



## **AMORE E PSICHE AI TEMPI DEL DIABETE**



# **La sessualità nella persona con diabete: evidenze cliniche e pratica quotidiana**

***“La disfunzione erettile:  
indicatore di rischio  
cardiovascolare”***

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UOC di Medicina interna

Servizio di Endocrinologia e Diabetologia

Ospedale “San Sebastiano Martire” - Frascati (Roma)

# Disfunzione erettile

## Gruppo Italiano Studio Deficit Erettile

identificazione random eseguita da 143 MMG

uomini con età superiore a 18 anni

gennaio 96 - febbraio 97

numerosità del campione: 2010 uomini

prevalenza della DE: 12.8%

Parazzini F et al, Eur Urol, 37:43-49, 2000

*Francesco, 58 anni*

*Anamnesi Fisiologica*

- Familiarità per ipertensione, malattie cardiovascolari e DM2
- Sedentario
- Fumatore  $\approx$  20 sig/die da 30 anni
- Riferisce libido normale
- Da circa 3 anni difficoltà ad ottenere e mantenere l'erezione

## *Anamnesi Patologica Remota*

- Ipertensione arteriosa da 5 anni in terapia con perindopril 10 mg + indapamide 2.5 mg + amlodipina 5 mg
- Alterata glicemia a digiuno da alcuni anni

## *Anamnesi Patologica Prossima*

- Riferisce incremento ponderale di circa 6 kg negli ultimi 10 mesi in seguito a sospensione dell'attività fisica (trauma ginocchio destro)
- Da tre mesi astenia ingravescente, dispnea per sforzi di media entità con episodica precordialgia che regredisce con il riposo

## Anamnesi sessuologica

Riferisce normale desiderio sessuale. Da circa tre anni progressiva difficoltà ad ottenere, ma soprattutto a mantenere una normale erezione tale da poter concludere il rapporto sessuale.

Fa coincidere l'inizio di tale sintomatologia a difficoltà lavorative (Cassa integrazione) intervenute circa 3 anni e mezzo fa.

Spesso va a dormire presto al fine evitare contatti fisici con la partner.

## *EO:*

- Peso 79 kg, altezza 167 cm (BMI = 28.3 kg/m<sup>2</sup>)
- Obesità centrale, circonferenza addominale 109 cm
- Obiettività cardiaca: Azione cardiaca ritmica ( $\cong$  90 bpm)  
compenso cardiocircolatorio, PA 140/85 mmHg
- Polsi periferici isosfigmici
- Obiettività toracica e addominale nella norma
- Non ginecomastia
- Tono dell'umore depresso

# Esami ematochimici

## Profilo metabolico ed ormonale:

- Glicemia a digiuno: 117 mg/dL
- HbA1c: 5.7%
- Uricemia: 5.5 mg/dL
- TSH reflex: 1.2  $\mu$ UI/mL
- PRL: 9 ng/mL
- Testosterone: 3.5 ng/mL
- LH: 12 U/L
- PSA totale: 3.8 ng/mL con normale rapporto L/T
- Colesterolo totale: 169 mg/dL
- Colesterolo HDL: 50 mg/dL
- Trigliceridi: 150 mg/dL

## Esami ematochimici:

- Funzione epatica e renale nella norma
- Emocromo
- Elettroforesi proteica normale
- Microalbuminuria: 14  $\mu$ g/min (v.n. < 20  $\mu$ g/min)
- VES nella norma



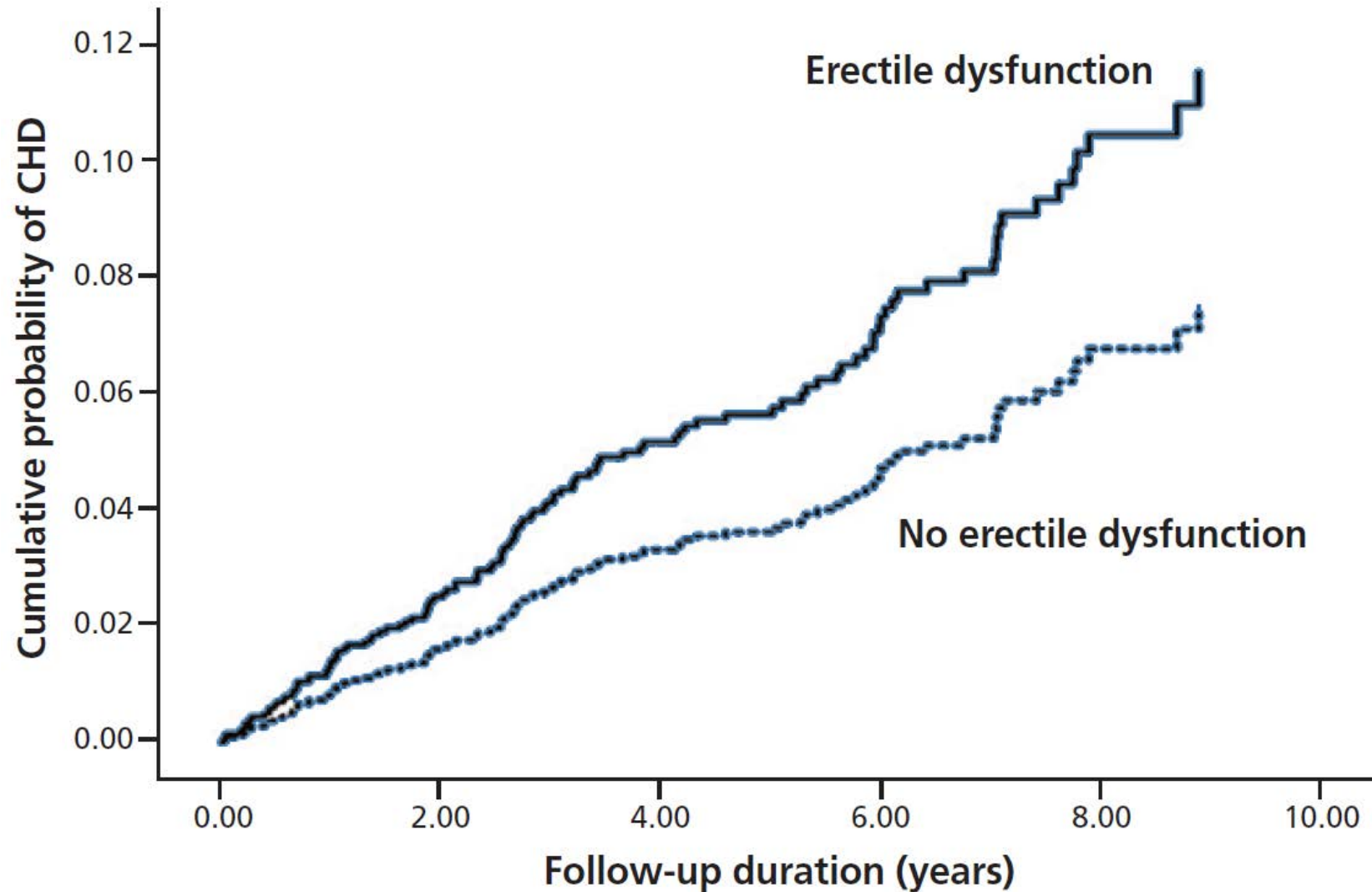
## Esami strumentali:

- ECG: Ritmo sinusale. Anomalie aspecifiche del tratto ST.
- Ecocardiogramma: Modesta ipertrofia della parete posteriore. Massa ventricolare sinistra aumentata. Buona cinesi globale e segmentaria. Ridotta compliance ventricolare sinistra.
- ECD dei tronchi sovraortici: Ispessimento medio-intimale diffuso a carico delle carotidi comuni; placca fibrosa alla biforcazione sinistra.
- Esame fundus oculi: Quadro di retinopatia ipertensiva di I - II grado.

In seguito alla comparsa di angor da sforzo mentre saliva le scale, effettua un test ergometrico che risulta positivo per ischemia.

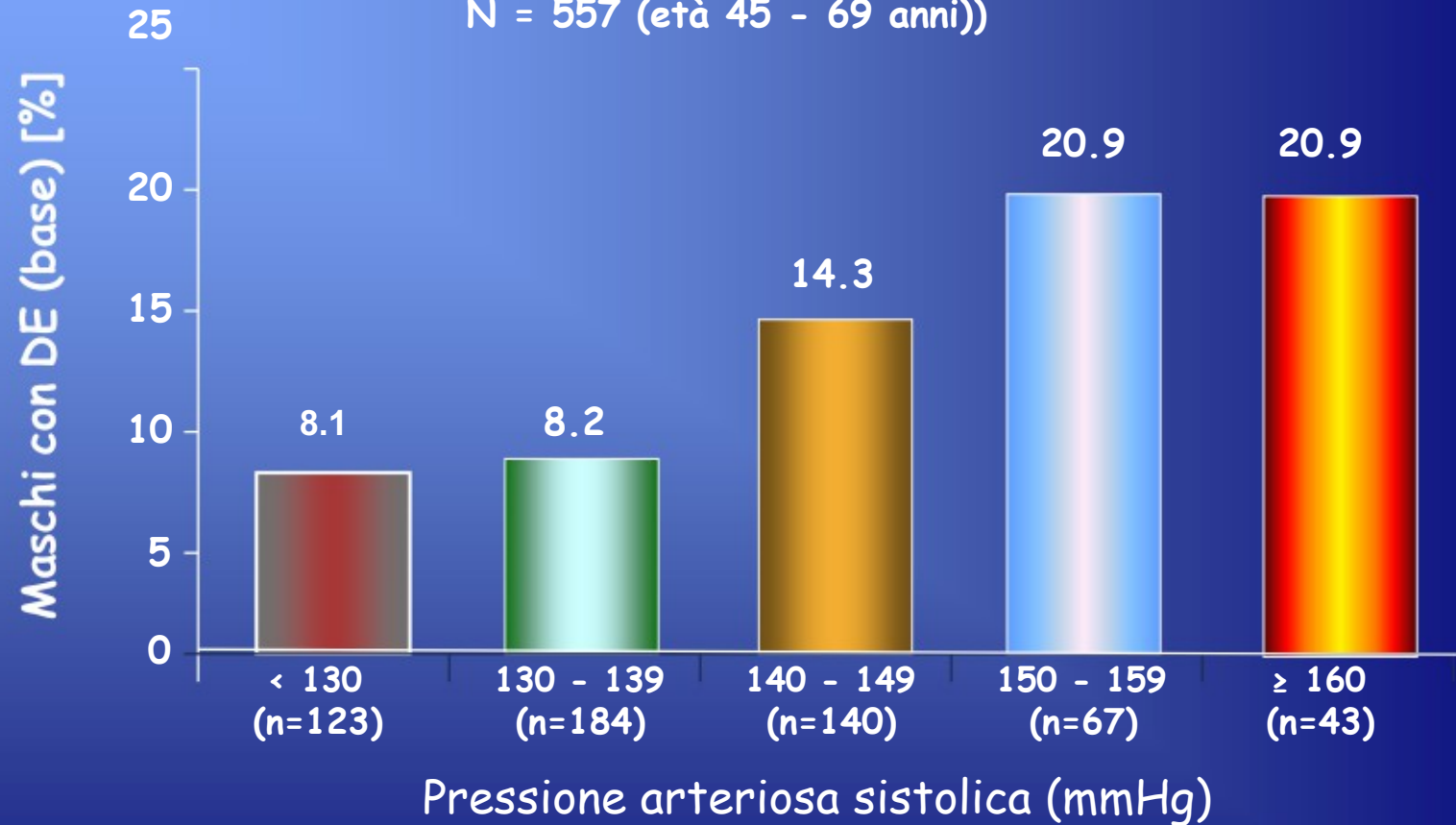
Viene sottoposto a coronarografia con riscontro di lesione critica sul ramo intermedio, trattata con PTCA + stent medicato.

**Figure 4.** Cumulative hazard ratio of coronary heart disease (CHD) events stratified by erectile dysfunction



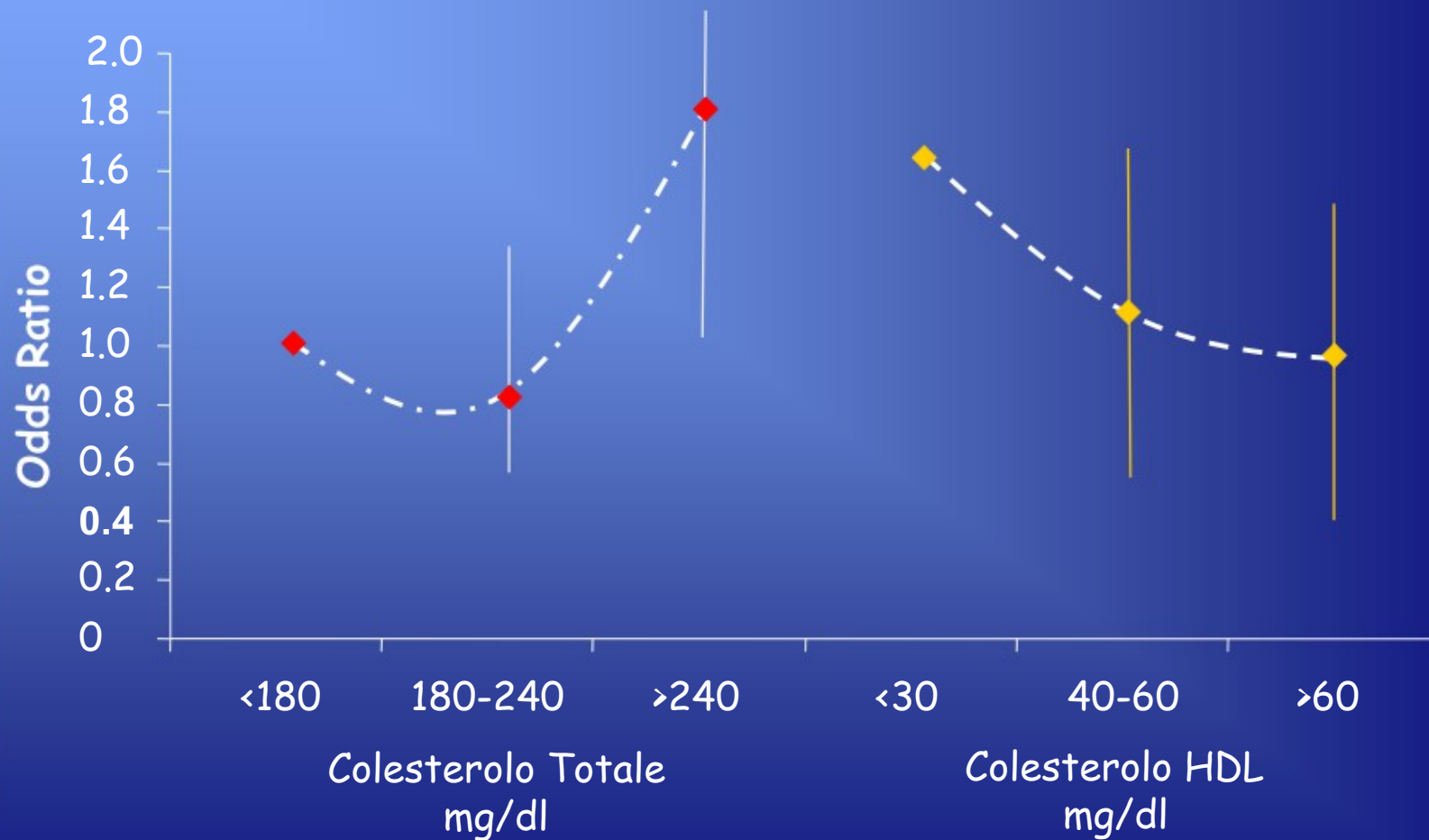
# Ipertensione e DE

Treatment of Mild Hypertension Study (TOMHS)  
N = 557 (età 45 - 69 anni)



