



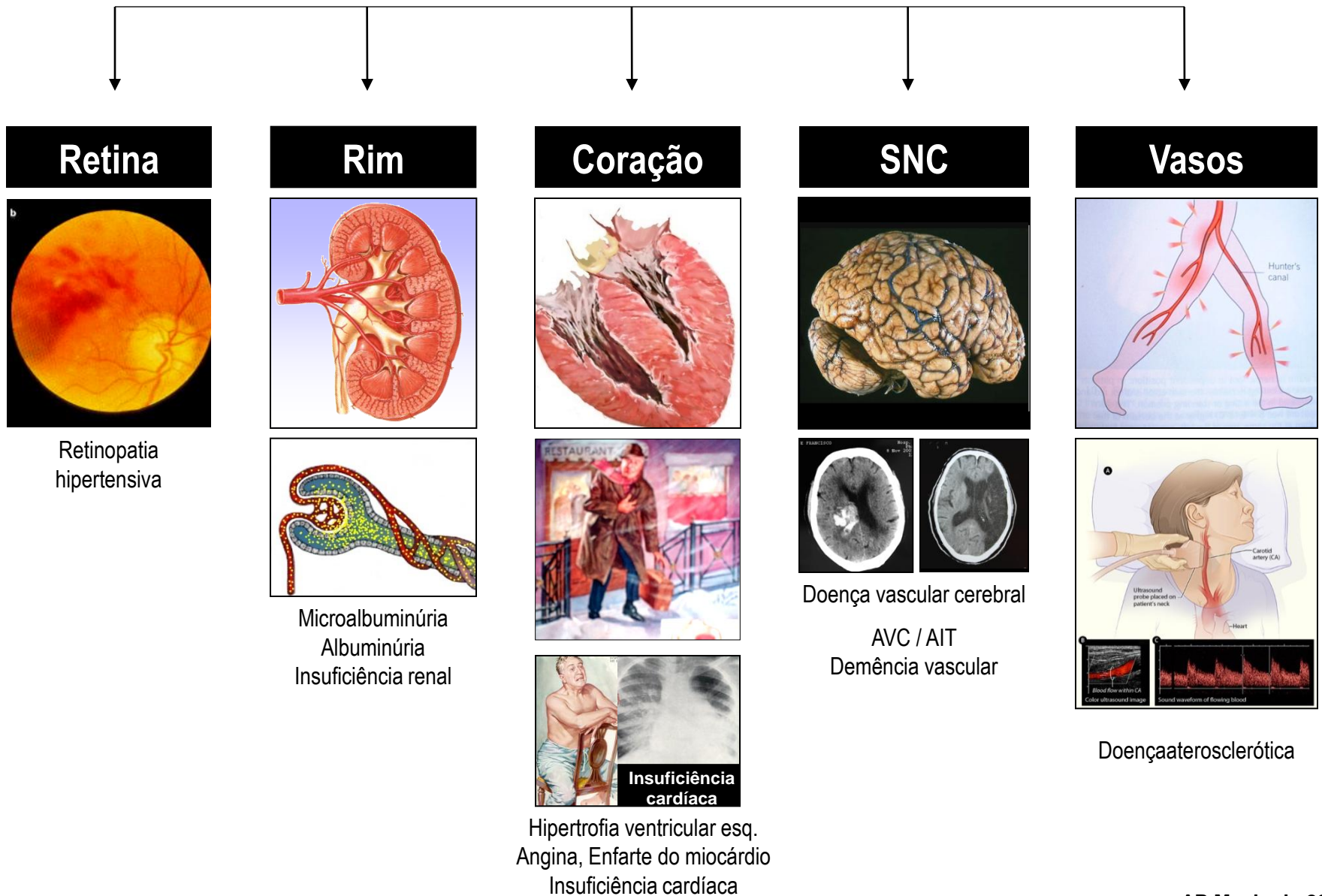
# **Sessão Televoter Hipertensão**

**Alexandra Fernandes**

**António Pedro Machado**

**Carlos Rabaçal**

# Orgãos alvo da HTA



# HTA: estratificação de risco e prognóstico

<b>Factores de Risco/ Doença</b>	Pressão Arterial (mmHg)				
	Normal PAS 120-129 ou PAD 80-84	Normal-alta PAS 130-139 ou PAD 85-89	Grau 1 PAS 140-159 ou PAD 90-99	Grau 2 PAS 160-179 ou PAD 100-109	Grau 3 PAS ≥ 180 ou PAD ≥ 110
0 FR			Baixo	Moderado	Elevado
1-2 FR	Baixo	Baixo	Moderado	Moderado	Muito Elevado
≥ 3 FR, SM, LOA ou Diabetes	Moderado	Elevado	Elevado	Elevado	Muito Elevado
Doença CV ou renal associada	Muito Elevado	Muito Elevado	Muito Elevado	Muito Elevado	Muito Elevado

