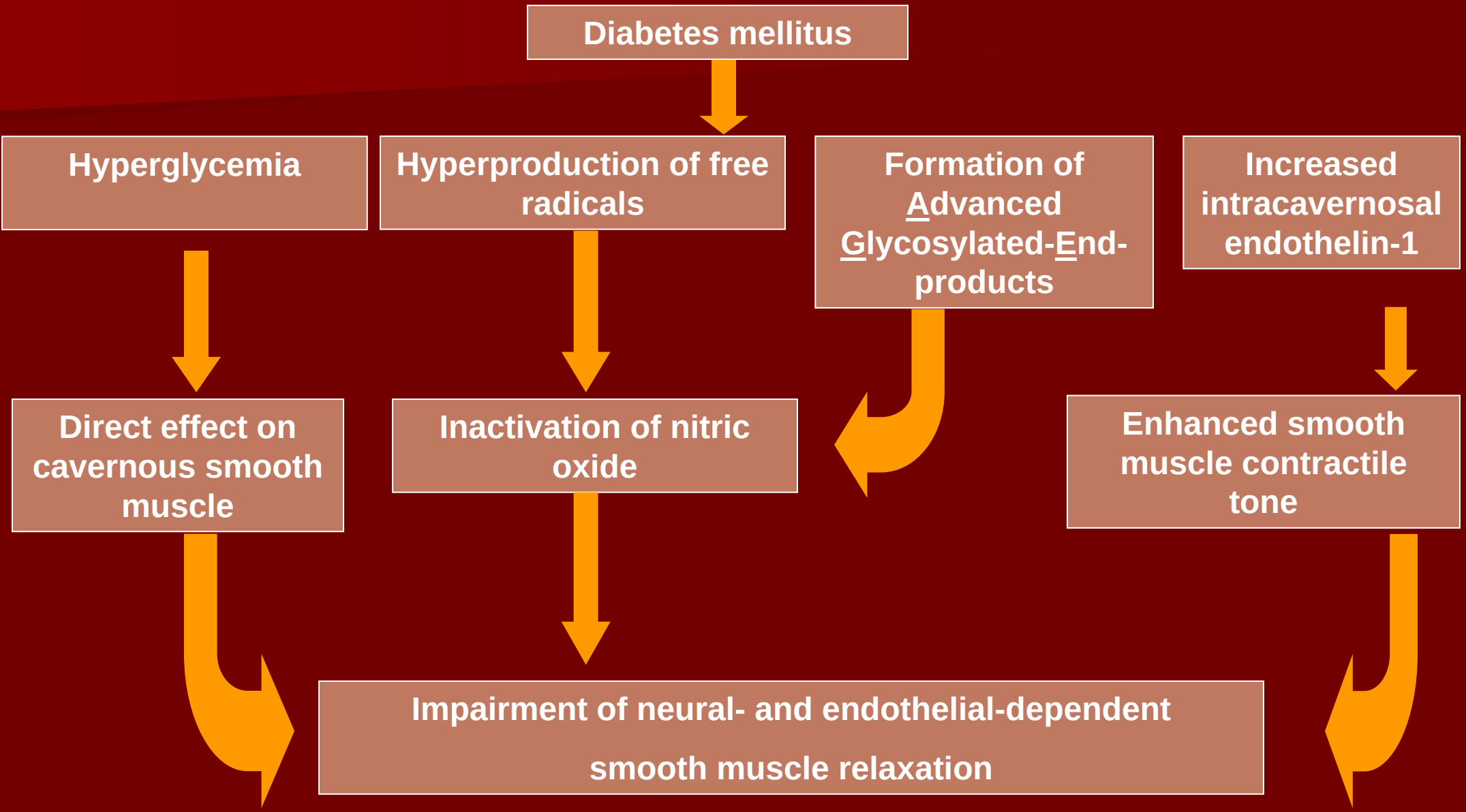


Group 1 = patients with newly diagnosed DM
Group 2 = patients with IFG
Group 3 = patients with normal FBG

FBG = Fasting Blood Glucose
IFG = Impaired Fast Glucose

K. Sairam et al., BJU International 2001

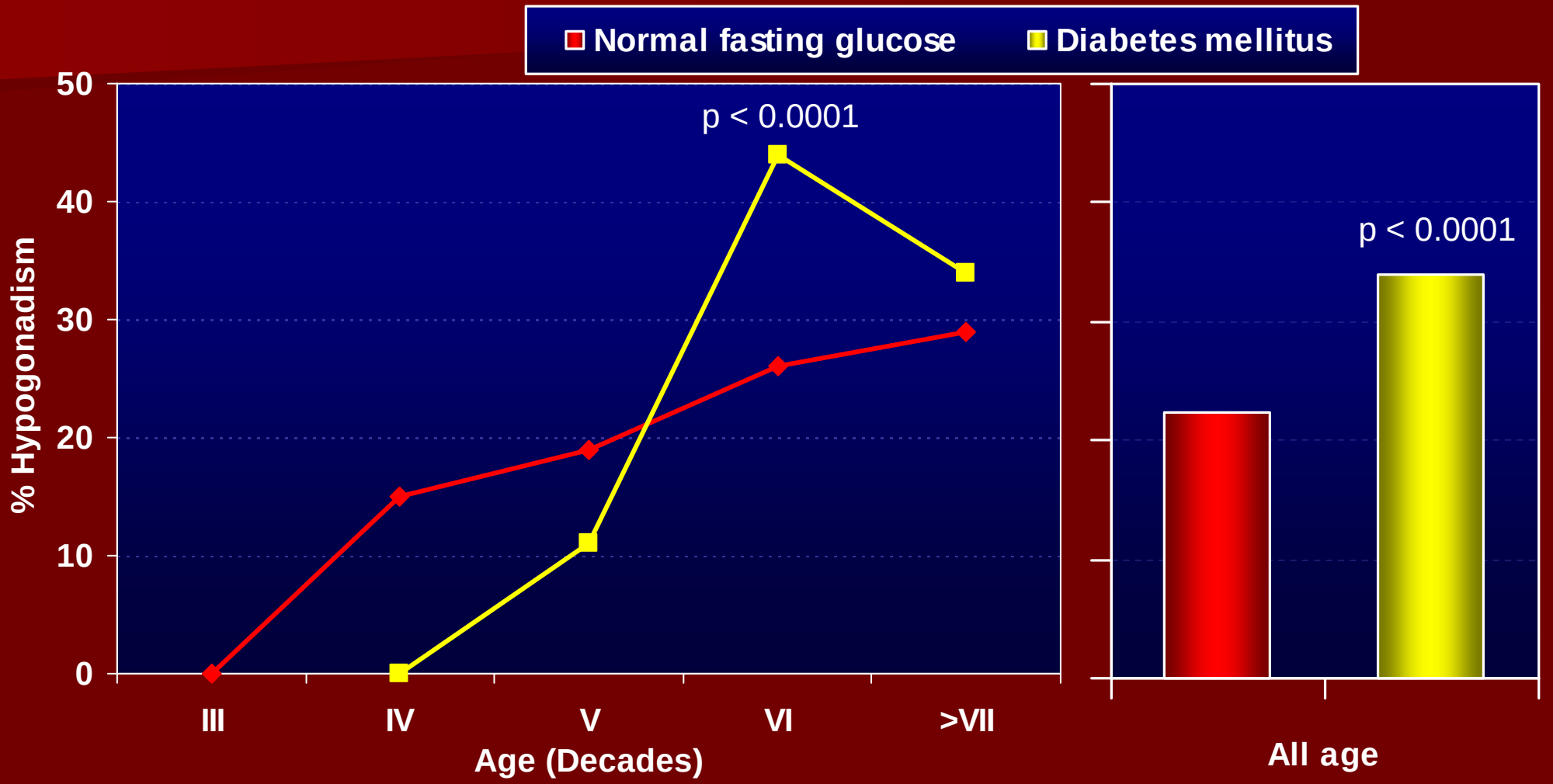
Possible pathophysiologic mechanisms of smooth muscle and endothelial dysfunction in diabetic ED



ED and diabetes: Pathophysiology

- Vascular Alterations
  - Microangiopathy
  - Macroangiopathy
- Neurological Alterations
  - Sensitive and motor
  - Autonomic
- Hormonal Alterations
- Psychological Alterations

Prevalence of Hypogonadism (T < 12 nmol/L) in 1,027 Diabetic and Nondiabetic Patients Presenting with ED



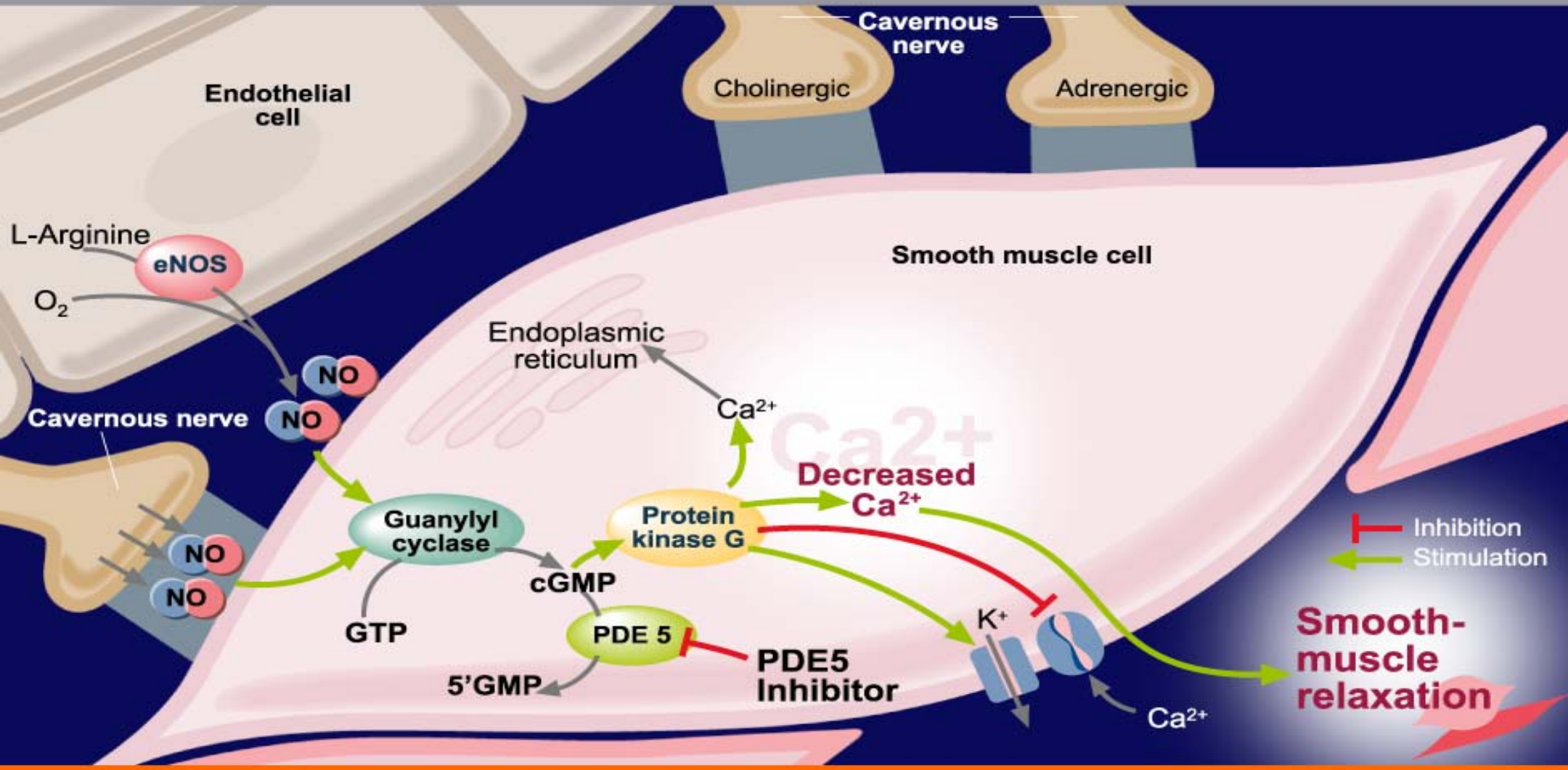
Corona G et al. Eur Urol 46(2): 222-228 (2004)

ED and diabetes: how to manage

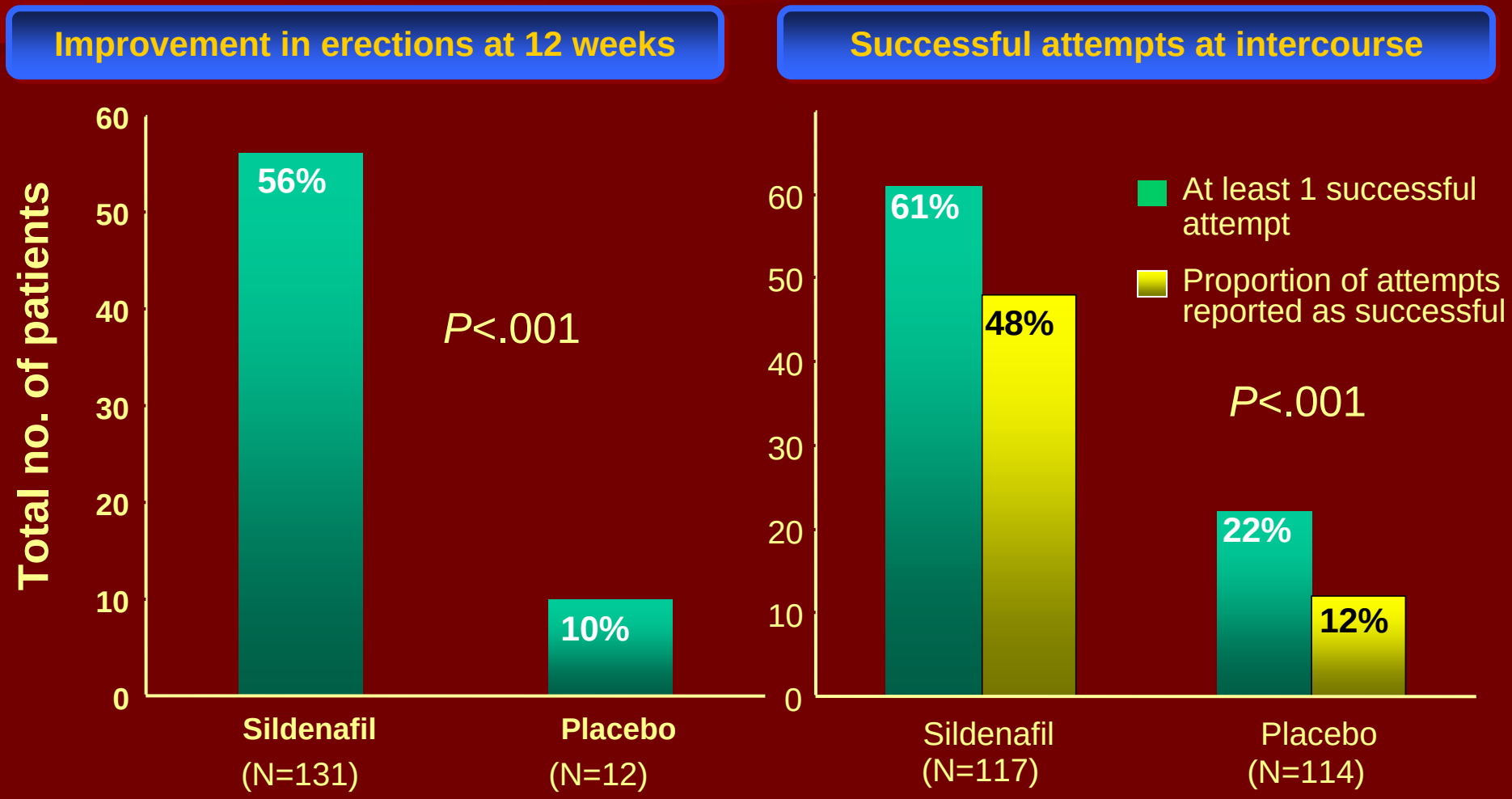
- Oral agents
  - PDE5 inhibitors
  - Testosterone (if deficiency occurs)
- Intracavernous injection (ICI) of vasoactive drugs
- Vacuum Devices
- Surgery or penile implants
- Psychosexual counselling

PDE Type 5 Inhibition Therapy: Mechanism of Action

Adapted from Lue T. *N Engl J Med* 2000; 342: 1802-1813.