Grimm RH, Hypertension 1997;29:8-14

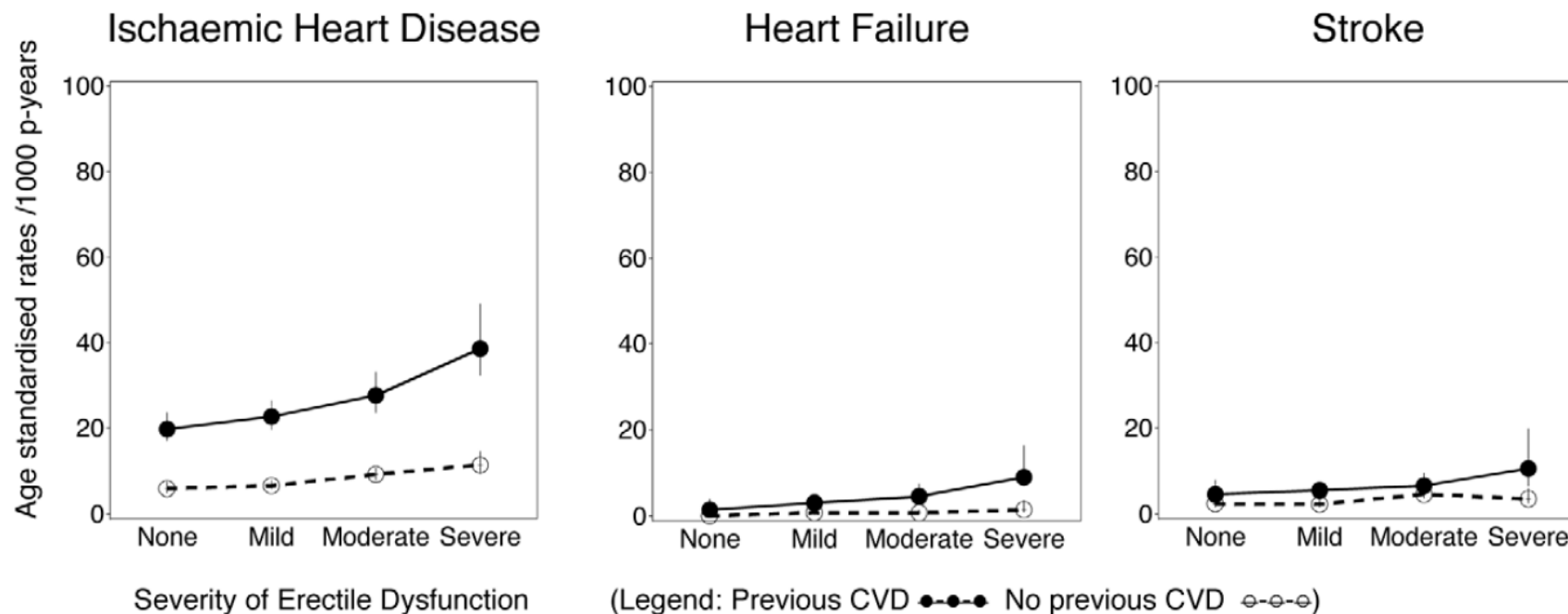
# Odds Ratio del DE in rapporto ai livelli di Colesterolo Totale e Colesterolo HDL



Braun M, J Impot Res 2001; 12: 305-11

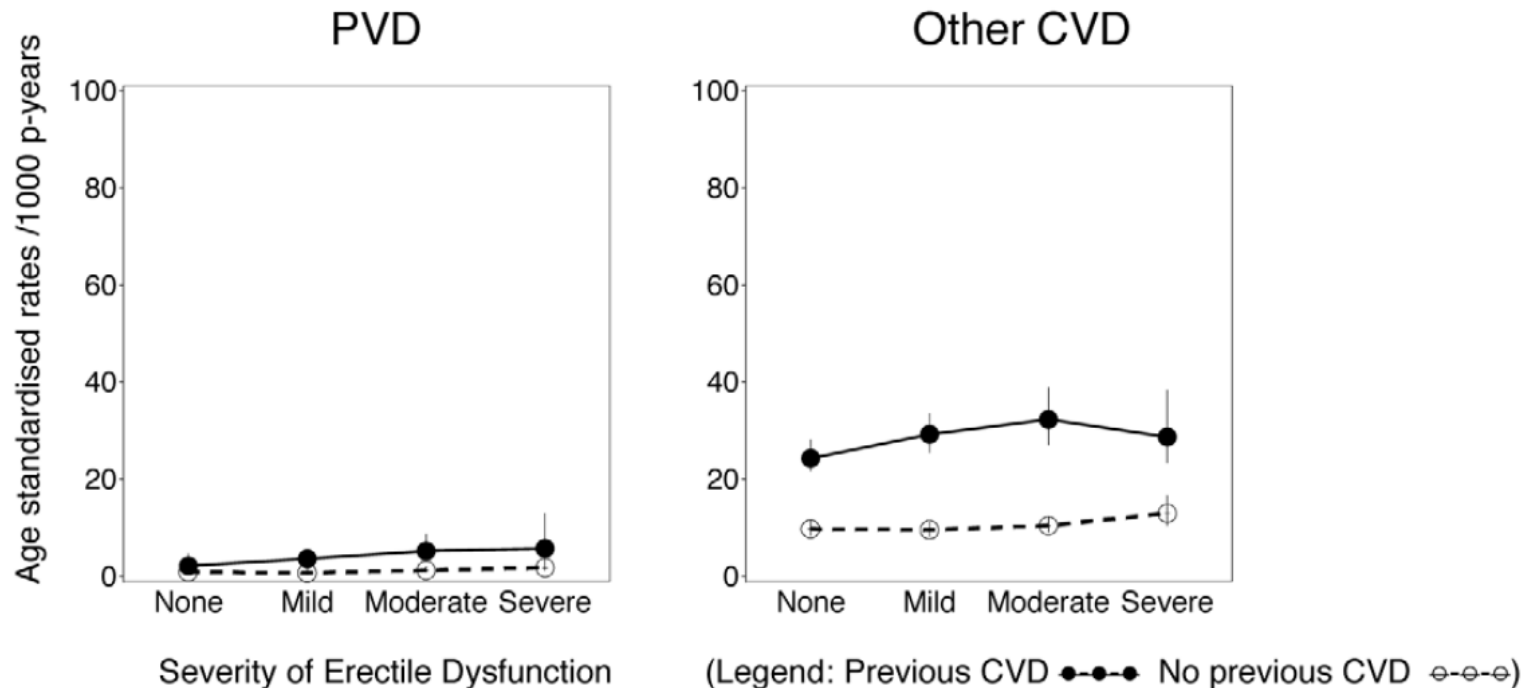
# Erectile Dysfunction Severity as a Risk Marker for Cardiovascular Disease Hospitalisation and All-Cause Mortality: A Prospective Cohort Study

Emily Banks<sup>1,2\*</sup>, Grace Joshy<sup>1</sup>, Walter P. Abhayaratna<sup>3</sup>, Leonard Kritharides<sup>4</sup>, Peter S. Macdonald<sup>5</sup>, Rosemary J. Korda<sup>1</sup>, John P. Chalmers<sup>6</sup>



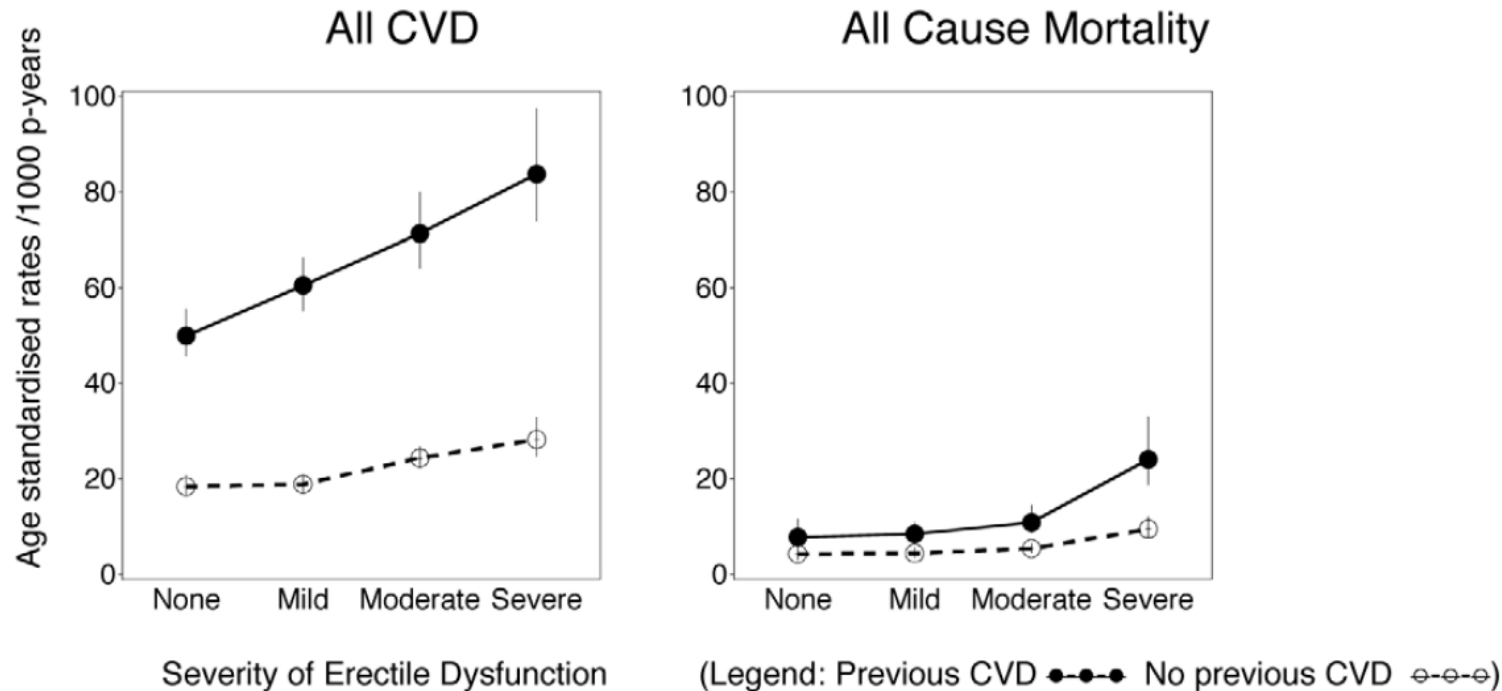
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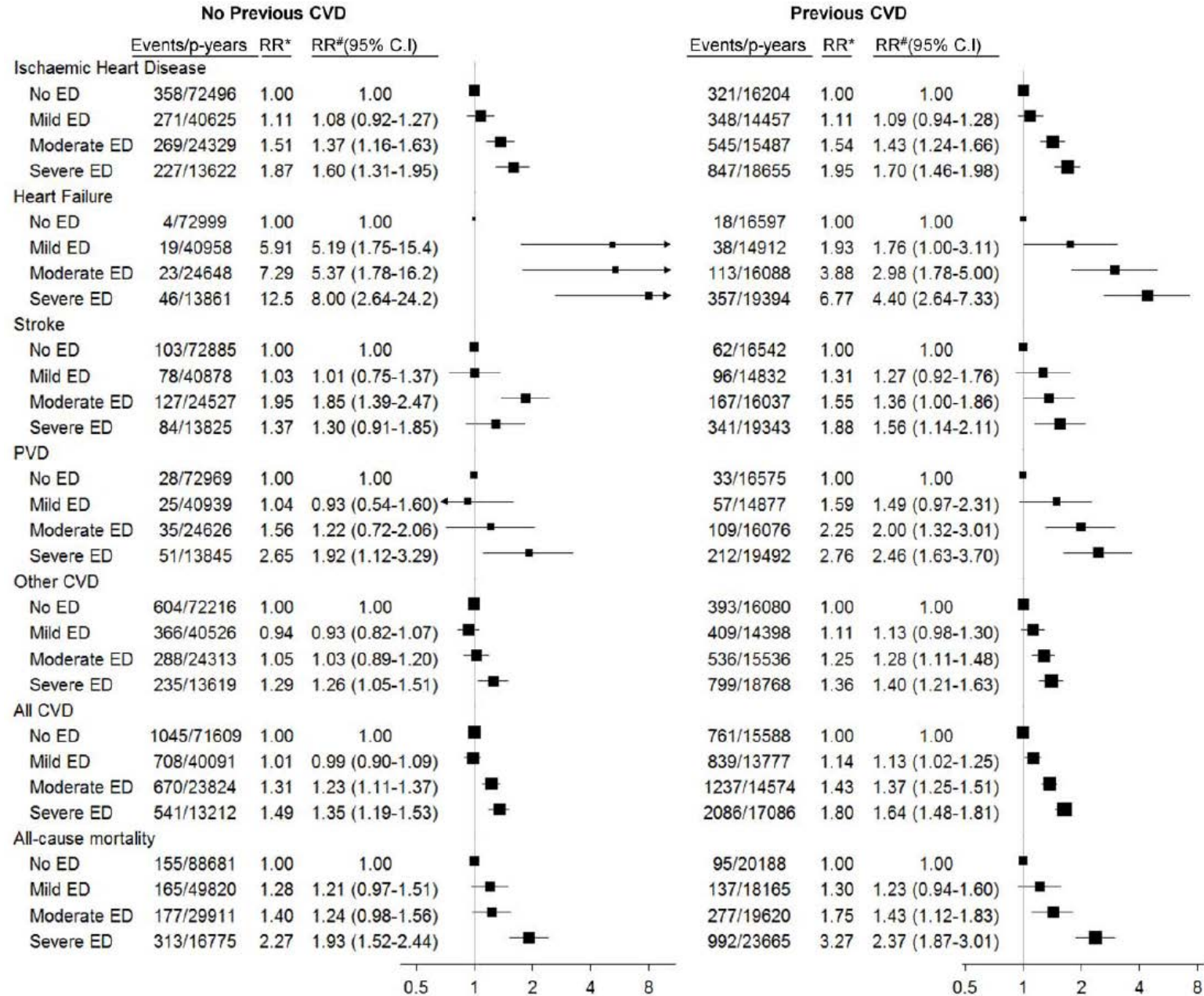
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# Rischio relativo di ricoveri per malattie cardiovascolari e mortalità per tutte le cause in funzione della severità della DE