**RA de DCV fatal (SCORE):** Baixo <4% ♦ Moderado 4-5% ♦ Elevado 5-8% ♦ Muito Elevado > 8%

# HTA: estratificação de risco e prognóstico

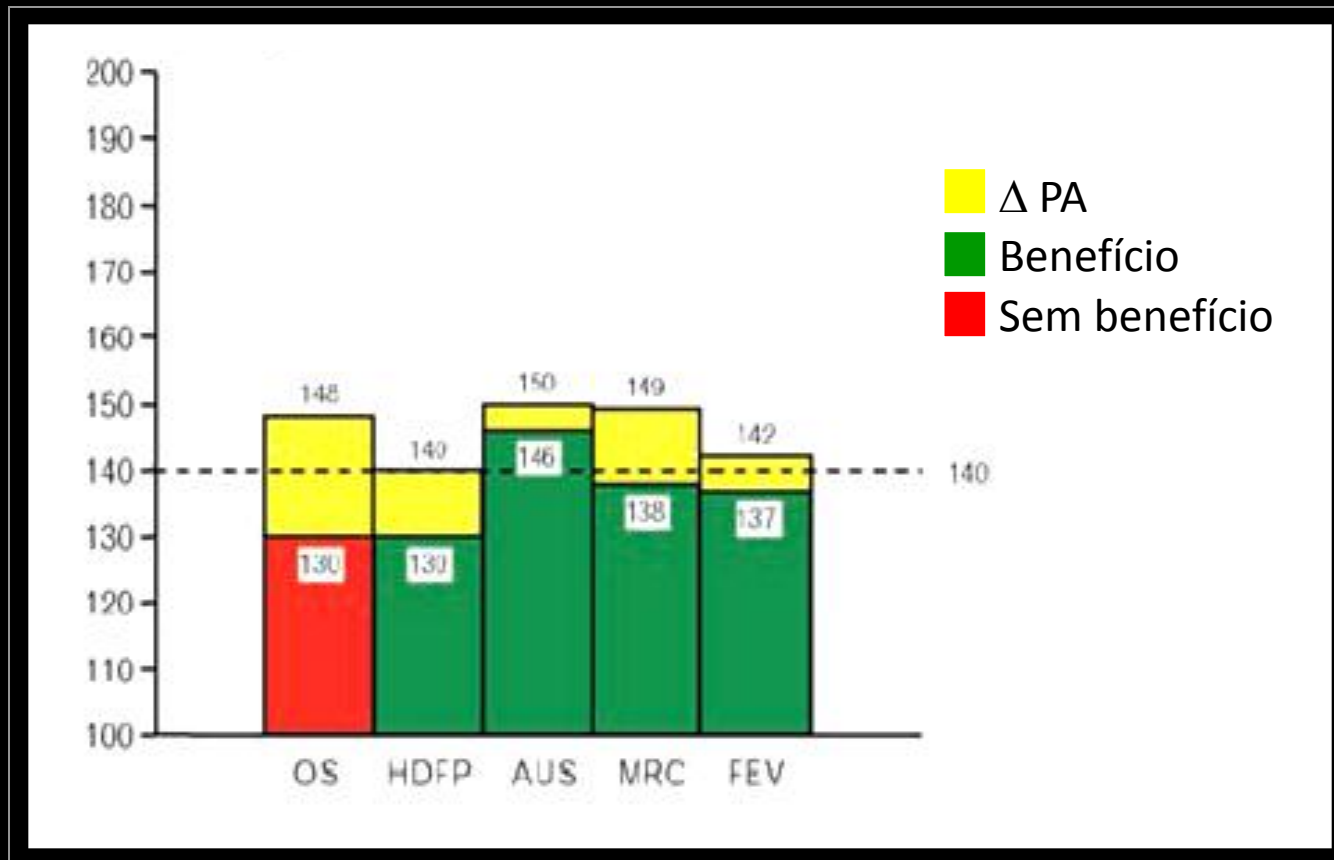
<b>Factores de Risco/Doença</b>	<b>Pressão Arterial (mmHg)</b>				
	<b>Normal PAS 120-129 ou PAD 80-84</b>	<b>Normal-alta PAS 130-139 ou PAD 85-89</b>	<b>Grau 1 PAS 140-159 ou PAD 90-99</b>	<b>Grau 2 PAS 160-179 ou PAD 100-109</b>	<b>Grau 3 PAS ≥ 180 ou PAD ≥ 110</b>
0 FR	Sem tratamento	Sem tratamento	MEV vários meses; depois Tx FARM (monoterapia) se PA elevada	MEV várias semanas; depois Tx FARM (monoterapia) se PA elevada	MEV + Tx FARM imediato
1-2 FR	MEV	MEV	MEV várias semanas; depois Tx FARM (monoterapia) se PA elevada	MEV várias semanas; depois Tx FARM (monoterapia) se PA elevada	MEV + Tx FARM imediato
≥ 3 FR, SM ou LOA	MEV	MEV + Considerar Tx FARM	MEV + Tx FARM	MEV + Tx FARM	MEV + Tx FARM imediato
Diabetes	MEV	MEV + Tx FARM	MEV + Tx FARM	MEV + Tx FARM	MEV + Tx FARM imediato
Doença CV ou renal associada	MEV + Tx FARM imediato	MEV + Tx FARM imediato	MEV + Tx FARM imediato	MEV + Tx FARM imediato	MEV + Tx FARM imediato

