Valori pressori e danno renale

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Hypertension and Kidney Disease: A Deadly Connection

Yousri M. Barri, MD

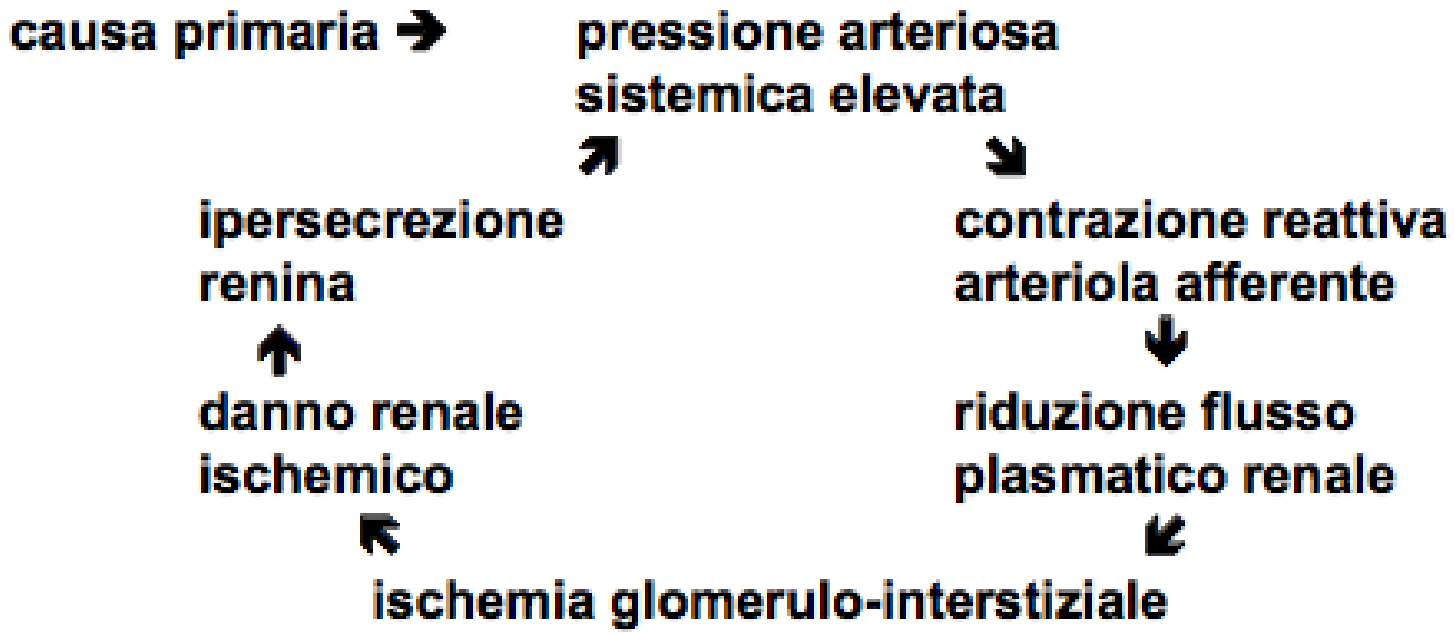
Current Cardiology Reports 2006, 8: 411-417

[…]The association between kidney disease and Hypertension has been complex, as **hypertension can cause kidney disease and conversely kidney disease can be complicated by the development of hypertension** […]

The combination of hypertension and kidney disease amplifies the rate of complications, specifically cardiovascular events. […]

Danno renale e ipertensione

→ Ipertensione come causa di danno renale



Hypertension and Prehypertension and Prediction of Development of Decreased Estimated GFR in the General Population: A Meta-analysis of Cohort Studies

Carlo Garofalo, MD,[1] Silvio Borrelli, MD,[1] Mario Pacilio, MD,[1] Roberto Minutolo, MD, PhD,[1] Paolo Chiodini, MSc,[2] Luca De Nicola, MD, PhD,[1] and Giuseppe Conte, MD[1]

Am J Kidney Dis. 2016;67(1):89-97

Predictors: Hypertension (BP . 140/90 mm Hg), prehypertension (systolic BP of 120-139 and/or diastolic BP of 80-89 mm Hg), and BP as a continuous variable.

Results: Data from 16 cohorts (315,321 participants) were analyzed The presence of prehypertension and hypertension increased renal risk (RRs of 1.19 [95% CI, 1.07-1.33; I2 5 23.8%] and 1.76 [95% CI, 1.58-1.97; I2 5 37.7%], respectively). Similarly, we found that every 10–mm Hg increase in systolic and diastolic BPs associated with higher risk for decreased eGFR (RRs of 1.08 [95% CI, 1.04-1.11; I2 5 60.0%] and 1.12 [95% CI, 1.04-1.20; I2 5 51.4%], respectively). Metaregression analysis showed greater risk with older age (P 5 0.03), whereas other covariates were not significant.

Conclusions: Prehypertension and hypertension, as BP levels, are independent predictors of decreased GFR in the general population, with the effect being more pronounced in the elderly.