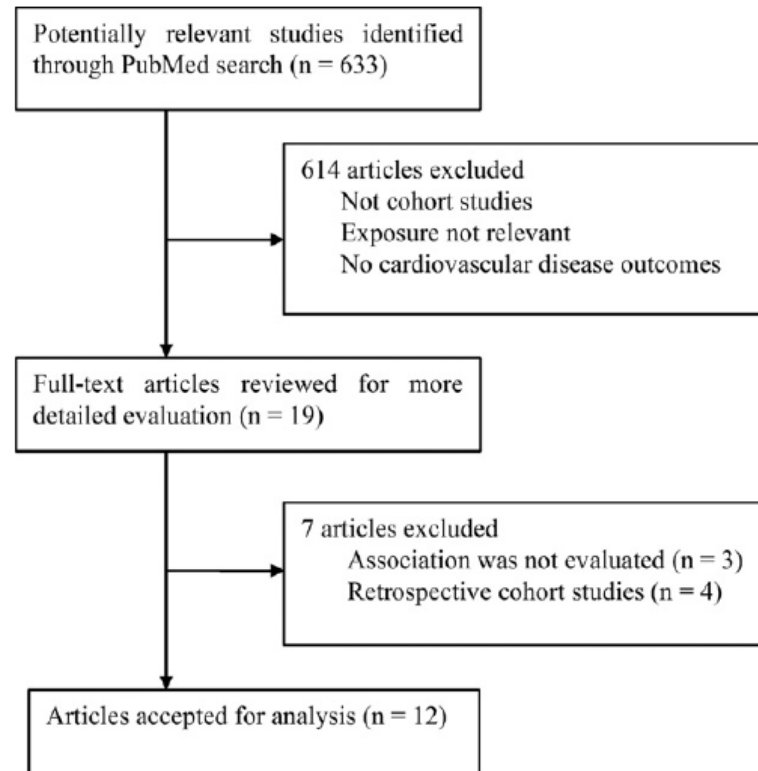


# Erectile Dysfunction and Risk of Cardiovascular Disease

## Meta-Analysis of Prospective Cohort Studies

Jia-Yi Dong, BSc,\* Yong-Hong Zhang, MD, PHD,† Li-Qiang Qin, MD, PHD\*

*Suzhou, China*

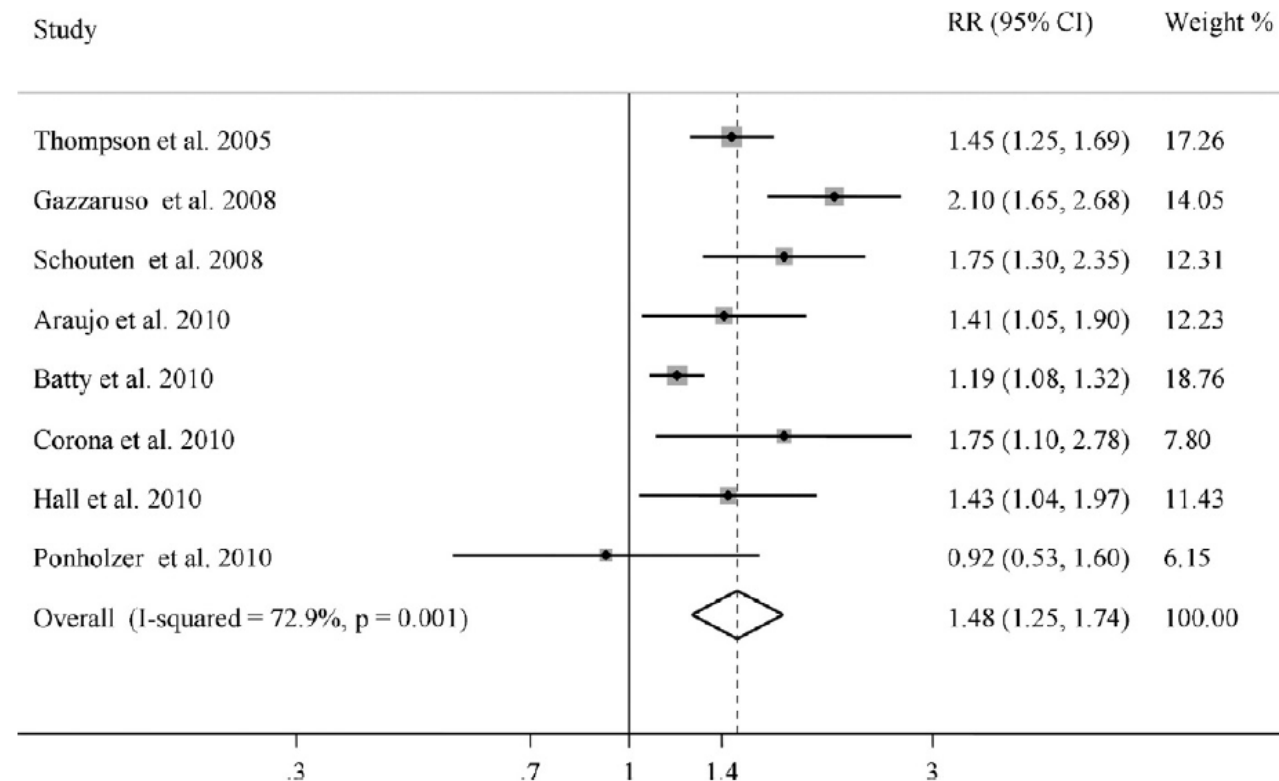


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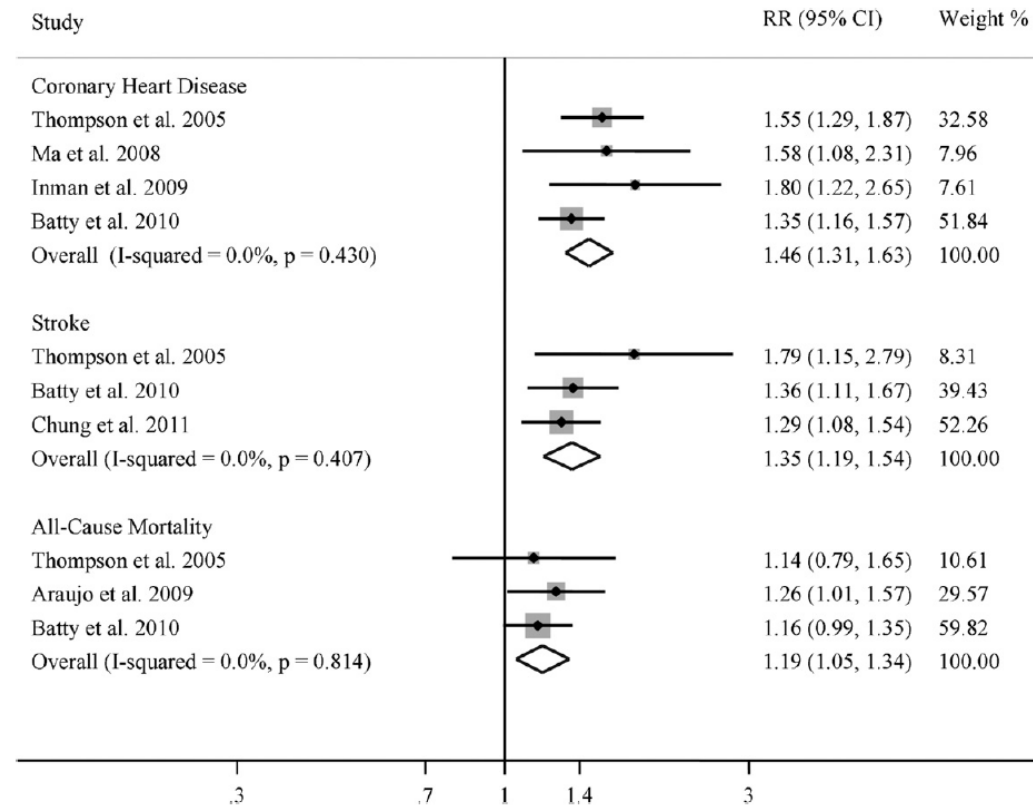


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**CLINICAL RESEARCH**

**Cardiovascular Risk**

## **Erectile Dysfunction and Later Cardiovascular Disease in Men With Type 2 Diabetes**

Prospective Cohort Study Based on the  
ADVANCE (Action in Diabetes and Vascular Disease:  
Preterax and Diamicron Modified-Release Controlled Evaluation) Trial

G. David Batty, PhD,<sup>\*†‡</sup> Qiang Li, MBIostat,<sup>†</sup> Sébastien Czernichow, MD, PhD,<sup>†§</sup>  
Bruce Neal, MD, PhD,<sup>†</sup> Sophia Zoungas, MD, PhD,<sup>†||</sup> Rachel Huxley, PhD,<sup>†</sup>  
Anushka Patel, MD, PhD,<sup>†</sup> Bastiaan E. de Galan, MD, PhD,<sup>†¶</sup> Mark Woodward, PhD,<sup>†#</sup>  
Pavel Hamet, MD, PhD,<sup>\*\*</sup> Stephen B. Harrap, MD, PhD,<sup>††</sup> Neil Poulter, MD, PhD,<sup>‡‡</sup>  
John Chalmers, MD, PhD,<sup>†</sup> on behalf of the ADVANCE Collaborative Group

*Glasgow and London, United Kingdom; Sydney and Melbourne, Australia; Bobigny, France;  
Nijmegen, the Netherlands; New York, New York; and Montreal, Quebec, Canada*

### Erectile Dysfunction and Later Cardiovascular Disease in Men With Type 2 Diabetes

Prospective Cohort Study Based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicros Modified-Release Controlled Evaluation) Trial

G. David Batt, PhD,<sup>1</sup> Qing Li, MBE<sup>2,3,4</sup>, Sebastian Carnicko, MD, PhD,<sup>5</sup> Bruce Neal, MD, PhD,<sup>6</sup> Sophie Zoungas, MD, PhD,<sup>7,8</sup> Rachel Hussey, PhD,<sup>9</sup> Anshika Patel, MD, PhD,<sup>1</sup> Benjamin E. de Galon, MD, PhD,<sup>10</sup> Mark Woodward, PhD,<sup>11</sup> Peter Haines, MD, PhD,<sup>12</sup> Stephen B. Harrop, MD, PhD,<sup>13</sup> Neil Powles, MD, PhD,<sup>14</sup> John Chalmers, MD, PhD,<sup>15</sup> on behalf of the ADVANCE Collaborative Group  
*Chengde and London, United Kingdom; Sydney and Melbourne, Australia; Beijing, P.R. China; Nijmegen, the Netherlands; New York, New York; and Montreal, Quebec, Canada*

JACC Vol. 55, No. 23, 2010  
November 30, 2010:1908-13

**Table 3**

**Multiple Adjusted Hazard Ratios (95% Confidence Intervals) for the Relation of Change in ED Status Between Baseline and 24-Month Follow-Up With Selected Health Outcomes in Men in the ADVANCE Trial (n = 5,427)**

| ED at Baseline    | ED at 24 Months | n     | Total Mortality (n = 388) | CVD (n = 965)    | CHD (n = 399)    | Cerebrovascular Disease (n = 221) | Dementia (n = 48) | Cognitive Decline (n = 913) |
|-------------------|-----------------|-------|---------------------------|------------------|------------------|-----------------------------------|-------------------|-----------------------------|
| No                | No              | 1,964 | 1.00 (reference)          | 1.00             | 1.00             | 1.00                              | 1.00              | 1.00                        |
| Yes               | No              | 814   | 1.05 (0.75-1.48)          | 1.24 (1.01-1.52) | 1.13 (0.81-1.56) | 1.18 (0.76-1.83)                  | 1.30 (0.34-5.00)  | 1.34 (1.10-1.65)            |
| No                | Yes             | 618   | 1.08 (0.74-1.56)          | 0.98 (0.78-1.25) | 1.07 (0.74-1.56) | 1.05 (0.65-1.70)                  | 3.70 (1.19-11.46) | 1.07 (0.85-1.36)            |
| Yes               | Yes             | 2031  | 1.29 (1.00-1.66)          | 1.28 (1.09-1.50) | 1.45 (1.13-1.85) | 1.44 (1.04-2.01)                  | 3.11 (1.18-8.18)  | 1.32 (1.12-1.55)            |
| p value for trend |                 | —     | 0.0419                    | 0.0081           | 0.0032           | 0.0365                            | 0.0089            | 0.0051                      |

Multiple adjustment as in Table 2. Analytical sample was based on a subgroup of men who did not develop any of the health outcomes of interest between baseline and follow-up at 24 months. Abbreviations as in Table 2.