MEV- Modificações do estilo de vida

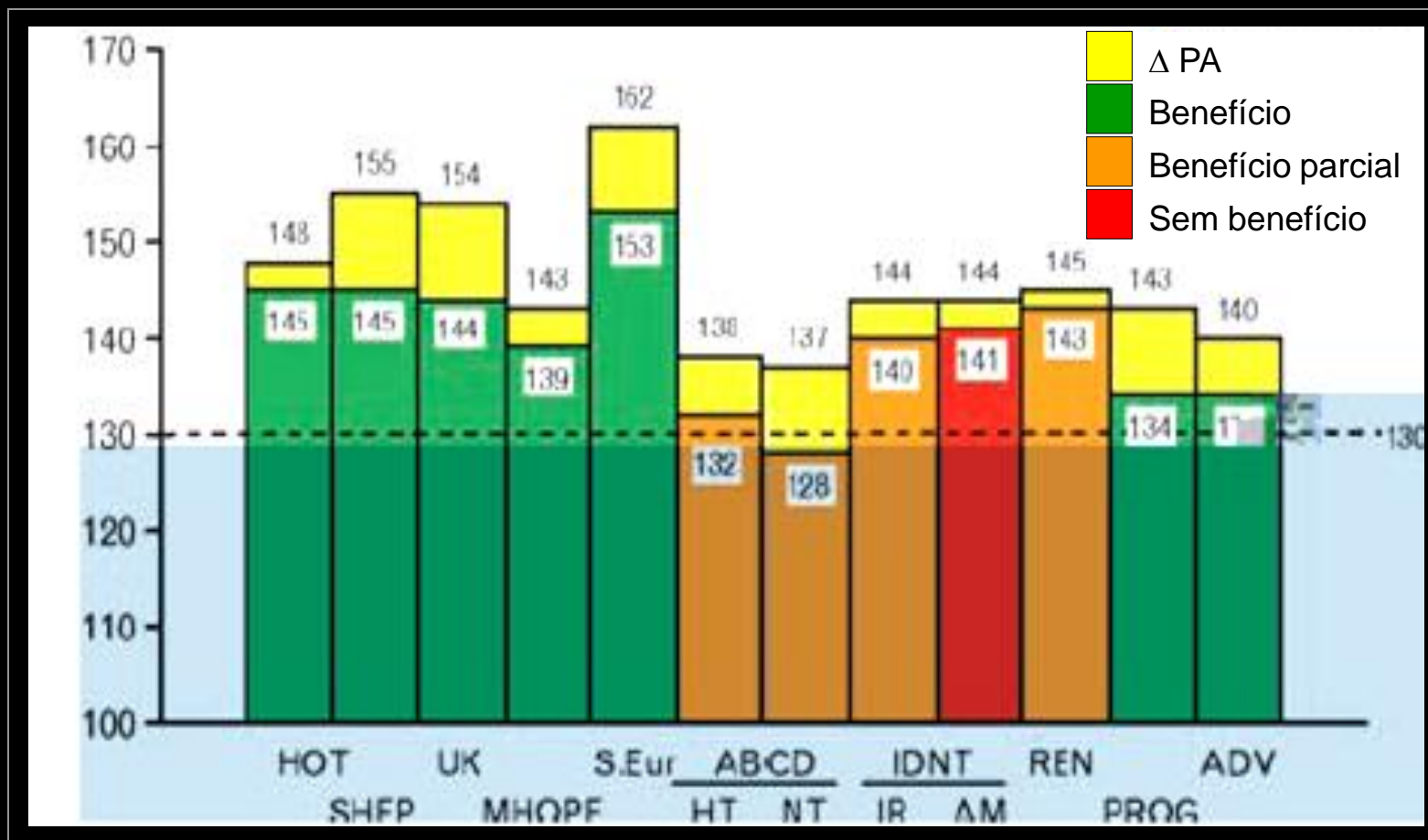
Tx FARM- Tratamento farmacológico

# HTA não complicada

PA alvo < 140 mmHg



# Benefício do tratamento da HTA no diabético



ORIGINAL ARTICLE

# Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group\*

## ABSTRACT

### BACKGROUND

There is no evidence from randomized trials to support a strategy of lowering systolic blood pressure below 135 to 140 mm Hg in persons with type 2 diabetes mellitus. We investigated whether therapy targeting normal systolic pressure (i.e., <120 mm Hg) reduces major cardiovascular events in participants with type 2 diabetes at high risk for cardiovascular events.

### METHODS

A total of 4733 participants with type 2 diabetes were randomly assigned to intensive therapy, targeting a systolic pressure of less than 120 mm Hg, or standard therapy, targeting a systolic pressure of less than 140 mm Hg. The primary composite outcome was nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The mean follow-up was 4.7 years.