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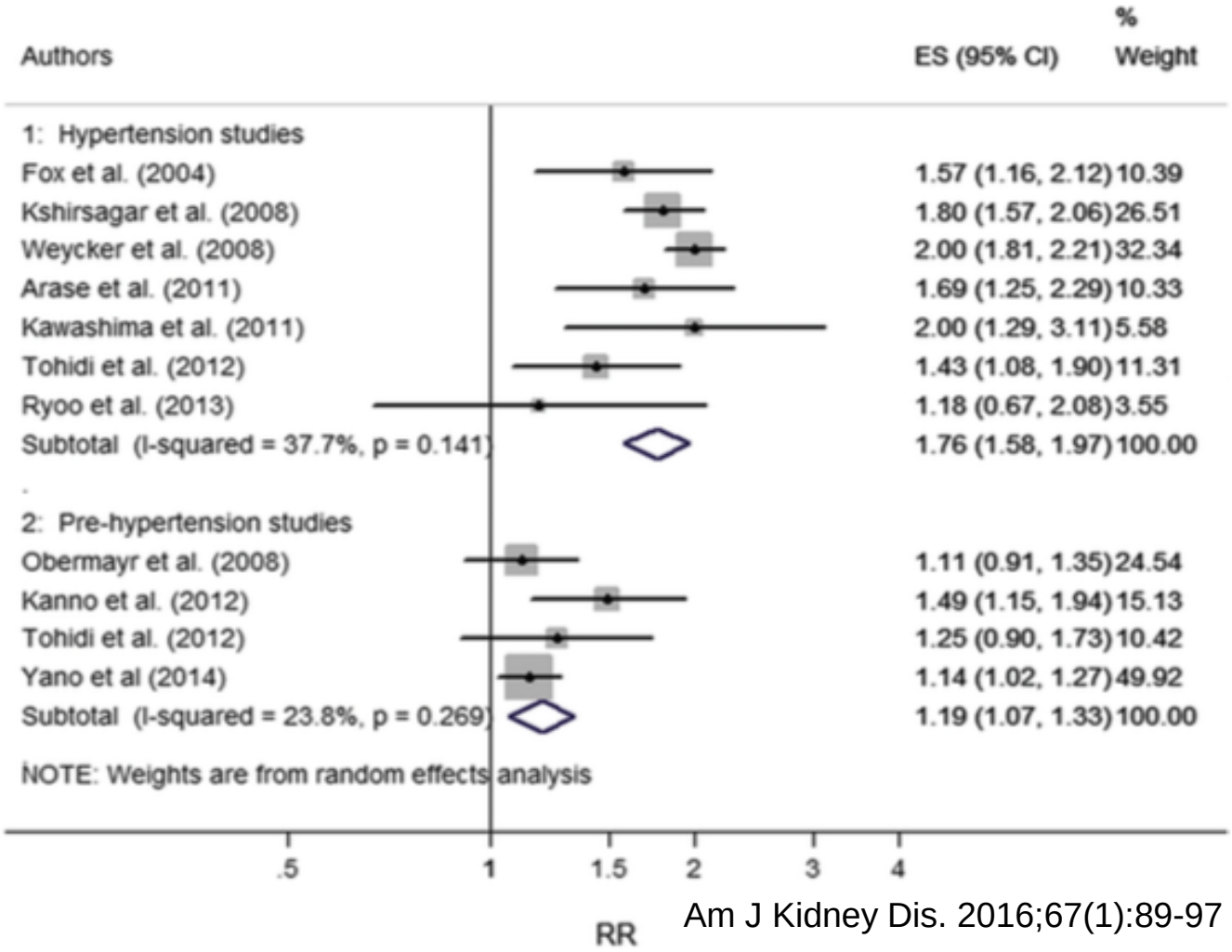

Am J Kidney Dis. 2016;67(1):89-97

Figure 2. Forest plot of comparison: (top) hypertension versus optimal blood pressure and (bottom) prehypertension versus optimal blood pressure; outcome: onset of decreased estimated glomerular filtration rate. Abbreviations: CI, confidence interval; ES, effect size; RR, relative risk.

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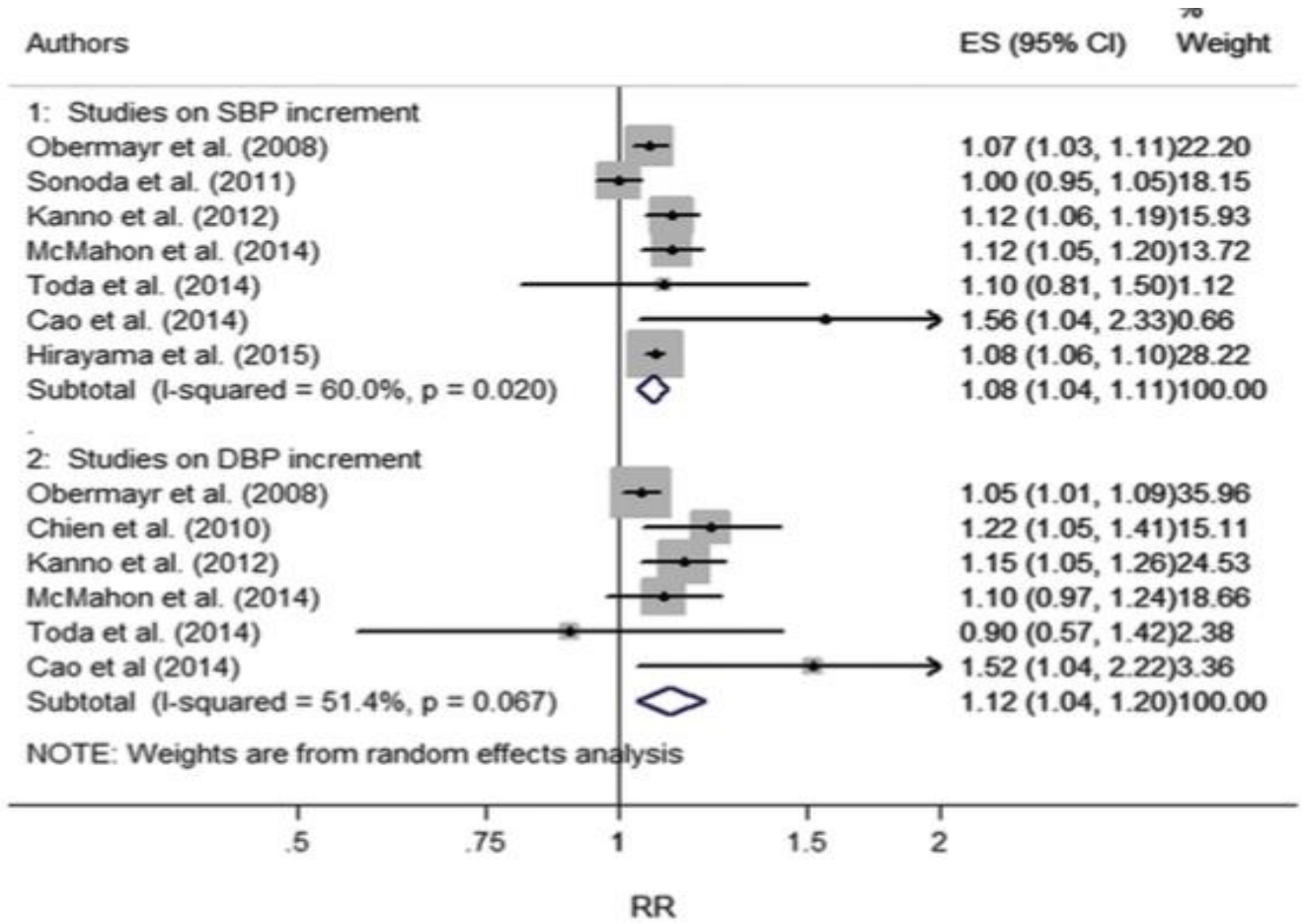

Figure 4. Forest plot of comparison: increments of 10 mm Hg of (top) systolic (SBP) and (bottom) diastolic blood pressure (DBP) versus optimal blood pressure, outcome: onset of decreased estimated glomerular filtration rate. Abbreviations: CI, confidence interval; ES, effect size; RR relative risk.

