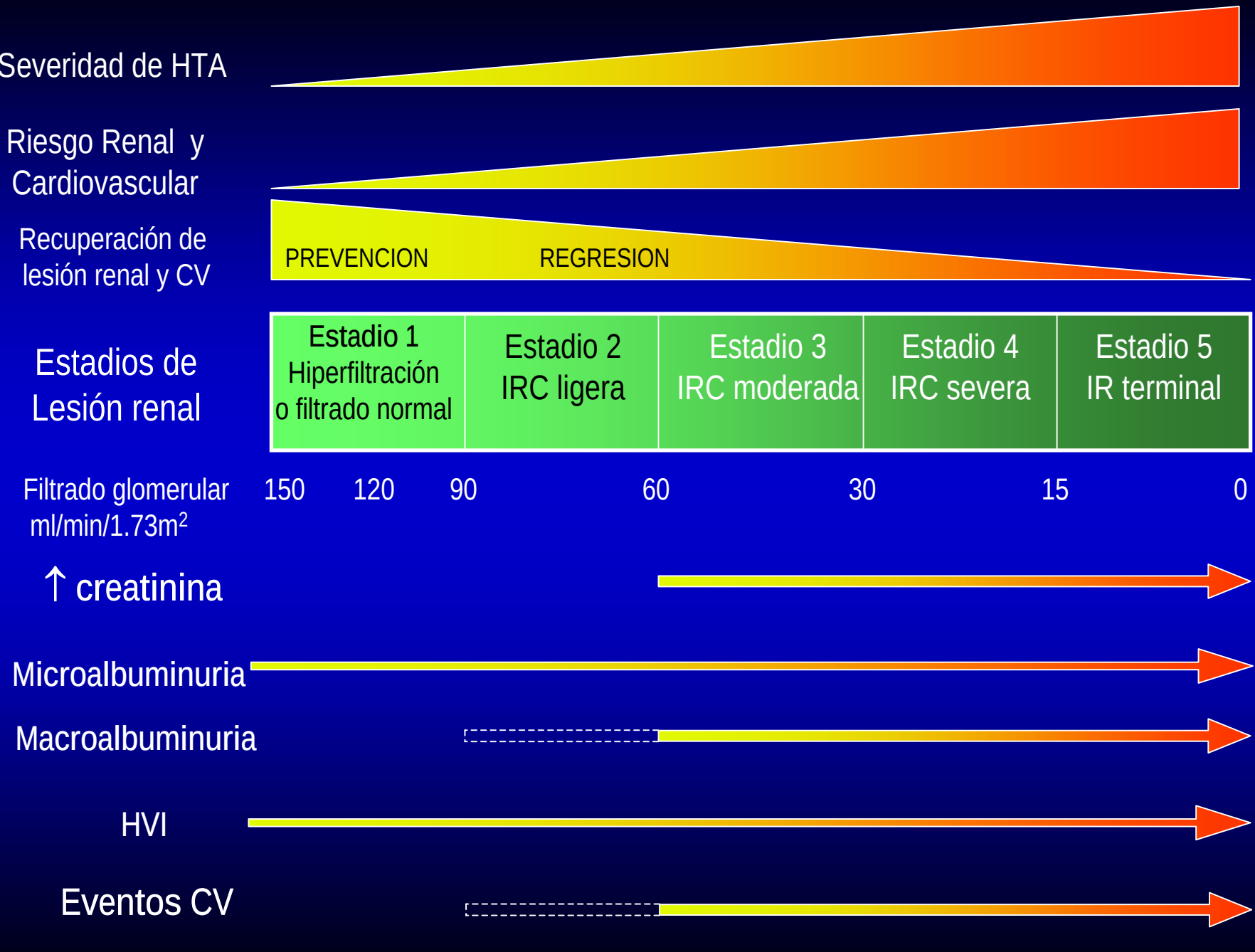
MÁS ALLÁ DEL DESCENSO DE LA PA ¿DISPONEMOS DE EVIDENCIAS EN…?

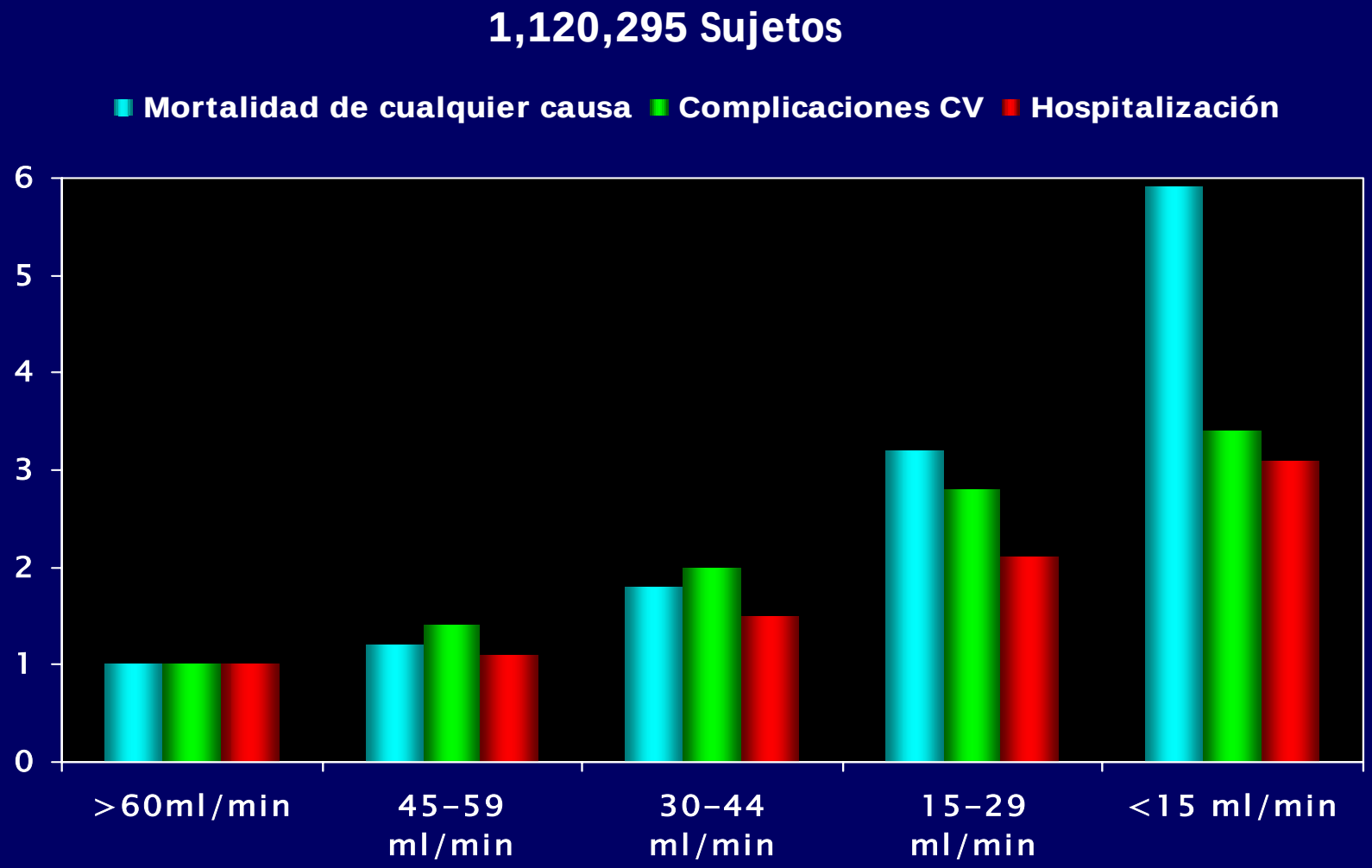
Protección renal

Dr. Julián Segura.
Unidad de Hipertensión Arterial. Servicio de Nefrología.
Hospital Universitario 12 de Octubre. Madrid.



Segura J et al. Kidney Int 2004; 66: S45-S49.

Riesgo ajustado de mortalidad de cualquier causa, complicaciones cardiovasculares y hospitalizaciones según el filtrado glomerular estimado

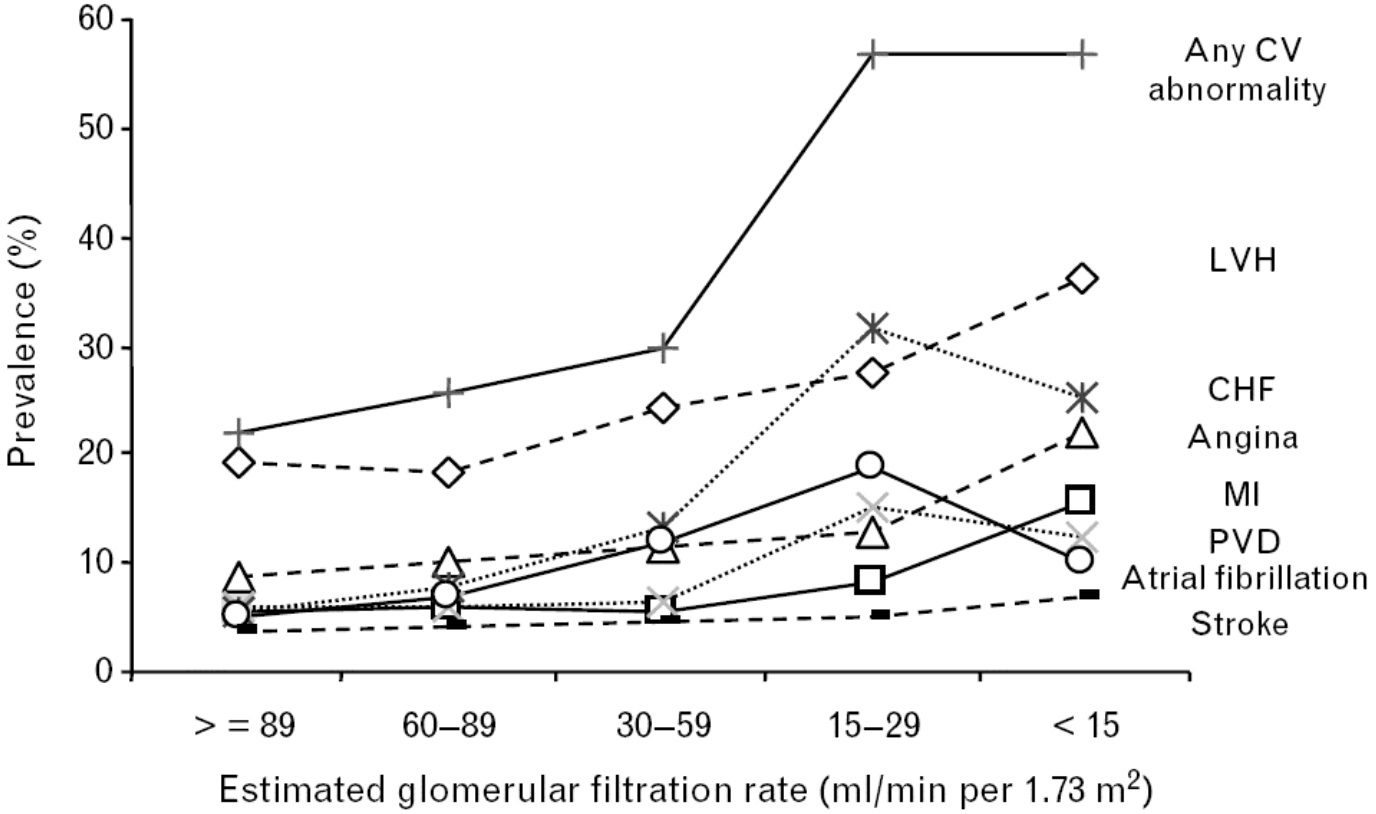


Go AS et al. N Engl J Med 2004;351:1296-1305

Kidney function and cardiovascular disease in the hypertensive population: the ERIC-HTA study

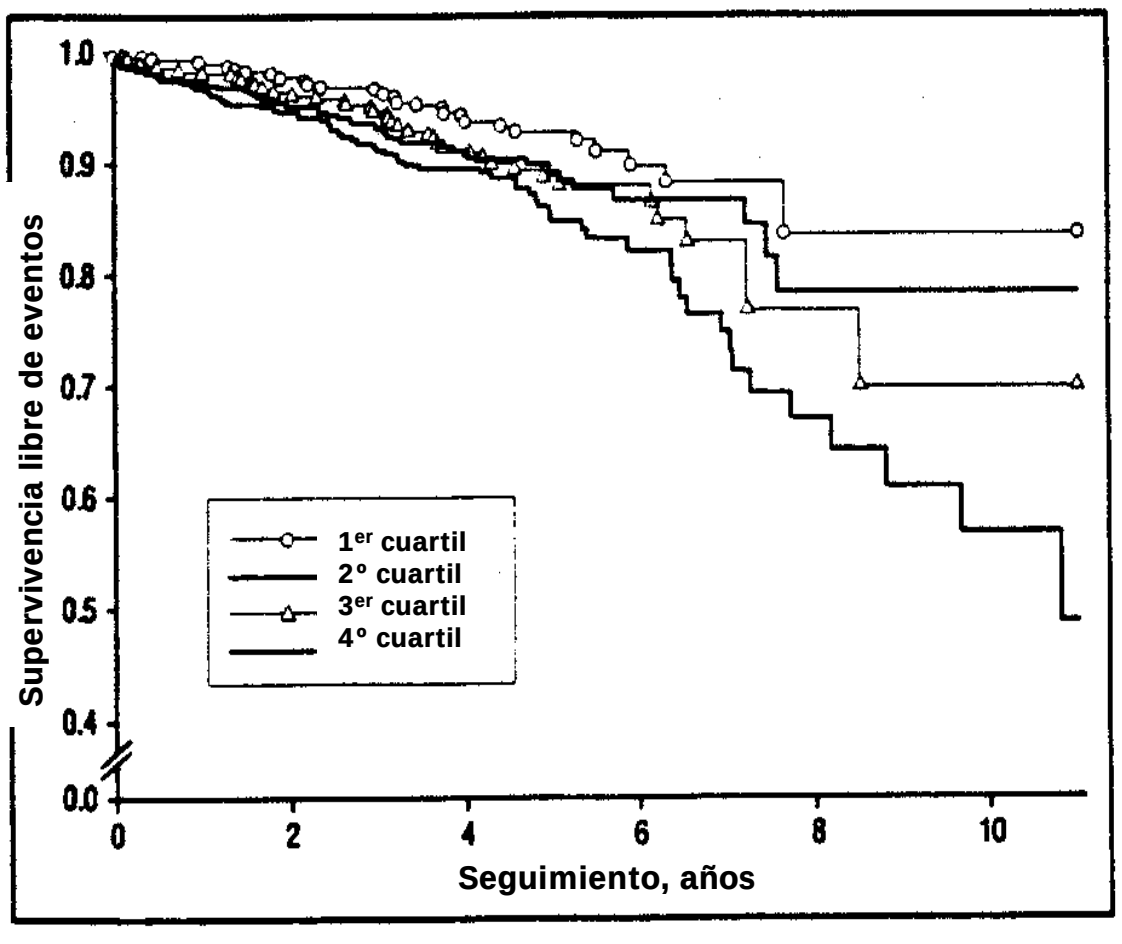
Josep Redon, Luis Cea-Calvo, Jose V. Lozano, Cristina Fernandez-Perez, Jorge Navarro, Alvaro Bonet and Jorge Gonzalez-Esteban on behalf of the investigators of the ERIC-HTA 2003 Study

Journal of Hypertension 2006;24:663.