### RESULTS

After 1 year, the mean systolic blood pressure was 119.3 mm Hg in the intensive-therapy group and 133.5 mm Hg in the standard-therapy group. The annual rate of the primary outcome was 1.87% in the intensive-therapy group and 2.09% in the standard-therapy group (hazard ratio with intensive therapy, 0.88; 95% confidence interval [CI], 0.73 to 1.06;  $P=0.20$ ). The annual rates of death from any cause were 1.28% and 1.19% in the two groups, respectively (hazard ratio, 1.07; 95% CI 0.85 to 1.35;  $P=0.55$ ). The annual rates of stroke, a prespecified secondary outcome, were 0.32% and 0.53% in the two groups, respectively (hazard ratio, 0.59; 95% CI, 0.39 to 0.89;  $P=0.01$ ). Serious adverse events attributed to antihypertensive treatment occurred in 77 of the 2362 participants in the intensive-therapy group (3.3%) and 30 of the 2371 participants in the standard-therapy group (1.3%) ( $P<0.001$ ).

### CONCLUSIONS

In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)

The members of the Writing Group (William C. Cushman, M.D., Gregory W. Evans, M.A., Robert P. Byington, Ph.D., David C. Goff, Jr., M.D., Ph.D., Richard H. Grimm, Jr., M.D., Ph.D., Jeffrey A. Cutler, M.D., M.P.H., Denise G. Simons-Morton, M.D., Ph.D., Jan N. Basile, M.D., Marshall A. Corson, M.D., Jeffrey L. Probstfield, M.D., Lois Katz, M.D., Kevin A. Peterson, M.D., William T. Friedewald, M.D., John B. Buse, M.D., Ph.D., J. Thomas Bigger, M.D., Hertz C. Gerstein, M.D., and Faramarz Ismail-Beigi, M.D., Ph.D.) assume responsibility for the integrity of the article. Address reprint requests to Dr. Cushman at the Preventive Medicine Section (111Q), Veterans Affairs Medical Center, 1030 Jefferson Ave., Memphis, TN 38104, or at [william.cushman@va.gov](mailto:william.cushman@va.gov).

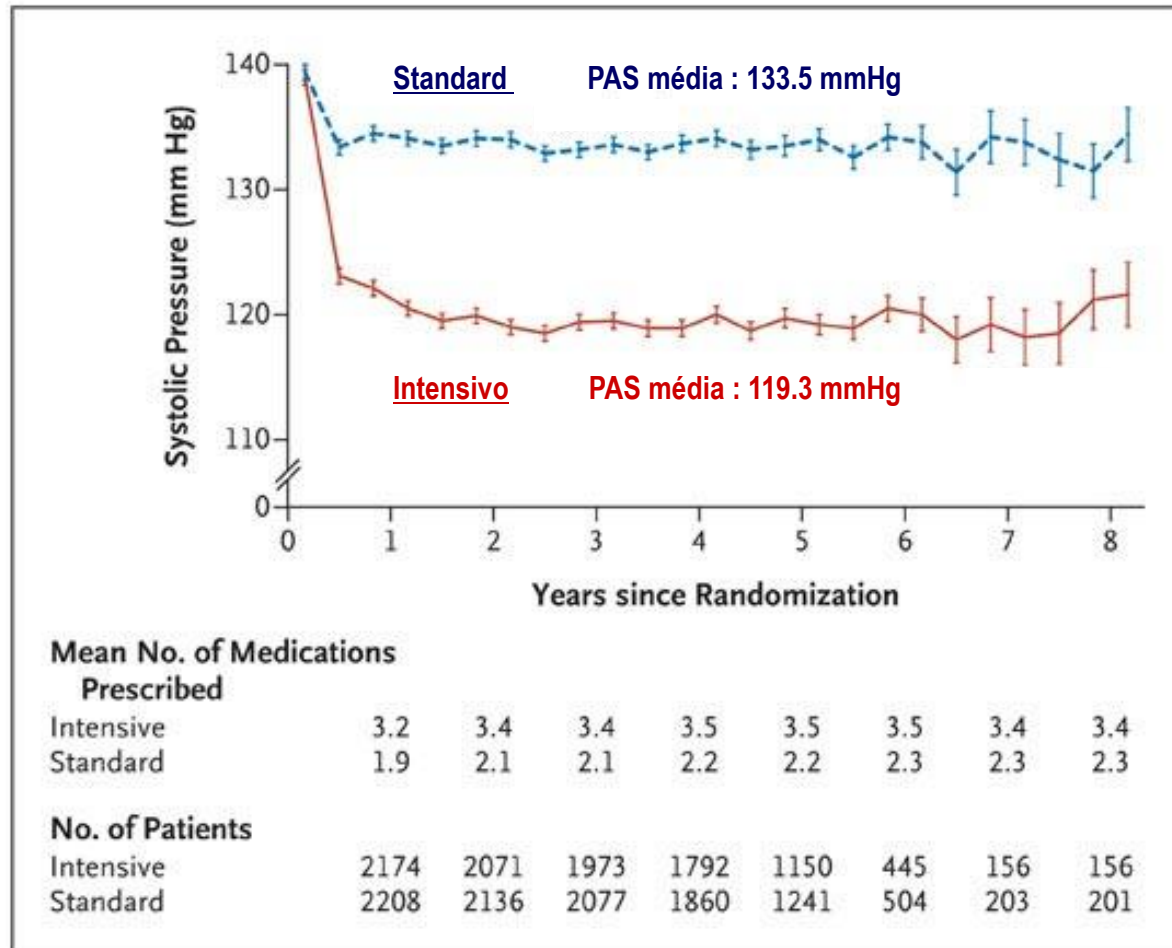
\*The members of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group are listed in Section 1 in Supplementary Appendix 1, available with the full text of this article at [NEJM.org](http://NEJM.org). The affiliations of the members of the Writing Group are listed in the Appendix.