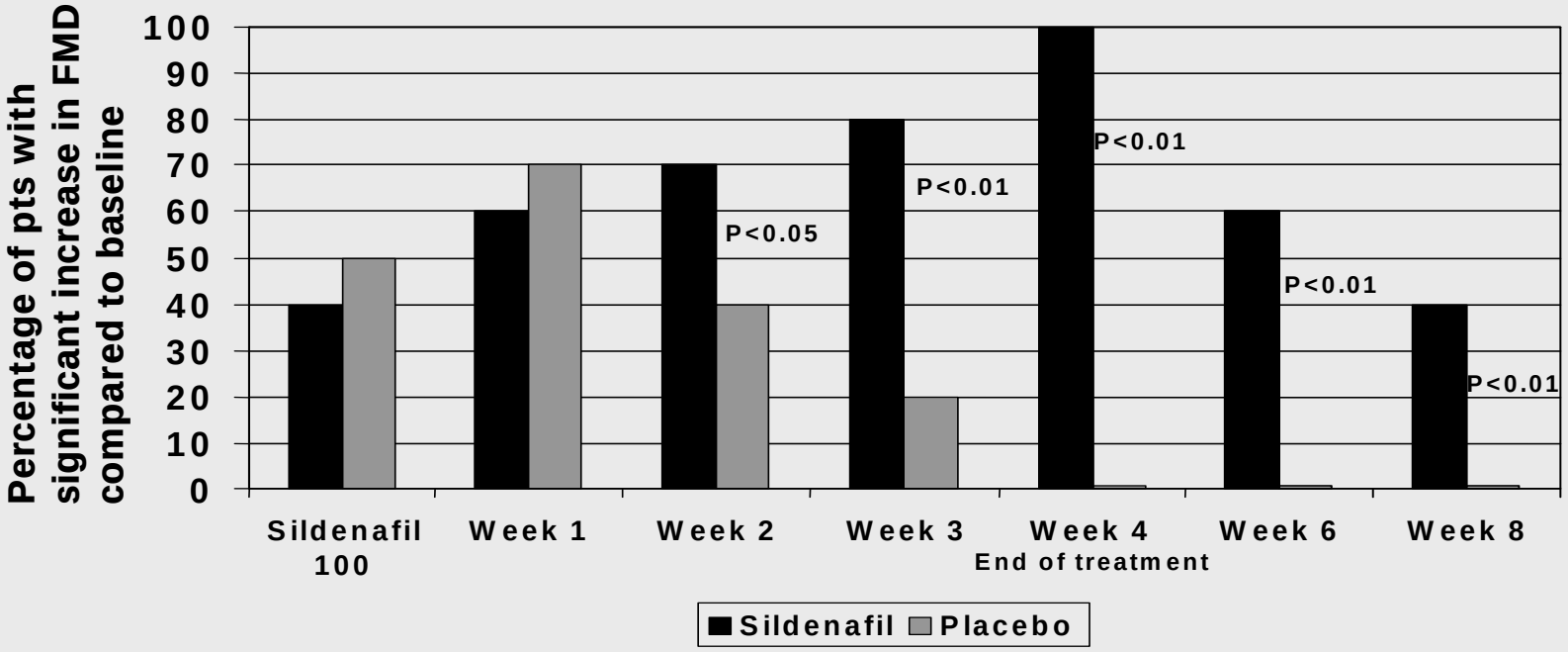


Sildenafil and diabetes: efficacy



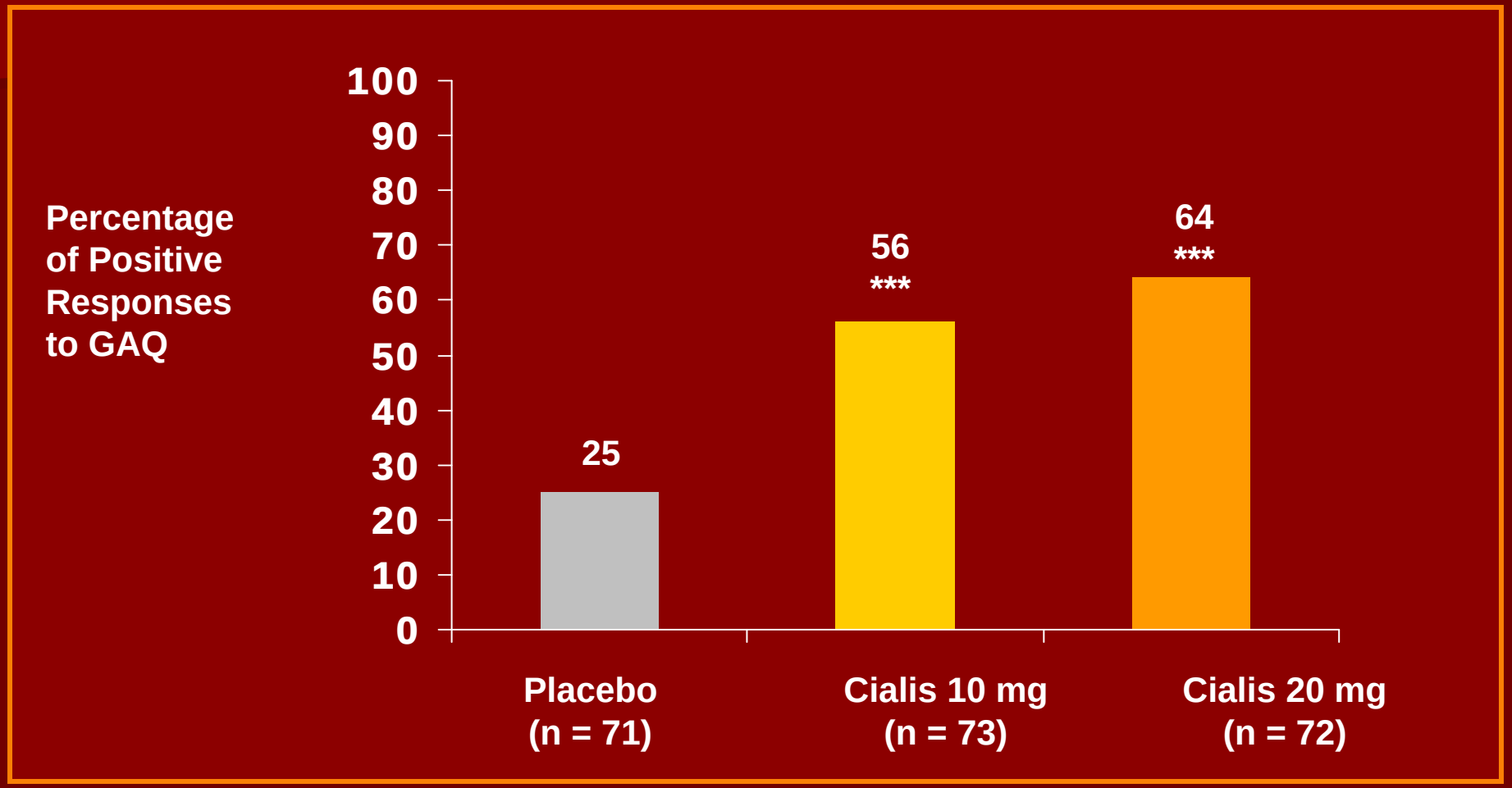
Rendell MS, et al. *JAMA.* 1999;281:421-426.

Daily Sildenafil and FMD in DM2



Vitale, Aversa et al. *unpublished data*

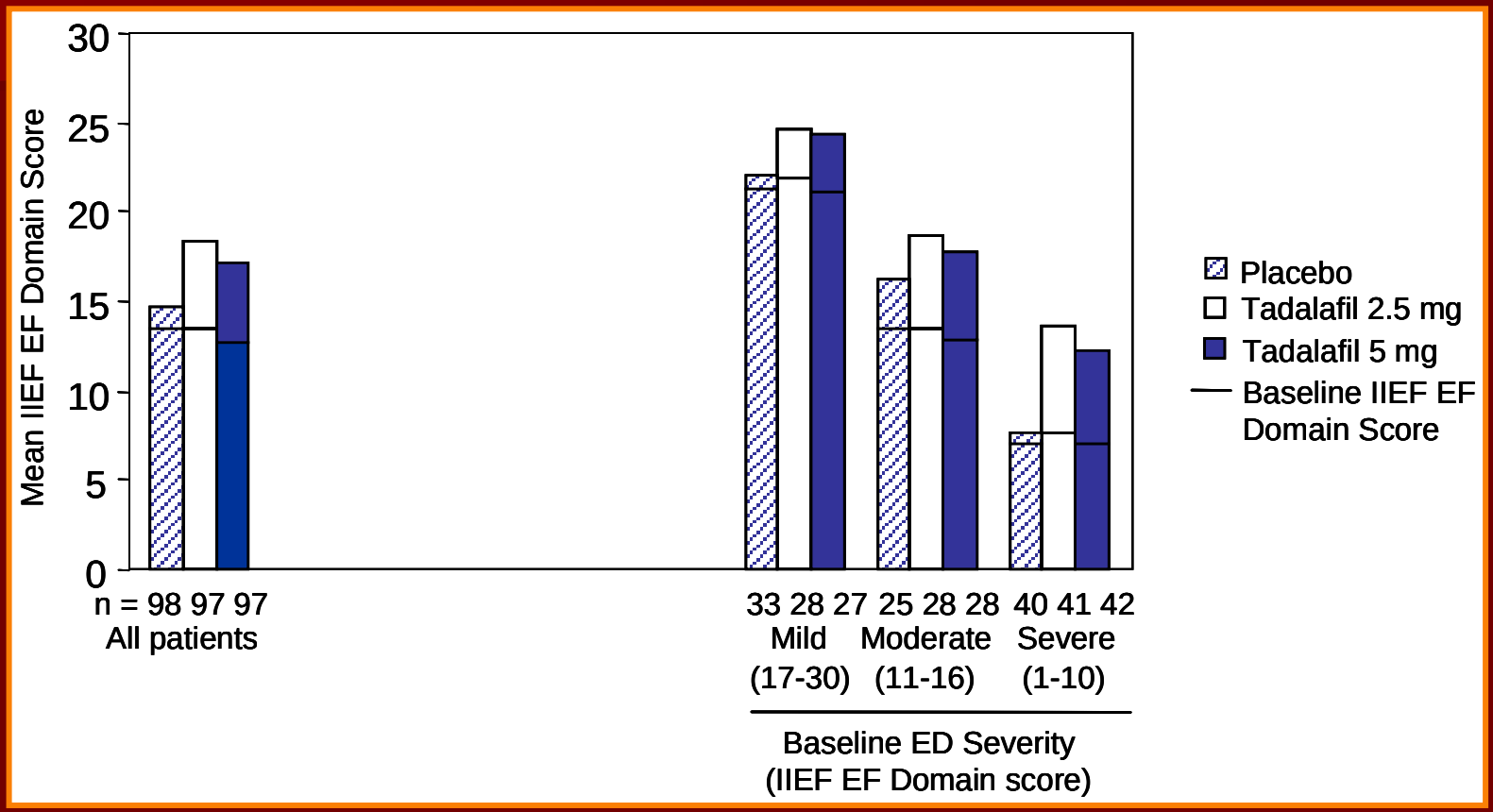
Taladafil and diabetes
Treatment Effect on Erections: GAQ†



†Has the treatment you have been taking improved your erections?
***P <0.001 versus placebo

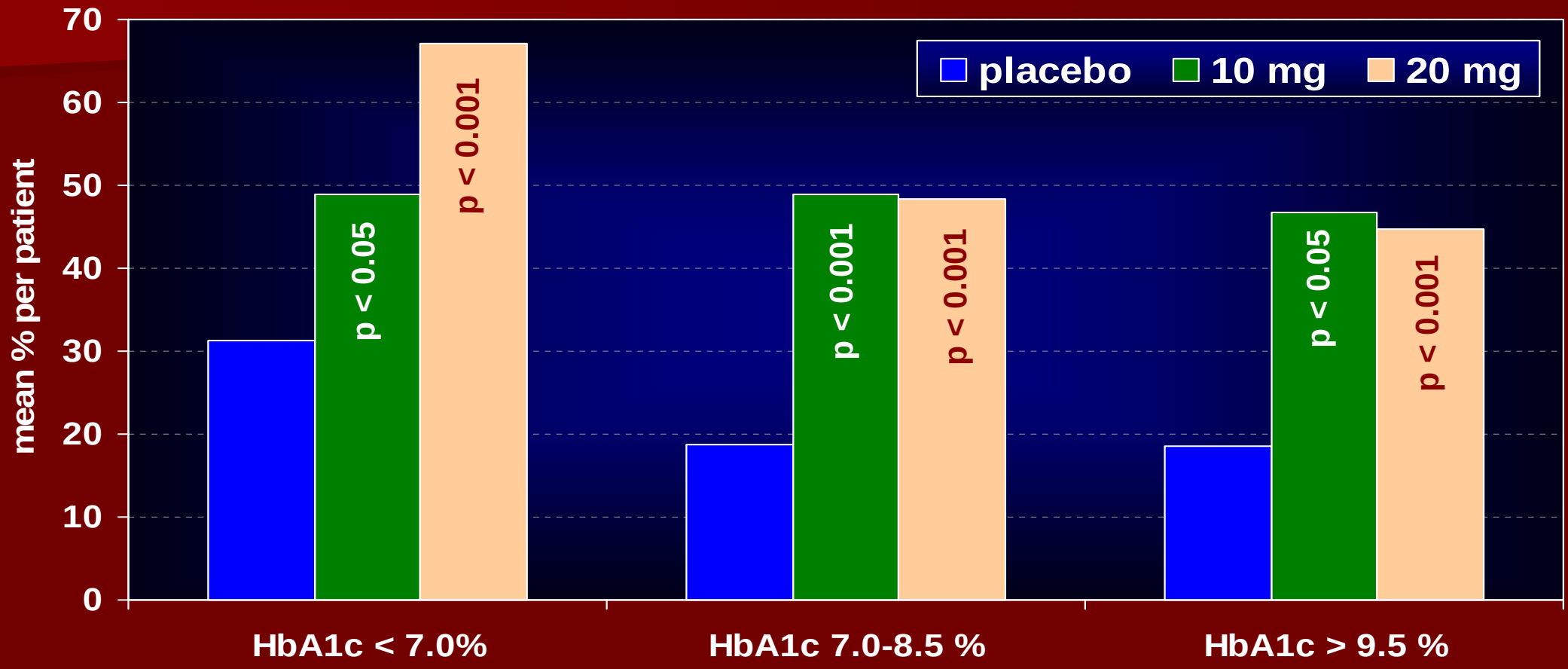
Saenz de Tejada et al. *Diabetes Care, 2002*

Daily Taladafil and DM2: Results from a multicenter study (N=298)



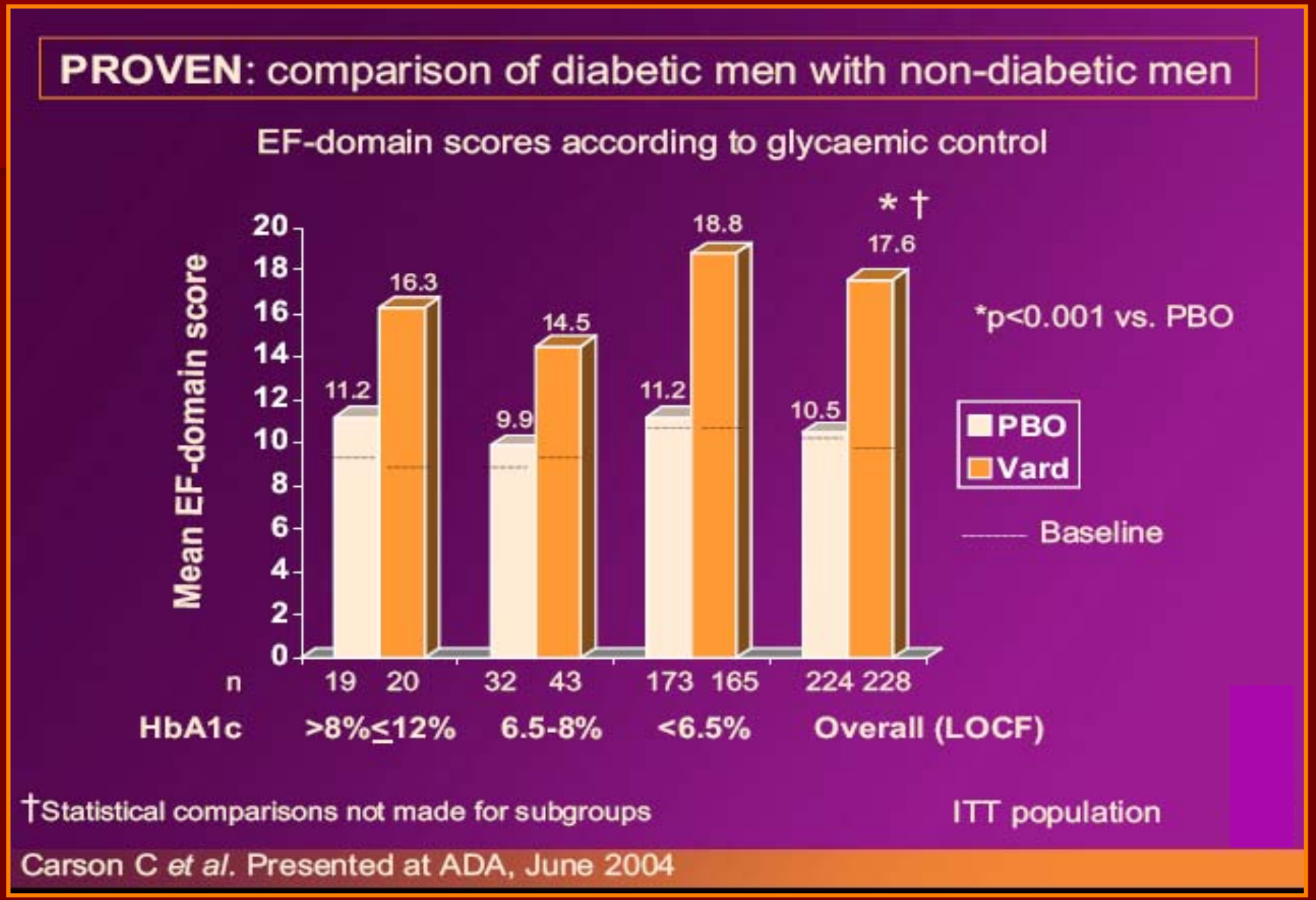
Hatzichristou, Spera et al. *submitted*

Tadalafil Treatment Efficacy in 519 Diabetic Patients as a Function of Glycaemic Control