2013 ESH/ESC Guidelines for the management of arterial hypertension

Valutazione del danno d'organo renale nell'ipertensione arteriosa

Kidney		
Measurement of serum creatinine and estimation of GFR is recommended in all hypertensive patients.[d]	I	B
Assessment of urinary protein is recommended in all hypertensive patients by dipstick.	I	B
Assessment of microalbuminuria is recommended in spot urine and related to urinary creatinine excretion.	I	B

Predictive value, availability, reproducibility and cost–effectiveness of some markers of organ damage

Marker	Cardiovascular predictive value	Availability	Reproducibility	Cost-effectiveness
Estimated glomerular filtration rate	+++	++++	++++	++++
Microalbuminuria	+++	++++	++	++++

Microalbuminuria proteinuria

2013 ESH/ESC Guidelines for the management of arterial hypertension

- […]Microalbuminuria has been shown to predict the development of overt diabetic nephro-pathy in both type 1 and type 2 diabetic patients.
- In both diabetic and non-diabetic hypertensive patients, microalbuminuria, even below the threshold values usually considered, has been shown to predict CV events.

Albuminuria come Target terapeutico?

Albuminuria Is an Appropriate Therapeutic Target in Patients with CKD: The Pro View

Hiddo J. Lambers Heerspink and Ron T. Gansevoort†*

Clin J Am Soc Nephrol 10, 2015.

Albuminuria is Not an Appropriate Therapeutic Target in Patients with CKD: The Con View

Linda F. Fried and Julia Lewis†*

Albuminuria Is an Appropriate Therapeutic Target in Patients with CKD: The Pro View

Hiddo J. Lambers Heerspink and Ron T. Gansevoort†*

- **L'albuminuria è causa di danno renale** → non solo marker di danno, ma anche causa stessa di danno renale. Effetto tossico diretto sul tessuto renale con progressiva perdita di funzionalità renale e danno tubulointerstiziale.

•**Albuminuria predice la comparsa di ESRD** → l'albuminuria è un potente marker di danno renale (ad oggi ancora il più potente anche rispetto ai nuovi marker emergenti)

•**La riduzione deli livelli di albuminuria mediante uso di farmaci porta a un miglioramento dell'outcome renale.**

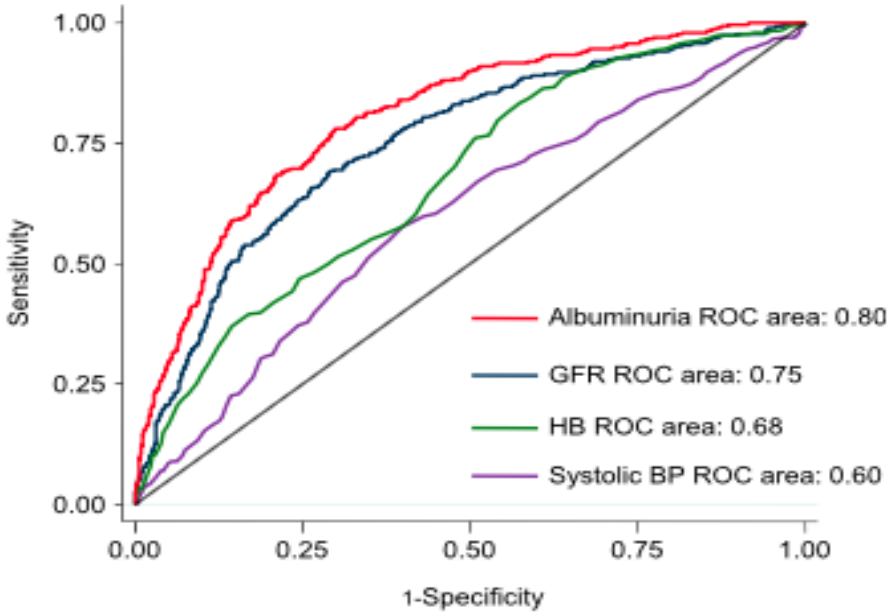

Figure 1. | Area under the receiver operating characteristic (ROC) curve for prediction of ESRD of different renal risk markers in patients with diabetic nephropathy. HB, hemoglobin.

Table 1. Short-term changes in albuminuria and subsequent renoprotection in different clinical trials

Study	Population	eGFR (ml/min per 1.73 m^2)	Proteinuria[a]/ Albuminuria	Intervention	Renal End Point	Renal Risk Reduction in Albuminuria
RENAAL (54)	Type 2 diabetes and nephropathy	40	1246 mg/g	Losartan versus placebo	Doubling serum creatinine, ESRD, or death	For each halving of albuminuria during the first 6 months, the risk of ESRD was statistically significantly reduced by one half
IDNT (64)	Type 2 diabetes and nephropathy	47	1500 mg/g	Irbesartan versus Amlodipine versus placebo	Doubling serum creatinine or ESRD	For each halving of albuminuria during the first 12 months, the risk of kidney failure was statistically significantly reduced by more than one half (56%)
AASK (65)	Hypertensive nephrosclerosis	46	80 mg/g[a]	Ramipril versus Metoprolol	ESRD	For each halving of albuminuria during the first 6 months, the risk of ESRD was statistically significantly reduced by more than one half (53%)
ROAD (55)	IgA nephropathy	31	1800 mg/24 h[a]	Losartan or Benazepril	Doubling serum creatinine, ESRD, or death	Renal risk was 80% lower among subjects with a >50% reduction in proteinuria compared with those with a <25% reduction in proteinuria
REIN (66)	Nondiabetic nephropathy	43	3500 mg/24 h[a]	Ramipril versus placebo	GFR decline	GFR decline was significantly slower in patients with a month 3 reduction in proteinuria

Table 1. (Continued)

Study	Population	eGFR (ml/min per 1.73 m^2)	Proteinuria[a]/ Albuminuria	Intervention	Renal End Point	Renal Risk Reduction in Albuminuria
MDRD (51) study A	Nondiabetic nephropathy	39	200 mg/24 h[a]	Low- versus usual protein diet		An initial reduction in proteinuria of 1.0 g/d was associated with a statistically significant 0.9-ml/min per year slower GFR decline during subsequent follow-up
MDRD (51) study B	Nondiabetic nephropathy	19	700 mg/24 h[a]			

RENAAL, Reduction of Endpoints in Non-Insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan; IDNT, Irbesartan Diabetic Nephropathy Trial; AASK, African-American Study of Kidney Disease and Hypertension; ROAD, Renoprotection of Optimal Antiproteinuric Doses; IgA, immunoglobin A; REIN, Ramipril Efficacy in Nephropathy; IRMA-2, Irbesartan Microalbuminuria Type 2 Diabetes in Hypertensive Patients 2; ONTARGET, Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial; MDRD, Modification of Diet in Renal Disease.

[a]Trials with proteinuria measurements.

Albuminuria is Not an Appropriate Therapeutic Target in Patients with CKD: The Con View

Linda F. Fried and Julia Lewis†*

→Non ci sono ad oggi Trial clinici progettati per valutare il ruolo dell'albuminuria come target terapeutico

NON si può assumere che tutti i trattamenti che riducono l'albuminuria riducano la progressione del danno renale.

Microalbuminuria in primary hypertension: a guide to optimal patient management?