This article (10.1056/NEJMoa1001286) was published on March 14, 2010, at [NEJM.org](http://NEJM.org).

N Engl J Med 2010.

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# PAS média ao longo do estudo



The ACCORD Study Group. N Engl J Med 2010;10.1056/NEJMoa1001286

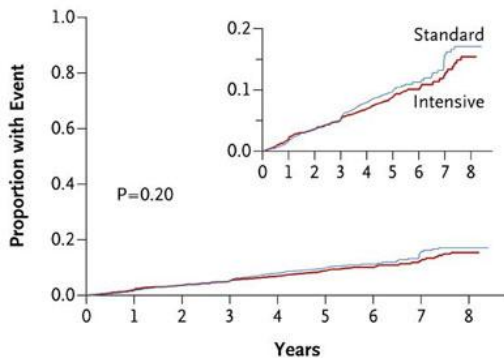


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# Kaplan-Meier Analyses of Selected Outcomes

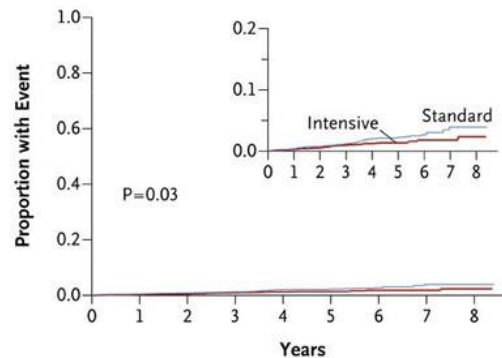
**A Primary Outcome**



**No. at Risk**

Intensive	2362	2273	2182	2117	1770	1080	298	175	80
Standard	2371	2274	2196	2120	1793	1127	358	195	108

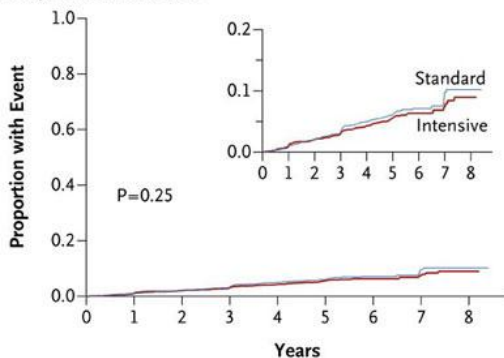
**B Nonfatal Stroke**



**No. at Risk**

Intensive	2362	2291	2223	2174	1841	1128	313	186	88
Standard	2371	2287	2235	2186	1879	1196	382	215	114

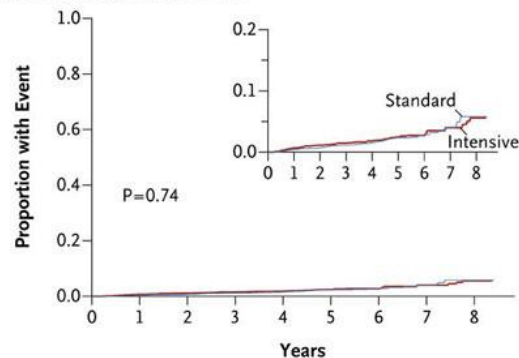
**C Nonfatal Myocardial Infarction**



**No. at Risk**

Intensive	2362	2278	2190	2133	1787	1087	299	177	82
Standard	2371	2278	2208	2141	1818	1145	365	201	112

**D Death from Cardiovascular Disease**



**No. at Risk**

Intensive	2362	2304	2252	2201	1870	1143	317	188	91
Standard	2371	2313	2268	2218	1922	1220	393	221	118

The ACCORD Study Group. N Engl J Med 2010;10.1056/NEJMoa1001286



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# Primary and Secondary Outcomes

**Table 3. Primary and Secondary Outcomes.**

Outcome	Intensive Therapy (N = 2363)		Standard Therapy (N = 2371)		Hazard Ratio (95% CI)	P Value
	no. of events	%/yr	no. of events	%/yr		
Primary outcome*	208	1.87	237	2.09	0.88 (0.73–1.06)	0.20
Prespecified secondary outcomes						
Nonfatal myocardial infarction	126	1.13	146	1.28	0.87 (0.68–1.10)	0.25
Stroke						
Any	36	0.32	62	0.53	0.59 (0.39–0.89)	0.01
Nonfatal	34	0.30	55	0.47	0.63 (0.41–0.96)	0.03
Death						
From any cause	150	1.28	144	1.19	1.07 (0.85–1.35)	0.55
From cardiovascular cause	60	0.52	58	0.49	1.06 (0.74–1.52)	0.74
Primary outcome plus revascularization or nonfatal heart failure	521	5.10	551	5.31	0.95 (0.84–1.07)	0.40
Major coronary disease event†	253	2.31	270	2.41	0.94 (0.79–1.12)	0.50
Fatal or nonfatal heart failure	83	0.73	90	0.78	0.94 (0.70–1.26)	0.67

\* The primary outcome was a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes.