**Erectile Dysfunction and Later Cardiovascular Disease in Men With Type 2 Diabetes**

Prospective Cohort Study Based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicros Modified-Release Controlled Evaluation) Trial

G. David Batty, PhD,<sup>1</sup> Qing Li, MSc,<sup>1</sup> Sebastian Carmichael, MD, PhD,<sup>1</sup> Bruce Neal, MD, PhD,<sup>2</sup> Sophie Zoungas, MD, PhD,<sup>1,3</sup> Rachel Hussey, PhD,<sup>1</sup> Anshika Patel, MD, PhD,<sup>1</sup> Benjamin E. de Galon, MD, PhD,<sup>1</sup> Mark Woodward, PhD,<sup>1</sup> Peter Haines, MD, PhD,<sup>4</sup> Stephen B. Harrop, MD, PhD,<sup>1</sup> Neil Powles, MD, PhD,<sup>1</sup> John Chalmers, MD, PhD,<sup>1</sup> on behalf of the ADVANCE Collaborative Group  
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**Table 3** Multiple Adjusted Hazard Ratios (95% CIs) for Dementia Between Baseline and 24-Month Follow-Up by ED Status in the ADVANCE Trial (n = 5,427)

| ED at Baseline    | ED at 24 Months | n     | Total M (n = 10,000) |
|-------------------|-----------------|-------|----------------------|
| No                | No              | 1,964 | 1.00 (reference)     |
| Yes               | No              | 814   | 1.05 (0.73-1.48)     |
| No                | Yes             | 618   | 1.08 (0.73-1.61)     |
| Yes               | Yes             | 2,031 | 1.29 (1.00-1.66)     |
| p value for trend |                 | —     | 0.0089               |

Multiple adjustment as in Table 2. Analytical sample was based on 5,427 men with type 2 diabetes. Abbreviations as in Table 2.

**Dementia**  
**(n = 48)**

---

**1.00**

---

**1.30 (0.34-5.00)**

---

**3.70 (1.19-11.46)**

---

**3.11 (1.18-8.18)**

---

**0.0089**

| ED Status         | Dementia (n = 48) | Cognitive Decline (n = 913) |
|-------------------|-------------------|-----------------------------|
| None              | 1.00              | 1.00                        |
| ED at baseline    | 1.30 (0.34-5.00)  | 1.34 (1.10-1.65)            |
| ED at 24 months   | 3.70 (1.19-11.46) | 1.07 (0.85-1.36)            |
| ED at both        | 3.11 (1.18-8.18)  | 1.32 (1.12-1.55)            |
| p value for trend | 0.0089            | 0.0051                      |

Interest between baseline and follow-up at 24 months.

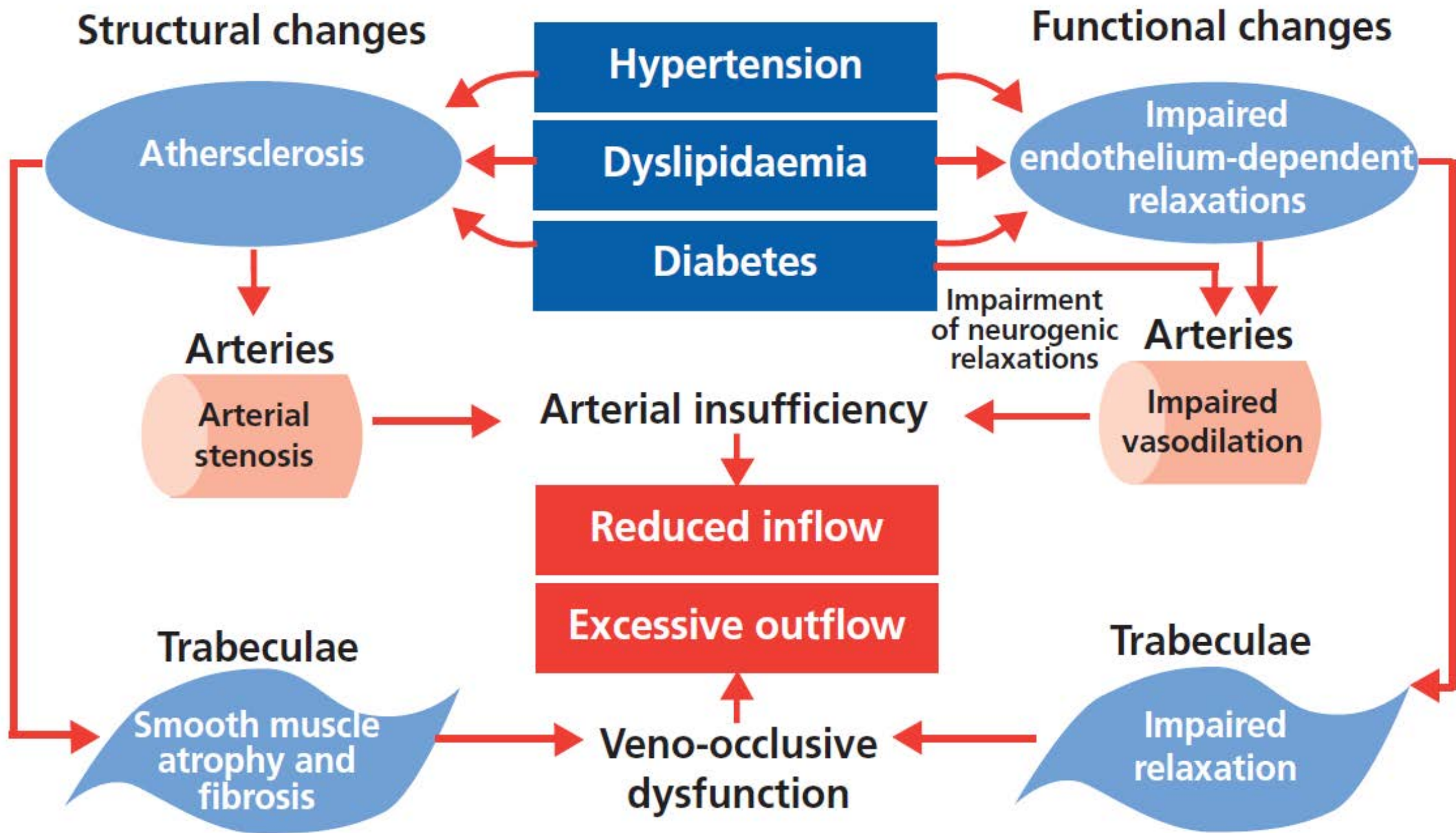
## ORIGINAL ARTICLE

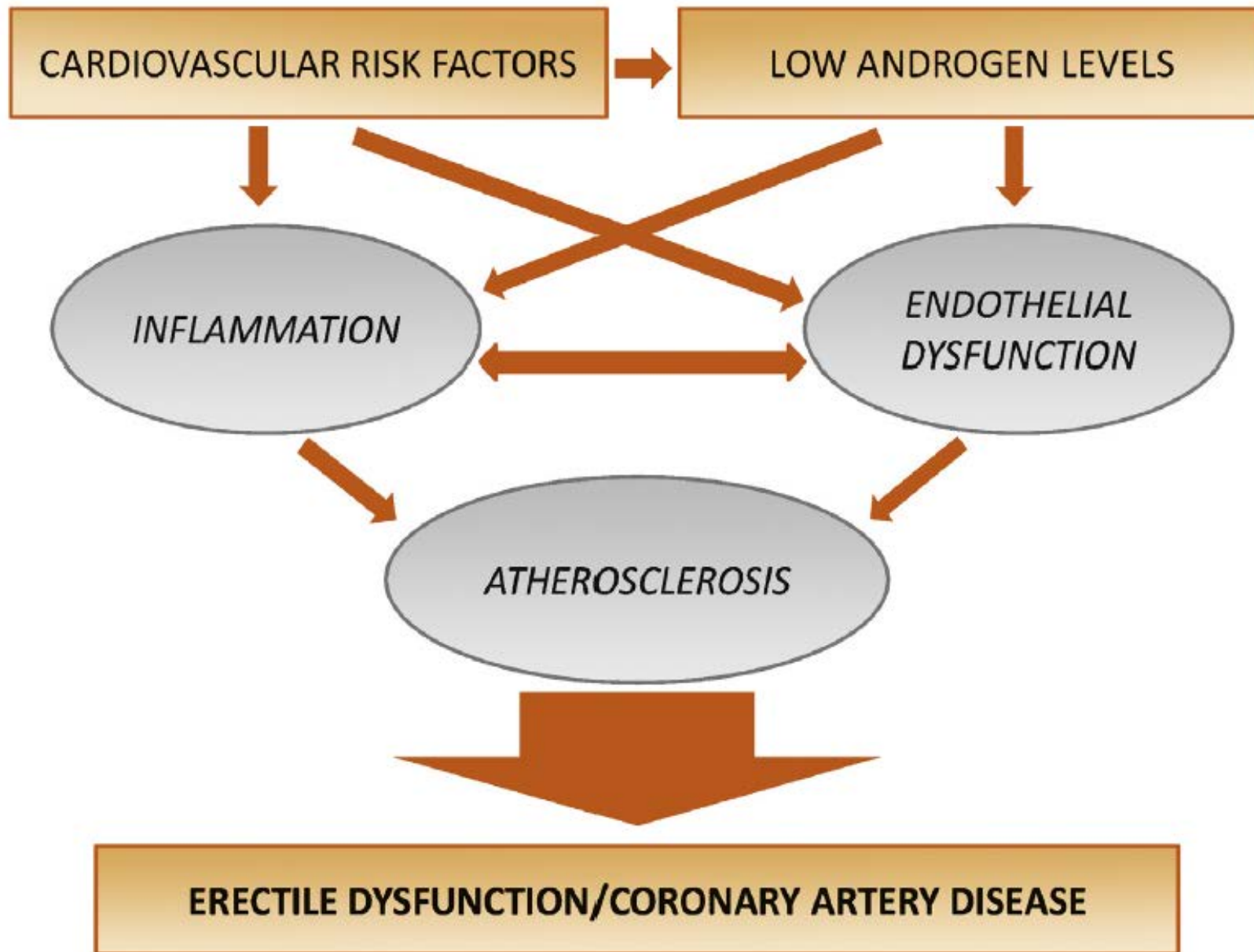
# Is penile atherosclerosis the link between erectile dysfunction and cardiovascular risk? An autopsy study

A Ponholzer<sup>1,5</sup>, J Stopfer<sup>2,5</sup>, G Bayer<sup>3</sup>, M Susani<sup>3</sup>, F Steinbacher<sup>1</sup>, F Herbst<sup>2</sup>, P Schramek<sup>1</sup>, S Madersbacher<sup>4</sup> and J Maresch<sup>3</sup>

Erectile dysfunction (ED) is increasingly linked to coronary heart disease risk. Aim of this study was to test the hypothesis whether this association is due to penile atherosclerosis. We evaluated the prevalence and severity of penile atherosclerosis in relation to coronary and peripheral atherosclerosis. Between January and June 2010, a consecutive series of 31 men underwent an autopsy at the Department of Pathology at the Medical University Vienna. Atherosclerosis at the following localizations were histologically classified: right coronary artery, left coronary artery, left circumflex artery, internal iliac artery, dorsal penile artery and deep penile artery (bilateral). Coronary and peripheral atherosclerosis was present in 87.1 and 77.4% of cases. Atherosclerosis of penile arteries was detectable in only 4 men (12.9%). The only factor linked to penile atherosclerosis was diabetes ( $P = 0.03$ ). All other parameters as assessed according to medical history, general finding from autopsy or histological results regarding arterial lesions in general were not correlated to penile arterial lesions. In contrast to the high prevalence of atherosclerosis in general, penile arterial lesions are rarely present.