J Nephrol (2016) 29:747–753

Francesca Viazzi, Francesca Cappadona, Roberto Pontremoli

→Studio LIFE (2005,Hypertension): la riduzione della microalbuminuria si accompagna alla riduzione degli eventi fatali

→Analisi secondarie dei dati dell'ACCOMPLISH trial (2010, Lancet 375: 1173-1181): associazione ACEi+Ca antagonisti è associato a miglior outcome CV rispetto all'associazione ACEi+diuretico, a dispetto di una maggior riduzione della microalbuminuria nel braccio ACEi+diuretico

→Analisi dei dati dell'ONTARGET trial (2011), J Am Soc Nephrol 22: 1353-1364): analisi dell'albuminuria indipendentemente dal braccio di trattamento hanno mostrato outcome migliore in pazienti che hanno avuto riduzione della microalbuminuria

→**Reduction of albumin urinary excretion is associated with reduced cardiovascular events in hypertensive and/or diabetic patients**. A meta-regression analysis of 32 RCT. (Int J Cardiol 2014, 172: 403-410) Savarese, Mosca et Al

Microalbuminuria in primary hypertension: a guide to optimal patient management?

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Conclusions

Albuminuria, a long-known powerful predictor of future cardiovascular risk in primary hypertension, may also turn out to be an independent target for treatment. In fact, recent studies seem to suggest that its changes over time parallel those in cardiovascular morbidity. If these findings are confirmed and if the time-dependent sequential relationship between changes in albuminuria and incidence of cardiovascular disease is confirmed, the role of albuminuria and its changes over time as a predictor of cardiovascular and renal outcome will be further strengthened. In the meantime, clinicians dealing with hypertensive and with high risk patients in general may rely on this simple, inexpensive and easy-to-use test to optimize the management of their patients.

Danno renale e ipertensione

→ **Insufficienza renale come fattore causante lo sviluppo di ipertensione**

lenta escrezione renale di sodio

↓

ritenzione idrosalina

↓

espansione volume extracellulare (ipervolemia)

↓

aumento gittata cardiaca

↓

ipertensione ad alto volume

Intensive Hemodialysis, Blood Pressure, and Antihypertensive Medication Use

George L. Bakris, MD,[1] John M. Burkart, MD,[2] Eric D. Weinhandl, PhD, MS,[3] Peter A. McCullough, MD, MPH,[4,5,6,7] and Michael A. Kraus, MD[8]

Pazienti dializzati → prevalenza ipertensione 95%in pz con GFR < 30 mL/min;

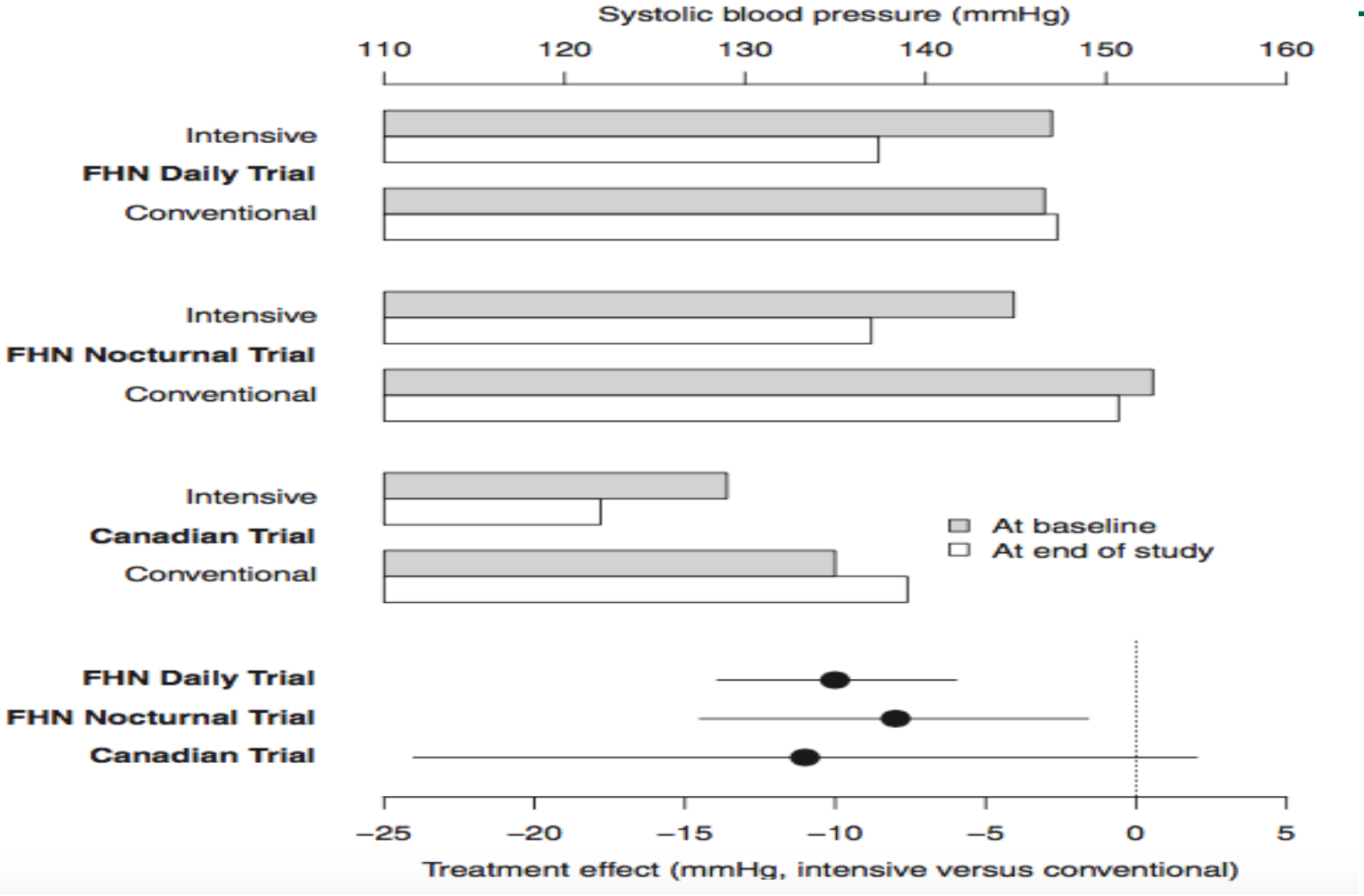
Patogenesi multifattoriale: ipervolemia, aumento resistenze periferiche (attivazione sistema RAA e aumento attività simpatica e NA circolante), ridotta attività dei vasodilatatori endogeni (NO e chinine).

Utilizzo di farmaci anti ipertensivi: 70% BB, 50%,calcio antagonisti and 40% ACEi

Significato prognostico della PA predialitica: curva ad U. Importanza prognostica della PA interdialitica → importanza del controllo della PA.