† Major coronary disease events, as defined in the protocol, included fatal coronary events, nonfatal myocardial infarction, and unstable angina.

The ACCORD Study Group. N Engl J Med 2010;10.1056/NEJMoa1001286



The NEW ENGLAND  
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# The International Verapamil-Trandolapril Study (INVEST): A Randomized Controlled Trial

## Caution Urged in Reducing Blood Pressure in Patients With Diabetes and Coronary Disease

*ScienceDaily* (Mar. 15, 2010) — For patients with diabetes and heart disease, less isn't always more -- at least when it comes to blood pressure.

New data show an increased risk of heart attack, stroke or death for patients having blood pressure deemed too high -- or too low, according to Rhonda Cooper-DeHoff, Pharm.D., an associate professor of pharmacy and medicine at UF. She reported her findings at the American College of Cardiology's 59th annual scientific session in Atlanta.

She recommends raising the systolic bar above 120 for blood pressure in patients with diabetes and coronary artery disease, saying that levels between 130 and 140 appear to be the most healthful.

**PAS alvo em diabéticos com doença coronária**

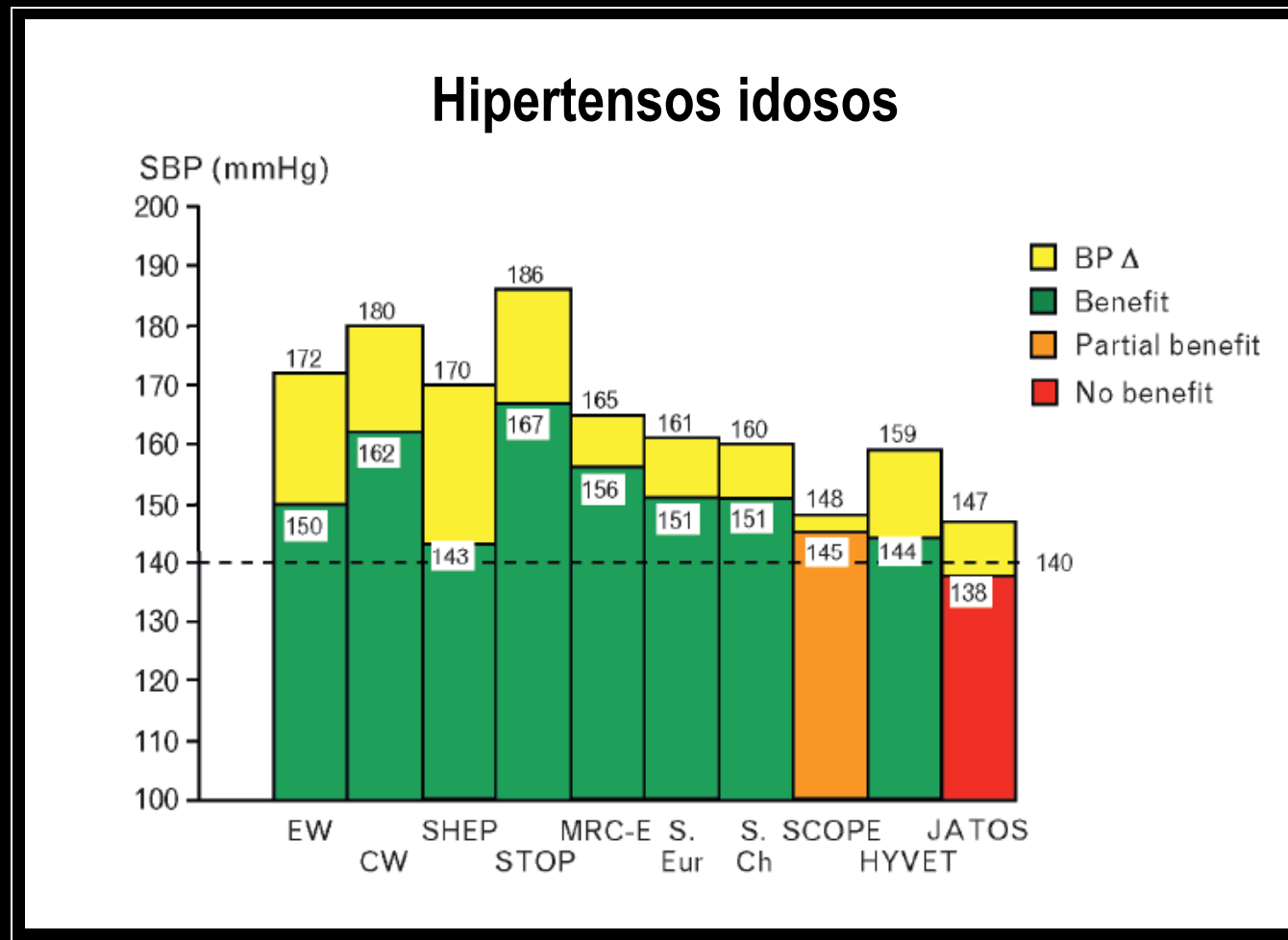
**130-140 mmHg**

# Risco cardiovascular global

## Indivíduos de alto risco e de muito alto risco

- PAS  $\geq 180$  mmHg e/ou PAD  $\geq 110$  mmHg
- **PAS > 160 mmHg e PAD baixa (<70 mmHg)**
- Diabetes
- Síndrome metabólica ( $\geq 3$  de 5 factores: obesidade abdominal, elevação da glicémia em jejum, PA > 130/85 mmHg, diminuição das HDL e elevação dos TG).
- $\geq 3$  factores de risco
- Uma ou mais das seguintes lesões subclínicas dos órgãos alvo
  - HVE
  - Espessamento ou placa carotídea (Eco)
  - Aumento da rigidez arterial
  - Insuficiência renal (elevação moderada da creatinina sérica ou redução da taxa de filtração glomerular ou da clearance da creatinina estimadas)
  - Microalbuminúria ou proteinúria
- Doença cardiovascular ou renal estabelecidas

PAS atingida em doentes aleatorizados para tratamento mais activo (parte inferior dos histogramas) e menos activo (parte superior dos histogramas) em ensaios com hipertensos idosos



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

FEBRUARY 13, 2003

VOL. 348 NO. 7

## A Comparison of Outcomes with Angiotensin-Converting-Enzyme Inhibitors and Diuretics for Hypertension in the Elderly

Lindon M.H. Wing, M.B., B.S., Christopher M. Reid, Ph.D., Philip Ryan, M.B., B.S., Lawrence J. Beilin, M.D., Mark A. Brown, M.B., B.S., M.D., Garry L.R. Jennings, M.D., Colin I. Johnston, M.B., B.S., John J. McNeil, M.B., B.S., Graham J. Macdonald, M.D., John E. Marley, M.D., M.B., Ch.B., Trefor O. Morgan, M.B., B.S., and Malcolm J. West, M.B., B.S., for the Second Australian National Blood Pressure Study Group\*

### ABSTRACT

#### BACKGROUND

Treatment of hypertension with diuretics, beta-blockers, or both leads to improved outcomes. It has been postulated that agents that inhibit the renin-angiotensin system confer benefit beyond the reduction of blood pressure alone. We compared the outcomes in older subjects with hypertension who were treated with angiotensin-converting-enzyme (ACE) inhibitors with the outcomes in those treated with diuretic agents.