Prevalence of cardiovascular (CV) damage according the estimated glomerular filtration rate. LVH, left ventricular hypertrophy; CHF, coronary heart failure; MI, myocardial infarction; PVD, peripheral vascular disease.

Creatinina plasmática normal-alta como predictor de riesgo cardiovascular en hipertensión

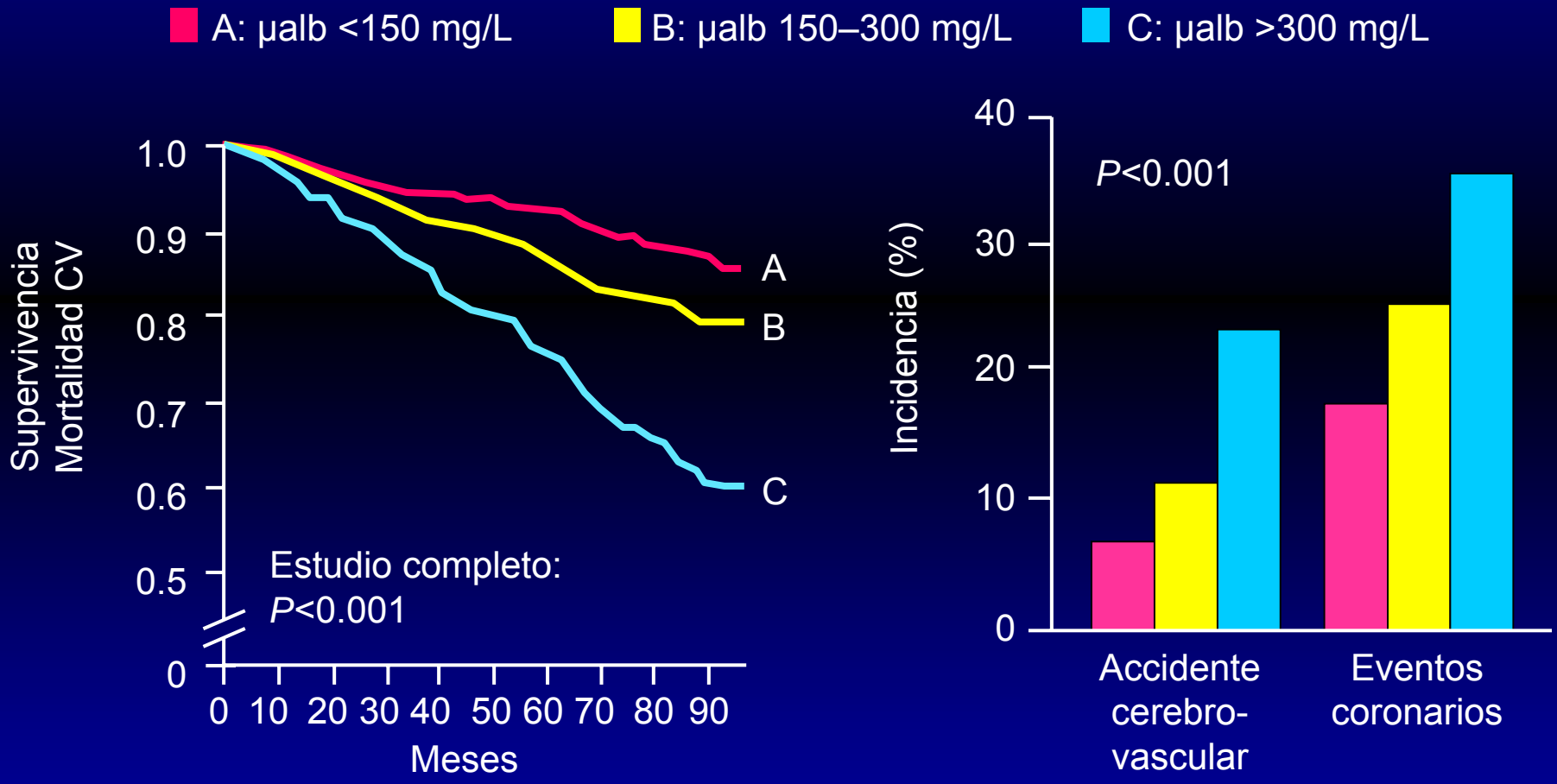


Cuartiles de Creat (mg/dl)

	Varones	Mujeres
1	<0.94	<0.79
2	0.94-1.04	0.79-0.86
3	1.04-1.17	0.86-0.95
4	>1.17	>0.95

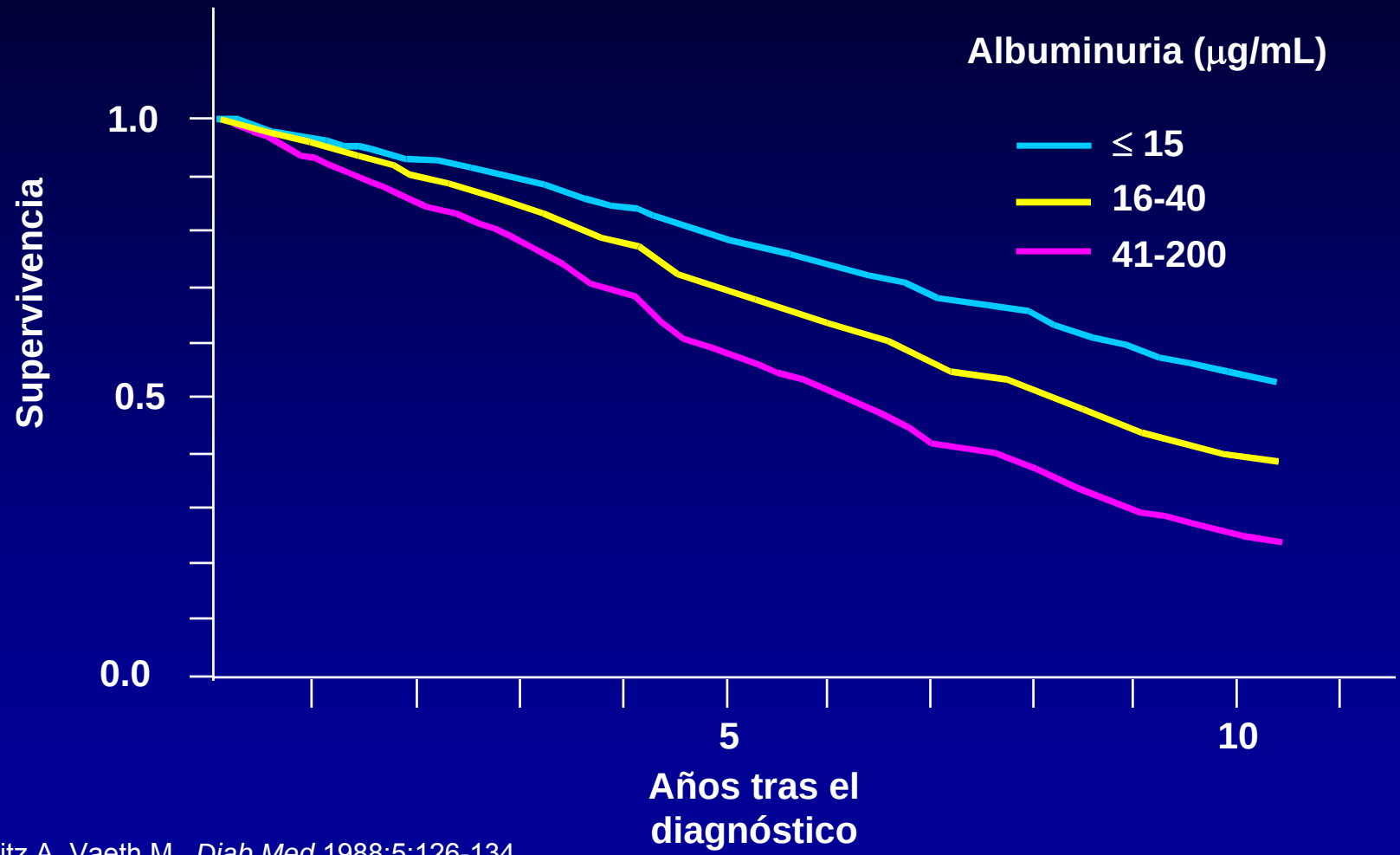
Schillaci G, et al. PIUMA study. Arch Intern Med 2001.

Proteinuria y riesgo de accidente cerebro-vascular y eventos coronarios en la diabetes tipo 2



Miettinen H et al. *Stroke.* 1996;27:2033–2039.

MICROALBUMINURIA COMO FACTOR DE RIESGO DE MUERTE EN LA DM TIPO 2



Schmitz A, Vaeth M. *Diab Med* 1988;5:126-134.

La albuminuria se relaciona con el riesgo cardiovascular

Joint National Committee - 7
FACTORES DE RIESGO CV

- Hipertensión*
- Tabaco
- Obesidad*
- Vida sedentaria
- Dislipemia*
- Diabetes mellitus*
- Microalbuminuria o TFG estimada <60 ml/min
- Edad (varones > 55 años, mujeres > 65 años)
- Antecedentes familiares de enfermedad CV prematura (en varones de < 55 años o mujeres < 65)

*Componentes del síndrome metabólico.

The JNC 7 Report. JAMA 2003; 289: 2560-2

Lesión de órganos diana

- Hipertrofia ventricular izquierda (ECG o ecocardiograma)

- Evidencia ultrasónica de espesamiento de la pared arterial (espesor íntima-media de la carótida ≥ 0,9 mm) o de placa aterosclerótica vascular

- Ligero incremento de la creatinina sérica (H:1,3-1,5 mg/dl; M:1,2-1,4 mg/dl)

- Microalbuminuria (30-300 mg/24 h; albúmina-creatinina: H ≥ 22, M ≥ 31 mg/g)

2003. ESH-ESC Guidelines. J Hypertens 2003; 21: 1011-1053

PRESIÓN ARTERIAL (mmHg)					
Otros factores de riesgo e historia de enfermedad	**Normal** **PAS 120-129, o** **PAD 80-84**	**Normal elevada** **PAS 130-130, o** **PAD 85-89**	**Grado 1** **PAS 140-159, o** **PAD 90-99**	**Grado 2** **PAS 160-179, o** **PAD 100-109**	**Grado 3** **PAS ≥180** **PAD ≥ 110**
Sin otros factores de riesgo	Riesgo normal	Riesgo normal	Riesgo añadido bajo	Riesgo añadido moderado	Riesgo añadido elevado
1-2 factores de riesgo	Riesgo añadido bajo	Riesgo añadido bajo	Riesgo añadido moderado	Riesgo añadido moderado	Riesgo añadido muy elevado
3 ó más factores de riesgo, o daño orgánico, o diabetes	Riesgo añadido moderado	Riesgo añadido elevado	Riesgo añadido elevado	Riesgo añadido elevado	Riesgo añadido muy elevado
Condiciones clínicas asociadas	Riesgo añadido elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado

2003. ESH-ESC Guidelines. J Hypertens 2003; 21: 1011-1053

Albuminuria in Hypertension Units

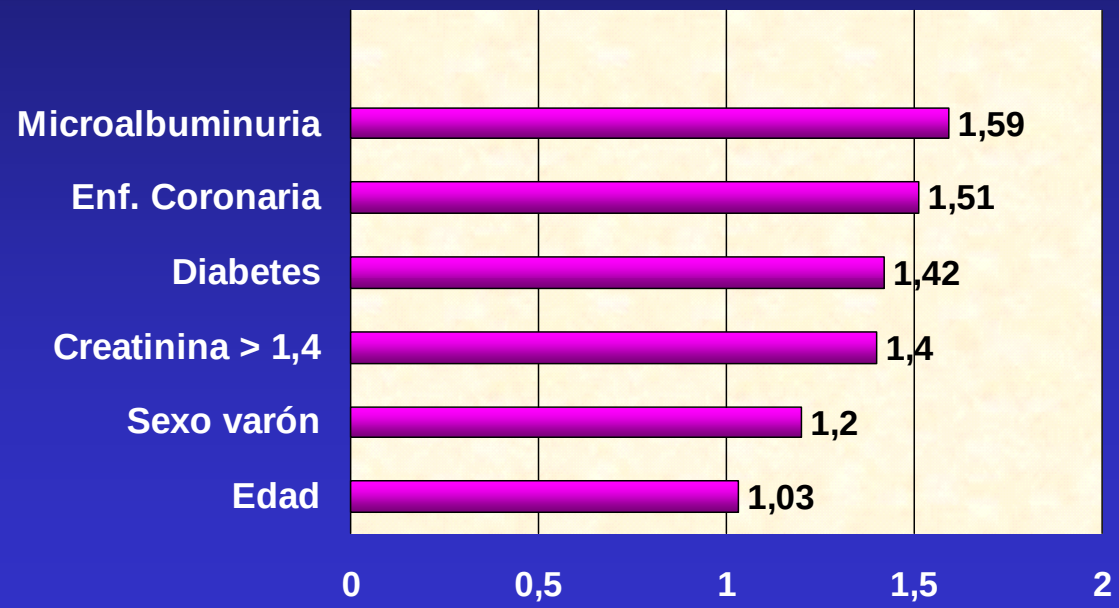
- **CLUE STUDY**
- **n= 4049 hypertensive patients**
- **ALBUMINURIA:**

30-300 mg/d	**29.4%**
300-1000 mg/d	**8.3%**
> 1000 mg/d	**5.7%**

Banegas JR, Segura J, et al, Hypertension 2004

Estudio HOPE: La microalbuminuria se asoció con un mayor riesgo de variable principal.