Diversi studi clinici hanno mostrato una riduzione della PA con la riduzione dell'intervallo interdialitico, permettendo una minor richiesta di farmaci per il controllo della PA.

Am J Kidney Dis. 68(5)(suppl 1):S15-S23. 2016



Effects of intensive versus conventional hemodialysis on predialysis systolic blood pressure in the Frequent Hemodial- ysis Network (FHN) Daily Trial,42 FHN Nocturnal Trial,42 and Canadian trial of nocturnal hemodialysis.46 Estimated treatment effects (solid dots) and associated 95% confidence intervals (solid lines) are displayed at the bottom.

Definizione e classificazione della pressione arteriosa clinica

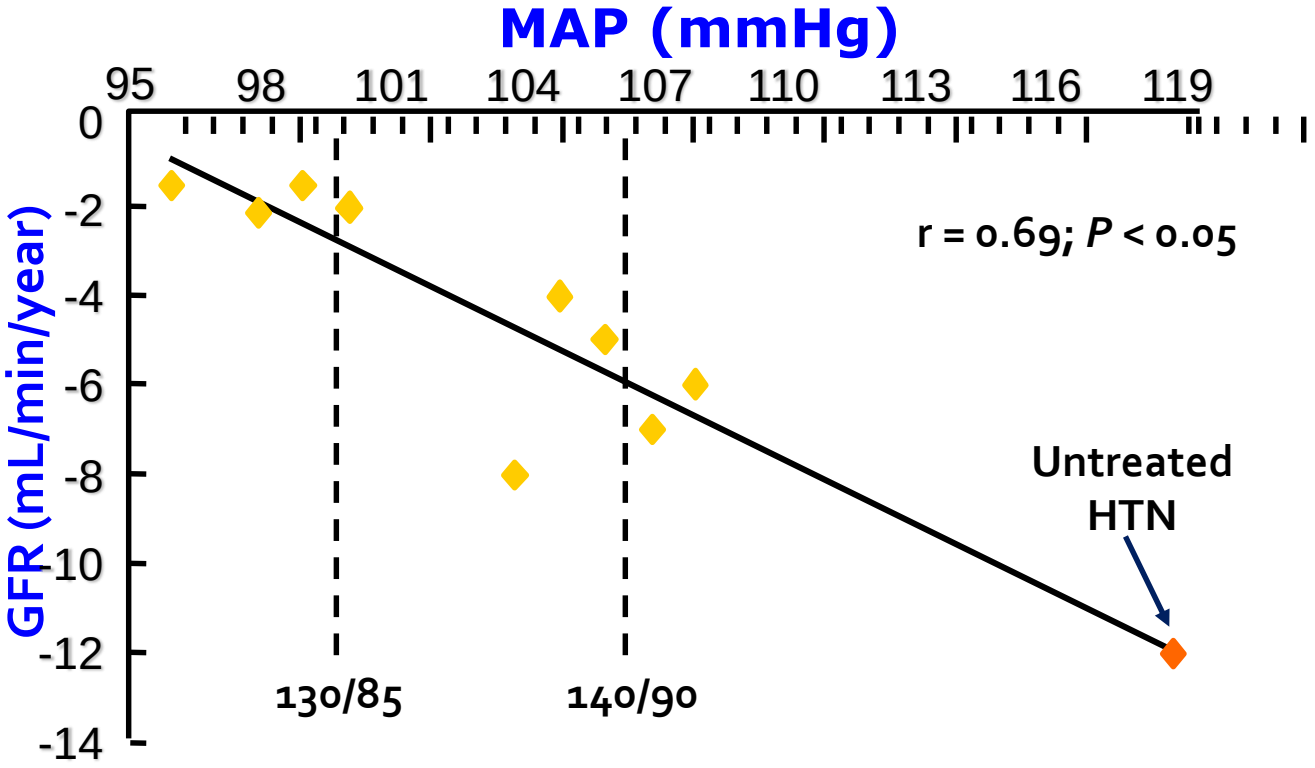
Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

2013 ESH-ESC Guidelines, J Hypertens 2013

Trattamento antipertensivo: target della pressione arteriosa

Recommendations	Class[a]	Level[b]	Ref.[c]
A SBP goal <140 mmHg:			
a) is recommended in patients at low–moderate CV risk;	I	B	266, 269, 270
b) is recommended in patients with diabetes;	I	A	270, 275, 276
c) should be considered in patients with previous stroke or TIA;	IIa	B	296, 297
d) should be considered in patients with CHD;	IIa	B	141, 265
e) should be considered in patients with diabetic or non-diabetic CKD.	IIa	B	312, 313
In elderly hypertensives less than 80 years old with SBP ≥160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A	265
In fit elderly patients less than 80 years old SBP values <140 mmHg may be considered, whereas in the fragile elderly population SBP goals should be adapted to individual tolerability.	IIb	C	-
In individuals older than 80 years and with initial SBP ≥160 mmHg, it is recommended to reduce SBP to between 150 and 140 mmHg provided they are in good physical and mental conditions.	I	B	287
A DBP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A	269, 290, 293