Fonseca V et al. Diabetologia 47: 1914-1923 (2005)

Vardenafil and DM2: PROVEN Study



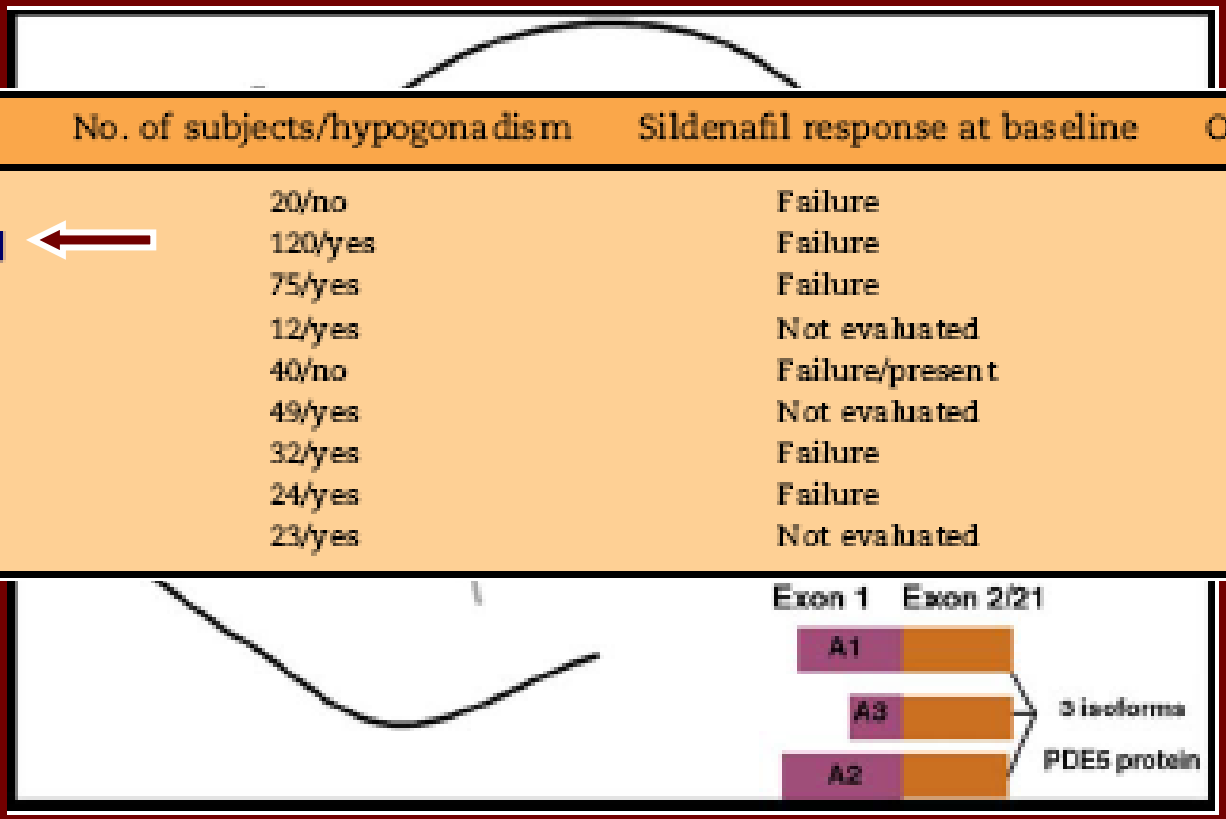
Review – Andrology

Combining Testosterone and PDE5 Inhibitors in Erectile Dysfunction: Basic Rationale and Clinical Evidences

Emanuela A. Greco, Giovanni Spera, Antonio Aversa *

Department of Medical Pathophysiology, University of Rome "La Sapienza", 00161 Rome, Italy

Authors	No. of subjects/hypogonadism	Sildenafil response at baseline	Overall efficacy/adverse events
Aversa et al. [9]	20/no	Failure	80%/none
Kalinchenko et al. [25]	120/yes	Failure	70%/none
Shabsigh et al. [10]	75/yes	Failure	70%/not evaluated
Chatterjee et al. [36]	12/yes	Not evaluated	100%/none
Shamloul et al. [26]	40/no	Failure/present	Improved/none
Greenstein et al. [37]	49/yes	Not evaluated	63%/18% skin irritation
Hwang et al. [27]	32/yes	Failure	57%/none
Rosenthal et al. [28]	24/yes	Failure	92%/1% headache
Tas et al. [38]	23/yes	Not evaluated	34%/none



Eur Urol, 2006

Intracavernous Injections and diabetes: efficacy

- ✓ PGE1 monotherapy 80%
- ✓ Papaverine monotherapy 61%
- ✓ Trimix (Pap/Fen/PGE1) 70-85%
- ✓ VIP/phentolamine 65-85%

- Re-oxigenation of cavernosal SMCs after 3-6 mo

ICI and CVD disease: safety

Study on efficacy of ICI in 106 pts with cardiovascular disease (CVD) and failure or controindications for Sildenafil

- ✓ Different drug combinations used (papaverine, phentolamine, alprostadil, atropine) in a 1 year follow-up study
- Immediately effective in 94% and after 1y in 96%
- AEs: prolonged erection (2%), subcutaneous hemorrhage (3%), fibrotic nodules (3%)

Israilov S et al, IJIR, 2002

TAKE-HOME MESSAGES

1. PDE5i monotherapy on-demand may be ineffective in as high as 40% of cases
2. Daily dosing PDE5i for diabetic ED has good cardiovascular safety and may improve overall efficacy (Kloner et al, AJC, 2006)
3. Combination of PDE5i plus testosterone (if testosterone deficiency occurs) is safe end effective and may salvage up to 30% non-responders to PDE5i (Aversa et al, The Endocrinologist, 2005)
4. ICI is safe and effective whenever PDE5i are ineffective or contraindicated

Update in Clinical Endocrinology
Verona, October 27-29,2006

Obesity, Lifestyle and Diet: is there a link with ED?

Miryam Ciotola

Divisione di Malattie del Metabolismo

A Prospective Study of Risk Factors for Erectile Dysfunction

Constance G. Bacon, Murray A. Mittleman, Ichiro Kawachi, Edward Giovannucci, Dale B. Glasser* and Eric B. Rimm†

43.235 men with an age range of 53 to 90 years

TABLE 2. *Risk of developing ED (poor or very poor) among men in HPFS who were healthy and had good or very good erectile function before the study*

	All Subjects RR (95% CI)	Prostate Ca Developed RR (95% CI)	No Known Prostate Ca* RR (95% CI)
No. ED/Total No.	3,905/22,086	726/1,225	3,179/20,861
Smoking status:			
Never smoked	1.0 —	1.0 —	1.0 —
Past smoker	1.1† (1.1–1.2)	1.1 (0.9–1.2)	1.2† (1.1–1.3)
Current smoker	1.4† (1.3–1.6)	1.4† (1.0–1.9)	1.5† (1.3–1.7)
Alcohol consumption (gm/day):			
0	1.0 —	1.0 —	1.0 —
0.1–4.9	1.0 (0.9–1.1)	1.0 (0.7–1.2)	1.0 (0.9–1.1)
5.0–14.9	1.0 (0.9–1.1)	1.1 (1.0–1.4)	0.9 (0.8–1.1)
15–29.9	1.0 (0.9–1.1)	1.0 (0.8–1.3)	1.0 (0.9–1.1)
30.0 or Greater	1.1 (1.0–1.2)	1.0 (0.7–1.3)	1.1 (1.0–1.2)
Physical activity			

Obesity (kg/m^2):

Less than 23	1.0 —
23.0–24.9	1.1† (1.0–1.2)
25.0–26.9	1.2† (1.1–1.3)
27.0–29.9	1.3† (1.1–1.4)
30.0 or Greater	1.7† (1.5–2.0)

* Defined as before 1986 or at any time before 2000 questionnaire.
† Statistically significant difference at $p < 0.05$.

TABLE 3. *Risk of developing ED among healthy participants who had good/very good erectile function before the study (and no prostate cancer through 2000) for specific types*

1986 Physical Activity Tertile (hrs/wk)	Age Adjusted RR (95% CI)
Walking:	
0	1.0 —
0.04–0.9	0.9 (0.8–1.0)
1.0–2.4	0.9* (0.8–1.0)
2.5 or greater	0.8* (0.7–0.9)

1 or greater	0.9* (0.8–1.0)	0.9 (0.8–1.0)	1.0 (0.8–1.1)
Swimming:			
0	1.0 —	1.0 —	1.0 —
0.04–0.1	0.9 (0.7–1.1)	0.9 (0.8–1.2)	1.0 (0.8–1.3)
0.2–0.9	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.9 (0.7–1.1)
1 or greater	0.8* (0.7–0.9)	0.8 (0.7–1.0)	0.8 (0.7–1.0)
Tennis:			
0	1.0 —	1.0 —	1.0 —
0.04–0.9	0.8* (0.7–1.0)	0.8 (0.7–1.0)	0.9 (0.7–1.1)
1–2.4	0.9 (0.8–1.0)	0.9 (0.8–1.1)	1.0 (0.8–1.2)
2.5 or greater	0.7* (0.6–0.8)	0.8* (0.7–0.9)	0.9 (0.7–1.0)
Squash/raquetball:			
0	1.0 —	1.0 —	1.0 —
0.04–0.9	0.9 (0.6–1.2)	0.9 (0.7–1.3)	1.0 (0.7–1.4)
1.0–2.4	0.9 (0.7–1.1)	0.9 (0.7–1.1)	1.1 (0.7–1.4)
2.5 or greater	0.7* (0.5–0.9)	0.7* (0.5–0.9)	0.8 (0.6–1.2)
Rowing/calisthenics/ exercise machine:			
0	1.0 —	1.0 —	1.0 —
0.04–0.4	0.9 (0.8–1.0)	1.0 (0.9–1.1)	0.9 (0.8–1.1)
0.5–1.4	0.8* (0.7–0.9)	0.9* (0.8–1.0)	0.9 (0.8–1.0)
1.5 or greater	0.7* (0.6–0.8)	0.8* (0.7–0.9)	0.8 (0.7–1.0)

* Independent variables include age (5-year groups), marital status (married/divorced/widowed vs. never married), smoking status (current/past vs. never), alcohol intake and BMI.
† Independent variables include total physical activity quintiles, age (5-year groups), marital status (married/divorced/widowed vs. never married), smoking status (current/past vs. never), alcohol intake and BMI.

J Urol. 2006 Jul;176(1):217-21

Heart Disease Risk Factors Predict Erectile Dysfunction 25 Years Later (The Rancho Bernardo Study)

Elizabeth Barrett-Connor, MD

1.810 men aged 30 to 69 years between 1972 and 1974

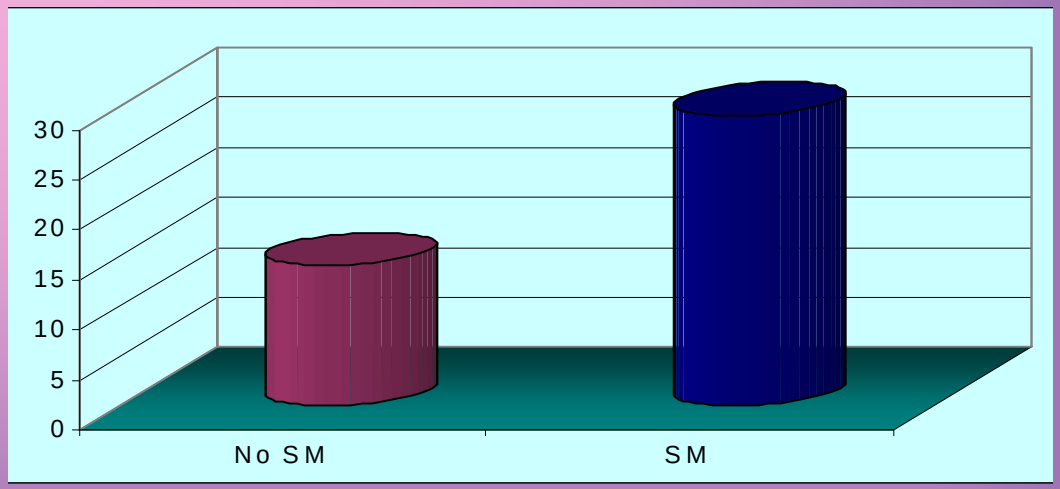
Independent risk factors for erectile dysfunction by multivariate logistic regression

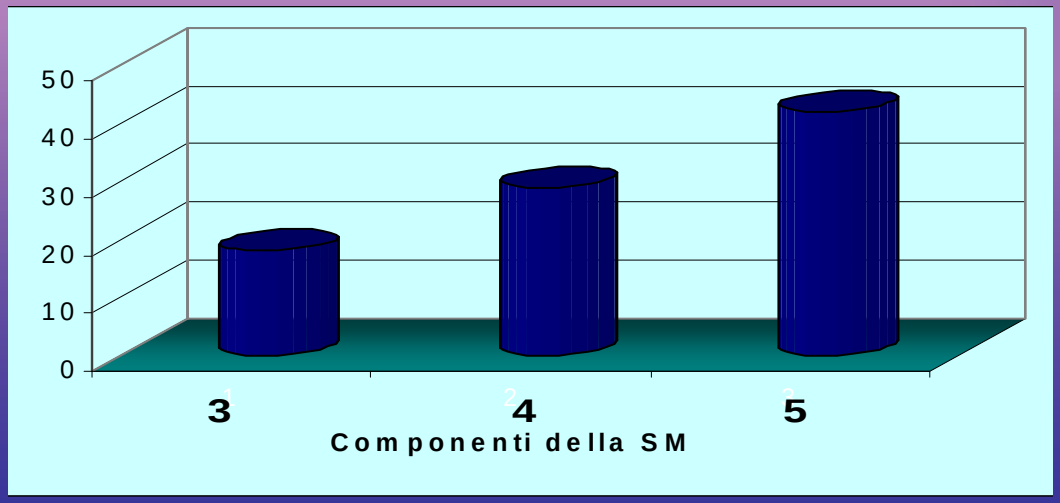
Variable	Odds Ratio	p Value	95% CI
Age, per 5 yr	1.38	<0.0001	1.24–1.53
Hypercholesterolemia	1.54	0.027	1.05–2.26
Overweight (BMI ≥28)	1.93	0.009	1.18–3.17