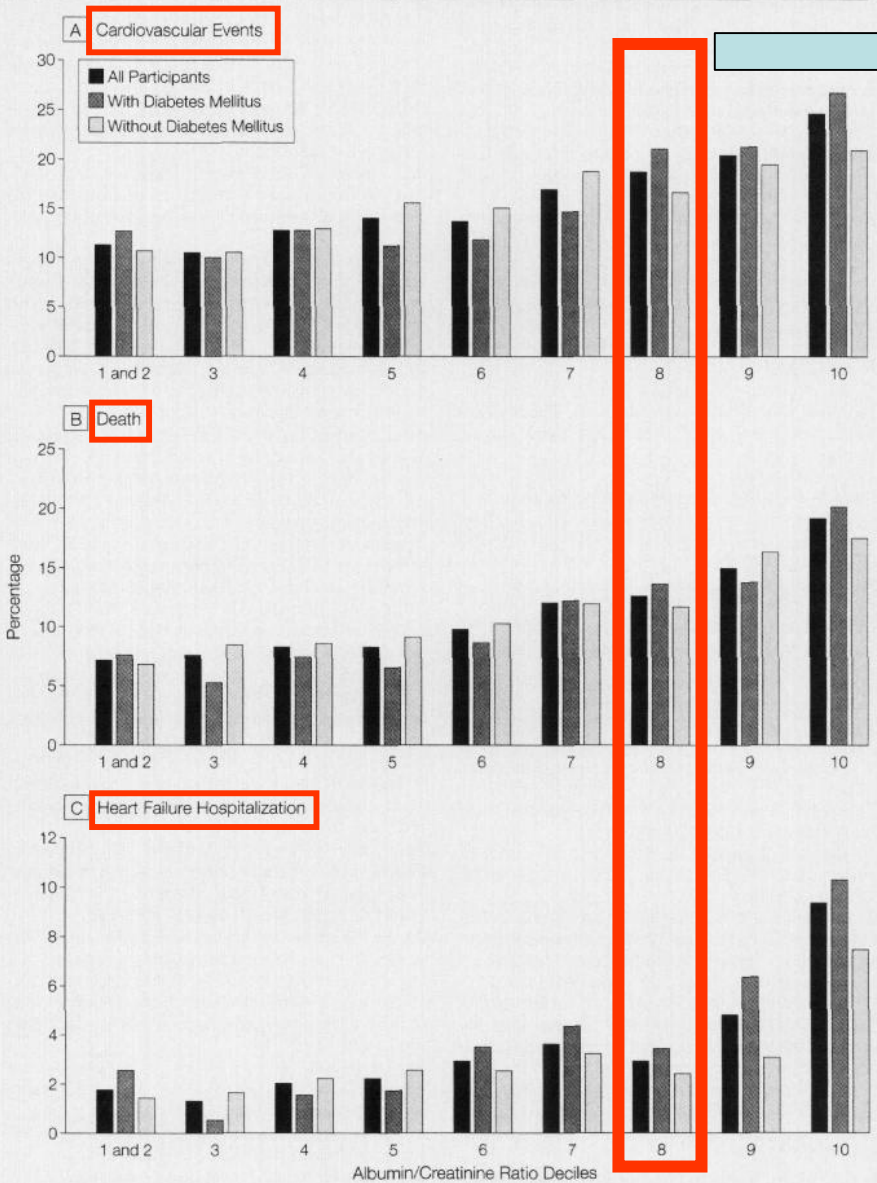
- En diabéticos y no diabéticos.
- El riesgo de evento cardiovascular se incrementó conforme aumentaban los niveles de microalbuminuria.



N: 9297

NEJM 2000; 342: 145-153.

Figure. Incidence of Cardiovascular Outcomes According to Degree of Albuminuria



Panels A, B, and C show the rate of major cardiovascular events (myocardial infarction, stroke, or cardiovascular death), all-cause mortality, and hospitalization for congestive heart failure in each decile of albumin/creatinine ratio (ACR) for all participants, participants with diabetes mellitus, and participants without diabetes mellitus. Decile 1 and 2 are combined because of very low incidence rates in these 2 deciles. The 8th decile includes ACR of 2 mg/mmol, which is the microalbuminuria threshold.

Cociente A/C 30 mg/g
EUA 30 mg/24h

JAMA 2001; 286: 421-427.

Time to abandon microalbuminuria?

Ruggenenti P, Remuzzi G.

Kidney Int 2006; Oct 70: 1214.

- The relationship between albuminuria and risk is not restricted to the microalbuminuric range and extends to as low as 2-5 microg/min.

- Albuminuria is a component of the metabolic syndrome and may represent a marker of the increased risk of renal and cardiovascular disease associated with insulin resistance and endothelial dysfunction.

- Albuminuria reflects functional and potentially reversible abnormalities initiated by glomerular hyperfiltration, proteinuria, a size-selective dysfunction of the glomerular barrier.

- Among subjects with albuminuria, there is a continuous relationship between albumin excretion and risk and no lower bound between normal albuminuria and microalbuminuria can be identified that segregates subjects at different risk.

Reduction in Albuminuria Translates to Reduction in Cardiovascular Events in Hypertensive Patients Losartan Intervention for Endpoint Reduction in Hypertension Study

Hans Ibsen; Michael H. Olsen; Kristian Wachtell; Knut Borch-Johnsen; Lars H. Lindholm; Carl Erik Mogensen; Björn Dahlöf; Richard B. Devereux; Ulf de Faire; Frej Fyhrquist; Stevo Julius; Sverre E. Kjeldsen; Ole Lederballe-Pedersen; Markku S. Nieminen; Per Omvik; Suzanne Oparil; Ying Wan

Hypertension. 2005;45:198.

- Measurement of albuminuria should be an integrated part of the management of arterial hypertension.

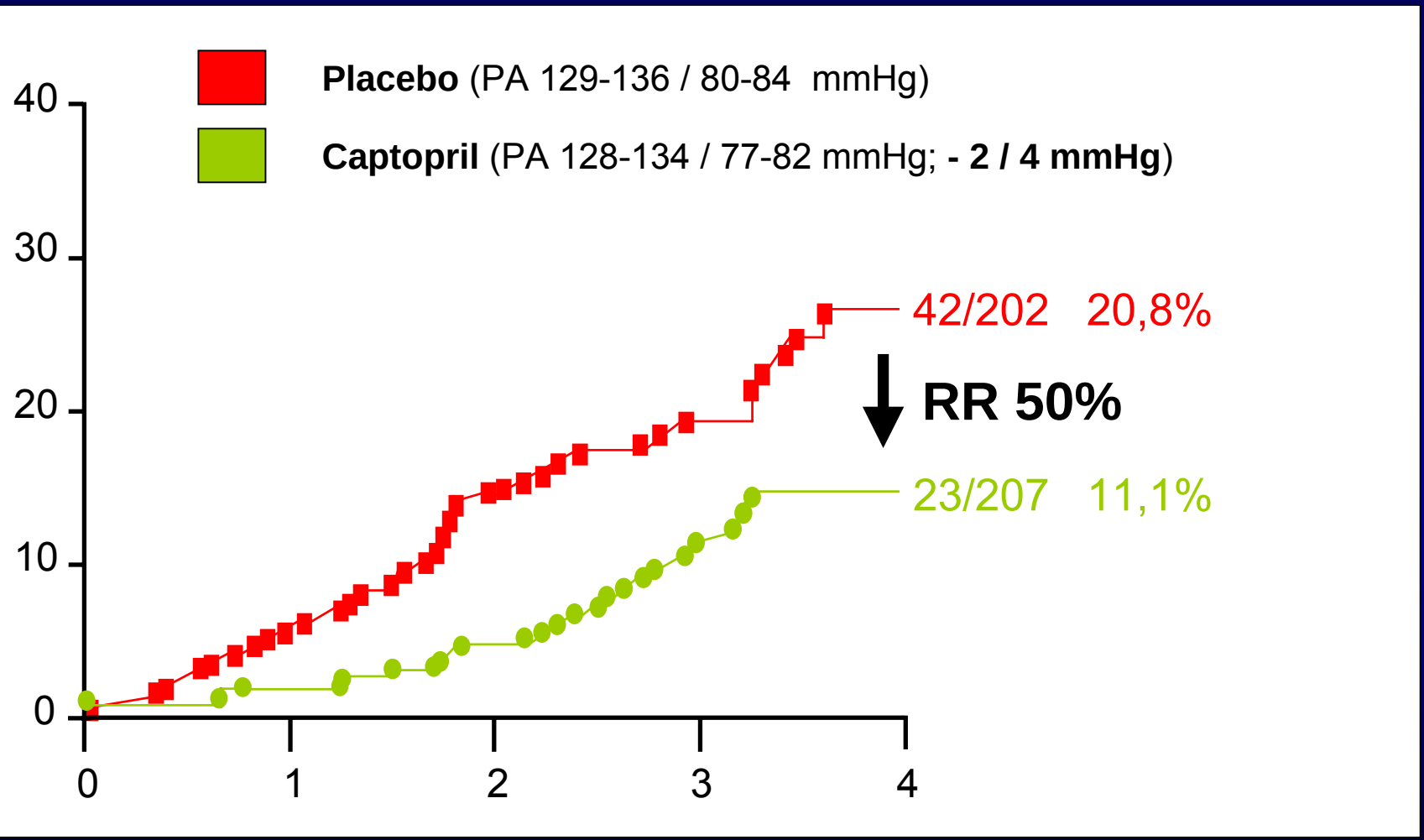
- It should be assessed before treatment and measured at yearly intervals.

- If the level remains high or not influenced by antihypertensive treatment, the clinician should carefully consider whether blood pressure is adequately controlled or whether other modifiable risk factors, such as smoking, lipid abnormalities, and glucose metabolism, need further intervention to decrease patient risk.

Nefroprotección
Diferentes estrategias

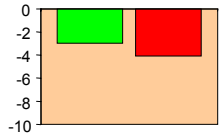
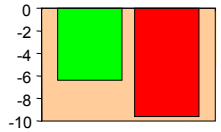
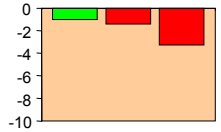
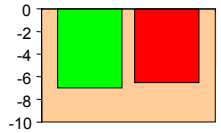
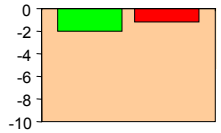
IECAs

EFECTO DEL CAPTOPRIL EN LA PROGRESIÓN DE LA NEFROPATÍA DIABÉTICA A DIÁLISIS, TRASPLANTE RENAL O MUERTE



Lewis EJ, et al. N Engl J Med 1993;329:1456-1462.

EL TRATAMIENTO IECA...
¿ FRENA LA PROGRESIÓN DE LA NEFROPATÍA ASOCIADA A LA DIABETES TIPO 2 ?