# Momento patogenetico comune

Ipertensione

Diabete

Dislipidemie

Fumo

Disfunzione Endoteliale

Disfunzione Erettile

Patologia Aterosclerotica

# Disunzione erettile e patologia cardiovascolare

## Le arterie pudende

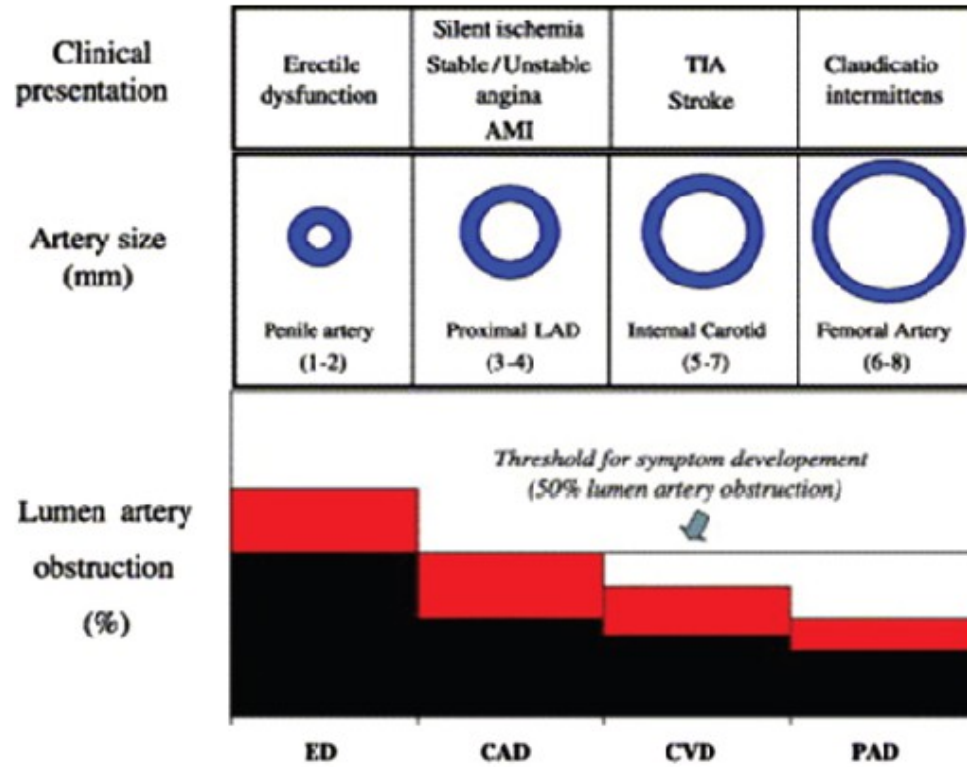
**Table 1** Artery size and atherothrombosis. A significant restriction to flow in the penile arteries may be subclinical in larger vessels.

| Artery   | Diameter (mm) | Clinical Event          |
|----------|---------------|-------------------------|
| Penile   | 1–2           | ED                      |
| Coronary | 3–4           | Ischaemic heart disease |
| Carotid  | 5–7           | TIA/stroke              |
| Femoral  | 6–8           | Claudication            |

# Erectile Dysfunction

## *A Disease Marker for Cardiovascular Disease*

*David Shin, MD,\* Gerard Pregoner, Jr., MA,† and Julius M. Gardin, MD‡*



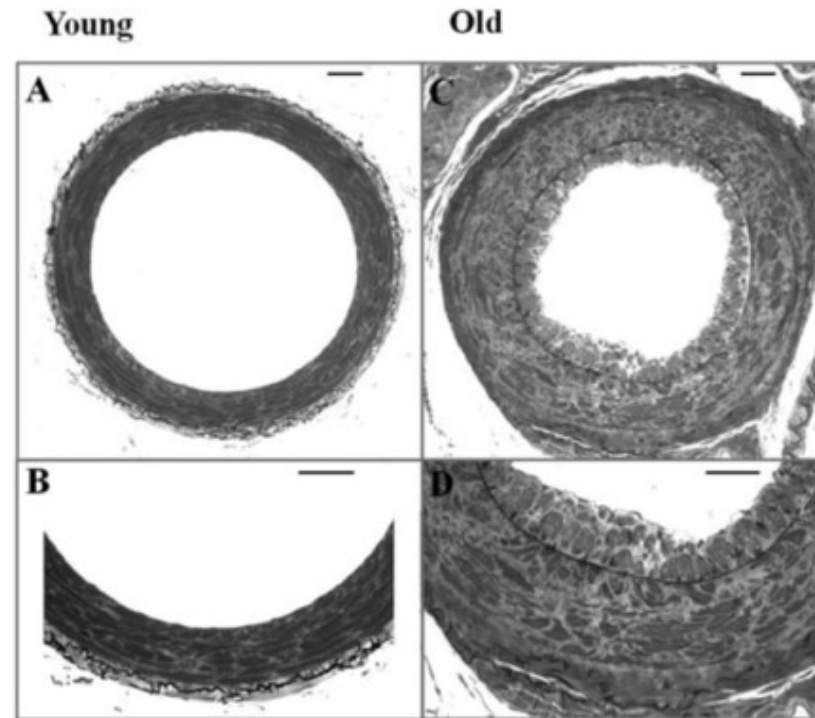
*(Cardiology in Review 2011;19: 5-11)*

# Impact of Hypertension, Aging, and Antihypertensive Treatment on the Morphology of the Pudendal Artery

Johanna L. Hannan, PhD,\* Mark C. Blaser, BEng,\* Judith J. Pang, Med Tech (Dip),\*\*  
Stephen M. Adams, BEng,\* Stephen C. Pang, PhD,† and Michael A. Adams, PhD\*‡

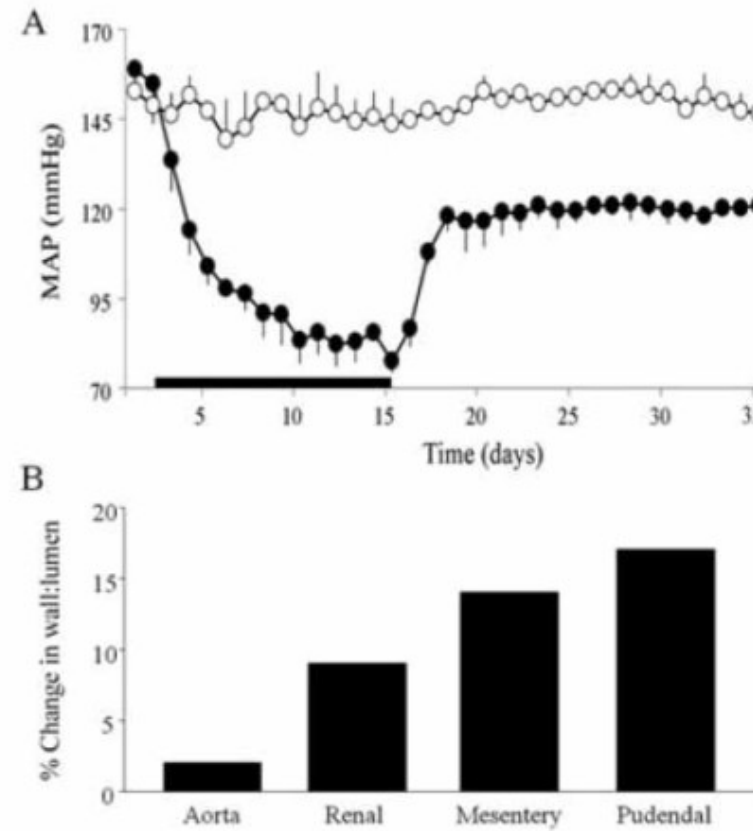
\*Department of Pharmacology & Toxicology, Queen's University, Kingston, Ontario, Canada; †Department of Anatomy, Queen's University, Kingston, Ontario, Canada; ‡Department of Urology, Queen's University, Kingston, Ontario, Canada

DOI: 10.1111/j.1743-6109.2010.02191.x



**Impact of Hypertension, Aging, and Antihypertensive Treatment on the Morphology of the Pudendal Artery**

Johanna L. Hannan, PhD,<sup>1</sup> Mark C. Bleuer, BEng,<sup>2</sup> Judith J. Pang, MScTech (Dist),<sup>1\*</sup> Stephen M. Adams, BEng,<sup>1</sup> Stephen C. Pang, PhD,<sup>1</sup> and Michael A. Adams, PhD<sup>1,2</sup>  
<sup>1</sup>Department of Pharmacology & Toxicology, Queen's University, Kingston, Ontario, Canada; <sup>2</sup>Department of Anatomy, Queen's University, Kingston, Ontario, Canada; <sup>3</sup>Department of Urology, Queen's University, Kingston, Ontario, Canada  
DOI: 10.1111/j.1743-1082.2010.02191.x



**Figure 4** (A) Treatment with enalapril and hydrochlorothiazide (closed circles) induced a significant reduction in mean arterial pressure (MAP) during treatment compared with controls (open circles) that persisted when treatment was withdrawn. The black bar represents the 2-week treatment period. Data is presented as 24-hour mean  $\pm$  standard deviation. (B) Percent changes in the wall-to-lumen ratio of aorta, left renal, first order mesenteric, and distal pudendal arteries after treatment was withdrawn.



# Internal Pudendal Artery Stenoses and Erectile Dysfunction: Correlation with Angiographic Coronary Artery Disease

Jason H. Rogers,<sup>1\*</sup> MD, Houshang Karimi,<sup>1</sup> MD, John Kao,<sup>1</sup> MD, Daniel Link,<sup>1</sup> MD, Javid Javidan,<sup>2</sup> MD, Dwayne S. Yamasaki,<sup>3</sup> PhD, Mark Dolan,<sup>3</sup> BS, John R. Laird,<sup>1</sup> MD, and Reginald I. Low,<sup>1</sup> MD

**TABLE III. Pelvic and Coronary Angiographic Findings**

| Pelvic Arteries          | Stenosis (%) | Diameter (mm) |
|--------------------------|--------------|---------------|
| Distal Aorta             | 8 ± 14       | 16.0 ± 2.5    |
| Common iliac             |              |               |
| Left                     | 25 ± 31      | 10.4 ± 1.4    |
| Right                    | 10 ± 13      | 10.8 ± 1.4    |
| Internal iliac           |              |               |
| Left                     | 15 ± 6.5     | 6.7 ± 1.7     |
| Right                    | 25 ± 19      | 6.4 ± 1.3     |
| Internal pudendal        |              |               |
| Left                     | 60 ± 32      | 2.7 ± 0.5     |
| Right                    | 52 ± 30      | 2.7 ± 0.4     |
| Coronary Arteries        |              |               |
| Left main                | 15 ± 17      | 4.6 ± 0.9     |
| Left anterior descending | 56 ± 28      | 3.0 ± 0.9     |
| Circumflex               | 55 ± 33      | 2.8 ± 0.7     |
| Right coronary artery    | 65 ± 29      | 3.5 ± 0.6     |

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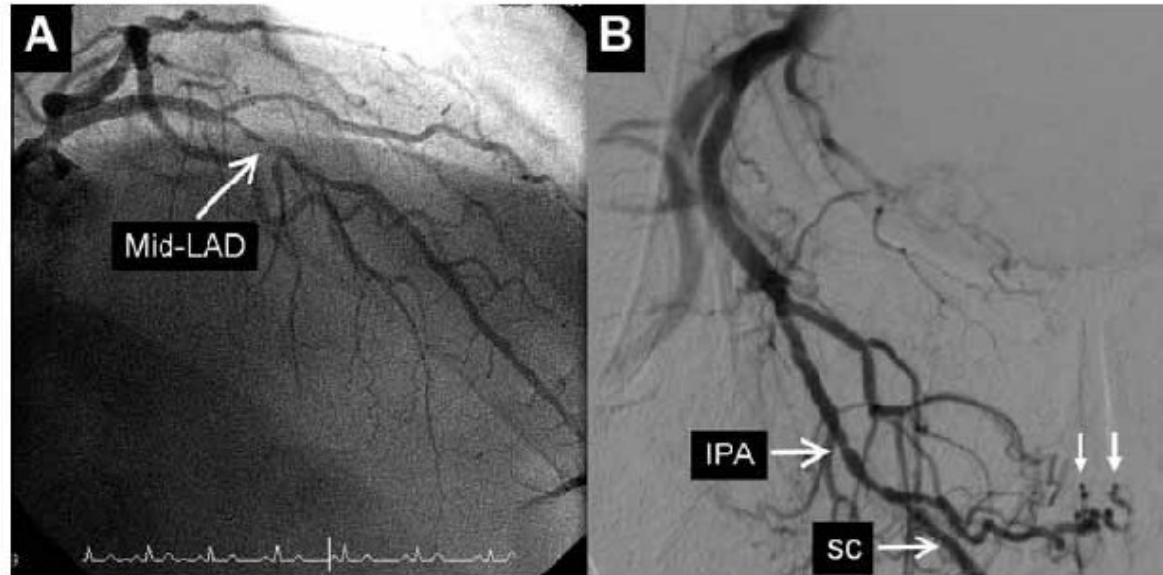
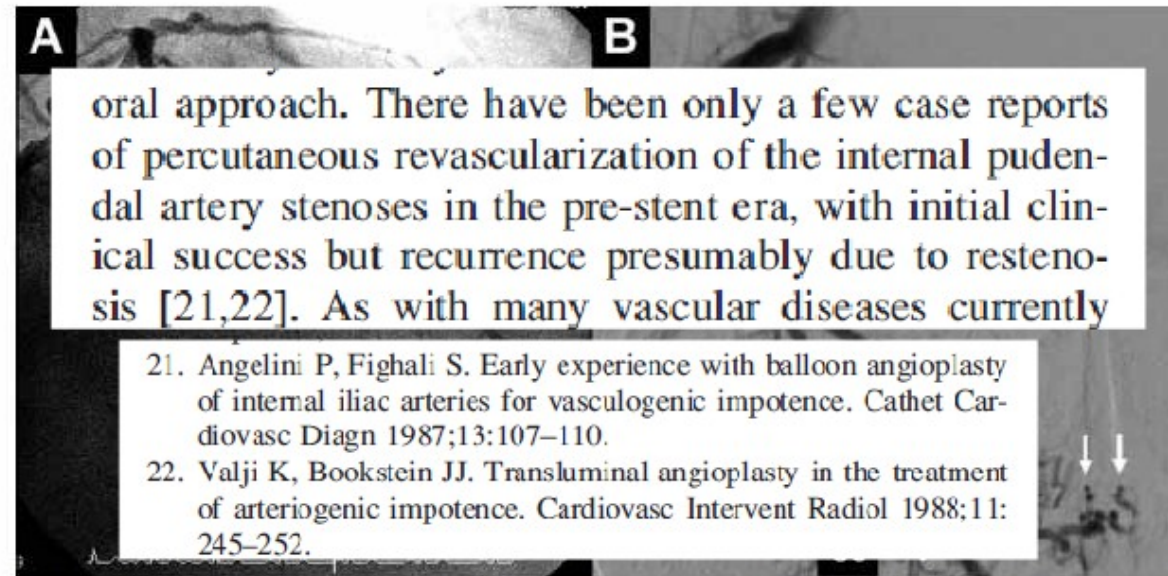


Fig. 2 Representative angiographic findings. A: Severe mid-left anterior descending coronary artery stenosis (arrow). B: In the same subject, severe focal unilateral distal right internal pudendal artery (IPA) stenosis before bifurcation into scrotal (sc) and cavernosal branches (double arrows) at the base of the penis.