2005 Dec 26;96(12B):3M-7M

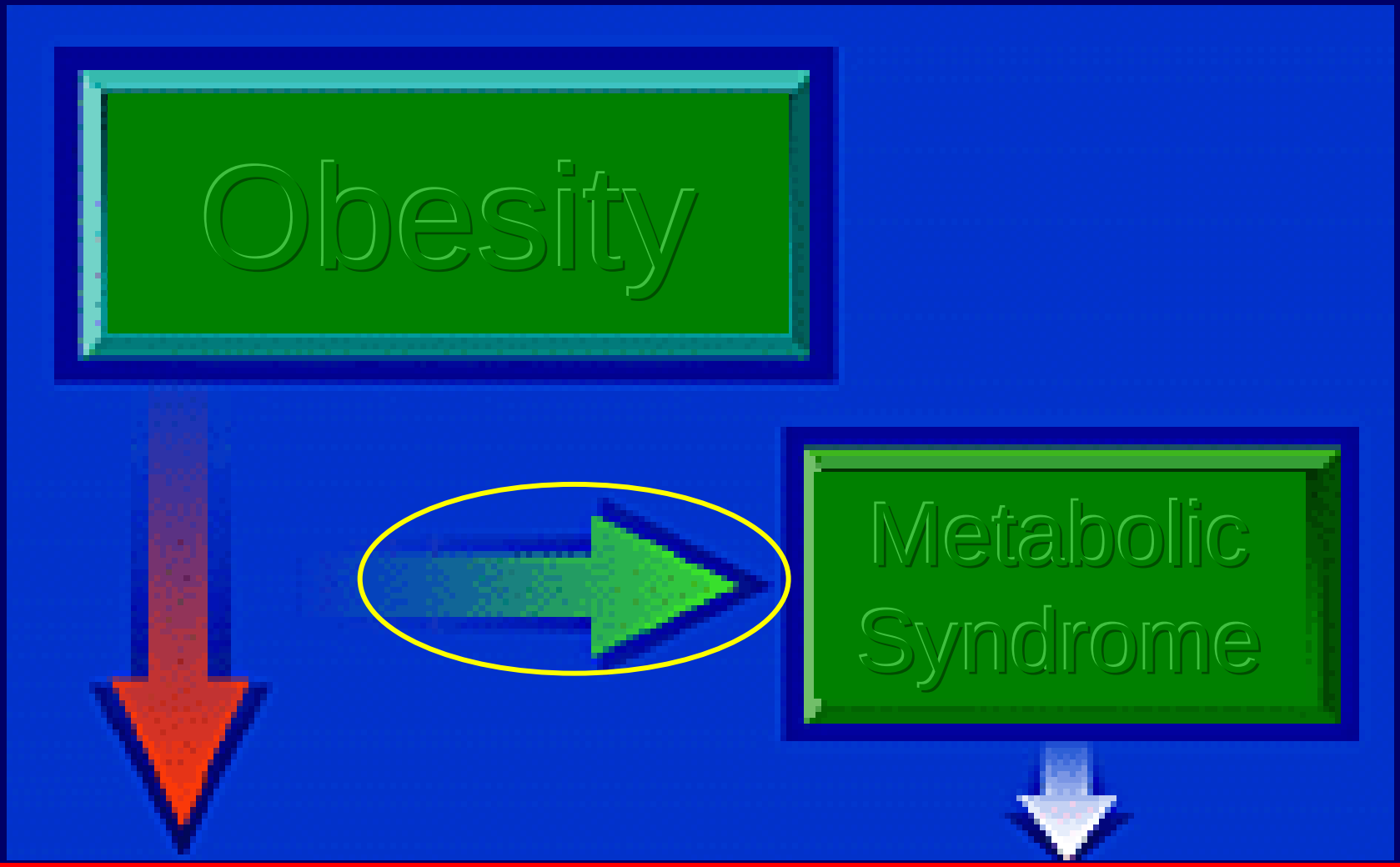
American Diabetes Association
Diabetes Care

ESPOSITO K. et al Diabetes Care May 2005

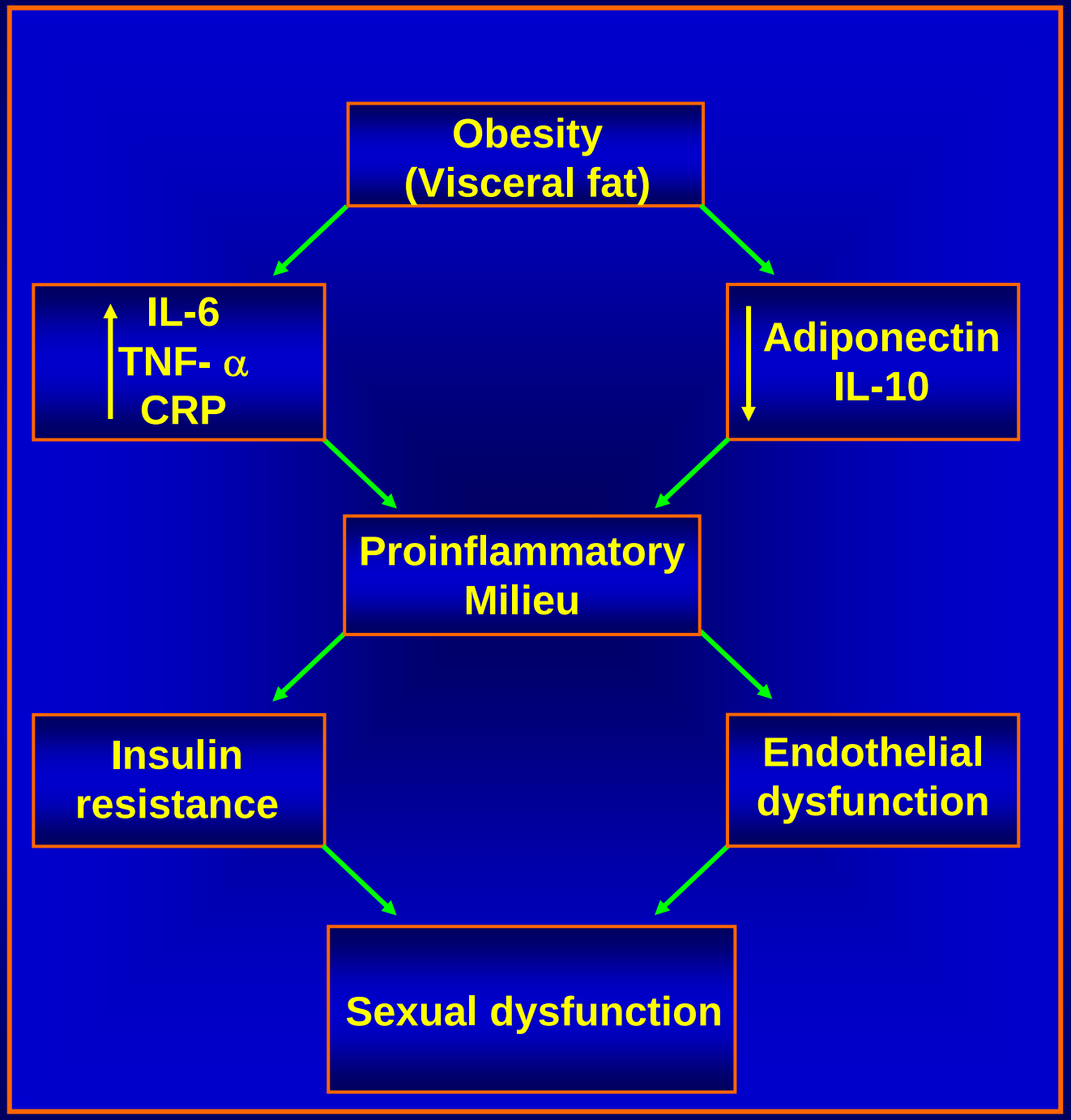




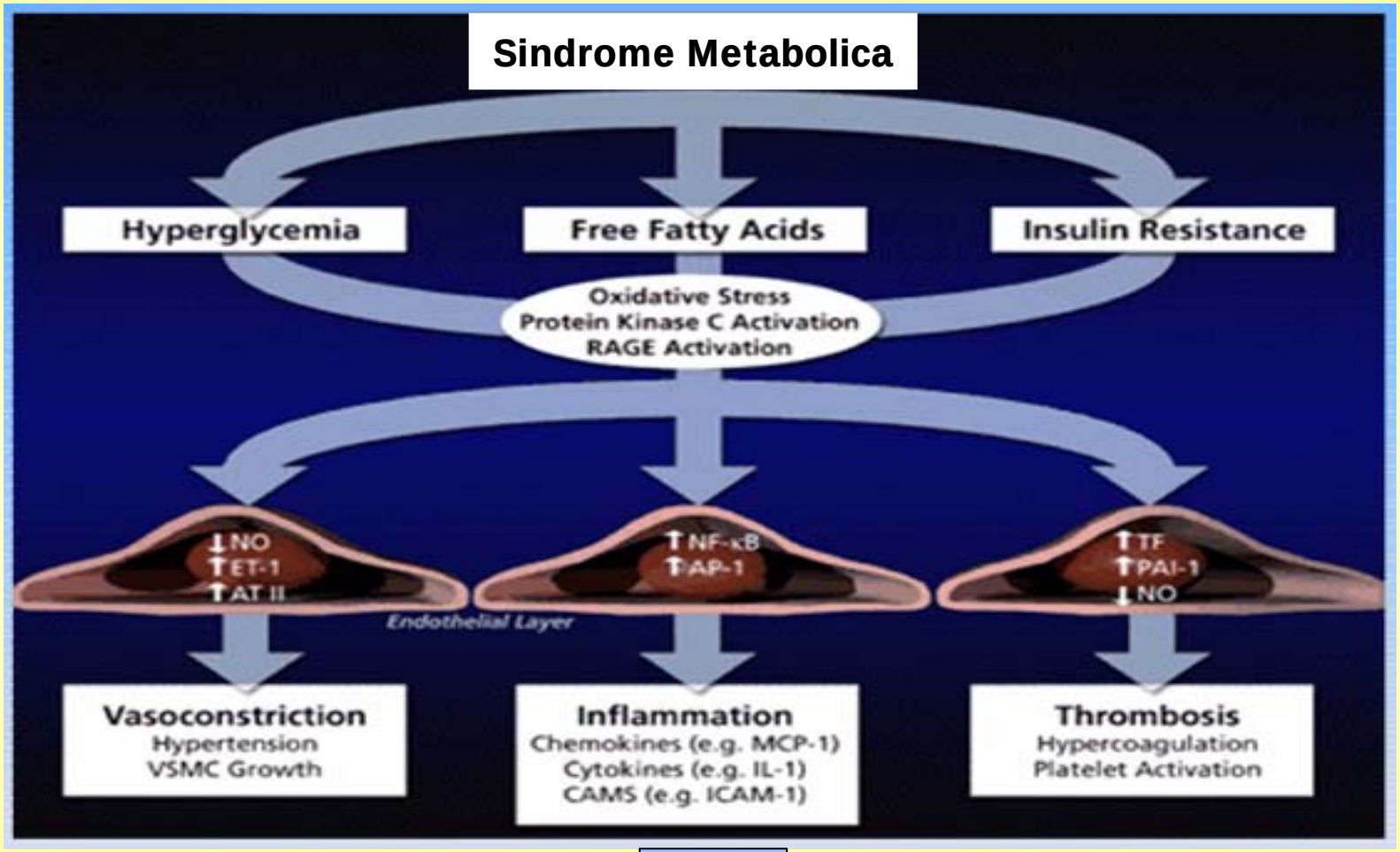
Prevalence of erectile dysfunction in men with the metabolic syndrome



Erectile Dysfunction


Obesity
(Visceral fat)
IL-6
TNF- α
CRP
Adiponectin
IL-10
Proinflammatory
Milieu
Insulin
resistance
Endothelial
dysfunction
Sexual dysfunction

Obesity



Erectile dysfunction

Intermediary Biological Mechanisms

Diet

Cardiac Rhythm

Lipid levels

High density lipoprotein Cholesterol

Low density Lipoprotein Cholesterol

Triglycerides

Lipoprotein(a)

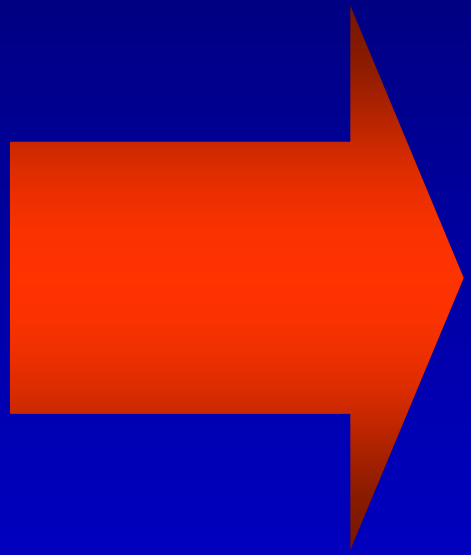
Blood Pressure

Endothelial function

Sistemic Inflammation

Insulin Sensitivity

Oxidative Stress



Risk of erectile dysfunction

JAMA

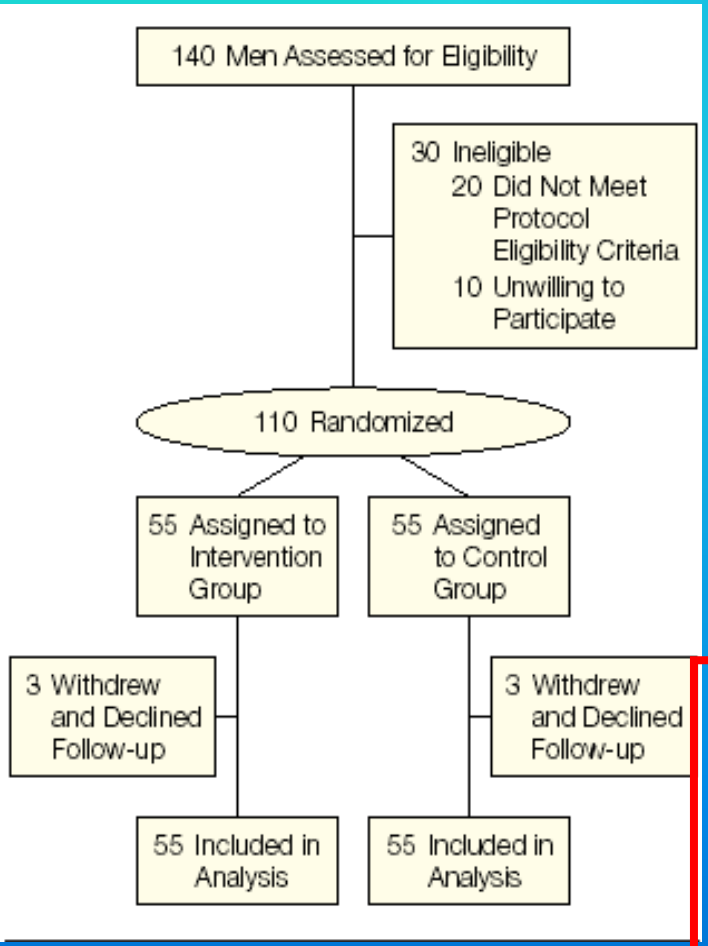


Table 1. Characteristics of the Study Participants*

Characteristic	Intervention Group (n = 55)	Control Group (n = 55)	*P* Value
Age, y	43.5 (4.8)	43 (5.1)	.62
Weight, kg	103 (9.4)	101 (9.7)	.55
Body mass index†	36.9 (2.5)	36.4 (2.3)	.65
Waist-to-hip ratio	1.02 (0.09)	1.01 (0.09)	.75
Erectile dysfunction score‡	13.9 (4)	13.5 (4)	.55
Blood pressure, mm Hg			
Systolic	127 (7.5)	128 (7.7)	.49
Diastolic	86 (3.7)	85 (4.1)	.48
Cholesterol level, mg/dL			
Total	213 (32)	210 (29)	.45
High-density lipoprotein	39 (10)	40 (9)	.76
Triglycerides, mg/dL	169 (56)	174 (51)	.23
Glucose, mg/dL	103 (10)	104 (11)	.77
Insulin, μU/mL	21 (8)	19 (7)	.35
Interleukin, pg/mL§			
6	4.5 (1.9-9)	4.4 (2-8.6)	.39
8	5.3 (2.3-10)	5.0 (2.2-9.7)	.45
C-reactive protein, mg/L§	3.3 (1.2-8.1)	3.4 (1.2-8.3)	.37
Response to L-arginine			
Platelet aggregation, %	−4 (2.2)	−3.6 (2.1)	.19
Mean blood pressure, mm Hg	−2.5 (1.3)	−2.4 (1.4)	.27

JAMA

Table 3. Nutrient Indices at Entry to Study and After 2 Years

Nutrient	Intervention Group (n = 55) Mean (SD) Baseline	Intervention Group (n = 55) Mean (SD) 2 Years	*P* Value	Control Group (n = 55) Mean (SD) Baseline	Control Group (n = 55) Mean (SD) 2 Years	*P* Value	Corrected Difference in Mean Change at 2 Years (95% CI)	*P* Value at 2 Years
Total energy, kcal/d	2340 (205)	1950 (168)	.01	2390 (215)	2340 (174)	.07	−340 (−520 to −160)	.01
Carbohydrates, %								
Regular	57 (2.5)	55 (2.9)	.01	57 (2.1)	57 (2.9)	.56	−2 (−3.4 to −0.6)	.02
Complex	43 (3.7)	50 (2.5)	.001	39 (2.4)	40 (2.2)	.15	6 (2 to 4)	.001
Fiber, g/d	15 (1.5)	25 (1.7)	.01	15 (1.6)	16 (1.8)	.10	9 (5 to 13)	.009
Protein, %	13 (1.9)	16 (1.7)	.02	13 (1.8)	14 (1.7)	.08	2.0 (0.5 to 3.5)	.04
Fat, %	30 (2.6)	29 (2.7)	.06	30 (3.3)	29 (2.9)	.59	0 (−1 to 1)	.90
Saturated	14 (2.5)	9 (1.3)	.01	14 (2.4)	14 (2.5)	.90	−5 (−9 to −1)	.001
Monounsaturated	9 (1.4)	14 (1.7)	.01	10 (1.6)	10 (1.4)	.95	5 (1.5 to 8.5)	.01
Polyunsaturated	7 (1.2)	6 (0.9)	.07	6 (1.1)	5 (0.8)	.09	0 (−1.5 to 1.5)	.88
Ratio of omega-6 to omega-3 fatty acid	12 (2.4)	6 (0.9)	.001	13 (2.1)	12 (1.9)	.08	−5 (−9 to −1)	.001
Cholesterol, mg/d	360 (39)	276 (26)	.01	356 (40)	327 (31)	.05	−53 (−95 to −11)	.02