ESTUDIO	N	DURACIÓN AÑOS	DISMINUCIÓN FG ML / MIN / AÑO
Walker *et al* JASN 92	**86**	**3**	
Lebovitz *et al* Kidney Int 94	**46**	**3**	
Bakris *et al* Kidney Int 96	**52**	**5**	
Nielsen *et al* Diabetes 97	**36**	**3**	
Fogari *et al* J Hum Hypertens 99	**36**	**2**	

IECA

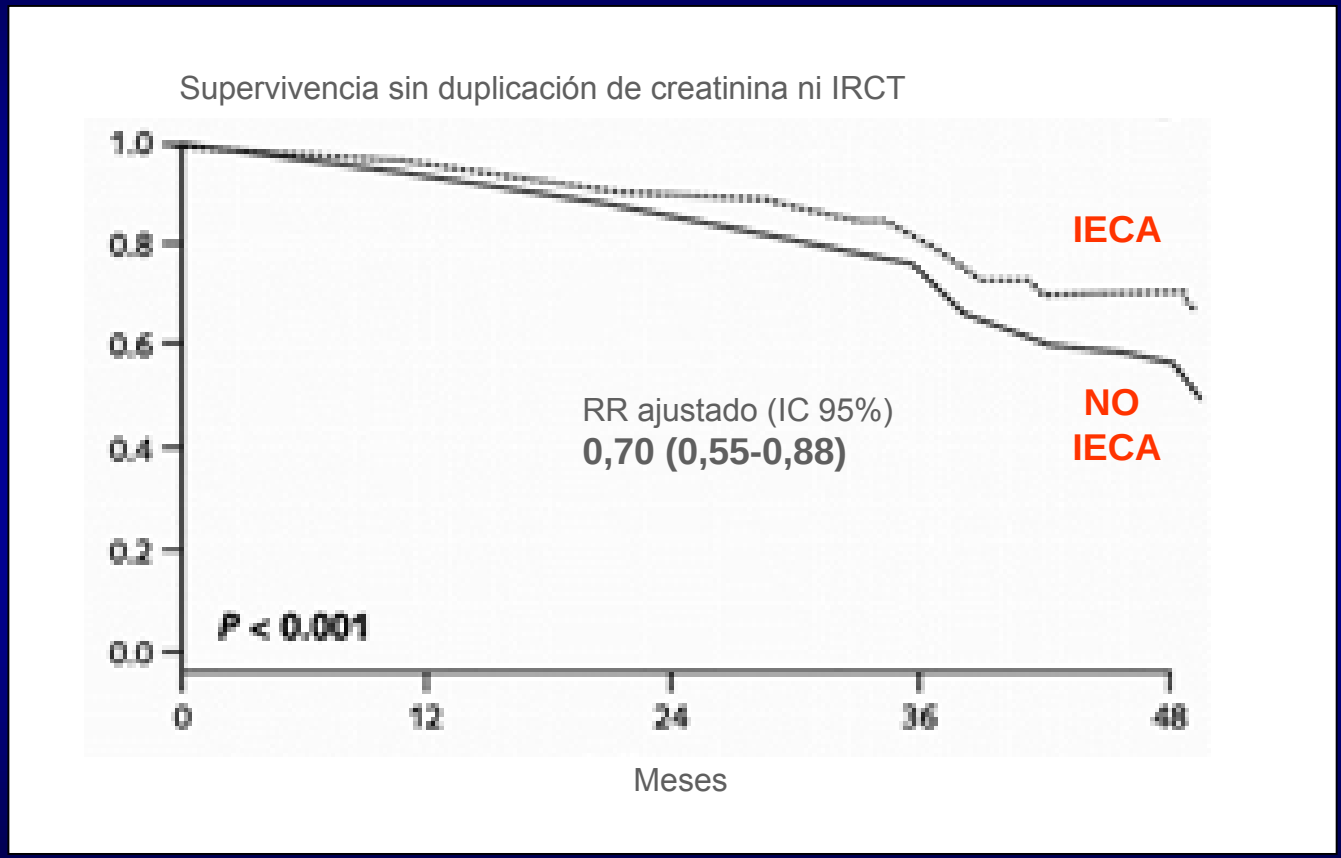
NO IECA

EL TRATAMIENTO IECA...
¿ FRENA LA PROGRESIÓN DE LA ENFERMEDAD RENAL NO DIABÉTICA ?

ESTUDIO	N	IECA vs NO IECA
Zucchelli *et al* (1992)	**121**	**Igual**
Kamper *et al* (1992)	**70**	**Mejor**
Brenner *et al* (1993)	**112**	**Igual**
Toto *et al* (1993)	**124**	**Igual**
Hannedouche *et al* (1994)	**100**	**Mejor**
Bannister *et al* (1995)	**51**	**Igual**
Ihle *et al* (1996)	**70**	**Mejor**
Maschio *et al* AIPRI (1996)	**583**	**Mejor**
Van Essen *et al* (1997)	**103**	**Igual**
GISEN REIN (1997)	**352**	**Mejor**
Segura *et al* (2001)	**295**	**Mejor**
Marín *et al* ESPIRAL (2001)	**241**	**Mejor**

ACE Inhibition in Progressive Renal Disease Study Group

METAANÁLISIS

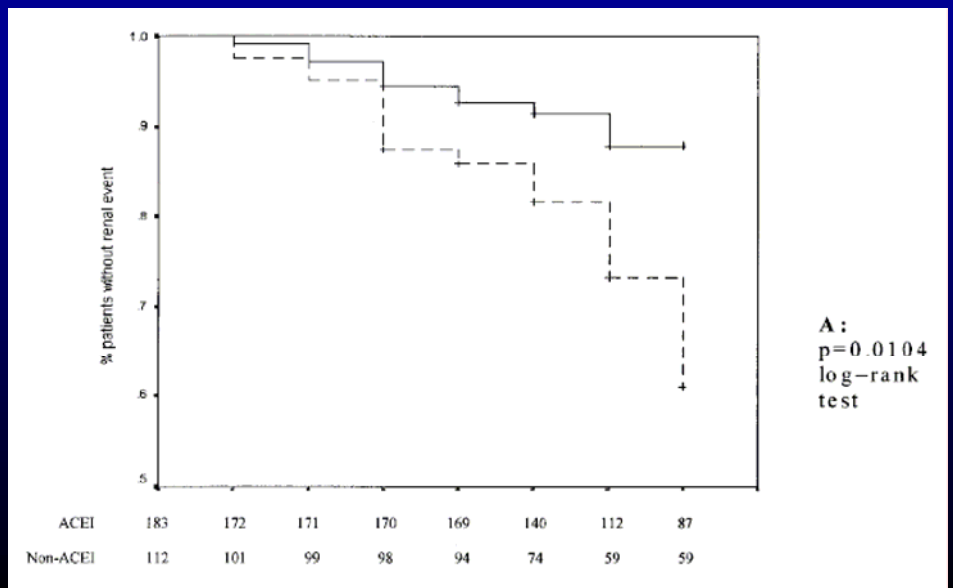


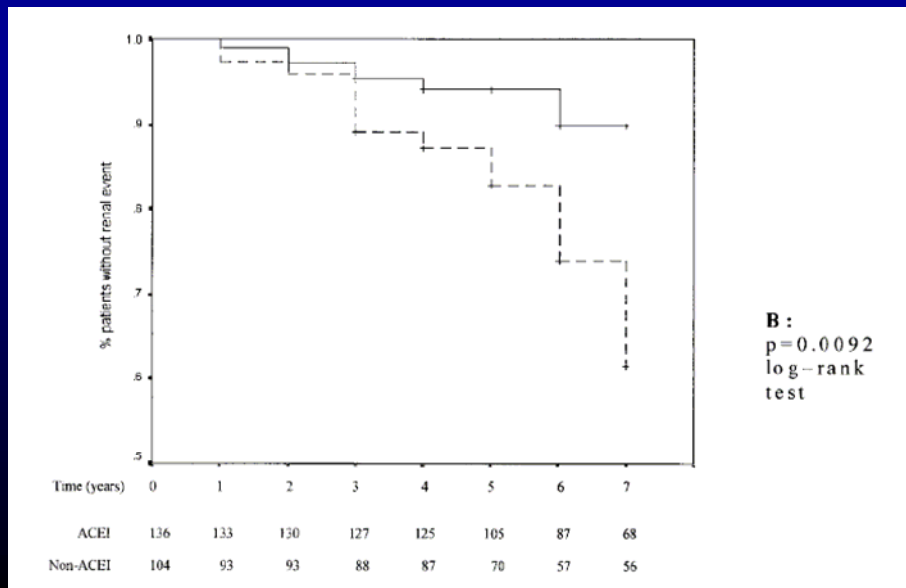
Jafar TH, et al. Ann Intern Med 2001;135:73-87.

ACE Inhibitors and Appearance of Renal Events in Hypertensive Nephrosclerosis

Julián Segura, Carlos Campo, José L. Rodicio, Luis M. Ruilope

Abstract—Nephrosclerosis constitutes a major cause of end-stage renal disease. Independently of blood pressure control, ACE inhibitors (ACEIs) are considered to be more nephroprotective than other antihypertensive agents. We have reviewed the long-term evolution of renal function in our series of essential hypertensive patients diagnosed as having nephrosclerosis when first seen in our unit. The analysis was performed depending on whether or not their antihypertensive therapy contained an ACEI alone or in combination for the whole follow-up. The end point was defined as the confirmation of a 50% reduction in creatinine clearance or entry in a dialysis program. A historical cohort of 295 patients was included in the analysis. Mean follow-up was 7.4±3.9 years. Diabetes prevalence was higher in ACEI-treated patients (25.7% versus 7.1%, $P=0.000$), but the diagnosis of diabetic nephropathy could not be confirmed on clinical grounds, including renal biopsy. Twenty-three out of 183 (12.6%) patients in the ACEI group and 23 out of 112 (20.5%) patients in the non-ACEI group experienced a renal event ($P=0.0104$ by log rank test). Similar results were observed when only nondiabetic patients were considered for the analysis. Cox regression analysis showed that baseline serum creatinine, absence of ACEI administration, mean proteinuria during follow-up, and age were independent predictors for the development of a renal event. In hypertensive nephrosclerosis, therapy containing an ACEI alone or in combination significantly reduces the incidence of renal events. This effect is independent of blood pressure control.
(*Hypertension*. 2001;38[part 2]:645-649.)





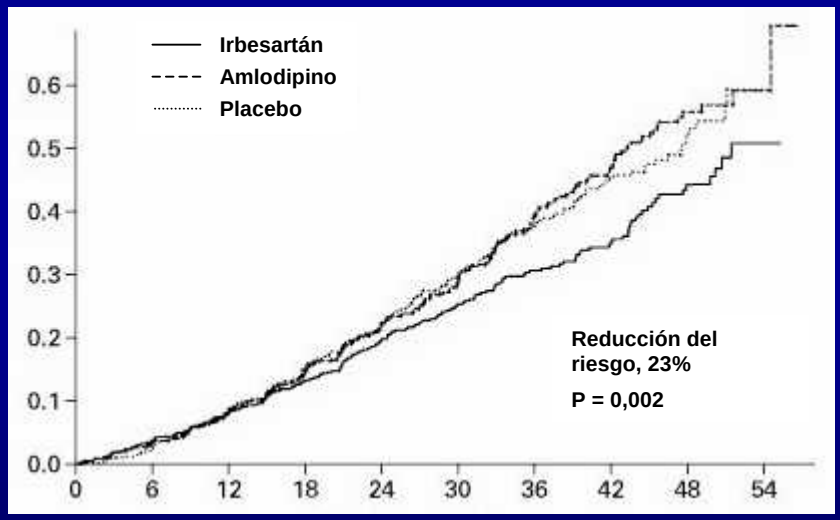
ARAs

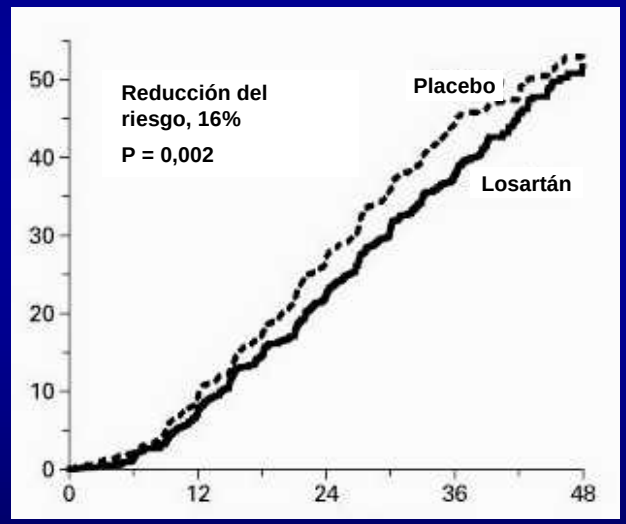
EFECTO DE LOS ARA2 EN LA PROGRESIÓN DE LA NEFROPATÍA ESTABLECIDA ASOCIADA A DIABETES TIPO 2

IDNT

RENAAL

Porcentaje de pacientes que sufren una duplicación de la creatinina, IRCT o muerte





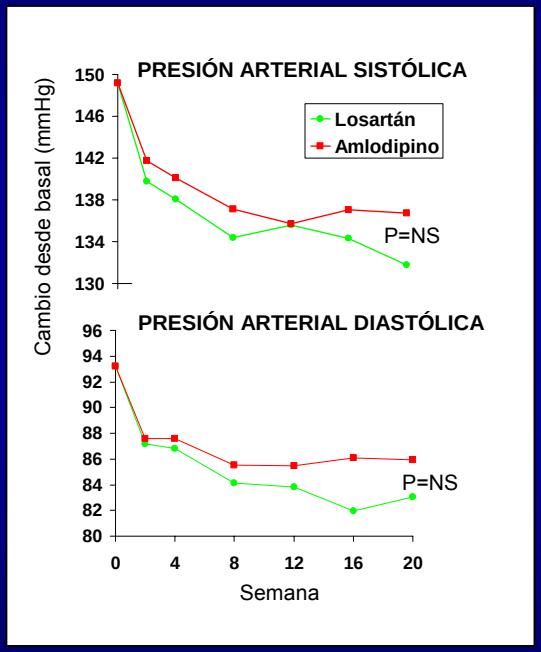
Meses de seguimiento

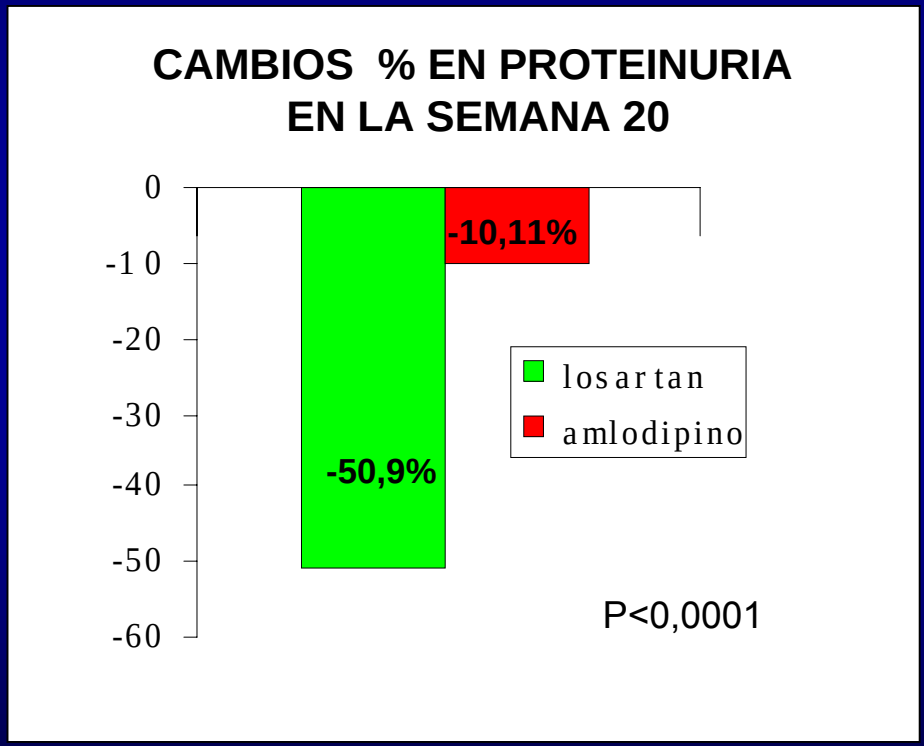
Lewis EJ, et al.
N Engl J Med 2001;345:851-860.