#### METHODS

We conducted a prospective, randomized, open-label study with blinded assessment of end points in 6083 subjects with hypertension who were 65 to 84 years of age and received health care at 1594 family practices. Subjects were followed for a median of 4.1 years, and the total numbers of cardiovascular events in the two treatment groups were compared with the use of multivariate proportional-hazards models.

#### RESULTS

At base line, the treatment groups were well matched in terms of age, sex, and blood pressure. By the end of the study, blood pressure had decreased to a similar extent in both groups (a decrease of 26/12 mm Hg). There were 695 cardiovascular events or deaths from any cause in the ACE-inhibitor group (56.1 per 1000 patient-years) and 736 cardiovascular events or deaths from any cause in the diuretic group (59.8 per 1000 patient-years; the hazard ratio for a cardiovascular event or death with ACE-inhibitor treatment was 0.89 [95 percent confidence interval, 0.79 to 1.00];  $P=0.05$ ). Among male subjects, the hazard ratio was 0.83 (95 percent confidence interval, 0.71 to 0.97;  $P=0.02$ ); among female subjects, the hazard ratio was 1.00 (95 percent confidence interval, 0.83 to 1.21;  $P=0.98$ ); the  $P$  value for the interaction between sex and treatment-group assignment was 0.15. The rates of nonfatal cardiovascular events and myocardial infarctions decreased with ACE-inhibitor treatment, whereas a similar number of strokes occurred in each group (although there were more fatal strokes in the ACE-inhibitor group).

#### CONCLUSIONS

Initiation of antihypertensive treatment involving ACE inhibitors in older subjects, particularly men, appears to lead to better outcomes than treatment with diuretic agents, despite similar reductions of blood pressure.

From the School of Medicine, Flinders University, Adelaide (L.M.H.W.); the Baker Heart Research Institute, Melbourne (C.M.R., G.L.R.J., C.I.J.); the Department of Public Health, University of Adelaide, Adelaide (P.R.); the Department of Medicine, University of Western Australia, Perth (L.J.B.); the Department of Nephrology, University of New South Wales, Sydney (M.A.B.); the Department of Epidemiology and Preventive Medicine, Monash University, Melbourne (J.J.M.); Merck Sharp & Dohme, Sydney (G.J.M.); the Faculty of Health, University of Newcastle, Newcastle (J.E.M.); the Department of Physiology, University of Melbourne, Melbourne (T.O.M.); and the Department of Medicine, University of Queensland, Brisbane (M.J.W.) — all in Australia. Address reprint requests to Dr. Reid at the Baker Heart Research Institute, P.O. Box 6492, St. Kilda Rd. Central, Melbourne, VIC 3008, Australia, or at [chris.reid@baker.edu.au](mailto:chris.reid@baker.edu.au).




\*Investigators in the Second Australian National Blood Pressure Study (ANBP2) are listed in the Appendix.

*N Engl J Med* 2003;348:583-92.