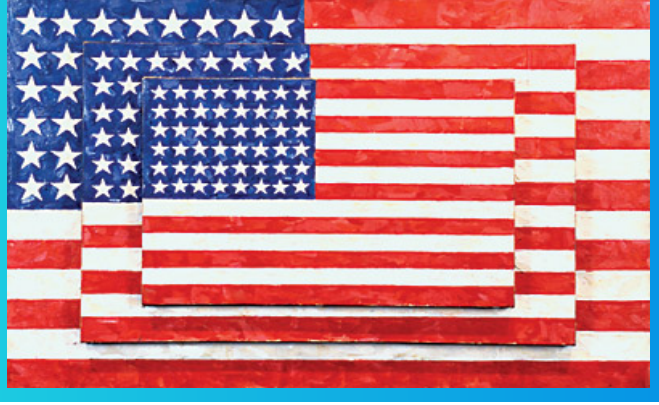


Table 4. Clinical and Metabolic Characteristics of the Study Participants after 2 Years*

Characteristic	Intervention Group (n = 55)			Control Group (n = 55)			Corrected Difference in Mean Change at 2 Years (95% CI)	*P* Value at 2 Years
	2 Years	Mean Change	*P* Value	2 Years	Mean Change	*P* Value		
Weight, kg	88 (8.5)	−15	<.001	99 (9.2)	−2	.27	−13 (−18 to −11)	.007
Body mass index†	31.2 (2.1)	−5.7	<.001	35.7 (2.5)	−0.7	.19	−5 (−7.5 to −2.5)	<.001
Waist-to-hip ratio	0.93 (0.08)	−0.09	<.001	1.00 (0.09)	−0.01	.56	−0.08 (−0.12 to −0.06)	.01
Erectile dysfunction score‡	17 (5)	3.01	<.001	13.6 (4.1)	0.1	.89	3 (1.2 to 4.8)	.008
Blood pressure, mm Hg								
Systolic	124 (7.4)	−3	.04	127 (7.8)	−1	.50	−2 (−3 to −1)	.01
Diastolic	82 (3.6)	−4	.02	85 (4.5)	0	.98	−4 (−6.5 to −1.5)	.009
Cholesterol level, mg/dL								
Total	202 (24)	−11	.04	212 (31)	2	.72	−13 (−23 to −3)	.02
High-density lipoprotein	48 (9)	9	.001	40 (9)	0	.99	9 (5 to 13)	.01
Triglycerides, mg/dL	150 (45)	−19	.04	170 (47)	−4	.67	−15 (−29 to −1)	.05
Glucose, mg/dL	95 (8)	−8	.02	103 (11)	−1	.34	−7 (−12 to −2)	.02
Insulin, μU/mL	14 (5)	−7	.04	17 (7)	−2	.09	−5 (−9 to −1)	.04
Interleukin, pg/mL§								
6	3.1 (0.9-7)	−1.4	.04	4.5 (2.1-8.8)	0.1	.67	−1.5 (−2.9 to 0.3)	.03
8	4.1 (1.3-8.9)	−1.2	.05	4.7 (1.4-8.4)	−0.3	.23	−0.9 (−2.0 to 0.3)	.07
C-reactive protein, mg/L§	1.9 (0.9-7.1)	−1.4	.01	3.4 (1.3-8.2)	0	.67	−1.4 (−2.5 to −0.3)	.02
Response to L-arginine								
Platelet aggregation, %	−11 (4.8)	−7	.01	−4.3 (3.2)	−0.7	.17	−6.3 (−9.3 to −3.3)	.02
Mean blood pressure, mm Hg	−5.1 (1.9)	−2.6	.001	−2.6 (1.5)	−0.2	.47	−2.4 (−3.2 to −1.6)	.02

JAMA

Effect of Lifestyle Changes on Erectil Dysfunction in Obese Men

A Randomized Controlled Trial

Esposito K et al

2004 Jun;291:2978-2984

International Journal of Impotence Research
The Journal of Sexual Medicine

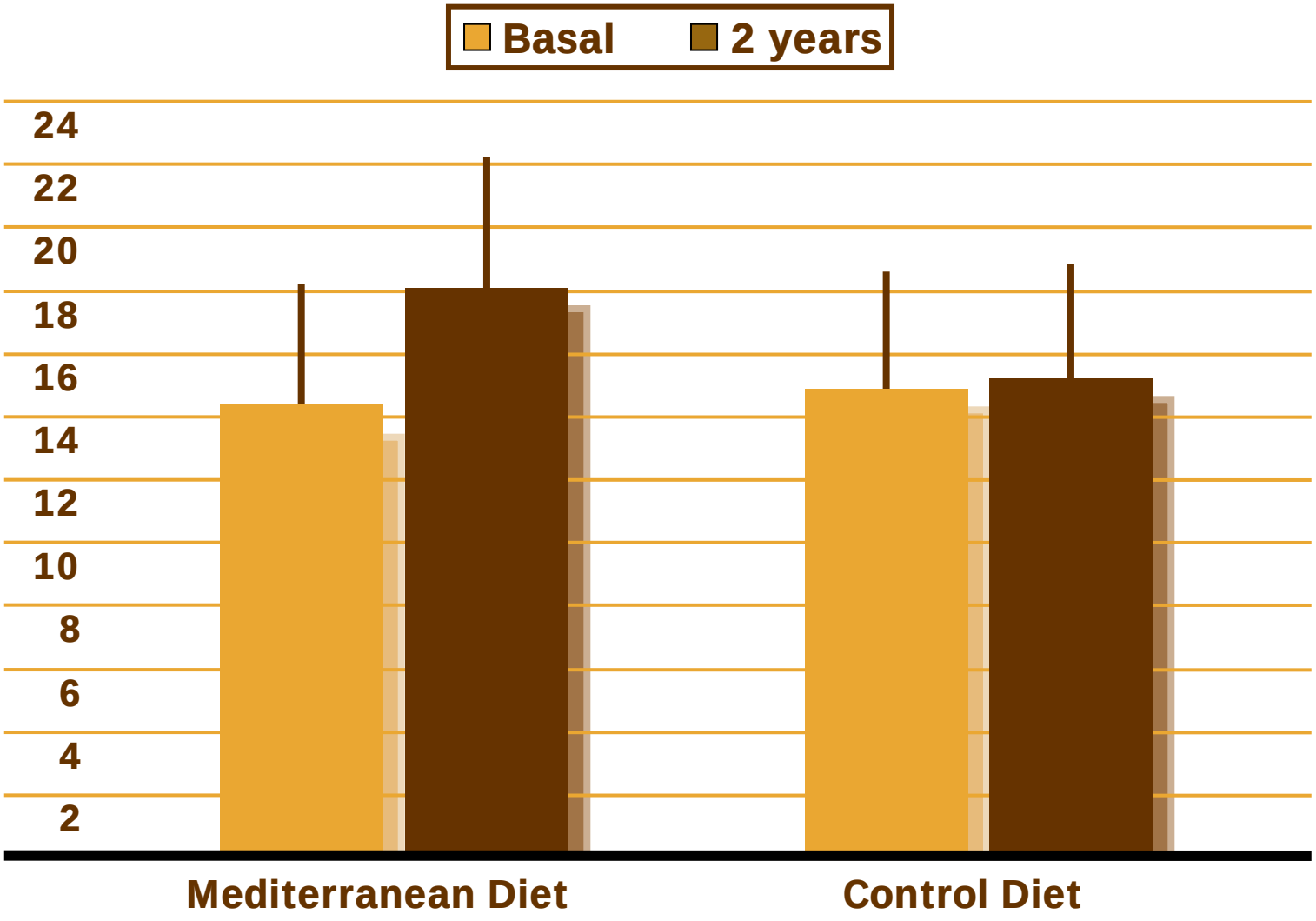
Original Article

International Journal of Impotence Research 2006 Jul-Aug;18(4):405-10

Mediterranean diet improves erectile function in subjects with the metabolic syndrome

Esposito K, Ciotola M, Giugliano F, De Sio M, Giugliano G, D'armiento M, Giugliano D.

CHANGES IN IIEF SCORE BETWEEN THE TWO GROUPS



nature publishing group

International Journal of Impotence Research
The Journal of Sexual Medicine

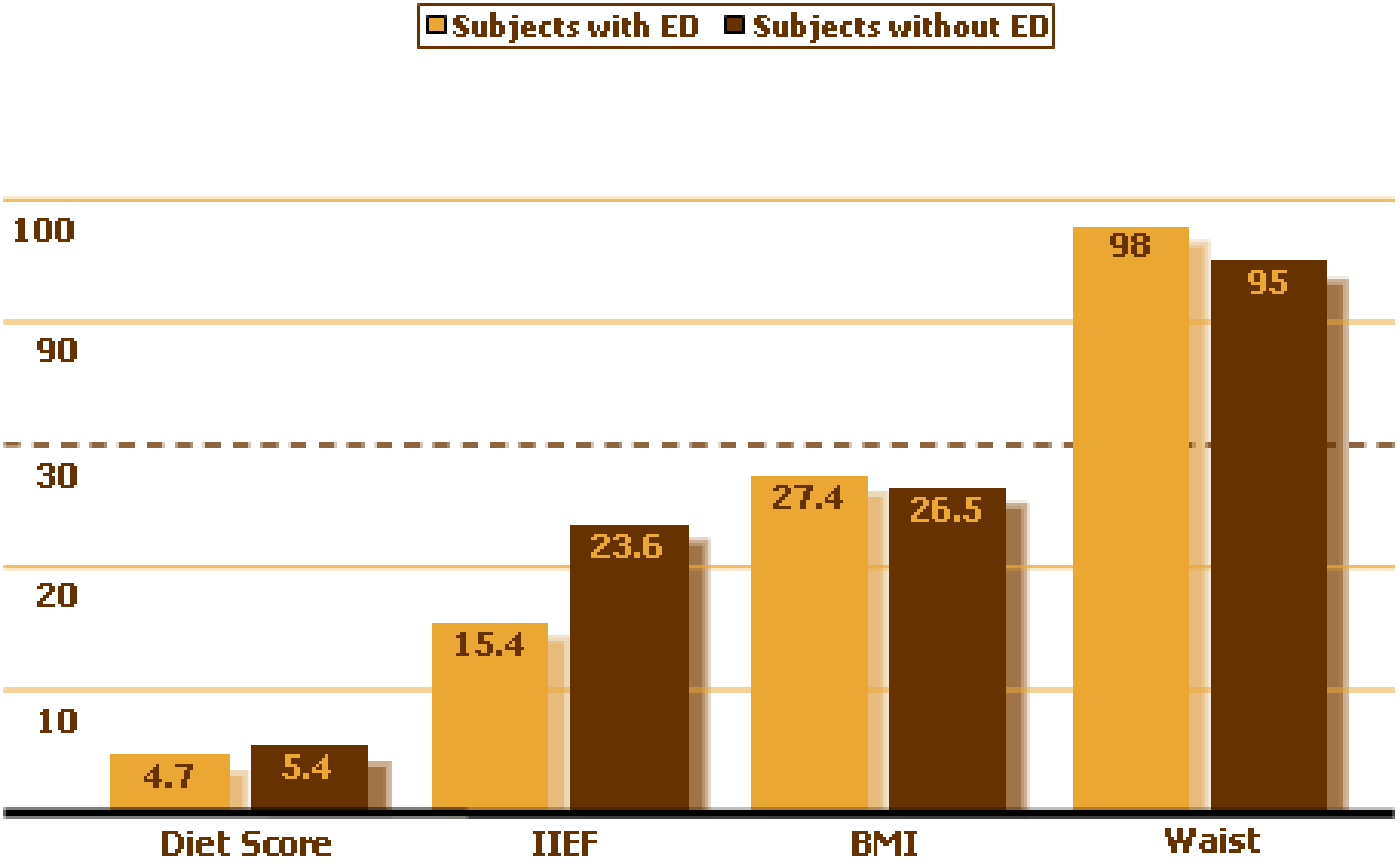
Dietary Factors in Erectile Dysfunction

Esposito K et al

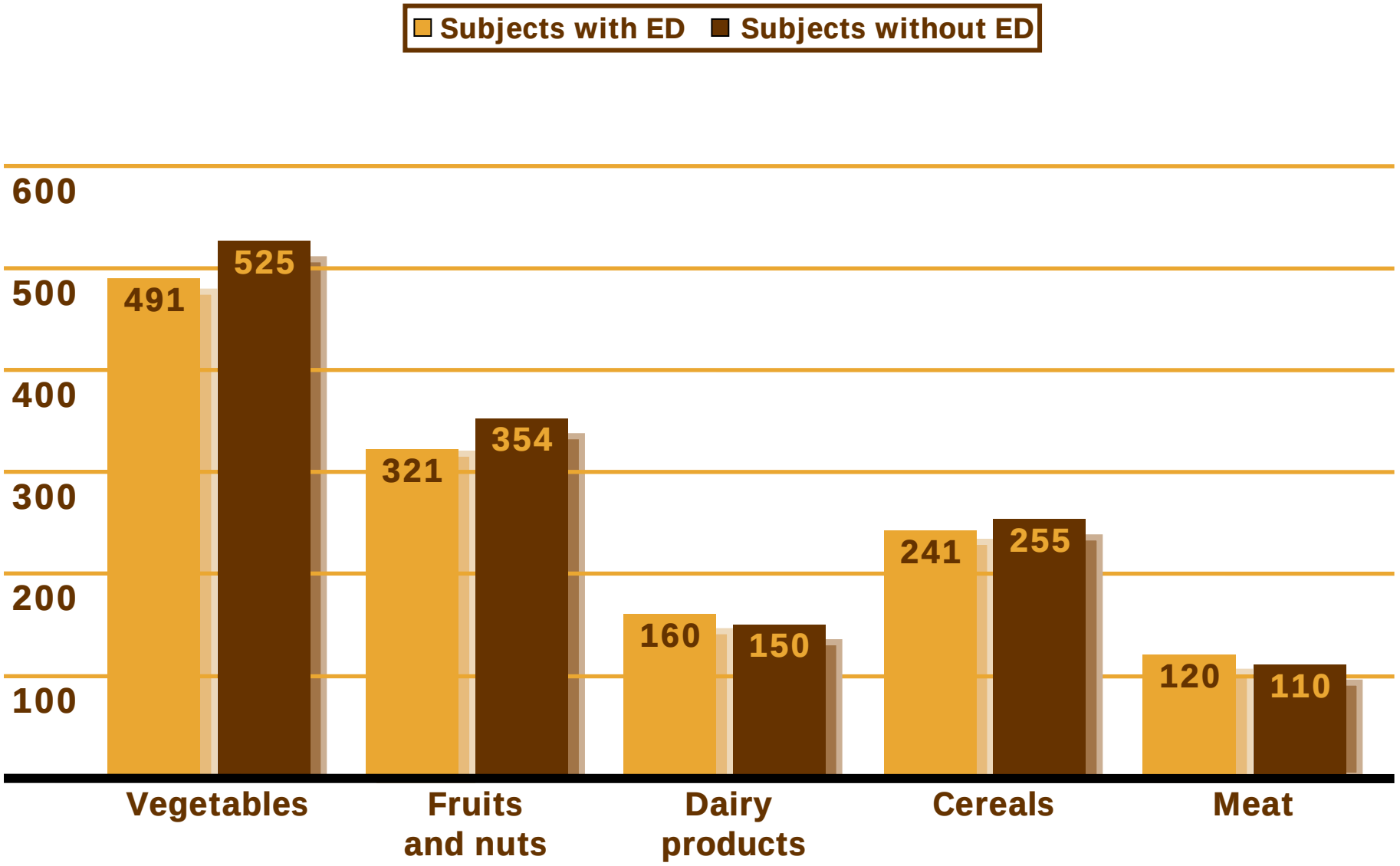
One hundred men with ED were compared with 100 age-matched men without ED. A scale indicating the degree of adherence to the Mediterranean diet was constructed: the total Mediterranean-diet score ranged from 0 (minimal adherence to the Mediterranean diet) to 9 (maximal adherence).