Brenner BM, et al.
N Engl J Med 2001;345:861-869.

Estudio GLOMERULAAR

Eficacia de losartán versus amlodipino en pacientes con nefropatía crónica proteinúrica no diabética

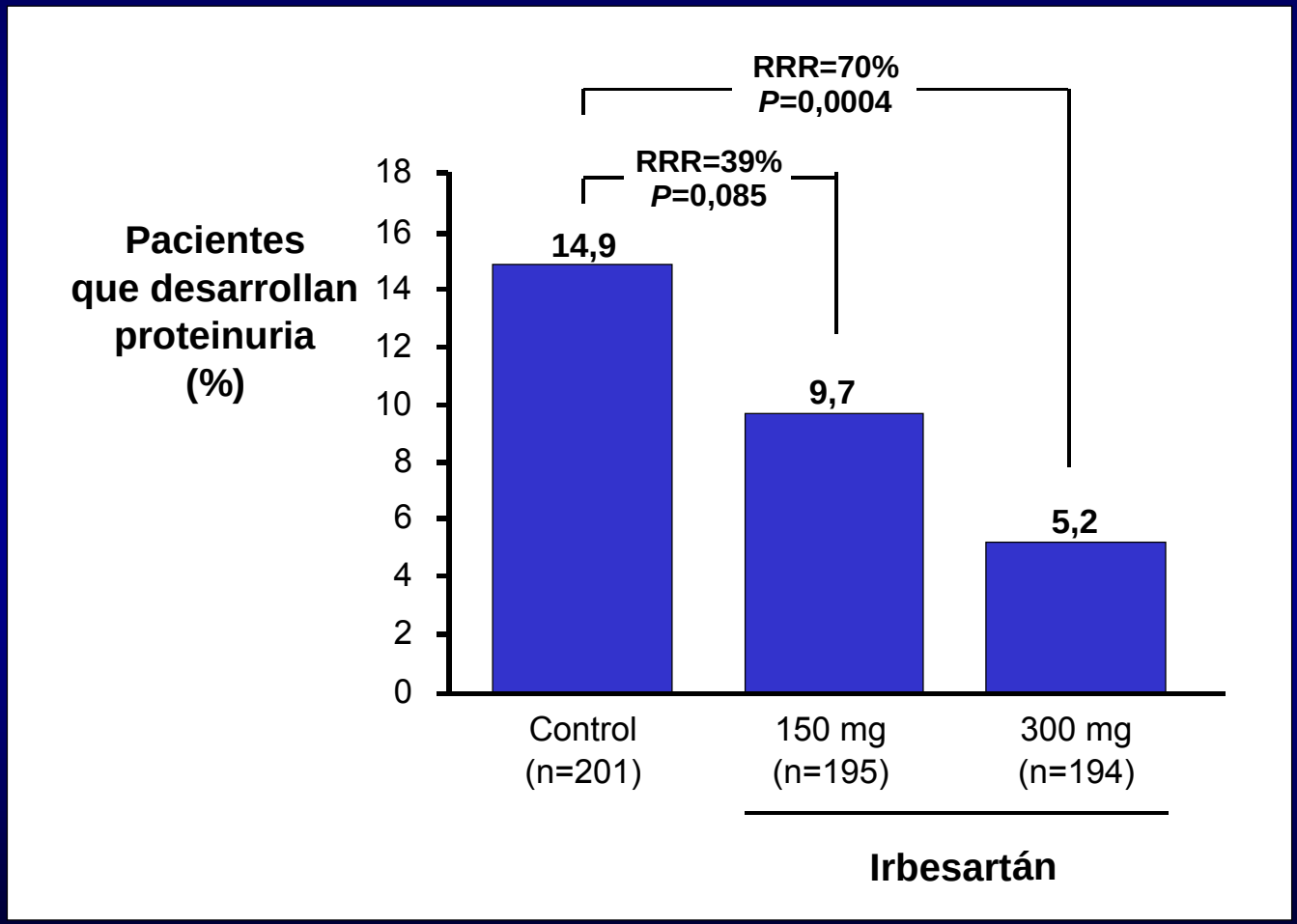




Praga, et al. Nephrol Dial Transplant 2003; 18: 1806-1813.

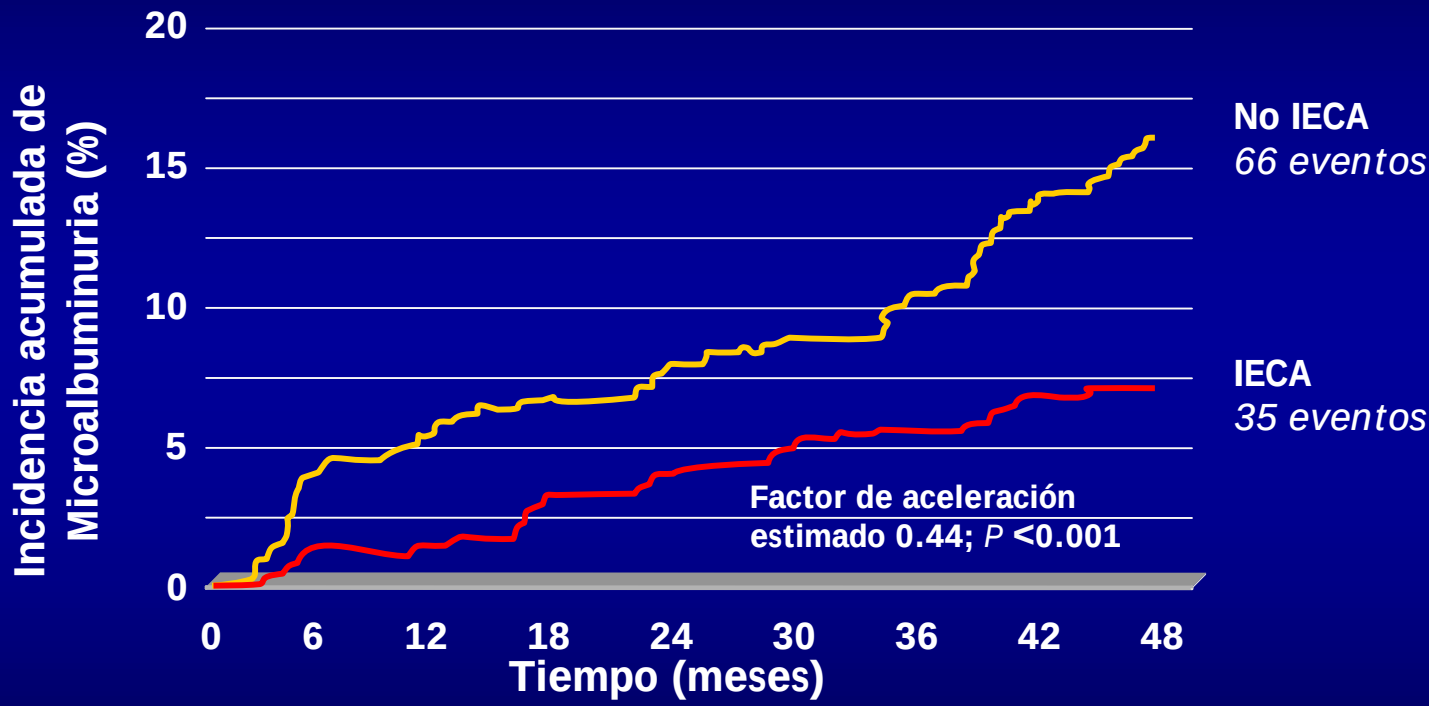
EFECTO DE IRBASARTÁN EN EL DESARROLLO DE NEFROPATÍA EN PACIENTES CON DIABETES TIPO 2

IRMA 2



Parving HH, et al. N Engl J Med 2001;345:870-878.

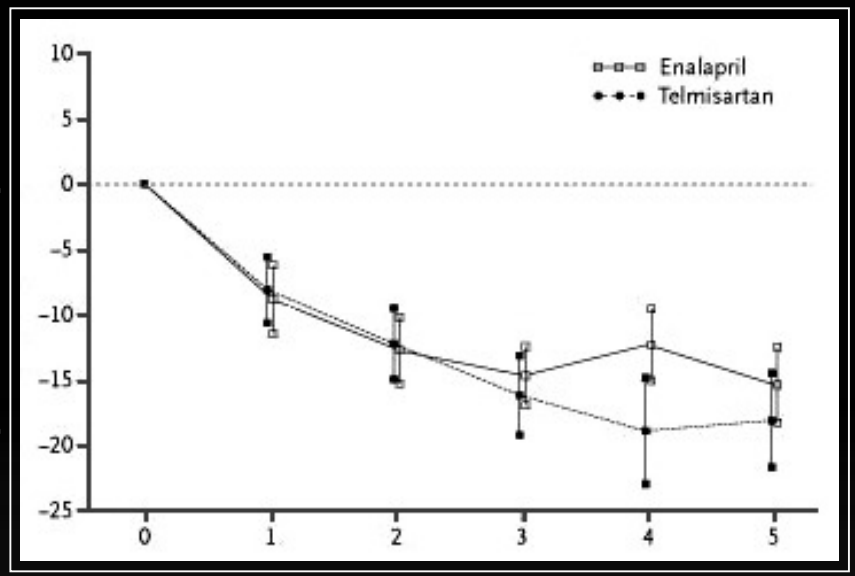
INCIDENCIA DE MICROALBUMINURIA A LO LARGO DEL TIEMPO: IECA VERSUS NO IECA



No. al riesgo									
ACE inhibitor	601	503	469	441	417	399	380	311	220
No ACE inhibitor	603	463	424	405	376	357	338	270	188

Ruggenenti P et al. N Engl J Med 2004; 351: 1941-51.

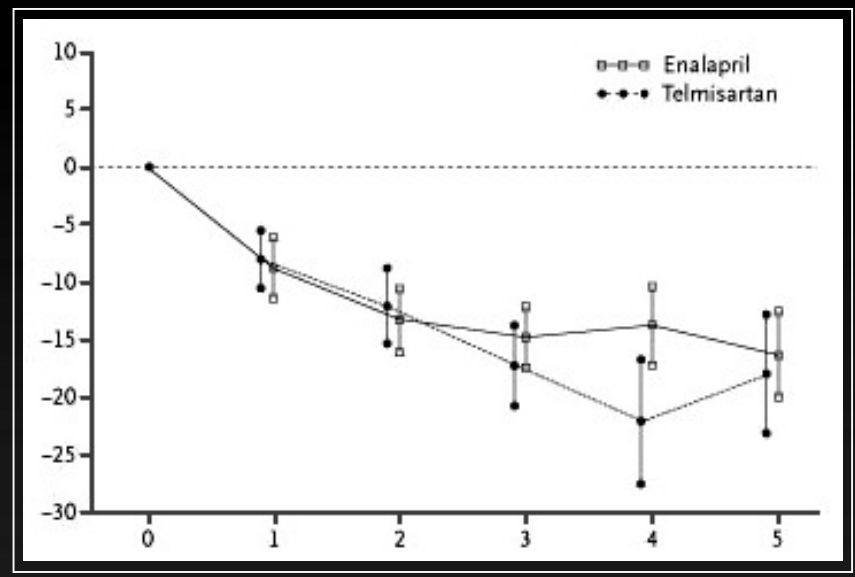
IECA VS ARA2: Estudio DETAIL



Nº con riesgo – Nº total (nº realizado)

Enalapril	103(0)	110(22)	113(23)	113(40)	113(39)
Telmisartán	86(0)	99(23)	102(21)	102(31)	103(41)