# Internal Pudendal Artery Stenoses and Erectile Dysfunction: Correlation with Angiographic Coronary Artery Disease

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**Fig. 2** Representative angiographic findings. **A:** Severe mid-left anterior descending coronary artery stenosis (arrow). **B:** In the same subject, severe focal unilateral distal right internal pudendal artery (IPA) stenosis before bifurcation into scrotal (sc) and cavernosal branches (double arrows) at the base of the penis.



# The Princeton III Consensus Recommendations for the Management of Erectile Dysfunction and Cardiovascular Disease

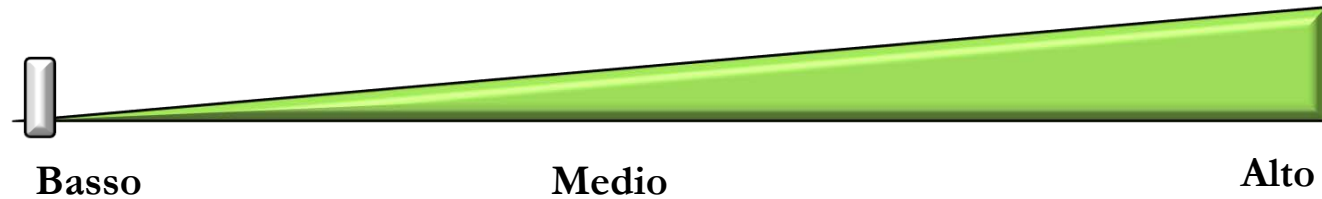
Ajay Nehra, MD; Graham Jackson, FRCP, FESC; Martin Miner, MD; Kevin L. Billups, MD;  
Arthur L. Burnett, MD, MBA; Jacques Buvat, MD; Culley C. Carson, MD;  
Glenn R. Cunningham, MD; Peter Ganz, MD; Irwin Goldstein, MD; Andre T. Guay, MD;  
Geoff Hackett, MD; Robert A. Kloner, MD, PhD; John Kostis, MD; Piero Montorsi, MD;  
Melinda Ramsey, PhD; Raymond Rosen, PhD; Richard Sadovsky, MD;  
Allen D. Seftel, MD; Ridwan Shabsigh, MD; Charalambos Vlachopoulos, MD;  
and Frederick C. W. Wu, MD

**TABLE 1. Relative Risks for Men With Erectile Dysfunction**

|                        | Relative risk | 95% Confidence interval | P value |
|------------------------|---------------|-------------------------|---------|
| Overall                | 1.48          | 1.25-1.74               | <.001   |
| Coronary heart disease | 1.46          | 1.31-1.63               | <.001   |
| Stroke                 | 1.35          | 1.19-1.54               | <.001   |
| All-cause mortality    | 1.19          | 1.05-1.34               | .005    |

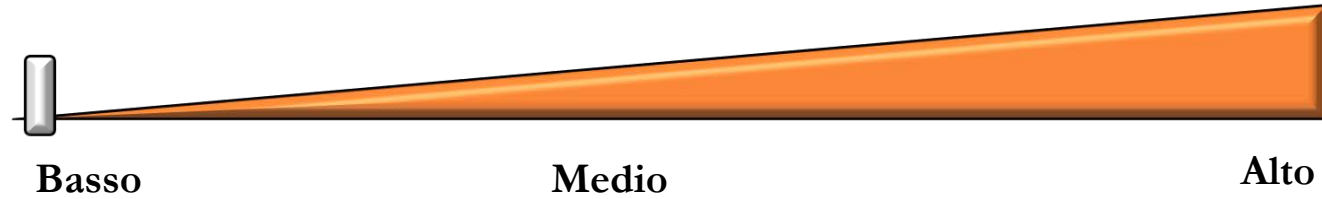
Adapted from *J Am Coll Cardiol.*<sup>15</sup>

## Basso rischio



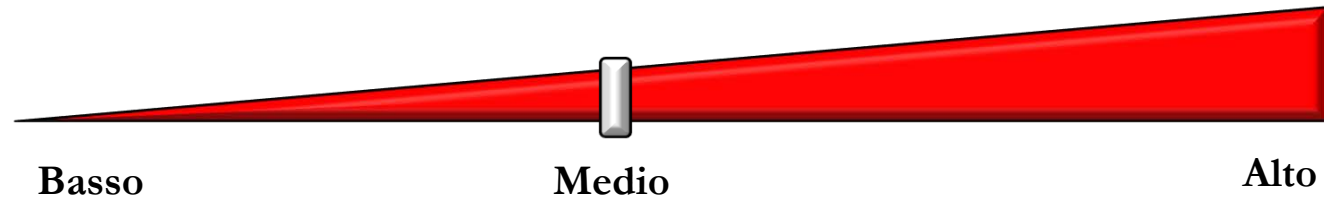
- ✓ Ipertensione ben controllata
- ✓ Angina stabile lieve
- ✓ Malattia coronarica stabile (ad esempio pazienti sottoposti con successo a precedente rivascolarizzazione)
- ✓ Infarto miocardico non complicato (> 6 – 8 settimane)
- ✓ Valvulopatie lievi
- ✓ Pazienti asintomatici con meno di tre fattori di rischio cardiovascolare (genere escluso)
- ✓ Insufficienza cardiaca congestizia lieve (NYHA I)
- ✓ Vasculopatia periferica

## Basso Intermedio



- ✓ Angina stabile moderata
- ✓ Recente infarto miocardico o stroke (2 - 6 settimane)
- ✓ Aritmia da cause non note
- ✓ Pazienti asintomatici con  $\geq$  tre fattori di rischio cardiovascolare (genere escluso)
- ✓ Insufficienza cardiaca congestizia lieve - moderata (NYHA II)
- ✓ Malattia aterosclerotica non cardiaca (vasculopatia periferica o stroke)

## Alto rischio

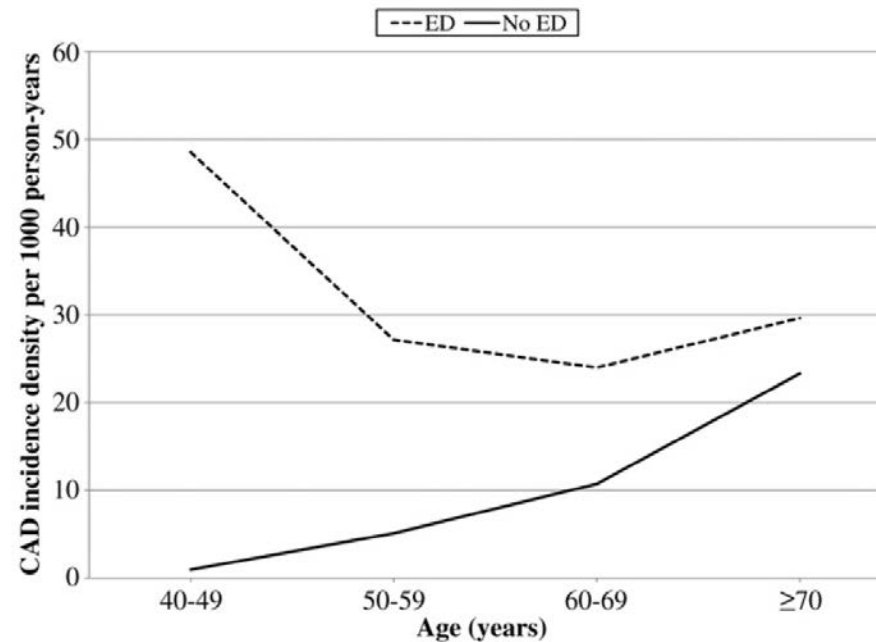


- ✓ Angina instabile o refrattaria
- ✓ Ipertensione non controllata
- ✓ Recente infarto miocardico o stroke (< 2 settimane)
- ✓ Aritmie ad alto rischio
- ✓ Cardiomiopatia ipertrofica od altre cardiomiopatie
- ✓ Valvulopatie moderato - severe
- ✓ Insufficienza cardiaca congestizia moderata - severa (NYHA III - IV)



# Prognostic utility of erectile dysfunction for cardiovascular disease in younger men and those with diabetes

Martin Miner, MD,<sup>a</sup> Allen D. Seftel, MD, FACS,<sup>b</sup> Ajay Nehra, MD,<sup>c</sup> Peter Ganz, MD,<sup>d</sup> Robert A. Kloner, MD, PhD,<sup>e</sup> Piero Montorsi, MD,<sup>f</sup> Charalambos Vlachopoulos, MD,<sup>g</sup> Melinda Ramsey, PhD,<sup>h</sup> Mark Sigman, MD,<sup>i</sup> Peter Tilkemeier, MD,<sup>j</sup> and Graham Jackson, MD, FRCP<sup>k</sup> *Providence, RI; Camden, NJ; Chicago, IL; San Francisco, and Los Angeles, CA; IRCCS, Italy; Athens, Greece; Philadelphia, PA; and London, United Kingdom*



Coronary artery disease incidence densities in patients with and without erectile dysfunction.<sup>14</sup>

**Table III.** Prognostic markers of cardiovascular disease in the patient with erectile dysfunction<sup>52</sup>

| <b>Biomarkers</b>              | <b>Association with vasculogenic ED</b> | <b>Overall CVD predictive value</b> | <b>Association with CV prevalence in ED</b> | <b>CVD predictive value in ED</b> | <b>Response to treatment</b> | <b>Availability</b> | <b>Cost</b> |
|--------------------------------|---|-------------------------------------|---|-----------------------------------|------------------------------|---------------------|-------------|
| Testosterone                   | +++                                     | ++                                  | +   | +                                 | +                            | ++++                | +           |
| hsCRP                          | ++                                      | +++                                 | +   | -                                 | +                            | ++++                | +           |
| Fibrinogen, IL-6               | +++                                     | ++                                  | +   | -                                 | +                            | ++                  | ++          |
| IMT                            | +++                                     | +++                                 | +   | -                                 | +                            | ++                  | ++          |
| Aortic stiffness               | ++                                      | +++                                 | +   | -/+                               | +                            | ++                  | ++          |
| ABI                            | ++                                      | +++                                 | +   | -                                 | -                            | +++                 | +           |
| CCTA                           | ++                                      | +++                                 | +   | -                                 | -                            | +                   | +++         |
| CAC                            | ++                                      | ++                                  | +   | -                                 | -                            | +                   | +++         |
| Endothelial dysfunction        | +++                                     | ++                                  | +   | -                                 | ++                           | ++                  | ++          |
| Albuminuria (micro- or macro-) | +                                       | +++                                 | +   | +                                 | -                            | ++++                | +           |
| Penile color Doppler           | ++++                                    | -                                   | +   | +                                 | ++                           | +                   | +++         |

Association with ED, availability, response to treatment, prognostic value and cost of biomarkers (scored from 0 to 4+).

ABI, Ankle-brachial index; CAC, Coronary artery calcium.

# Should patients with erectile dysfunction be evaluated for cardiovascular disease?

Kenneth A Ewane<sup>1</sup>, Hao-Cheng Lin<sup>1,2</sup> and Run Wang<sup>1,3</sup>

**Table 1** Relationship between erectile dysfunction (ED) and early vascular endothelial dysfunction

| Author (year)                                   | Study design       | No. with/no. without ED | Evaluation   | Intervention  | Results  |
|---|--------------------|-------------------------|--|---|--|
| Kaiser <i>et al.</i> <sup>13</sup> (2004)       | Case-control       | 30/27                   | Systemic vascular parameters<br>penile Doppler<br>IIEF | Carotid/brachial artery compliance/<br>distensibility<br>Aortic pulse wave velocity<br>Coronary calcification<br>Brachial artery vasodilation | Brachial artery FMD (1.3% vs. 2.4%,<br><i>P</i> =0.014)<br>Vasodilation to NTG (13.0% vs.<br>17.8%, <i>P</i> <0.05)  |
| Kaya <i>et al.</i> <sup>15</sup> (2006)         | Case-control       | 32/25                   | Penile Doppler US and IIEF                             | Endothelial-dependent BFMV and<br>brachial artery response to 0.4 mg<br>NTG   | Endothelial BFMV:<br>6.01±2.9 vs. 12.3±3.5<br>Brachial artery response to NTG:<br>12.8±4.2 vs. 17.8±5.2  |
| Uslu <i>et al.</i> <sup>16</sup> (2006)         | Case-control       | 30/25                   | IIEF and penile Doppler US                             | Aortic strain and distensibility,<br>endothelial-dependent brachial<br>artery FMD   | Aortic strain: 3.7%±2.7% vs.<br>9.5%±3.2%<br>Aortic distensibility: 1.5%±1.0% vs.<br>4.7%±2.9%<br>Brachial artery FMD: 4.1%±3.1%<br>vs. 9.7%±3.5%; <i>P</i> <0.001 |
| Baumhake and Bohm <sup>17</sup> (2007)          | Cohort             | 154/38                  | IIEF<br>High-risk CVD                                  | MRI or angiography to determine<br>LVEF   | Decreased LVEF (EF ≤40%)<br>associated with ED   |
| Lojanapiwat and Weerusawin <sup>18</sup> (2009) | Case-control       | 41/38                   | IIEF-5   | Brachial artery FMD   | Brachial artery FMD change:<br>8.7%±1.0% vs.<br>5.1%±0.6% ( <i>P</i> =0.007)   |
| Polonsky <i>et al.</i> <sup>19</sup> (2009)     | Prospective cohort | 310/380                 | IIEF   | ABI to screen for PAD   | PAD prevalence<br>32% vs. 16%  |

# Should patients with erectile dysfunction be evaluated for cardiovascular disease?

Kenneth A Ewane<sup>1</sup>, Hao-Cheng Lin<sup>1,2</sup> and Run Wang<sup>1,3</sup>