Int J Impot Res. 2006 Jul-Aug;18(4):370-4

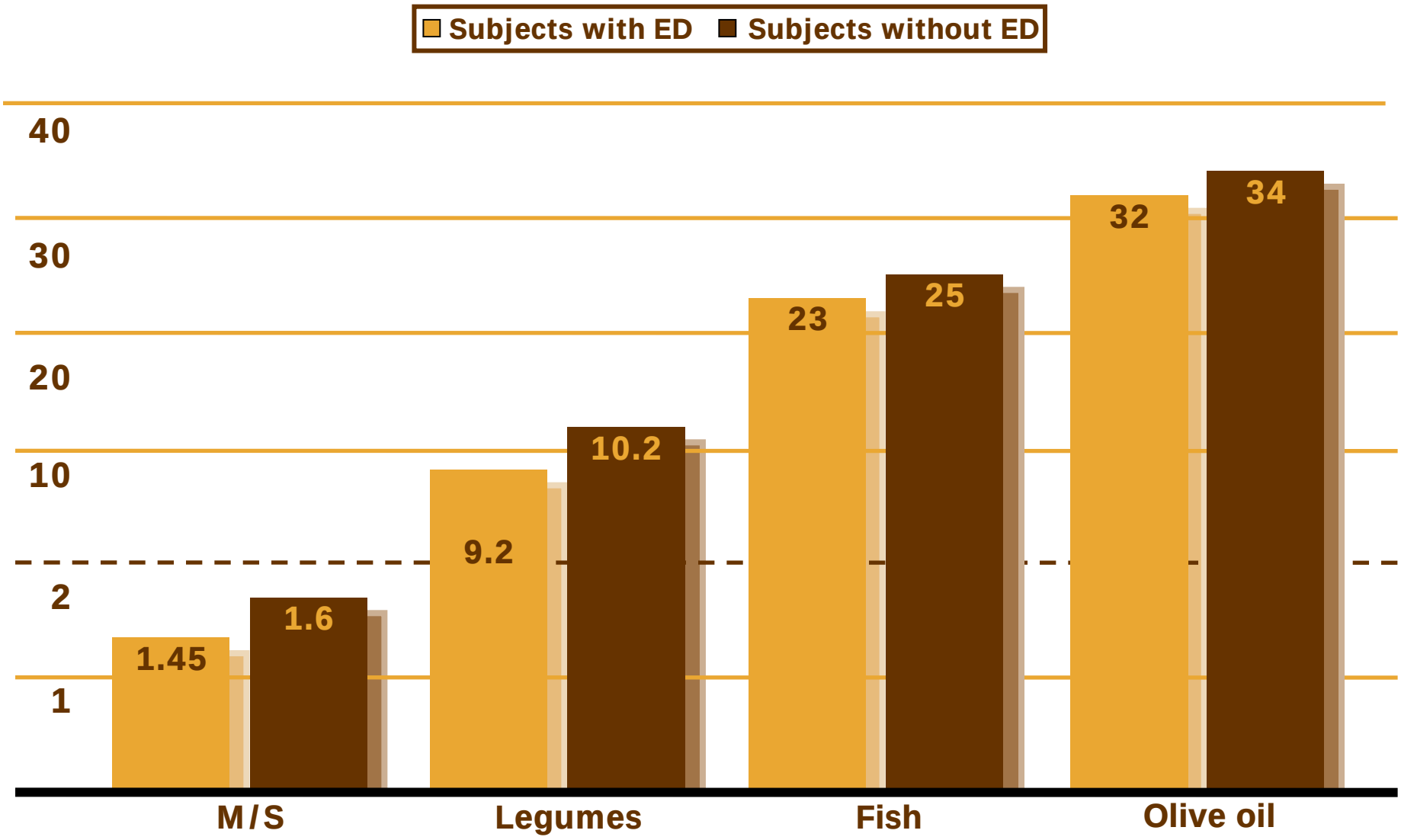
LIFESTYLE AND CLINICAL CHARACTERISTIC OF SUBJECTS WITH AND WITHOUT ERECTILE DYSFUNCTION



DAILY DIETARY INTAKE OF SEVERAL FOOD GROUPS IN THE TWO GROUPS OF SUBJECTS



DAILY DIETARY INTAKE OF SEVERAL FOOD GROUPS IN THE TWO GROUPS OF SUBJECTS



nature publishing group

International Journal of Impotence Research
The Journal of Sexual Medicine

Dietary Factors in Erectile Dysfunction

Esposito et al

In conclusion, the results of the present study show that dietary factors may be important in the development of ED: adoption of healthy diets would hopefully help preventing ED.

Int J Impot Res. 2006 Jan 5; [Epub ahead of print]

World Health Organization

Salon Des Refuses 1863

LA SALUTE SESSUALE

È PARTE INTEGRANTE

DELLA SALUTE DELL'INDIVIDUO

1972'

6th AME National Meeting – 3rd Joint Meeting with AACE

Erectile Dysfunctions (ED) in Internal Medicine

Verona Italy October 28 2006

Is sexual rehabiltation possible?

Ferdinando Valentini, MD

Endocrine Unit

"San Camillo-Forlanini" Hospital

Rome

BACKGROUND

- Results from SURE study: 42% of pts prefer tri weekly administration vs on demand
  - Mirone et al, Eur Urol, 2005
- Tri-weekly Tadalafil (3 mo) improves spontaneous erections in ED patients without vascular disease
  - Caretta et al, Eur Urol, 2005
- Efficacy and safety of daily tadalafil in men with erectile dysfunction previously unresponsive to on demand tadalafil
  - McMahon C, J Sex Med, 2006
- Circulating endothelial progenitor cells and endothelial function after chronic Tadalafil treatment in subjects with erectile dysfunction
  - Foresta C. et al, Int J Impotence Res, 2006

Vascular and Endothelial Function and Dysfunction and PDE5i

Improvement with PDE5i

Desouza C *Diabetes Care* 2002
(DM, *n*=16)
Gori T *Circulation* 2005
(Healthy, *n*=10)
Katz S *JACC* 2000
(CHF,*n*=39)
Kimura M *Hypertension* 2003
(Smokers, *n*=20)
Schofield et al *AJH* 2003
(CTR&HTN *n*=15)
Vlachopoulos C et al *AJH* 2004
(Smokers, *n*=14)

No improvement with PDE5i

Dishy V Clin Pharm & Ther 2003
(Smokers, *n*=9)
Dishy V Brit J Clin Pharm 2003
(Healthy, *n*=17)
Robinson SD Heart 2005
(CAD,*n*=24)

European Urology

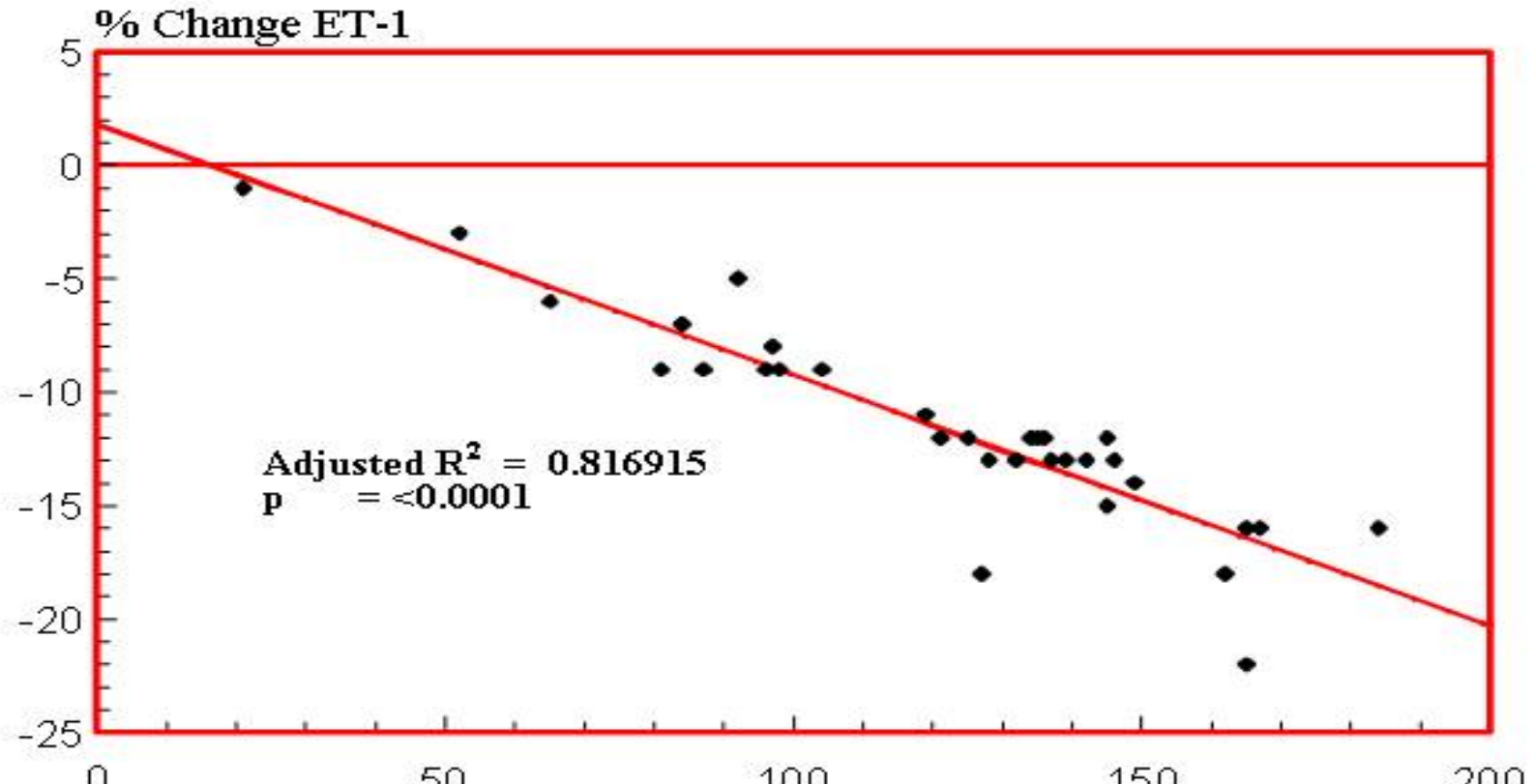
European Urology 47 (2005) 214–222

Chronic Treatment with Tadalafil Improves Endothelial Fun

Giusep
Massir
[a]Cardiovas
[b]Departme
[c]Departme
me, Italy

Accepted 4
Available o

Figure 4



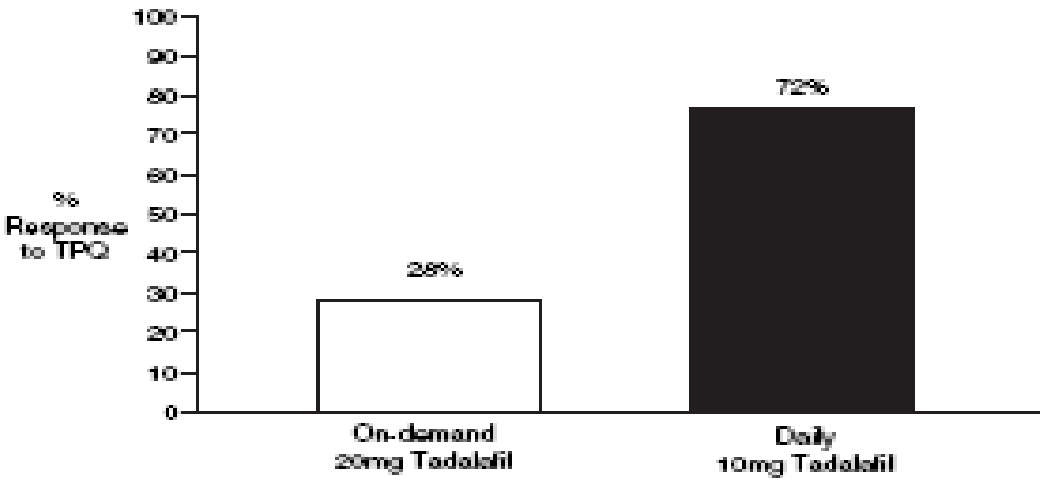
CHRONIC USE of PDE5i for TREATING ED

Comparison of Efficacy, Safety, and Tolerability of On-Demand Tadalafil and Daily Dosed Tadalafil for the Treatment of Erectile Dysfunction

Chris McMahon, MD, FACSHP

Australian Centre for Sexual Health, Sydney, NSW, Australia

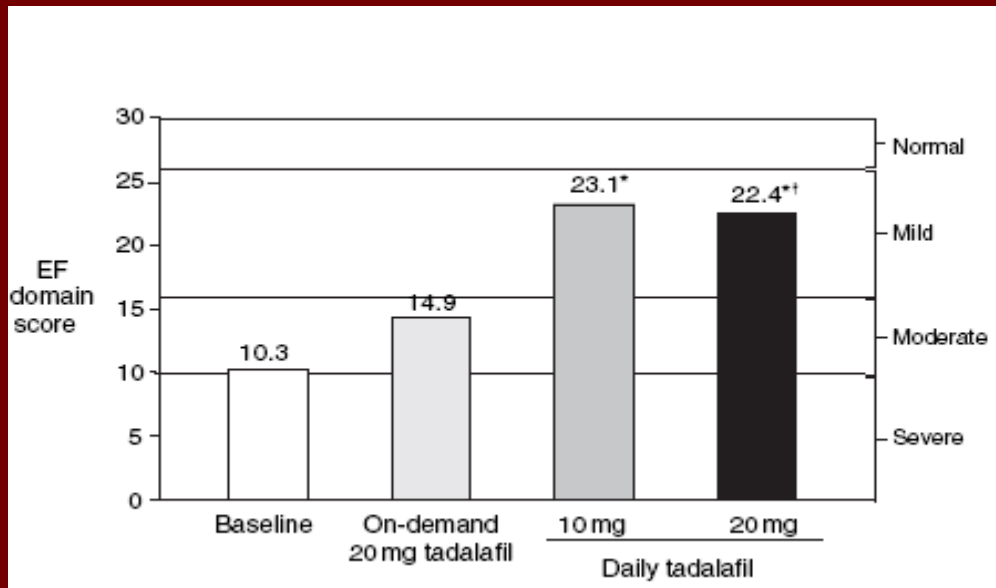
Corresponding Author: Chris McMahon, MD, FACSHP, Australian Centre for Sexual Health, Suite 2-4, 1A Berry Road, St Leonards, Sydney, New South Wales 2065, Australia. Tel: +61 294373906; Fax: +61 299065900; E-mail: cmcmahon@acsh.com.au

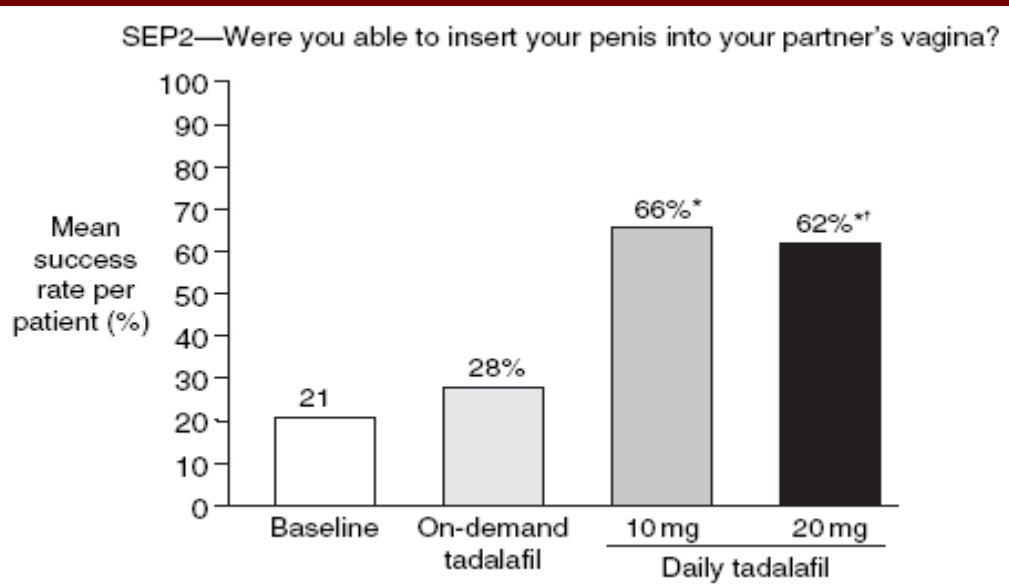


J Sex Med 2005; 2: 415–427

Efficacy and Safety of Daily Tadalafil in Men with Erectile Dysfunction Previously Unresponsive to On-demand Tadalafil

Chris McMahon, MD
Australian Centre for Sexual Health, Sydney, Australia.