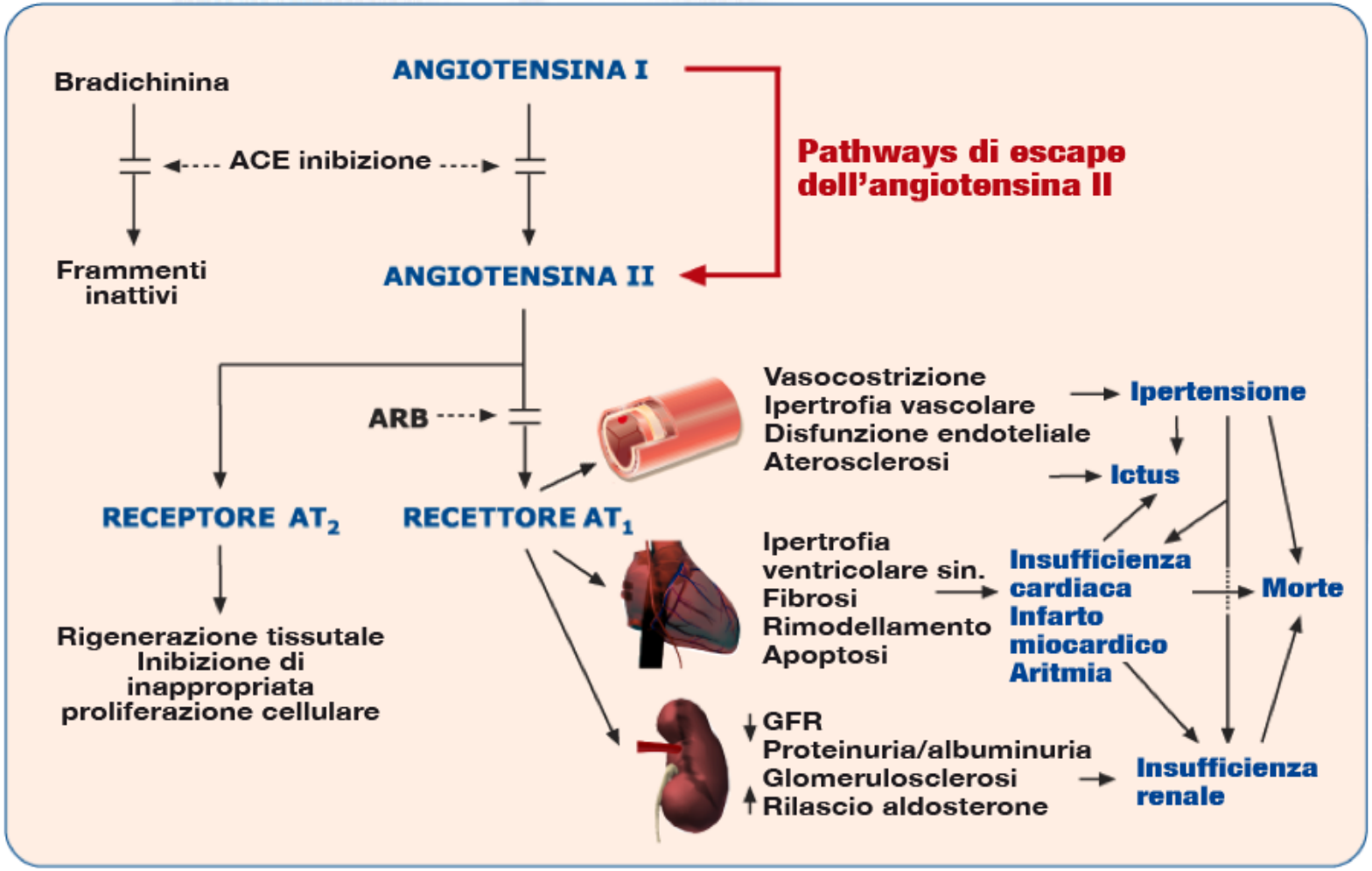
PIÙ BASSI VALORI DI PA MEDIA RALLENTANO IL DECLINO DEL GFR IN DIABETICI E NON DIABETICI



Parving HH, et al. Br Med J 1989. Maschio G, et al. N Engl J Med 1996. Viberti GC, et al. JAMA 1993. Bakris GL, et al. Kidney Int 1996. Klahr S, et al. N Eng J Med 1994. Bakris GL. Hypertension 1997. Hebert L, et al. Kidney Int 1994. The GISEN Group. Lancet 1997. Lebovitz H, et al. Kidney Int 1994.