**Table 2 Association between erectile dysfunction (ED) and other known cardiovascular disease (CVD) risk factors**

| <i>Author (year)</i>                          | <i>Study design</i>      | <i>Patients (age)</i>                         | <i>ED (%)</i> | <i>Risk factor correlate</i>                                   | <i>Results</i>   |
|---|--------------------------|---|---------------|--|--|
| Feldman <i>et al.</i> <sup>3</sup> (2000)     | Prospective cohort       | 513 (40–70)                                   | 18            | Smoking<br>BMI $\geq 28$ kg m <sup>-2</sup>                    | Baseline smoking almost doubled the likelihood of moderate/severe ED                 |
| Kloner <i>et al.</i> <sup>21</sup> (2003)     | Cohort                   | 76 (40–82)                                    | 70            | Chronic stable CAD   | ED common in patient with chronic stable CAD   |
| Roumeguere <i>et al.</i> <sup>22</sup> (2003) | Prospective cohort       | 315 (35–75)                                   | 68.3          | Hyperlipidemia   | 70.6% prevalence of hypercholesterolemia in the ED group                             |
| Sesayama <i>et al.</i> <sup>23</sup> (2003)   | Population               | 6112 (30–70)                                  | 81            | CVD<br>Diabetes  | 65% CVD and DM among patients with severe/moderate ED                                |
| Mittawae <i>et al.</i> <sup>24</sup> (2006)   | Cohort                   | 800 (28–75)                                   | 43.2          | Hypertension   | Statistical correlation between duration of HTN and ED                               |
| Montorsi <i>et al.</i> <sup>25</sup> (2006)   | Cohort                   | 285 (53.6 $\pm$ 8.5)                          | 22–65         | Coronary syndrome  | Age, multiple vessels and chronic coronary syndrome as opposed to acute predicted ED |
| Selvin <i>et al.</i> <sup>4</sup> (2007)      | Cross-sectional          | 2126 ( $\geq 20$ )                            | 18.4          | Diabetes<br>Hypertension                                       | 51.3% prevalence among men in the ED group with DM                                   |
| Chang <i>et al.</i> <sup>26</sup> (2009)      | Prospective cohort       | 141 (54 $\pm$ 10.3)                           | 100           | Metabolic syndrome   | The presence of MS and number of MS components influence the severity of ED          |
| Lee <i>et al.</i> <sup>27</sup> (2011)        | Randomized control trial | 176 (mild ED)<br>14 537 (database)<br>(18–89) | 100           | Hypertension, diabetes, dyslipidemias and hypercholesterolemia | The two groups were very similar in terms of risk factors                            |

# Should patients with erectile dysfunction be evaluated for cardiovascular disease?

Kenneth A Ewane<sup>1</sup>, Hao-Cheng Lin<sup>1,2</sup> and Run Wang<sup>1,3</sup>

**Table 3 Association between erectile dysfunction (ED) and future cardiovascular disease (CVD)**

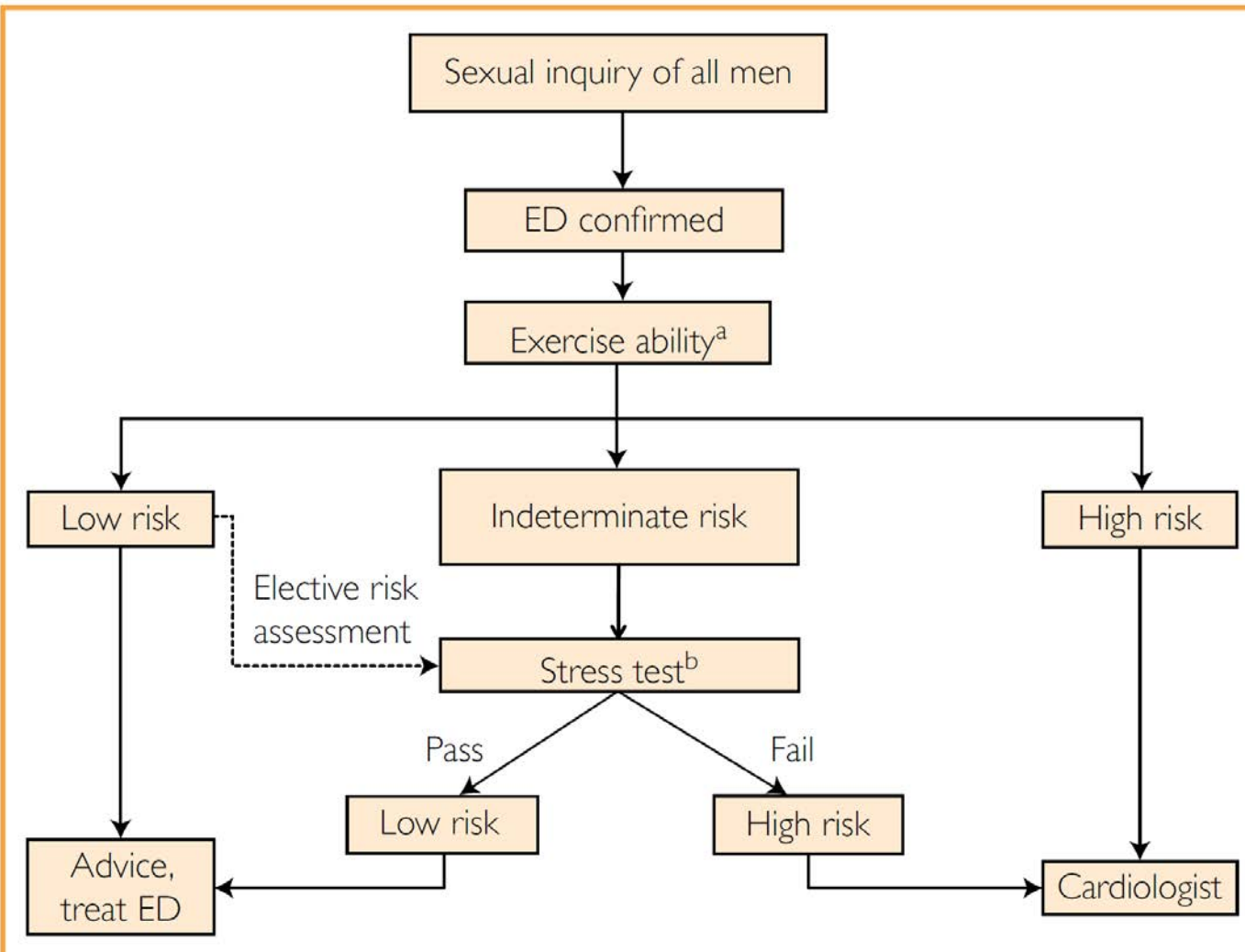
| <i>Author (year)</i>                         | <i>Study design</i>                  | <i>Patients (age)</i> | <i>ED (%)</i> | <i>ED timing/results</i>   |
|--|--------------------------------------|-----------------------|---------------|--|
| Montorsi <i>et al.</i> <sup>28</sup> (2003)  | Prospective cohort                   | 300 (33–86)           | 49            | Angina preceded ED in >70% patients  |
| El-Sakka and Morsy <sup>29</sup> (2004)      | Cohort                               | 303 (59.8±7.3)        | 76.2          | 31.4% of IHD<br>Association between IHD and arterigenic ED<br>Higher grade IHD correlated with decreasing PSV ( $P<0.05$ ) |
| Thompson <i>et al.</i> <sup>11</sup> (2005)  | Prospective randomized control trial | 4247 (62±6)           | 65 at 7 years | 11% CVE at 5 years in men with incident ED   |
| Min <i>et al.</i> <sup>30</sup> (2006)       | Prospective cohort                   | 221 (23–88)           | 54.8          | ED patient showed severe CHD (MPS summed stress score >8): 43.0% vs. 17.0%   |
| Hodges <i>et al.</i> <sup>31</sup> (2007)    | Case–control                         | 207 vs. 165 (61±9)    | 66 vs. 37     | ED may precede CVD by as much as 5 years   |
| Stuckey <i>et al.</i> <sup>32</sup> (2007)   | Case–control                         | 49 vs. 50 (40–70)     | 50            | Standing pulse pressure and flow debt repayment were both lower in the ED group  |
| Ma <i>et al.</i> <sup>33</sup> (2008)        | Cohort                               | 2306 (54.2±12.7)      | 26.7          | Incidence of CHD higher in ED than non-ED group  |
| Gazzaruso <i>et al.</i> <sup>34</sup> (2008) | Prospective cohort                   | 291 (54.8±7)          | 40.5          | 61.2% vs. 36.4% between ED and non-ED patients in experiencing major adverse cardiac event                                 |
| Schouten <i>et al.</i> <sup>35</sup> (2008)  | Population cohort                    | 1248 (50–75)          | 31.5          | 11.7% population attributable risk fraction for ED   |
| Chew <i>et al.</i> <sup>36</sup> (2010)      | Retrospective cohort                 | 2318 (20–89)          | 100           | Men with ED had a higher incidence of atherosclerotic cardiovascular event   |

# Should patients with erectile dysfunction be evaluated for cardiovascular disease?

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**Table 4** Erectile dysfunction (ED) as an independent risk predictor for cardiovascular disease (CVD)

| <i>Author (year)</i>                         | <i>Patients (age)</i>                    | <i>Study design</i>          | <i>Evaluations</i>   | <i>Results</i>   | <i>Comments</i>  |
|--|--|------------------------------|--|--|--|
| Ponholzer <i>et al.</i> <sup>38</sup> (2005) | 2495 (30–69)                             | Cohort                       | IIEF-5<br>10-year CHD risk estimate using the Framingham risk profile algorithm                              | CHD within 10 years: 13.2% vs. 8.0% for moderate/severe ED vs. no ED   | Moderate/severe ED is associated with increased risk for CHD within 10 years unlike mild ED                                  |
| Salem <i>et al.</i> <sup>39</sup> (2009)     | 183 with CAD and 134 without CAD (40–69) | Case–control                 | Logistic regression analysis to assess the effects of classic risk factors and ED severity on CAD            | ED prevalence was 88.5% in the CAD group and 64.2% in non-CAD group<br>Significant association between severe ED and CAD (OR: 2.22; 95% CI: 1.11–6.03; <i>P</i> <0.05) | ED associated with CAD, severe ED an independent risk predictor  |
| Inman <i>et al.</i> <sup>7</sup> (2009)      | 1402 (40–79)                             | Prospective cohort           | Brief male sexual function inventory (BMSFI)<br>Biennial screening<br>Incidence densities for CAD calculated | Association between ED and incident CAD declined with age;<br>48.52 (40–49) vs. 27.15 (50–59) vs. 23.97 (60–69) vs. 29.63 (≥70)  | ED associated with marked increase in the risk of future cardiovascular event in young men; no prognostic value in older men |
| Araujo <i>et al.</i> <sup>8</sup> (2010)     | 1057 (40–70)                             | Prospective population-based | 23-item questionnaire on sexual activity<br>CVD: self-report, MMAS linkage to NDI and medical records        | 261 new cases of CVD<br>ED associated with CVD after controlling for age, FRS, <i>etc.</i><br>ED did not improve prediction for CVD                                    | ED does not improve prediction for CVD beyond the traditional risk factors   |



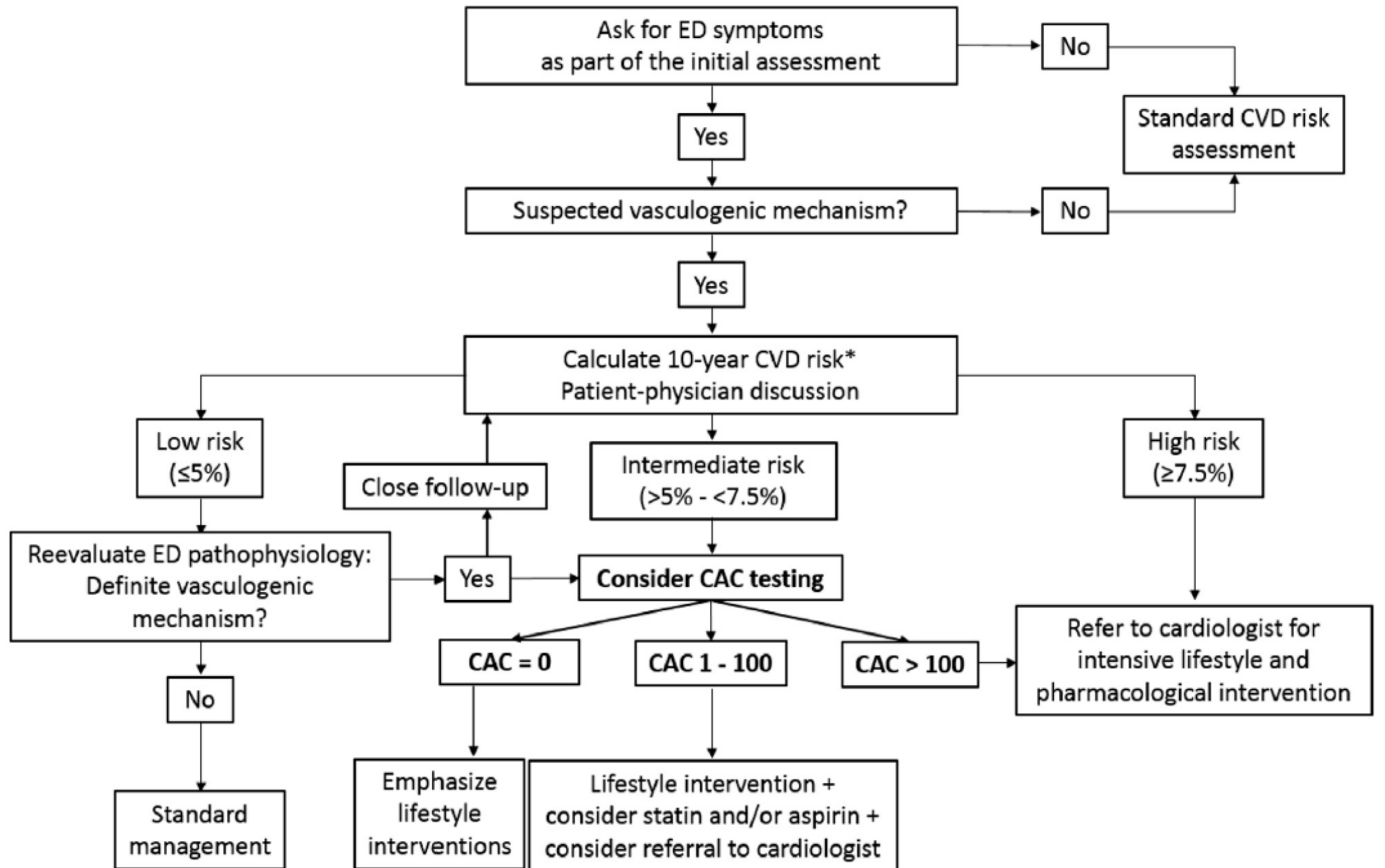
**FIGURE.** Management of erectile dysfunction (ED) in all men with ED, especially those with known cardiovascular disease. <sup>a</sup>Sexual activity is equivalent to walking 1 mile on the flat in 20 minutes or briskly climbing 2 flights of stairs in 10 seconds. <sup>b</sup>Sexual activity is equivalent to 4 minutes of the Bruce treadmill protocol.