DM2 + malb (n= 250)
Seguimiento 5 años



Barnett et al. NEJM 2004: 351: 1952-61

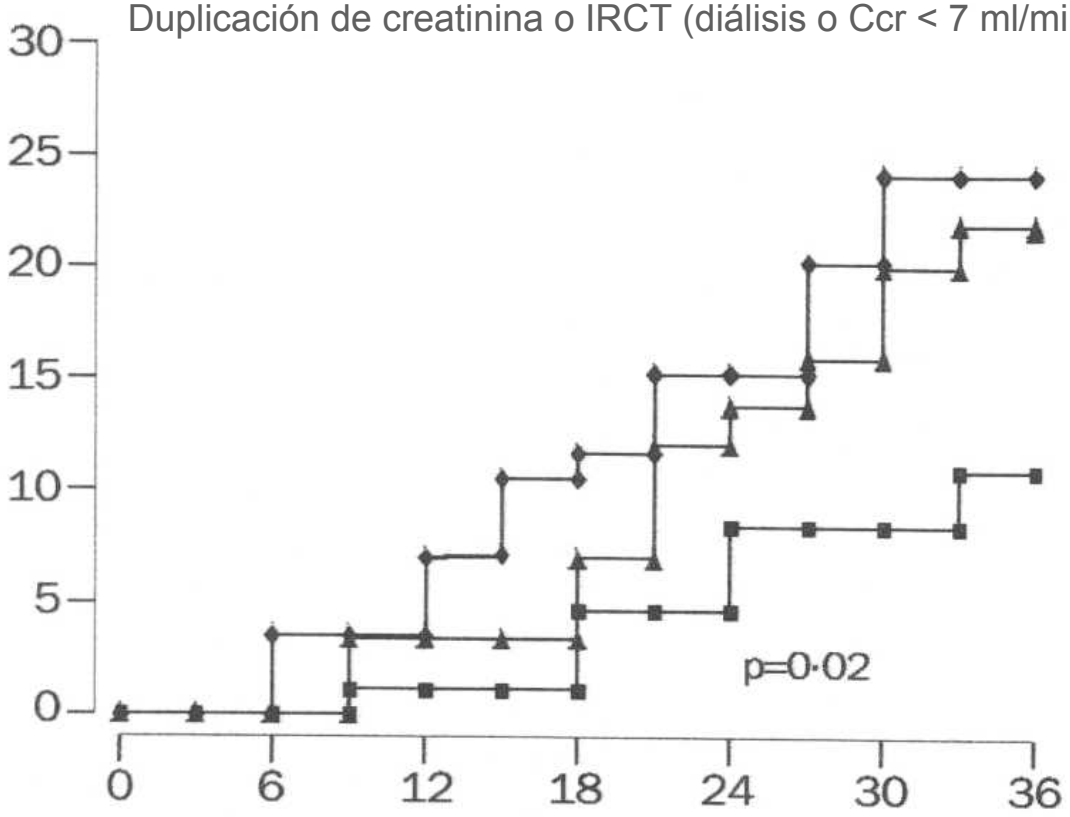
IECAs + ARAs

ESTUDIO	N	PACIENTES	FÁRMACOS	EFECTO PROTEINURIA	EFECTO PA
Russo et al Am J Kidney Dis 1999	**16**	**Nefropatía IgA**	ENA 10-20 mg LOS 50-100 mg	↓	≈
Mogensen et al BMJ 2000	**199**	**DM 2 + μ Alb**	LIS 20 mg CAN 16 mg	↓	↓
Ruilope et al J Hypertens 2000	**108**	**IRC**	BEN 5 ó 10 mg VAL 80 ó 160 mg	↓	↓
Agarwal Kidney Int 2001	**16**	**IRC**	LIS 40 mg LOS 50 mg	↔	↔
Ferrari et al J Hypertens 2002	**10**	**GN no DM**	FOS 20 mg IRB 150 mg	↓	↓
Laverman et al Kidney Int 2002	**9**	**Proteinuria no DM**	LIS 10-20-40 mg LOS 50-100-150	↓	↓
Kincaid-Smith et al NDT 2002	**60**	**IRC**	Varios IECA CAN 8 mg	↓	↓
Jacobsen et al NDT 2002	**21**	**DM 1 + Proteinuria**	Varios IECA IRB 300 mg	↓	↓
Luño et al Kidney Int 2002	**45**	**Nefropatía primaria**	LIS 40-20 mg CAN 32-16 mg	↓	↔
Campbell et al Kidney Int 2003	**24**	**Nefropatía no DM**	BEN 20-10 mg VAL 160-80 mg	↓	↔

Estudio COOPERATE

Porcentaje de pacientes que sufren un evento principal

Duplicación de creatinina o IRCT (diálisis o Ccr < 7 ml/min/1,73 m^2)



Trandolapril (20, 23%)

Losartán (20, 23%)

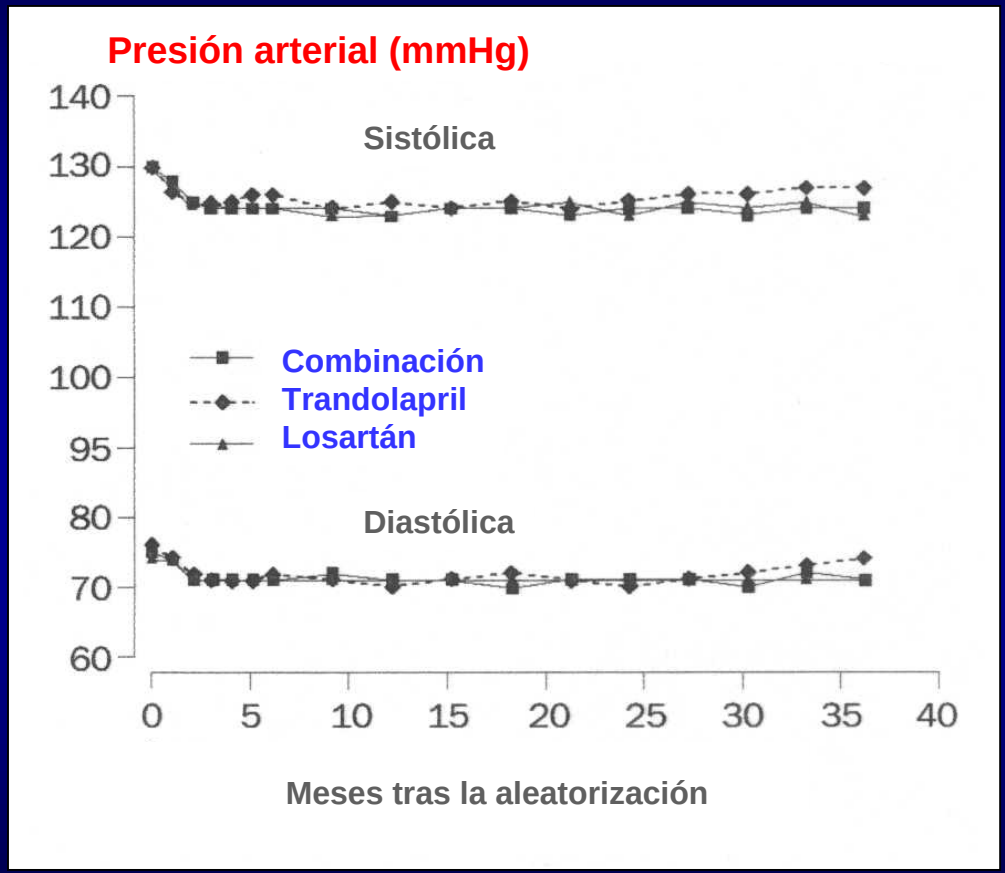
Combinación (10, 11%)

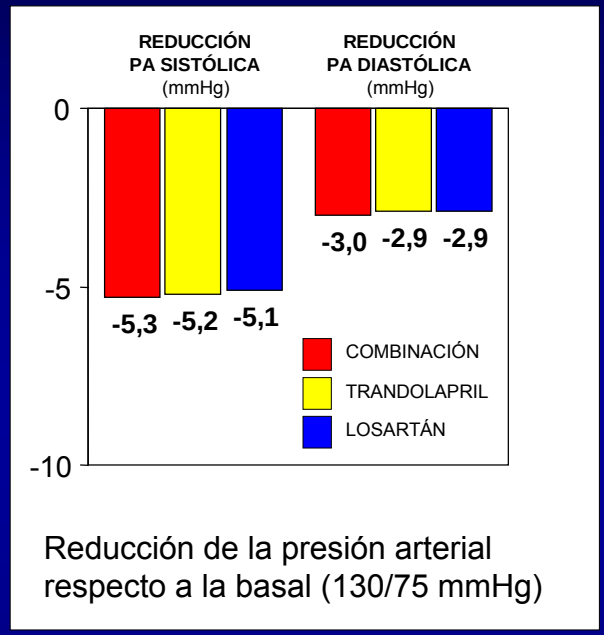
HR 0,40 IC 95% 0,17-0,69
Combinación vs. Losartán

HR 0,38 IC 95% 0,18-0,63
Combinación vs. Trandolapril

Nakao N, et al. Lancet 2003;361:117-124.

Estudio COOPERATE





Reducción de la presión arterial respecto a la basal (130/75 mmHg)

Presión arterial por grupo de tratamiento

Nakao N, et al. Lancet 2003;361:117-124.

Keywords: angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, renin-angiotensin system inhibition, mild renal insufficiency, proteinuria

Combination is better than monotherapy with ACE inhibitor or angiotensin receptor antagonist at recommended doses

Julián Segura, Manuel Praga, Carlos Campo, José L Rodicio, Luis M Ruilope

Hypertension Unit, Nephrology Department, Hospital 12 de Octubre, Madrid, Spain

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Accepted for publication 24th January 2003

JRAAS 2003:**4**:43–7

Abstract

Objective

The combination of an angiotensin-converting enzyme (ACE) inhibitor and an angiotensin II (Ang II) receptor antagonist (ARB) could provide a higher degree of blockade of the renin-angiotensin system(RAS) than either agent alone. The primary aim of this study was to look at the effect of three therapeutic regimens (titrated ACE inhibitor (ACE-I) versus titrated ARB versus the combination of an ACE-I and an ARB) on the attainment of adequate blood pressure (BP) control and antiproteinuric effect. Both ACE-I and ARB were titrated as monotherapy up to the maximal recommended dose.

Methods

A pilot randomised, parallel group open-label study was conducted in 36 patients with primary renal disease, proteinuria above 1.5 g/day and BP >140/90 mmHg while on therapy with an ACE-I. Patients were randomly assigned to (1) benazepril, n=12; (2) valsartan, n=12; or (3) benazepril plus valsartan, n=12. Other antihypertensive therapies could also be added to attain goal BP (<140/90 mmHg). The primary endpoint was the change in proteinuria during six months of follow-up.

Results

In the presence of similar BP decreases and stable creatinine clearance values, mean proteinuria decreases were 0.5±1.7, 1.2±2.0 and 2.5±1.8 g/day in groups 1, 2 and 3, respectively. When compared with baseline values, only the fall induced by the combination of ARB and ACE-I attained statistical significance ($p<0.05$).

Conclusion

The antiproteinuric capacity of monotherapy at recommended doses with either an ACE-I or an ARB is lower than that obtained with the combination of the two drugs.

Figure 1 Evolution of proteinuria during follow-up

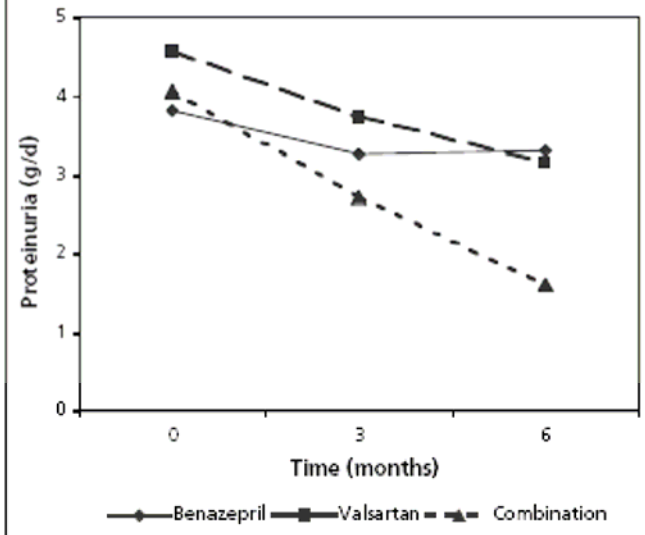
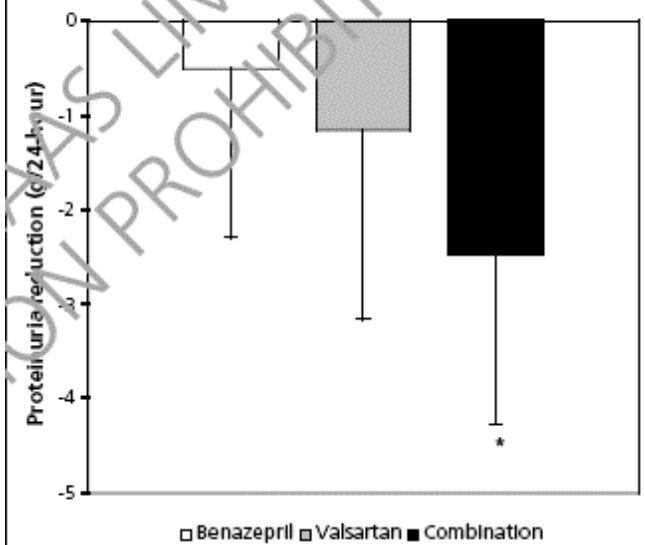
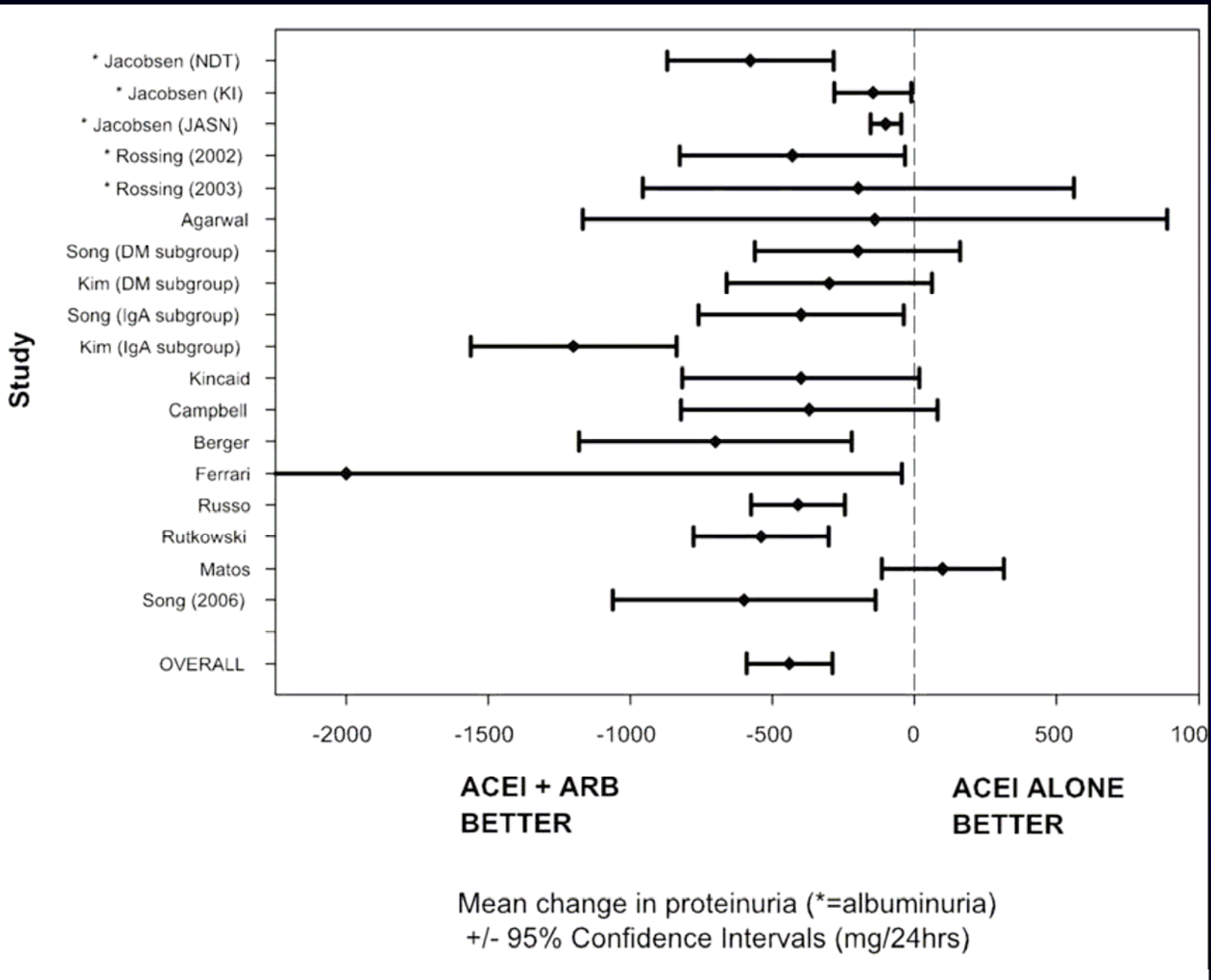