Blocco farmacologico del sistema RAA con ACE-I e sartani

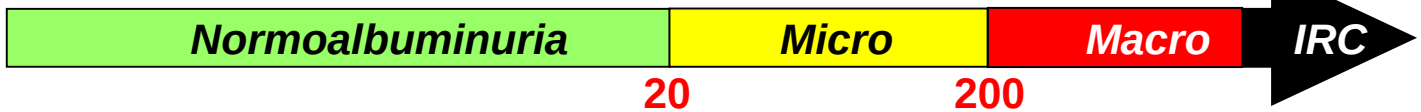
Renina ← **DIR**



Adattato da: Chung, Unger., Am J Hypertens 1999;12:150S–156S

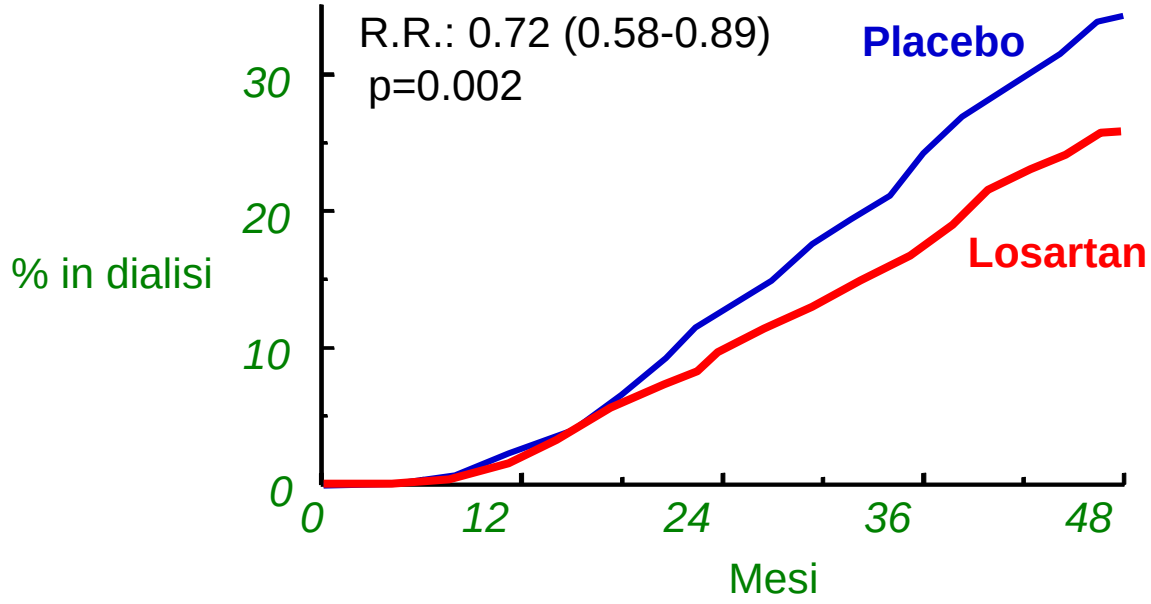
NORMOALBUMINURIA→MICROALBUMINURIA →PROTEINURIA →IRC

RENAAL, IDNT



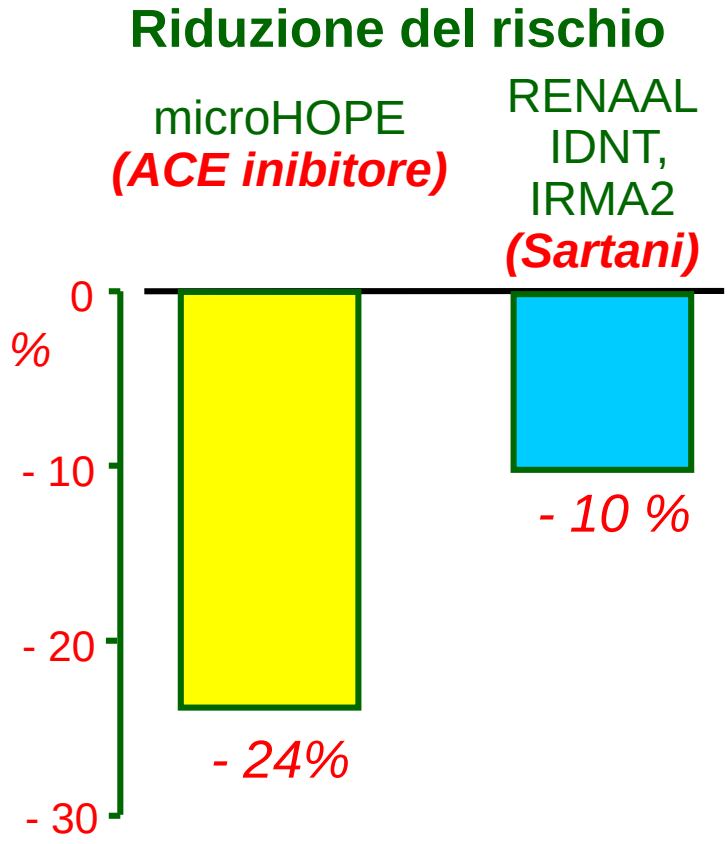
UAE (µg/min) 20 200

Durata diabete (anni) 0 13 18 25



INIBIZIONE DEL SRAA NEL DIABETE DI TIPO 2
- EFFETTI SULLA MORTALITÀ -

	pazienti (*n*)	mortalità (%)
MicroHOPE		
casi	1808	10.8
controlli	1769	14.0
RENAAL, IDNT, IRMA2		
casi	1719	14.4
controlli	1542	16.1



Linee guida 2013 ESH-ESC: possibili combinazioni di farmaci antipertensivi

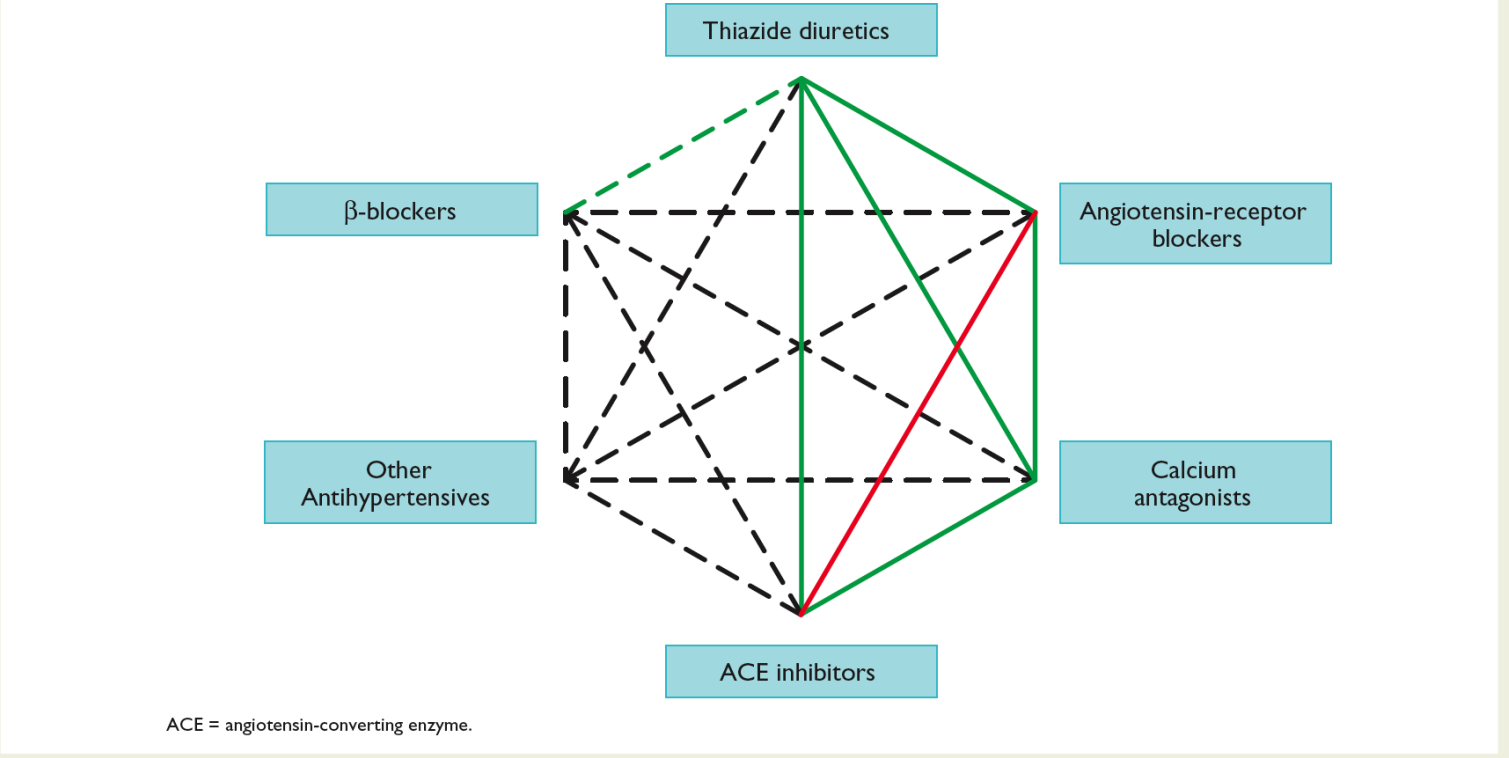
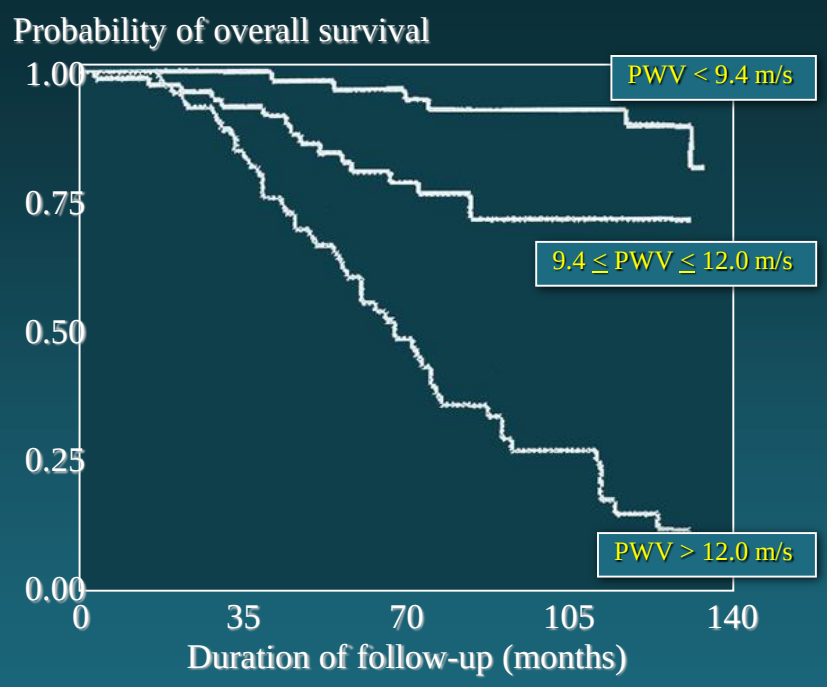