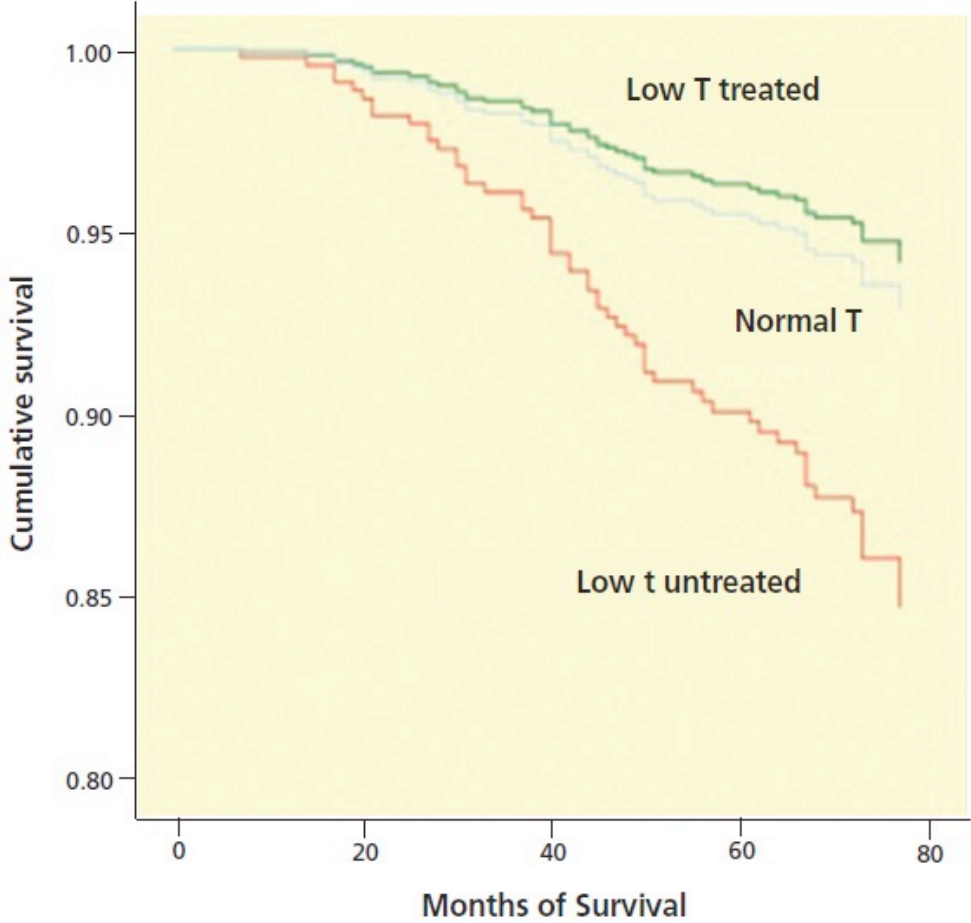
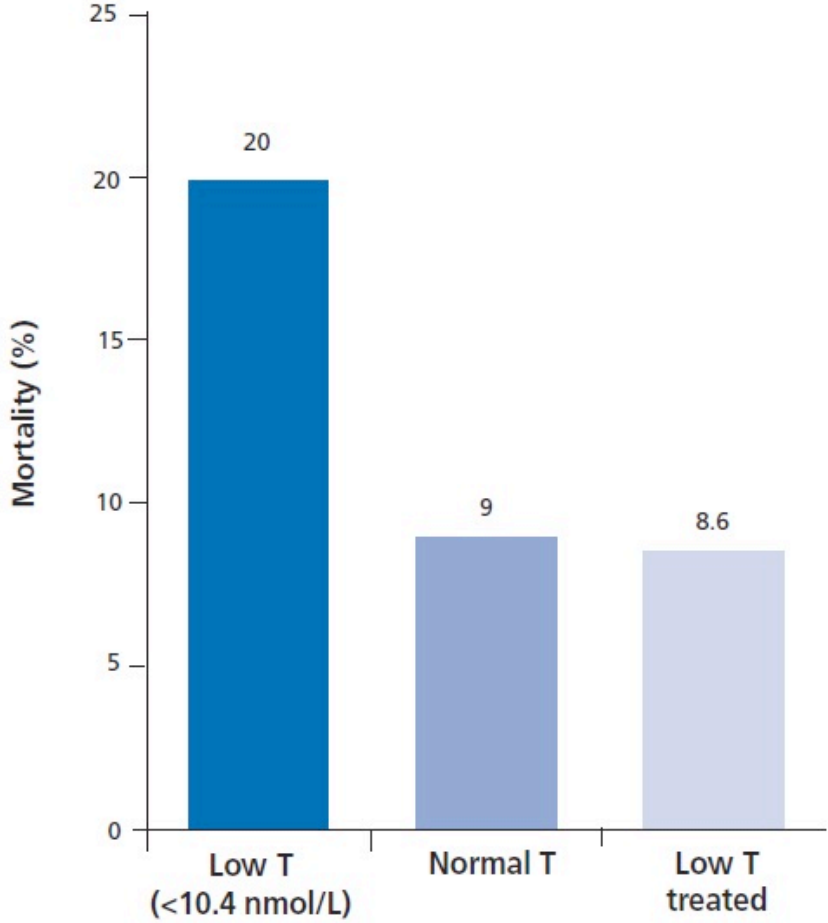


# All Men with Vasculogenic Erectile Dysfunction Require a Cardiovascular Workup

Martin Miner, MD,<sup>a</sup> Ajay Nehra, MD,<sup>b</sup> Graham Jackson, MD,<sup>c</sup> Shalender Bhasin, MD,<sup>d</sup> Kevin Billups, MD,<sup>e,f</sup> Arthur L. Burnett, MD,<sup>f</sup> Jacques Buvat, MD,<sup>g</sup> Culley Carson, MD,<sup>h</sup> Glenn Cunningham, MD,<sup>i</sup> Peter Ganz, MD,<sup>j</sup> Irwin Goldstein, MD,<sup>k</sup> Andre Guay, MD,<sup>l</sup> Geoff Hackett, MD,<sup>m</sup> Robert A. Kloner, MD, PhD,<sup>n</sup> John B. Kostis, MD,<sup>o</sup> K. Elizabeth LaFlamme, PhD,<sup>p</sup> Piero Montorsi, MD,<sup>q</sup> Melinda Ramsey, PhD,<sup>p</sup> Raymond Rosen, PhD,<sup>r</sup> Richard Sadovsky, MD,<sup>s</sup> Allen Seftel, MD,<sup>t</sup> Ridwan Shabsigh, MD,<sup>u</sup> Charalambos Vlachopoulos, MD,<sup>v</sup> Frederick Wu, MD<sup>w</sup>

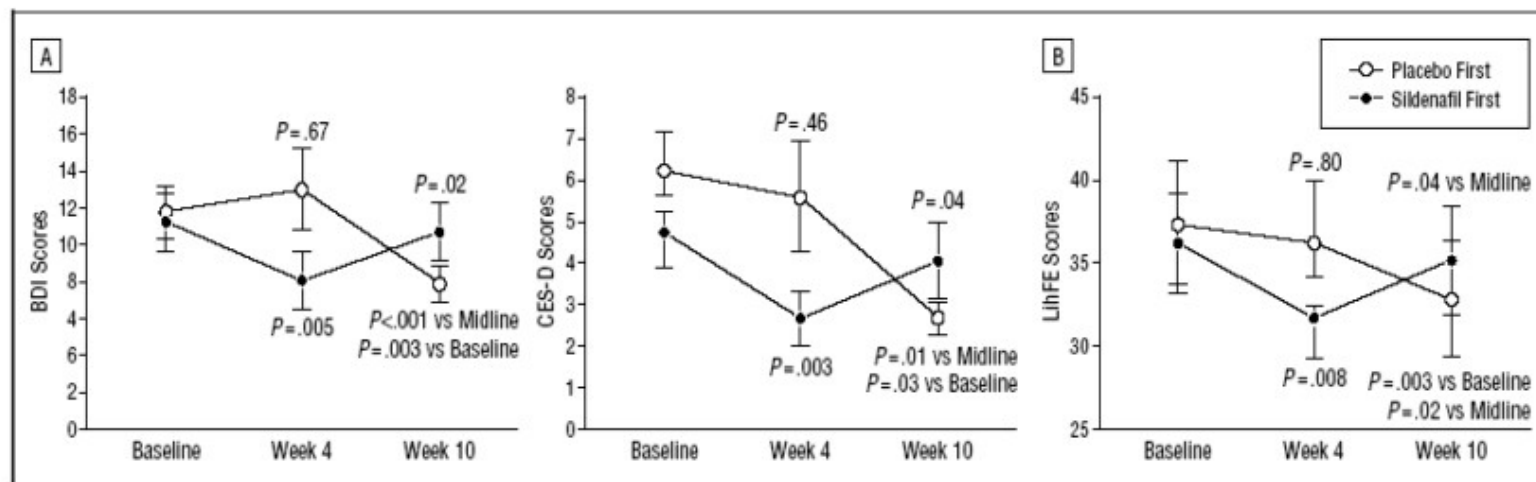


**Figure 6.** Testosterone replacement therapy and mortality in UK men with type 2 diabetes mellitus



PDE5 inibitori e polifarmacoterapia:  
interazioni nel paziente con comorbidità

## Use of Sildenafil for Safe Improvement of Erectile Function and Quality of Life in Men With New York Heart Association Classes II and III Congestive Heart Failure



**Figure 3.** Depression (A) and quality-of-life scores (B) at baseline and 6 and 12 weeks for the placebo-sildenafil citrate crossover protocol. BDI indicates Beck Depression Inventory; CES-D, Center for Epidemiological Studies-Depression Scale; LihFE, Minnesota Living With Heart Failure Questionnaire.

**Conclusion:** Sildenafil is a safe and effective treatment for ED in men with New York Heart Association classes II and III CHF and provides relief of depressive symptoms, explaining an improvement in the perception of quality of life.

# PDE 5 inibitori e terapia antiipertensiva:

## Hypertension and erectile dysfunction

Erectile dysfunction is a prevalent condition in hypertensive patients and a predictor of future cardiovascular events. Screening and treatment of erectile dysfunction improves management of cardiovascular risk factors. After initiating therapy with phosphodiesterase (PDE) 5 inhibitors, patients are more likely to take antihypertensive medication and BP control is improved [272].

Older antihypertensive drugs (diuretics,  $\beta$ -blockers, centrally acting drugs) exert negative effects, whereas newer drugs have neutral or beneficial effects (calcium antagonists, ACE inhibitors, angiotensin receptor antagonists, nebivolol) [273].

Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document

Journal of Hypertension 2009, 27:2121–2158

***Erectile Dysfunction Drugs Safe After MI.  
Outcomes actually better among users in Swedish database***

43.145 uomini (età  $\leq$  80 anni) con primo evento ischemico cardiac (inclusi in un database svedese dal 2007 al 2013 collegato a registri nazionali di prescrizione cardiaca e cause di morte).

Riduzione del 40% del rischio di ospedalizzazione per scompenso cardiaco e una incidenza significativamente minore di MACE (major adverse cardiovascular events) nei pazienti che assumevano farmaci inibitori delle fosfodiesterasi di tipo 5



## **Table 2 – Association between erectile dysfunction and cardiovascular disease: practice points**

---

- ED is common, especially with advancing age.
- ED and CVD share the same risk factors.
- ED and CVD have a common pathophysiologic background.
- ED is highly prevalent in CAD patients.
- ED is a marker of generalized vascular disease.
- ED precedes a CVD event by 2–5 yr (average: 3 yr).
- ED predicts cardiovascular events and all-cause mortality.
- ED patients with an intermediate-risk score need further evaluation of CV risk.
- ED treatment should include CVD risk reduction.

## **Table 3 – Association between erectile dysfunction and cardiovascular disease: issues to be addressed**

---

- How can young ED patients be stratified appropriately?
- Why do some patients with multivessel coronary disease not have ED?
- Is ED a target of organ damage in hypertensive patients?
- Is development of ED after CAD onset a marker of CAD progress?
- Can ED meaningfully reclassify patients that have been characterized with SCORE/FRS to higher or lower risk categories?
- Does aggressive risk reduction in men with asymptomatic CVD and concomitant/preceding ED lead to a reduction of the CVD event rate?
- What are the dose-dependent effects of statins (intensive vs nonintensive use) on erectile function?
- Can testosterone replacement therapy improve the cardiac event rate over time?
- Does long-term PDE-5 inhibition reduce the CVD event rate?

*'A man with erectile dysfunction and no cardiac symptoms is a cardiac patient until proven otherwise'* (Jackson, 2006)

- Erectile dysfunction is common
- It is an independent risk factor for cardiovascular disease, equivalent to a current moderate smoker
- Men presented with ED **for 38 months on average before** developing acute chest pain
- The penile arteries are smaller in diameter than the coronary arteries

# Grazie per l'attenzione



Smoking leads to impotence . . .  
**Quit Smoking.**