Figure 2 Reduction of proteinuria after treatment. Data are expressed as mean reduction±standard deviation. * $p<0.05$ compared with benazepril group





MacKinnon M et al. Am J Kidney Dis 2006; 48: 8-20.

ARAs

Long-term safety of high-dose angiotensin receptor blocker therapy in hypertensive patients with chronic kidney disease

Adam J. Weinberg[a], Dion H. Zappe[b], Rajeev Ramadugu[c] and Marc S. Weinberg[b,c,d]

Background Reducing urinary protein excretion in patients with renal disease is an important therapeutic target to prevent the progression of renal and cardiovascular disease. Drugs such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (ARBs), which block the actions of the renin–angiotensin–aldosterone system, are recommended because they reduce blood pressure and proteinuria. Recently, the use of higher doses of ARBs, up to three times the maximal approved dose, resulted in further reductions in protein excretion. Despite the effectiveness of this therapeutic approach, no long-term safety analysis has been conducted in patients receiving high-dose ARB treatment.

Objective To study the long-term safety of high-dose ARB treatment.

Methods We observed 48 patients [44 men and 4 women; ages 64 ± 15 years (mean ± SD), weight 99 ± 28 kg, estimated glomerular filtration rate 53 ± 23 ml/min] receiving treatment with high doses (1.5–5 times greater than the maximum approved dose) of ARBs, for 40 ± 24 months (range 6–98 months).

Results The average ARB dose tended to increase over time and was 3.2 ± 1.2 times greater at the end of the study than that at the start. Systolic blood pressure was similar at the beginning and end of the study period (132 ± 20 and 125 ± 20 mmHg, respectively), but diastolic blood pressure showed a decrease throughout the study and was significantly reduced ($P < 0.05$) in association with 1.5× and 2× the maximum ARB dose (73 ± 11 and 72 ± 10 mmHg, respectively) when compared with baseline (78 ± 11 mm Hg). There was a trend ($P > 0.05$) for increases in concentrations of serum potassium (0.2 ± 0.9 mmol/l) and creatinine (0.3 ± 0.7 mg/dl) with increases in dose from baseline to the end of the study. Serum creatinine concentration was greater ($P < 0.05$) at the periods of 3× and 4× the maximum dose, but this represented increases of only 12 and 20% from baseline, respectively.

Conclusions High-dose ARB treatment in patients with chronic renal disease is not associated with any clinically significant long-term negative effects on serum creatinine or potassium and is thus a important therapeutic modality with which to achieve further reductions in urinary protein excretion. *J Hypertens* 24 (suppl 1):S95–S99 © 2006 Lippincott Williams & Wilkins.

Journal of Hypertension 2006, 24 (suppl 1):S95–S99

Keywords: angiotensin II type 1-receptor blockers, blood pressure, chronic kidney disease, hyperkalemia, hypertension, proteinuria, renin–angiotensin system, serum creatinine

the study. Most patients in this study ($n = 34$) were administered candesartan cilexetil; valsartan ($n = 6$), losartan ($n = 6$), irbesartan ($n = 3$) and olmesartan ($n = 2$) were also used. The mean age was 64 ± 15 years,

Long-Term Renoprotective Effects of Standard Versus High Doses of Telmisartan in Hypertensive Nondiabetic Nephropathies

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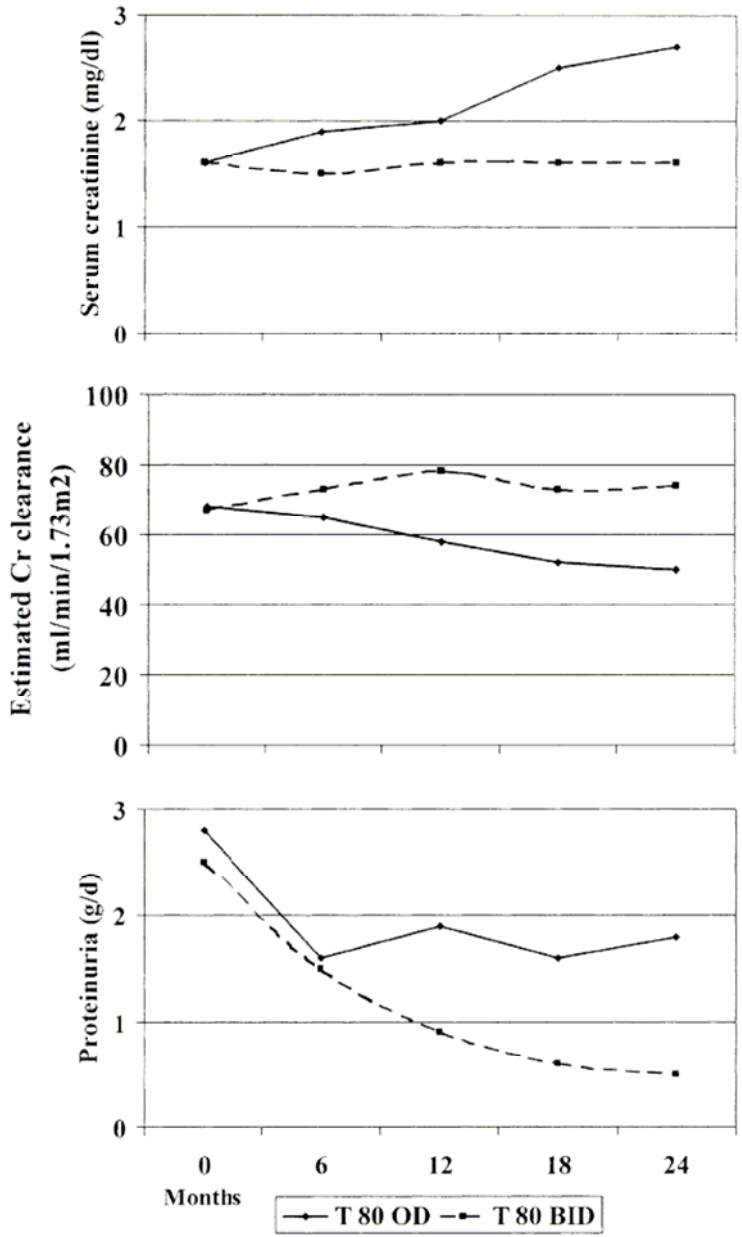
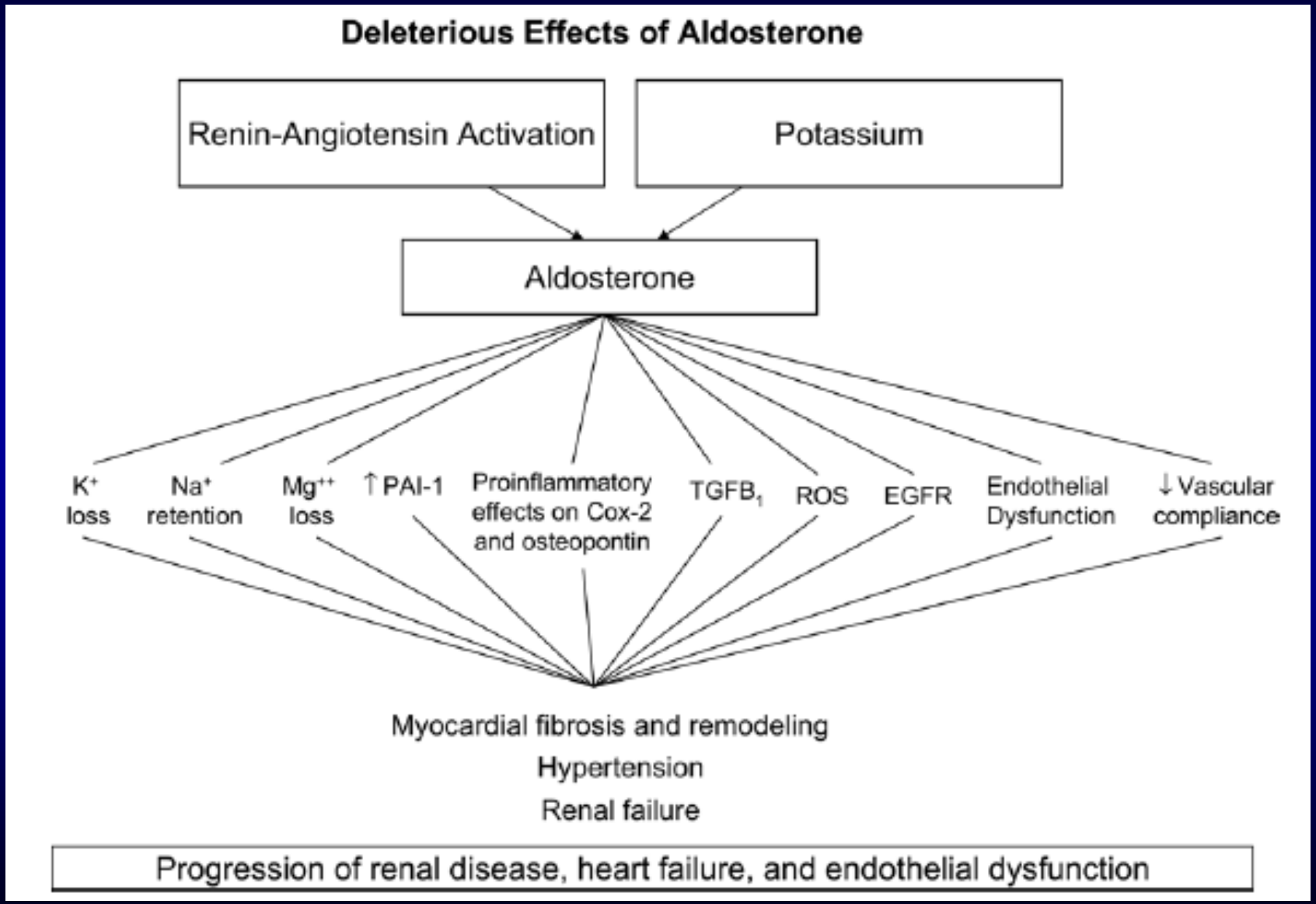
• *Background:* This report describes an open randomized study intended to evaluate the long-term renoprotective effects of "standard" (80 mg once daily) versus "high" (80 mg twice daily) doses of telmisartan in hypertensive patients without diabetes with biopsy-proven chronic proteinuric nephropathies. *Methods:* We included 78 patients (age, 43.5 ± 13.2 years; 71.8% men). After a 4-week wash-out period, patients were randomly assigned to telmisartan, 80 mg once daily (n = 40) or 80 mg twice daily (n = 38), during a mean follow-up of 24.6 ± 2.2 months. *Results:* Baseline characteristics were similar in both groups, including blood pressure, renal function, and proteinuria. Blood pressure control did not differ between groups during follow-up. In the group administered telmisartan, 80 mg once daily, serum creatinine level increased from 1.6 ± 0.6 to 2.7 ± 0.9 mg/dL (141 ± 52 to 239 ± 80 μmol/L), and estimated creatinine clearance declined from 68 ± 30 to 50 ± 34 mL/min (1.13 ± 0.50 to 0.83 ± 0.57 mL/s), whereas in those administered 80 mg twice daily, serum creatinine (1.6 ± 0.7 to 1.6 ± 0.8 mg/dL [141 ± 62 to 141 ± 71 μmol/L]) and estimated creatinine clearance values (67 ± 38 to 74 ± 38 mL/min [1.12 ± 0.63 to 1.23 ± 0.63 mL/s]) did not change during the study. The decrease in proteinuria was more pronounced ($P < 0.01$) in patients administered the high dose of telmisartan compared with those treated with the standard dose. Serum potassium levels and lipid profiles did not change significantly in either group. *Conclusion:* Long-term administration of high doses of telmisartan seems to improve the efficacy of the drug to decrease proteinuria and slow the progression to end-stage renal failure in nondiabetic hypertensive renal disease. *Am J Kidney Dis* 46:1074-1079.