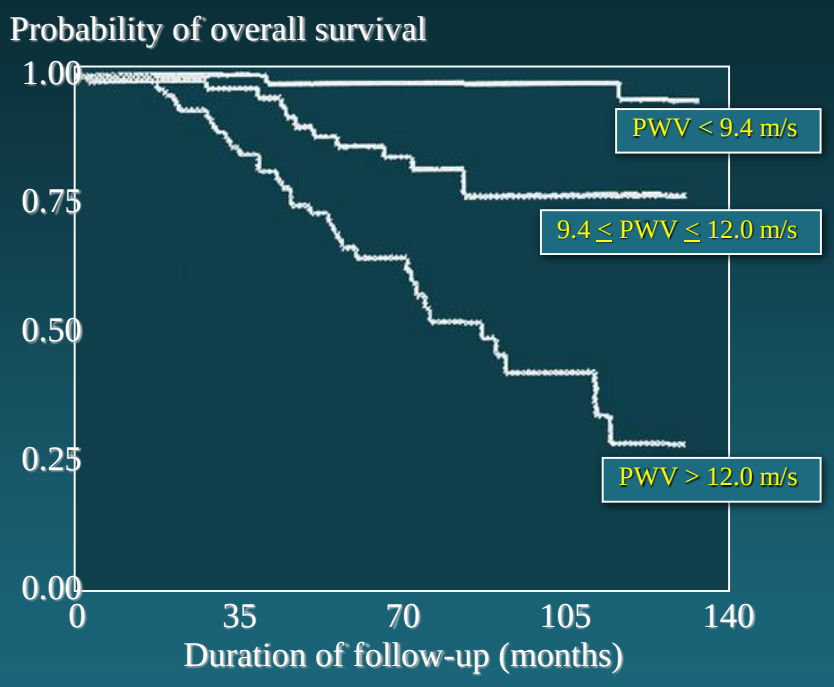
Figure 4 Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

Mancia G et al, Eur Heart J 2013

Probabilities of Overall Survival and Event-free Survival according to Level of PWV Tertiles



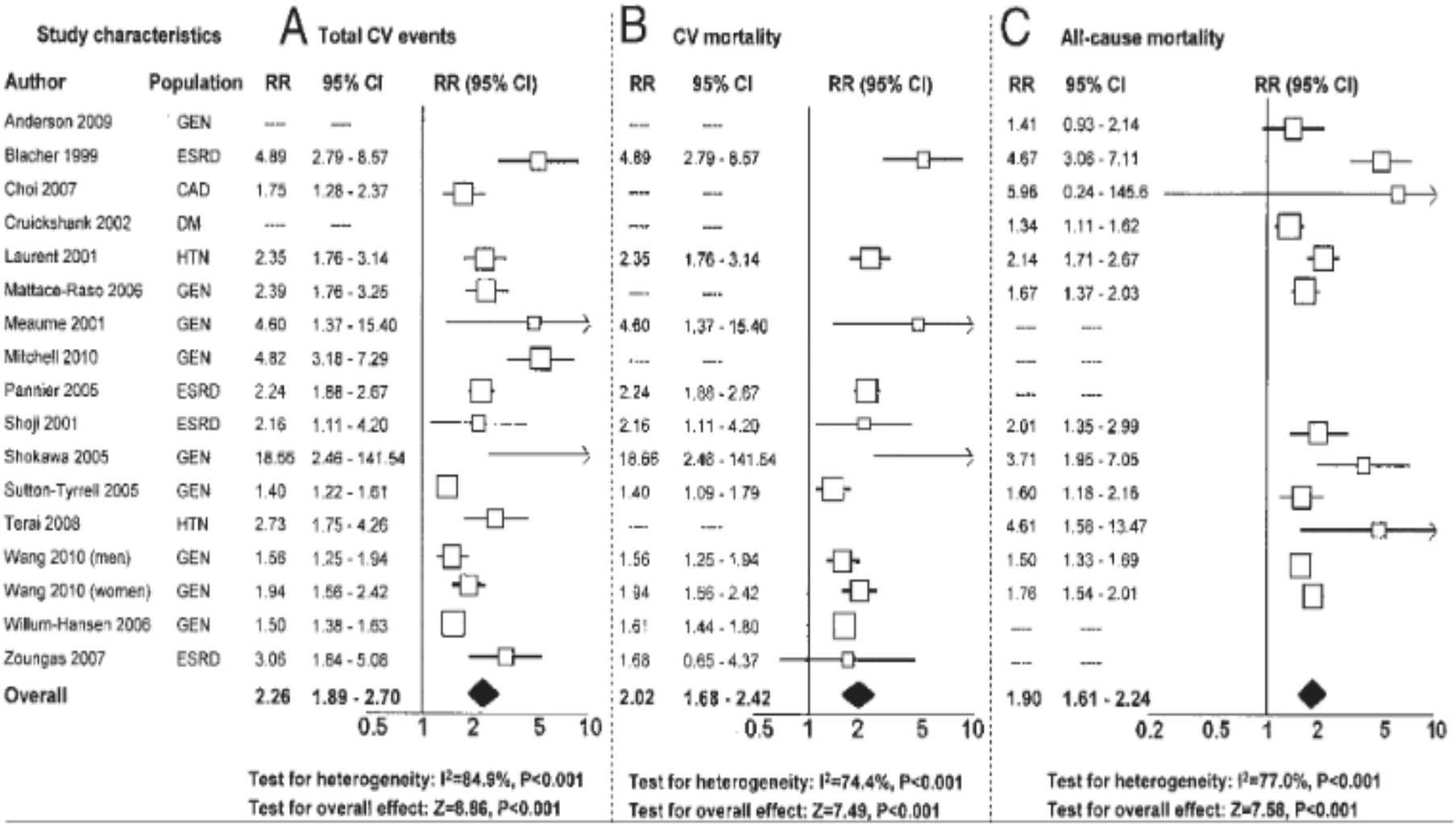
n	*81*	*81*	*78*	*77*	*75*
n	*80*	*75*	*67*	*64*	*64*
n	*80*	*69*	*46*	*35*	*29*



81	*81*	*80*	*80*	*79*
80	*78*	*71*	*68*	*68*
80	*70*	*57*	*49*	*46*

Blacher J et al., Circulation 1999; 99: 2434-2439

EVENTI CV



15877 subjectes; follow-up 7.7 years

Fonte: Vlachopoulos C et al. JACC. 2010; 55: 1318-27