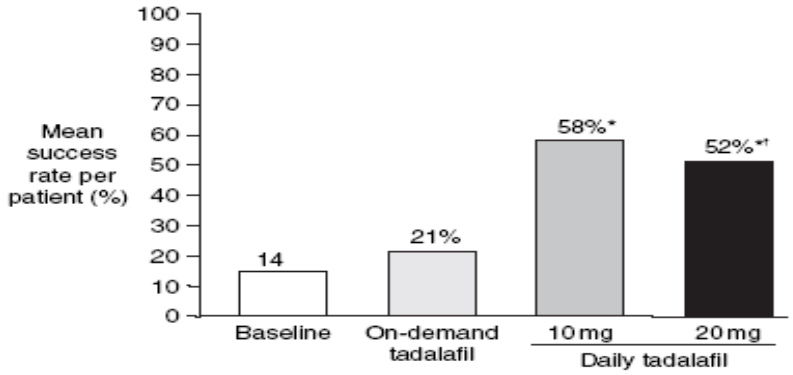


Efficacy and Safety of Daily Tadalafil in Men with Erectile Dysfunction Previously Unresponsive to On-demand Tadalafil

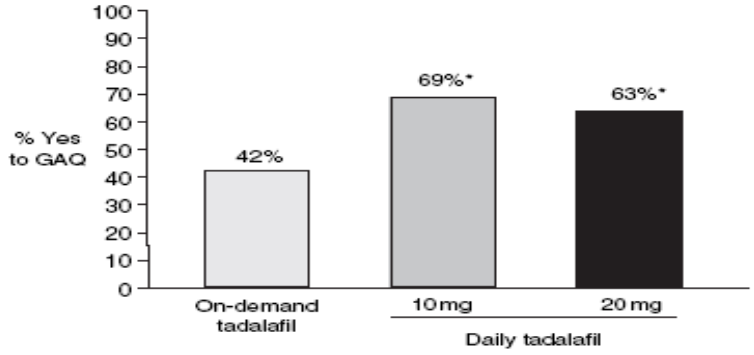
Chris McMahon, MD

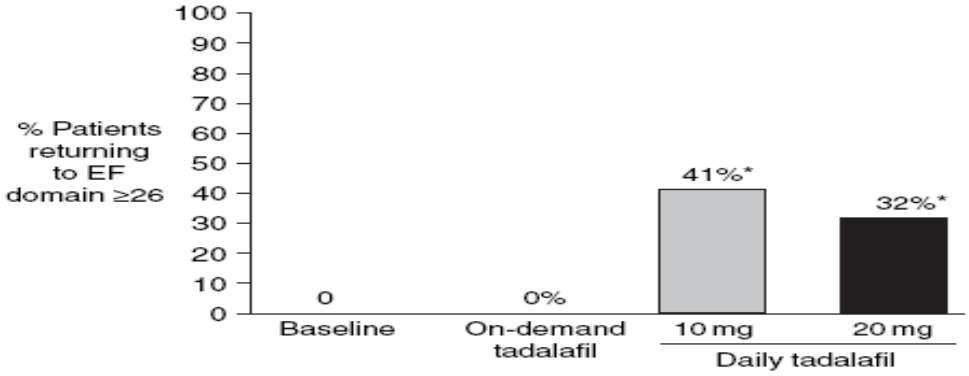
Australian Centre for Sexual Health, Sydney, Australia.

SEP3—Did your erection last long enough for you to have successful intercourse?



GAQ—Has the treatment you have taken over the past 4 weeks improved your erections?





International Journal of Impotence Research (2006), 1–8

0955-9930/06 $30.00
www.nature.com/ijir

ORIGINAL ARTICLE

Relationship between chronic tadalafil administration and improvement of endothelial function in men with erectile dysfunction: a pilot study

A Aversa, E Greco, R Bruzziches, M Pili, G Rosano and G Spera

Medical Pathophysiology, University of Rome La Sapienza, Roma, Italy

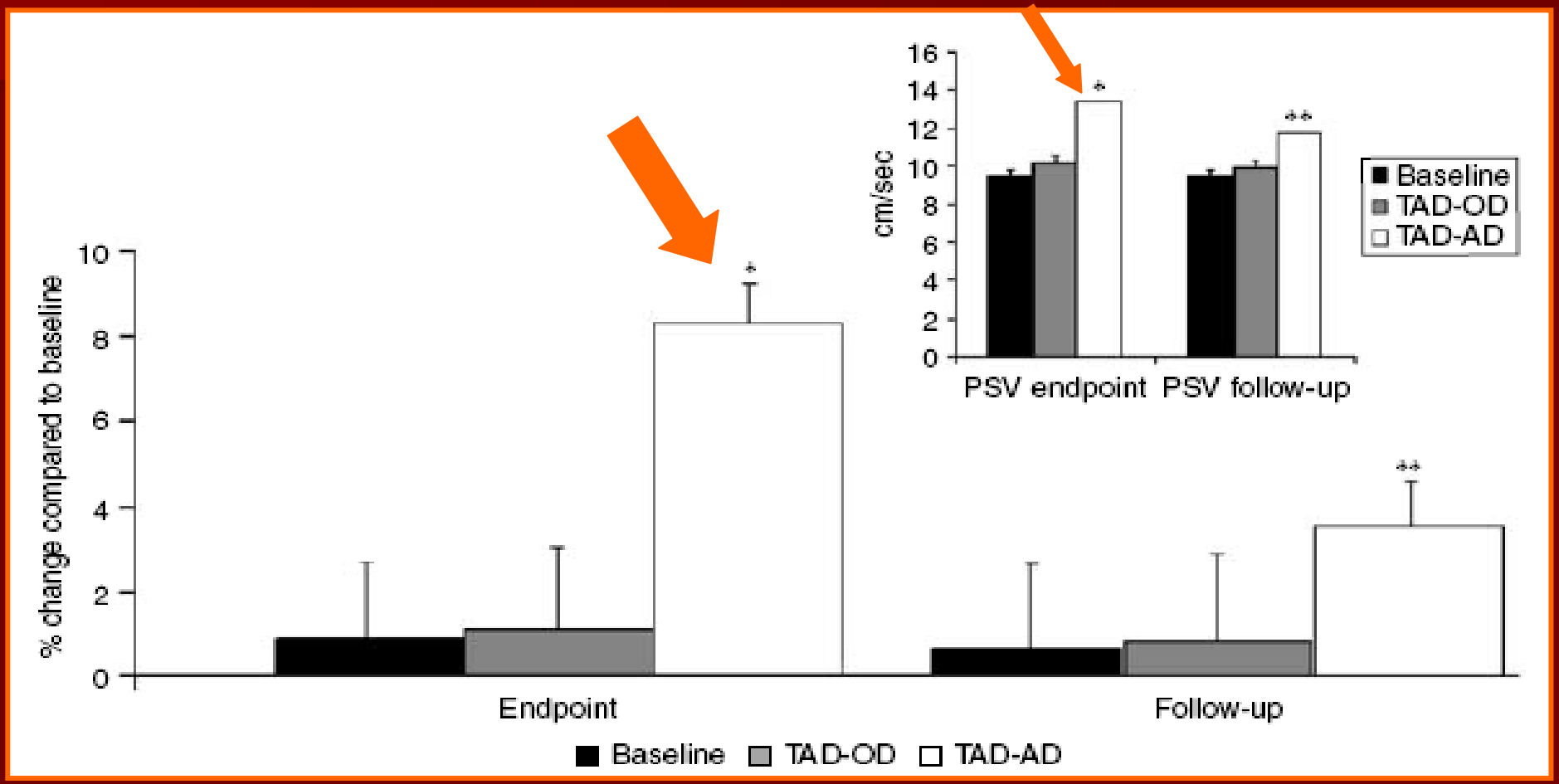
AIM OF THE STUDY:

To evaluate whether chronic exposure to TAD (AD) vs on demand (OD) may impact on cavernous circulation and markers of endothelial function in men with various ethiologies of ED

Int J Impotence Res 2006,1-8

RESULTS

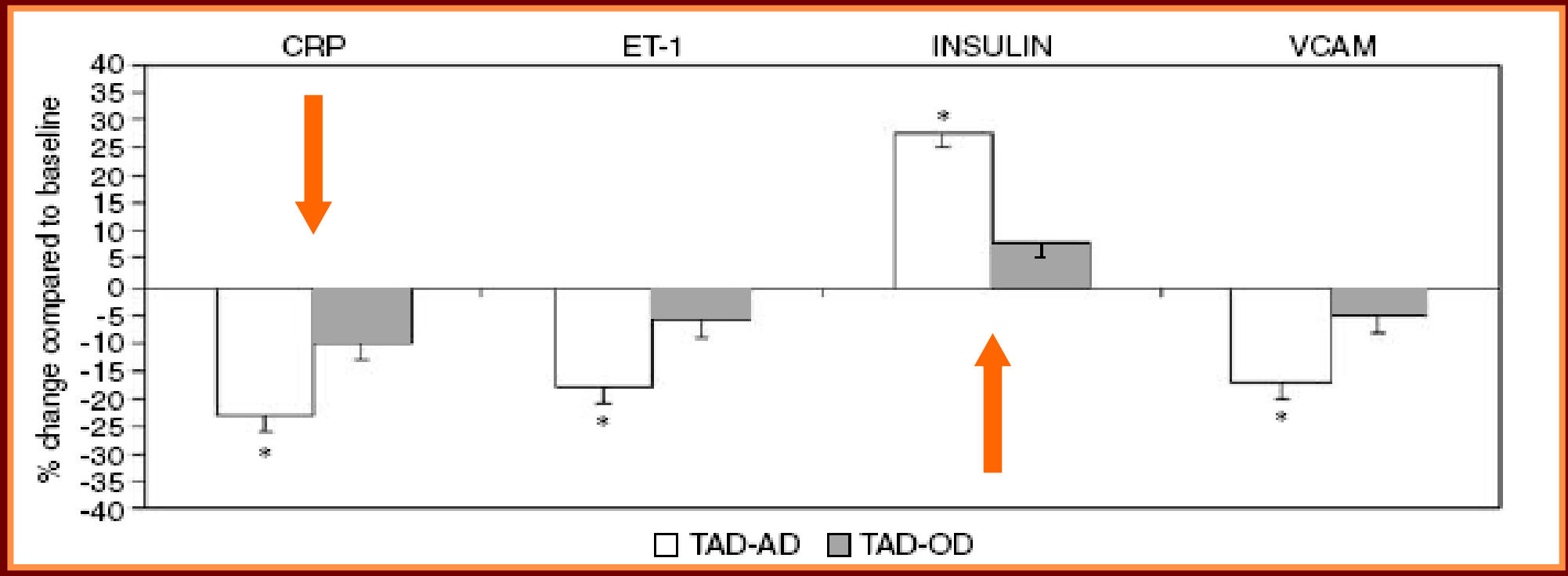
FMD of the cavernous arteries and basal CDU inflow



Int J Impotence Res (2006),1-8

RESULTS

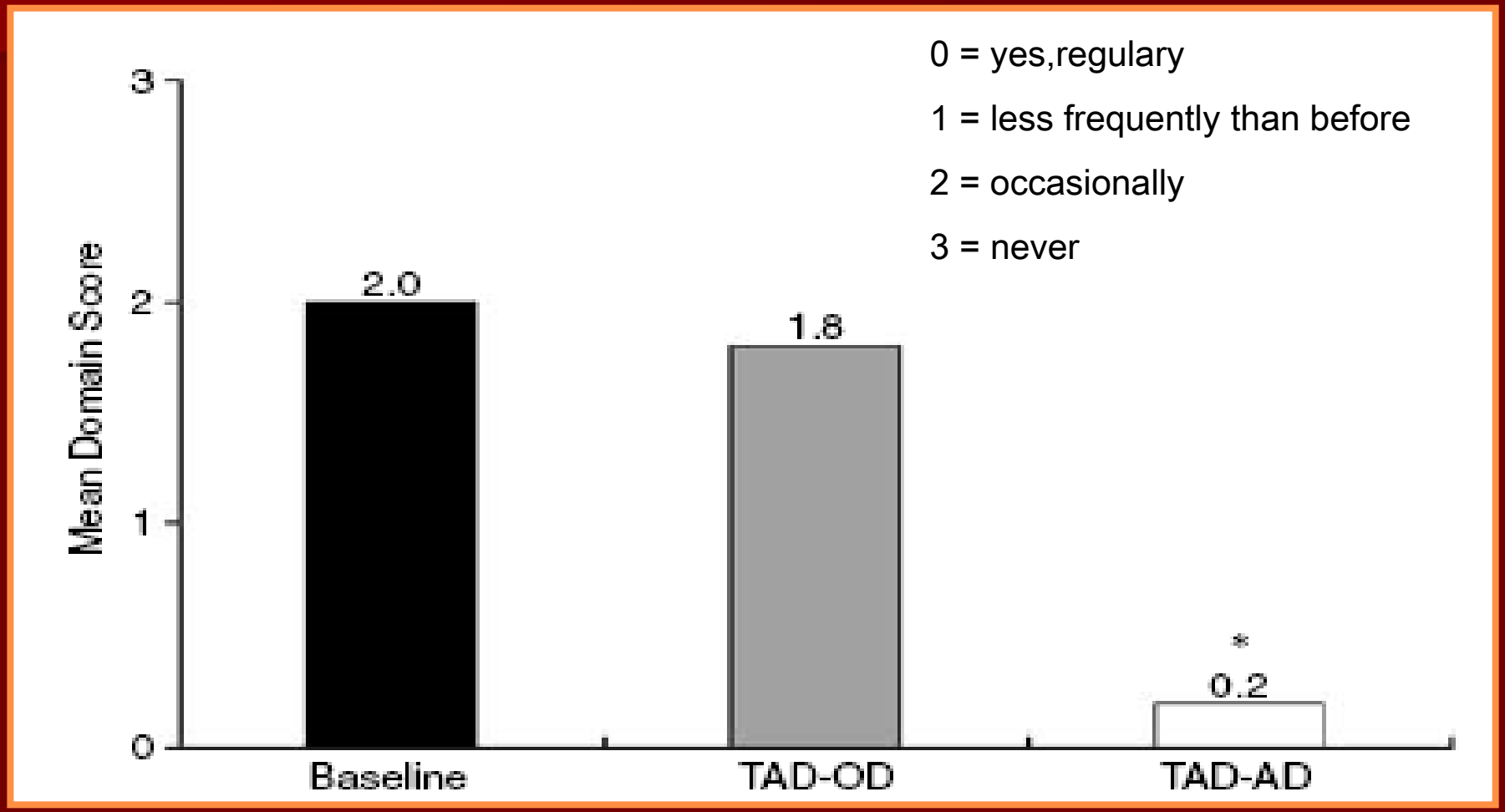
Endothelial functions markers



Int J Impotence Res (2006),1-8

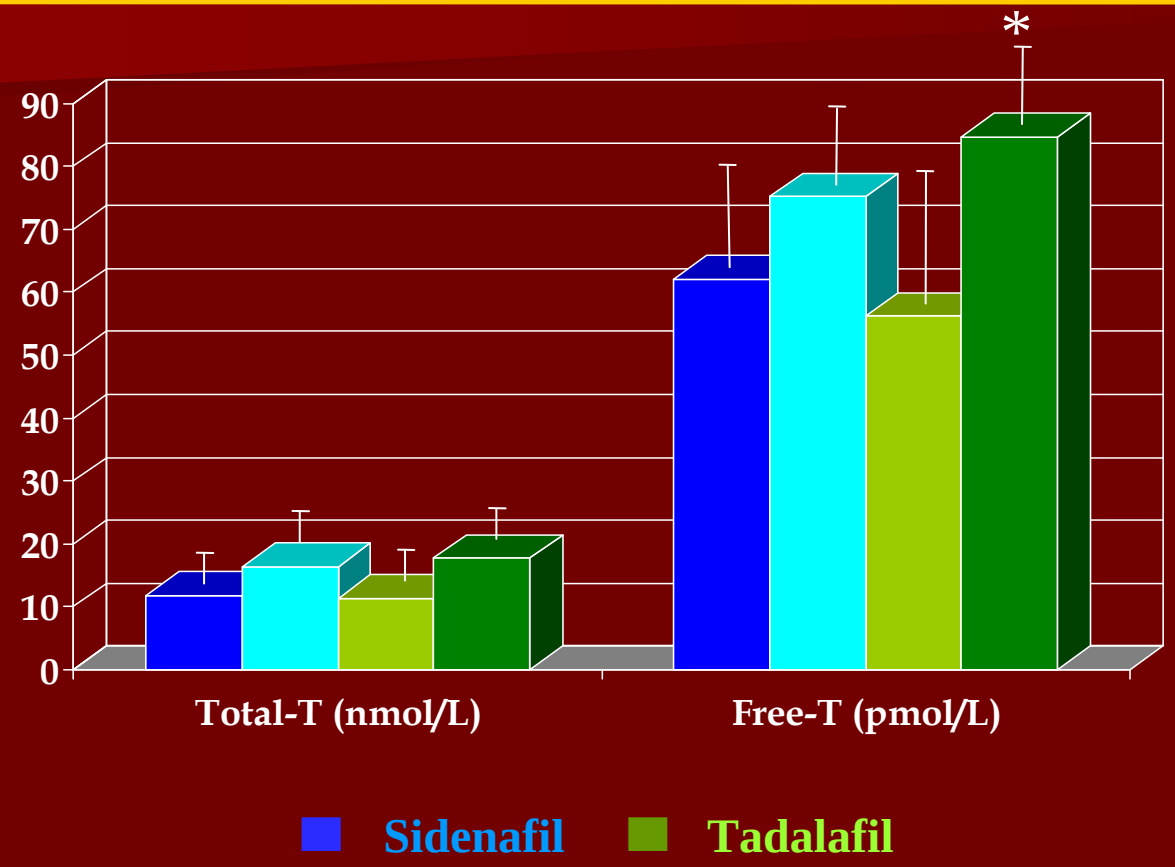
RESULTS Q13-SIEDY

In the last 4 weeks,did you ever make up with an erections?