Bloqueo de aldosterona

Efectos antiproteinúricos del bloqueo de aldosterona



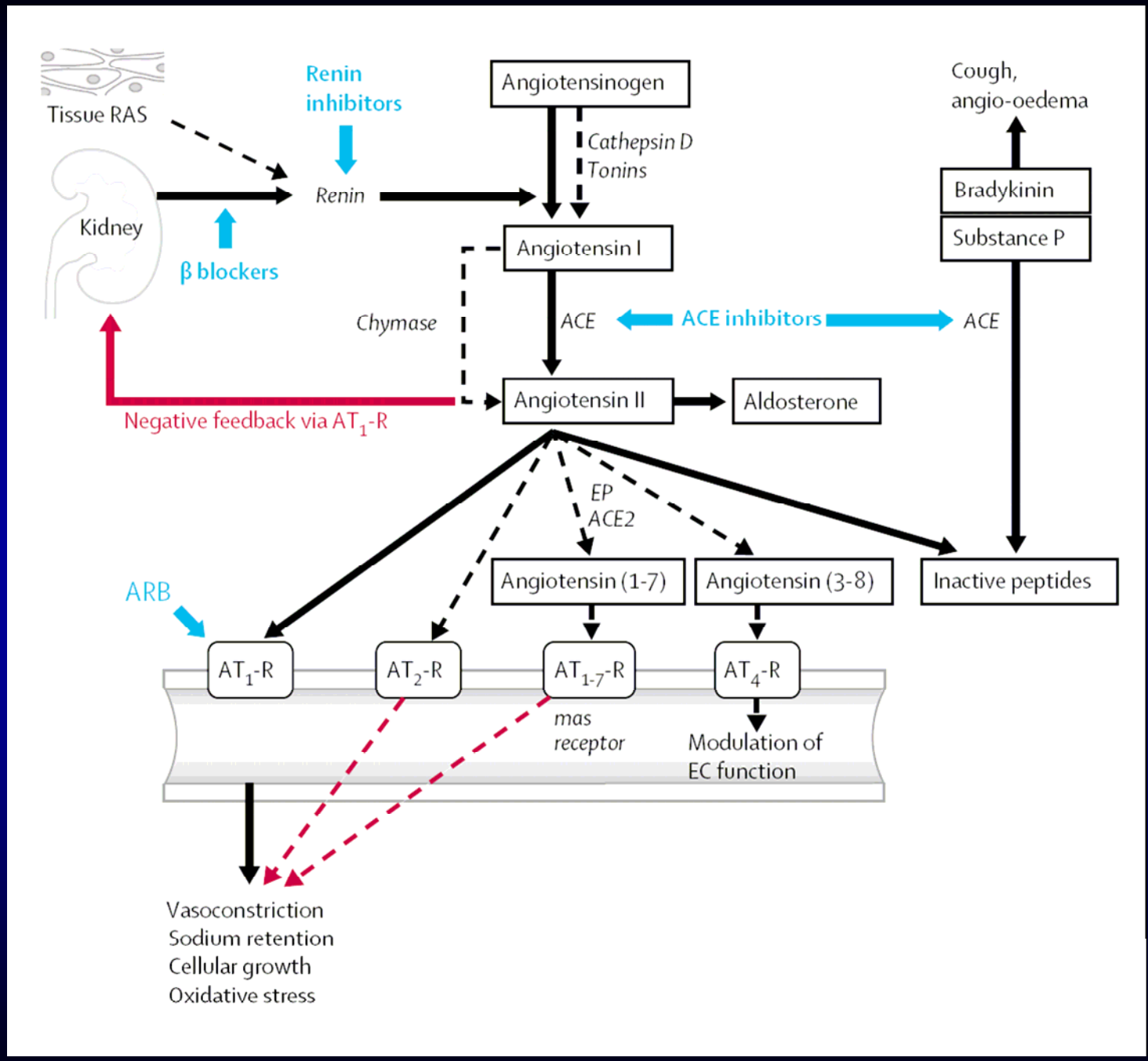
Epstein M. Am J Med 2006; 119: 912-919.

Efectos antiproteinúricos del bloqueo de aldosterona

Study	Study Design	Study Patients	No. of Pts	Intervention	Length	Endpoint	Results
Epstein et al, 2002[31]	Randomized, double-blind	Type 2 diabetics w/ mild to-moderate hypertension and microalbuminuria	215	EPL 200 mg/d vs ENAL 40 mg/d vs EPL 200 mg/d + ENAL 10 mg/d	24 wk	Change in UACR	↓ UACR
Epstein et al, 2006[32]	Randomized, double-blind, placebo-controlled, parallel group	Type 2 diabetics	268	EPL 50 mg/d vs EPL 100 mg/d vs placebo, all in addition to enalapril 20 mg/d	12 wk	Change in UACR	↓ UACR
Rachmani et al, 2004[33]	Randomized, prospective	Female type 2 diabetics	46	Cilazapril 5 mg/day or SPL 100 mg/day in addition to baseline atenolol and HCTZ	24 wk	Change in ACR	↓ ACR
Rossing et al, 2005[34]	Randomized, double-masked, placebo-controlled crossover	Type 2 diabetics w/nephropathy	20	SPL 25 mg/d in addition to baseline diuretics and maximally recommended doses of ACEI/ARBs	28-wk periods	Change in albuminuria	↓ Albuminuria
Schjoedt et al, 2005[35]	Randomized, double-masked, placebo-controlled crossover	Caucasian type 1 diabetics w/persistent microalbuminuria	20	SPL 25 mg/d in addition to baseline ACEI/ARB and diuretics	2 mo	Change in albuminuria (24-hr urine)	↓ Albuminuria
Sato et al, 2005[36]	Prospective, open-label, uncontrolled	Chronic renal disease w/ proteinuria persistently >0.5 g/d	32	SPL 25 mg/d added to baseline trandolapril	12 wk	Change in proteinuria (urine protein)	↓ Proteinuria
Bianchi et al, 2005[37]	Prospective, open-label, uncontrolled	CKD (eGFR* 20-138 mL/min)	42	SPL 25 mg/day added to baseline ACEI/ARB	8 wk	Change in proteinuria (urine protein)	↓ Proteinuria
Chrysostomou et al, 2006[38]	Randomized, double-blind, placebo-controlled	Persistent proteinuria >1.5 g/d	41	Ramipril 5 mg/d vs ramipril 5 mg/d + irbesartan 150 mg/d vs ramipril 5 mg/d + spironolactone 25 mg/d vs. ramipril 5 mg/d + irbesartan 150 mg/d + spironolactone 25 mg/d	3 mo	Change in proteinuria (urine protein)	↓ Proteinuria (there was a greater reduction in proteinuria in the 2 treatment regimens that incorporated spironolactone)

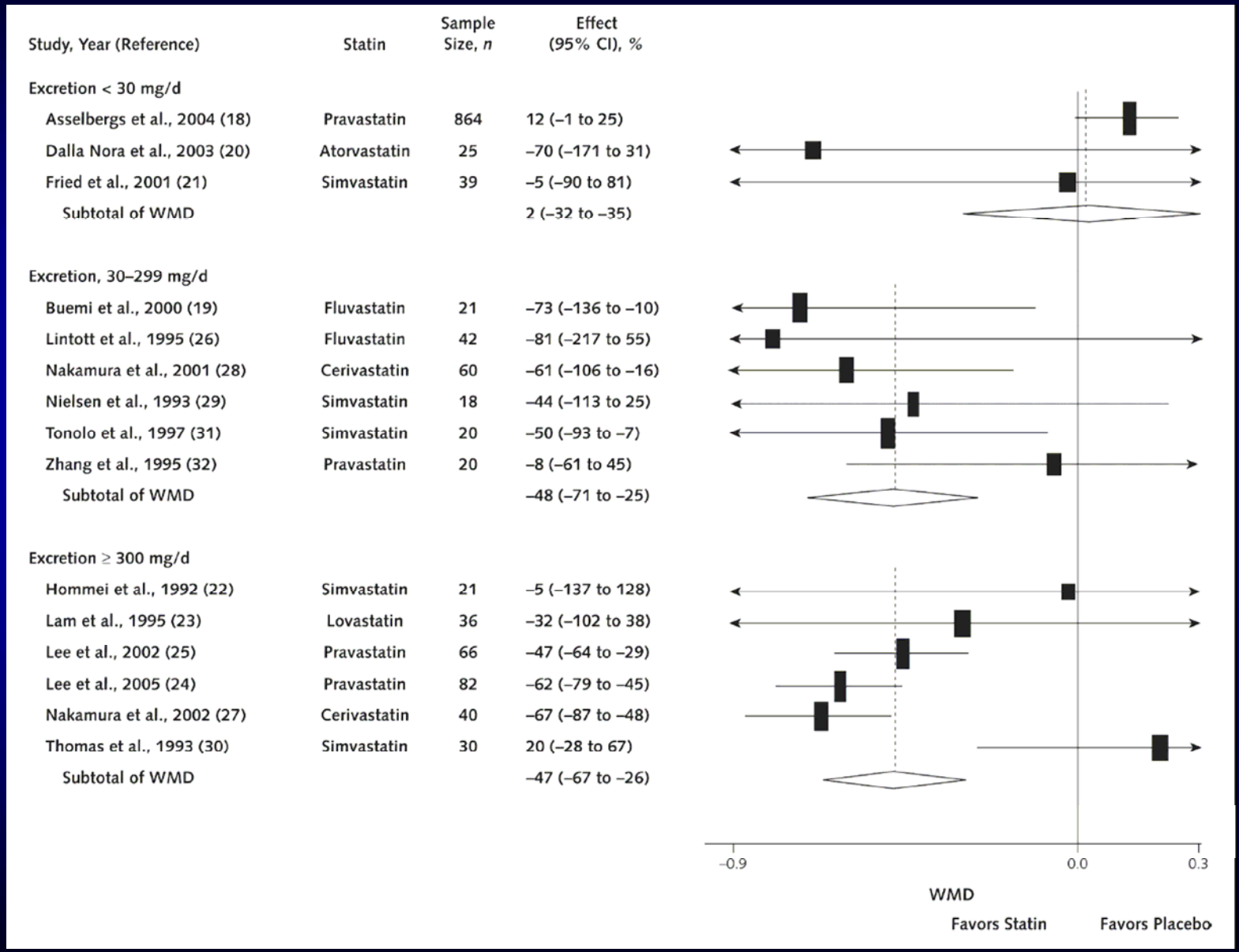
Epstein M. Am J Med 2006; 119: 912-919.

Inhibición de renina



Staessen JA, et al. Lancet 2006; 368: 1449-1456.

Efecto de las estatinas sobre la excreción urinaria de albúmina



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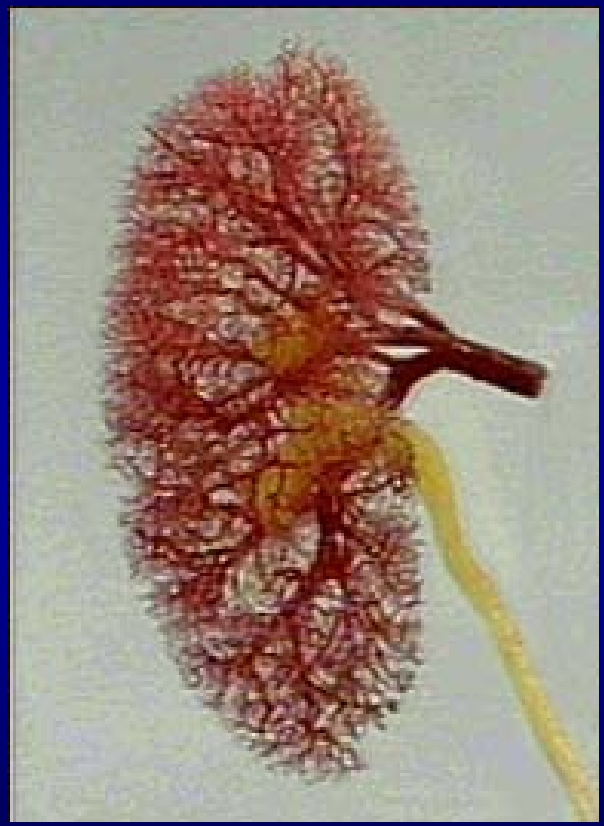

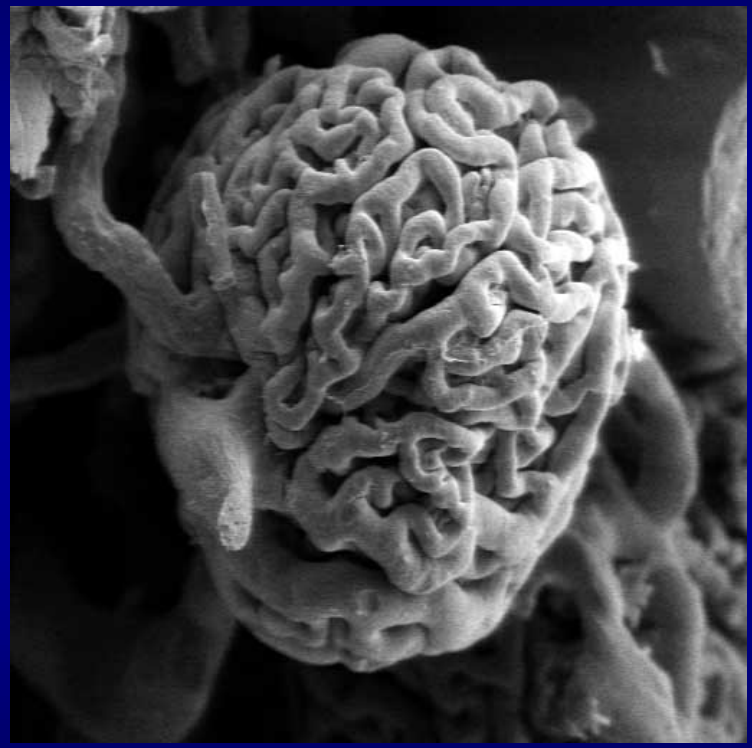

Lo que es bueno para el vaso, no debe ser malo para el riñón…