Int J Impotence Res (2006),1-8

3 months therapy with Tadalafil vs. Sildenafil on the sexual steroid hormones (N=74)

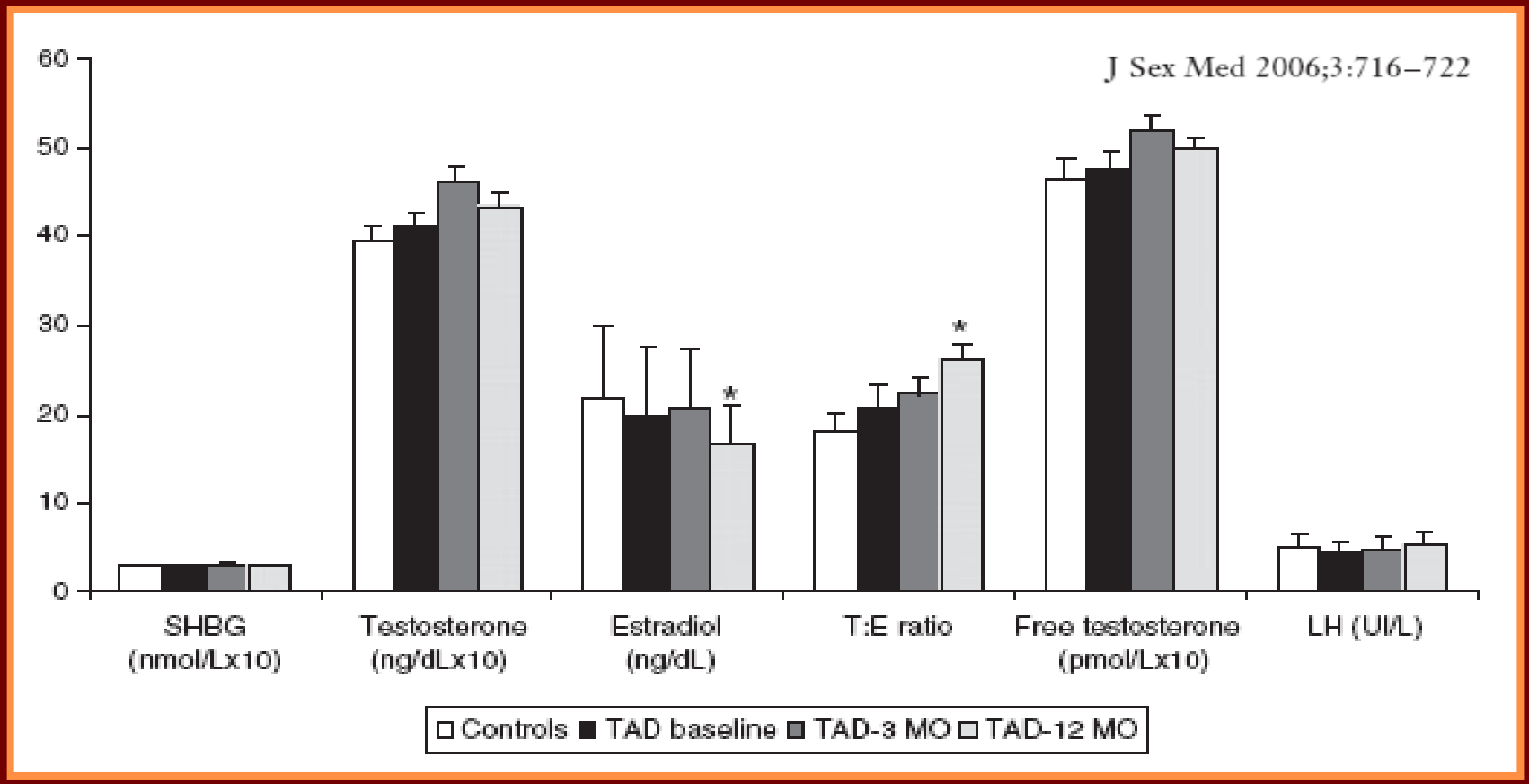


Carosa et al, Clin Endo, 2004

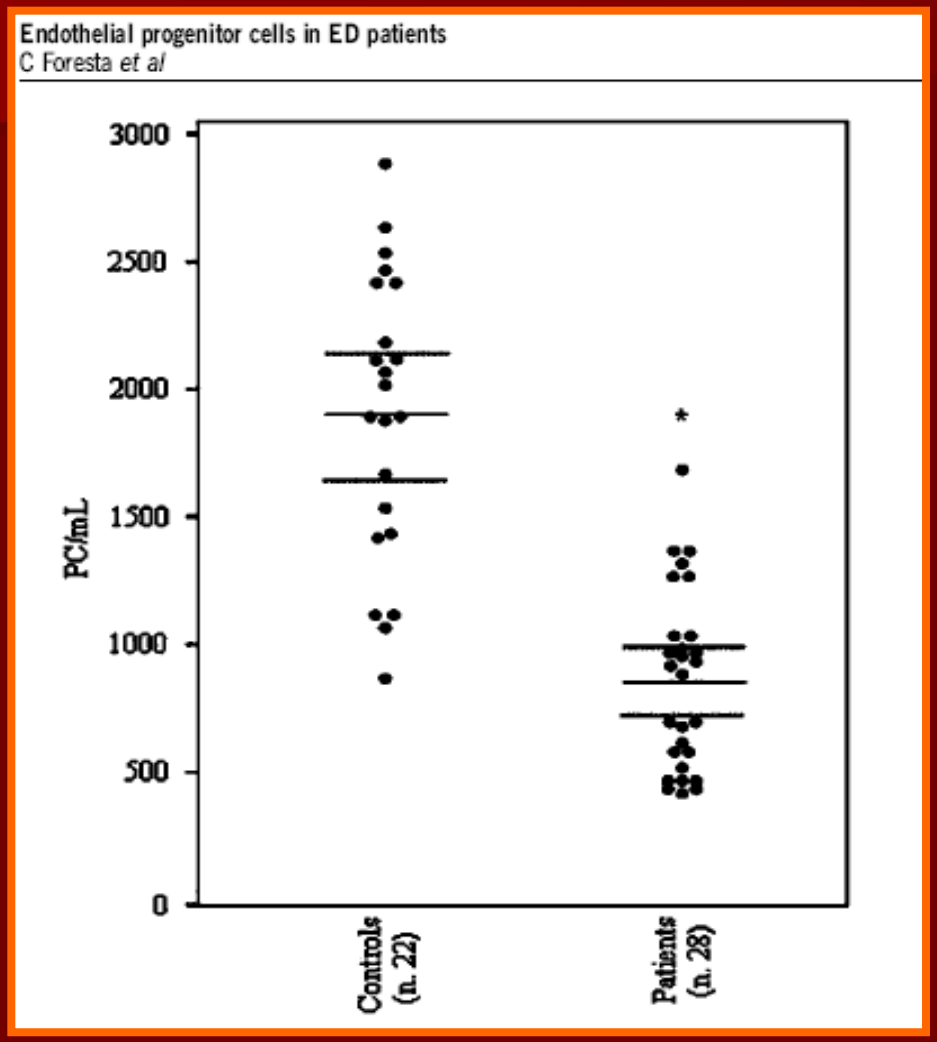
Testosterone:Estradiol Ratio Changes Associated with Long-Term Tadalafil Administration: A Pilot Study

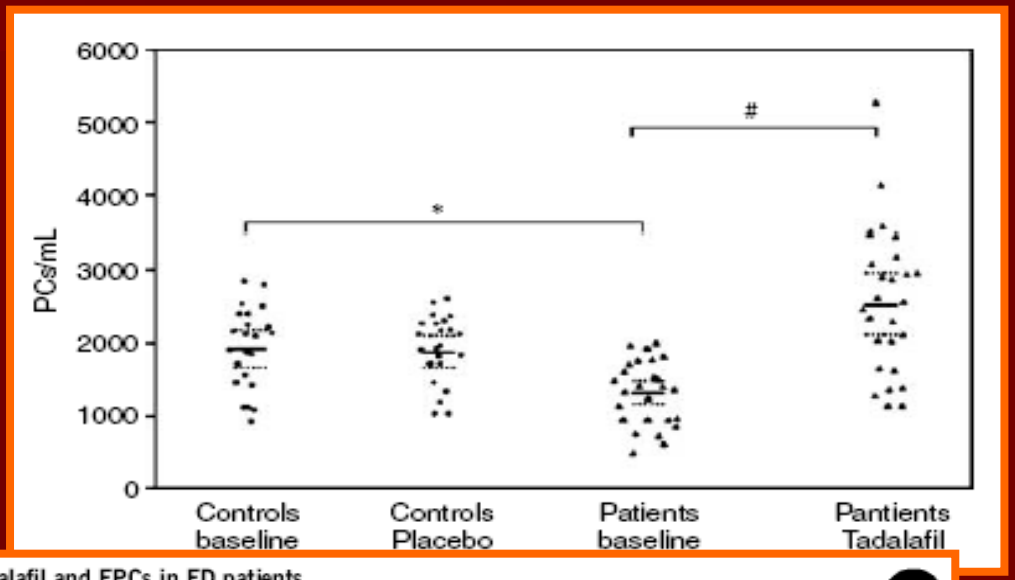
Emanuela A. Greco, MD,* Marcello Pili, MD,* Roberto Bruzziches, MD,* Giovanni Corona, MD,† Giovanni Spera, MD,* and Antonio Aversa, MD, PhD*

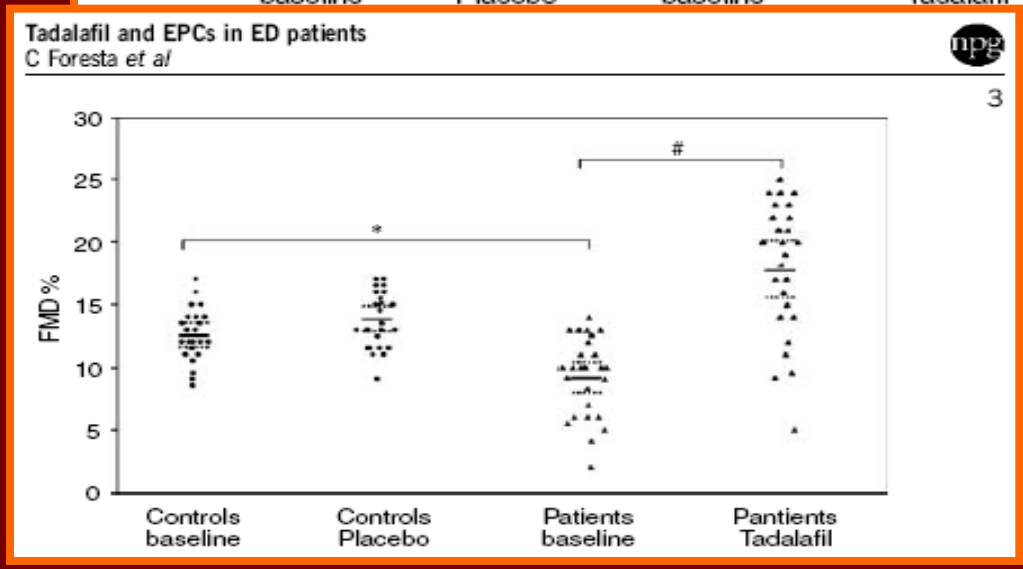
*Internal Medicine, Department of Medical Pathophysiology, University of Roma "La Sapienza," Rome, Italy; †Andrology Unit, Department of Clinical Pathophysiology, University of Florence, Florence, Italy



The circulating endothelial progenitor cells





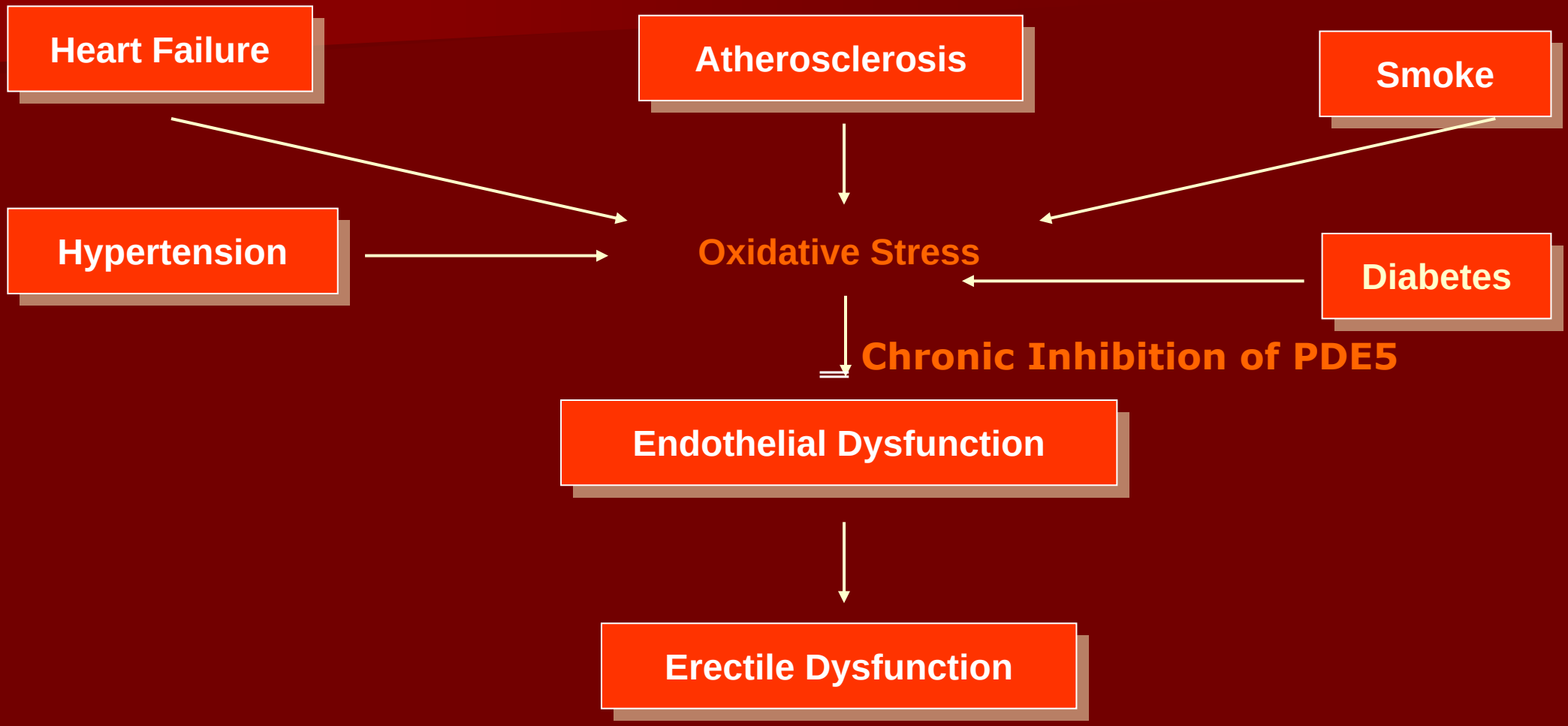


C.Foresta et al, Int J Impotence Res, 2006

FACTORS and THERAPY for ENDOTHELIAL DYSFUNTIONS

Associated Factors with Endothelial Dysfunction	Therapy for Endothelial Dysfunction
Aging	L-arginine
Male	Estrogens
Smoke	Stop
Familiarity for CHD	Antioxidants
<< HDL and >> LDL-COL	Statines
Hypertension	ACE-i
Hyperhomocystinemia	Folic Acid
Diabetes and Obesity	Physical Activity
Erectile Dysfunction	PDE5-i

Chronic Inhibition of PDE5 in Improvement of Endothelial Dysfunction associated with Erectile Dysfunction



Rubanyi GM. J Cardiovasc Pharmacol 1993; 22 (Suppl 4): S1–S4 mod.

PDE5i and Chronic Treatment : Conclusions

- Improvement of ED in patients non responders to PDE5i on demand
- Improvement of FMD (brachial and cavernous arteries)
- Improvement of markers of Endothelial Dysfunction
- Increase of Circulating Endothelial Progenitor Cells
- Improvement of Hormonal Pattern

Is sexual rehabiltation possible?
Yes

Tanks for your attention