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## Primary End Points among All Subjects, Male Subjects, and Female Subjects


### All Subjects

End Point	Hazard Ratio (95% CI)	P Value	ACE Inhibitors Superior		Diuretics Superior	
			0.2	1.0	5.0	
All cardiovascular events or death from any cause	0.89 (0.79–1.00)	0.05				
First cardiovascular event or death from any cause	0.89 (0.79–1.01)	0.06				
Death from any cause	0.90 (0.75–1.09)	0.27				

### Male Subjects

End Point	Hazard Ratio (95% CI)	P Value	ACE Inhibitors Superior		Diuretics Superior	
			0.2	1.0	5.0	
All cardiovascular events or death from any cause	0.83 (0.71–0.97)	0.02				
First cardiovascular event or death from any cause	0.83 (0.71–0.97)	0.02				
Death from any cause	0.83 (0.66–1.06)	0.14				

### Female Subjects

End Point	Hazard Ratio (95% CI)	P Value	ACE Inhibitors Superior		Diuretics Superior	
			0.2	1.0	5.0	
All cardiovascular events or death from any cause	1.00 (0.83–1.21)	0.98				
First cardiovascular event or death from any cause	1.00 (0.83–1.20)	0.98				
Death from any cause	1.01 (0.76–1.35)	0.94				



# Prevention of Stroke by Antihypertensive Drug Treatment in Older Persons With Isolated Systolic Hypertension

## Final Results of the Systolic Hypertension in the Elderly Program (SHEP)

SHEP Cooperative Research Group

**Objective.**—To assess the ability of antihypertensive drug treatment to reduce the risk of nonfatal and fatal (total) stroke in isolated systolic hypertension.

**Design.**—Multicenter, randomized, double-blind, placebo-controlled.

**Setting.**—Community-based ambulatory population in tertiary care centers.

**Participants.**—4736 persons (1.06%) from 447 921 screenees aged 60 years and above were randomized (2365 to active treatment, 2371 to placebo). Systolic blood pressure ranged from 160 to 219 mm Hg and diastolic blood pressure was less than 90 mm Hg. Of the participants, 3161 were not receiving antihypertensive medication at initial contact, and 1575 were. The average systolic blood pressure was 170 mm Hg; average diastolic blood pressure, 77 mm Hg. The mean age was 72 years, 57% were women, and 14% were black.

**Interventions.**—Participants were stratified by clinical center and by antihypertensive medication status at initial contact. For step 1 of the trial, dose 1 was chlorthalidone, 12.5 mg/d, or matching placebo; dose 2 was 25 mg/d. For step 2, dose 1 was atenolol, 25 mg/d, or matching placebo; dose 2 was 50 mg/d.

**Main Outcome Measures.**—*Primary.*—Nonfatal and fatal (total) stroke. *Secondary.*—Cardiovascular and coronary morbidity and mortality, all-cause mortality, and quality of life measures.

**Results.**—Average follow-up was 4.5 years. The 5-year average systolic blood pressure was 155 mm Hg for the placebo group and 143 mm Hg for the active treatment group, and the 5-year average diastolic blood pressure was 72 and 68 mm Hg, respectively. The 5-year incidence of total stroke was 5.2 per 100 participants for active treatment and 8.2 per 100 for placebo. The relative risk by proportional hazards regression analysis was 0.64 ( $P = .0003$ ). For the secondary end point of clinical nonfatal myocardial infarction plus coronary death, the relative risk was 0.73. Major cardiovascular events were reduced (relative risk, 0.68). For deaths from all causes, the relative risk was 0.87.

**Conclusion.**—In persons aged 60 years and over with isolated systolic hypertension, antihypertensive stepped-care drug treatment with low-dose chlorthalidone as step 1 medication reduced the incidence of total stroke by 36%, with 5-year absolute benefit of 30 events per 1000 participants. Major cardiovascular events were reduced, with 5-year absolute benefit of 55 events per 1000.

(JAMA. 1991;265:3255-3264)

THIS article presents the final results of the Systolic Hypertension in the El-

See the end of the article for a list of the principal investigators of the Systolic Hypertension in the Elderly Program.

Reprint requests to Clinical Trials Branch, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute, Federal Building, Room 5C-10B, 7550 Wisconsin Ave, Bethesda, MD 20892 (Dr Jeffrey L. Probstfield).

derly Program (SHEP), a double-blind, randomized, placebo-controlled trial of treatment for isolated systolic hypertension (ISH) in persons 60 years of age and older. The full-scale SHEP study, begun in 1984, set as its primary objective "the determination of whether antihypertensive drug treatment reduces risk of total stroke (nonfatal and fatal) in

a multi-ethnic cohort of men and women age 60 years and older with ISH."<sup>1</sup> Previous trials have demonstrated beneficial effects of antihypertensive treatment of diastolic hypertension on major morbidity and mortality, but none has investigated the ability to influence these events for persons with ISH.<sup>2-11</sup>

For editorial comment see p 3301.

Isolated systolic hypertension is increasingly prevalent with age, especially in those aged 60 years and above. Epidemiologic studies have demonstrated an increase in risk of stroke, other cardiovascular diseases, and death for those with ISH, independent of other risk factors.<sup>12-21</sup>

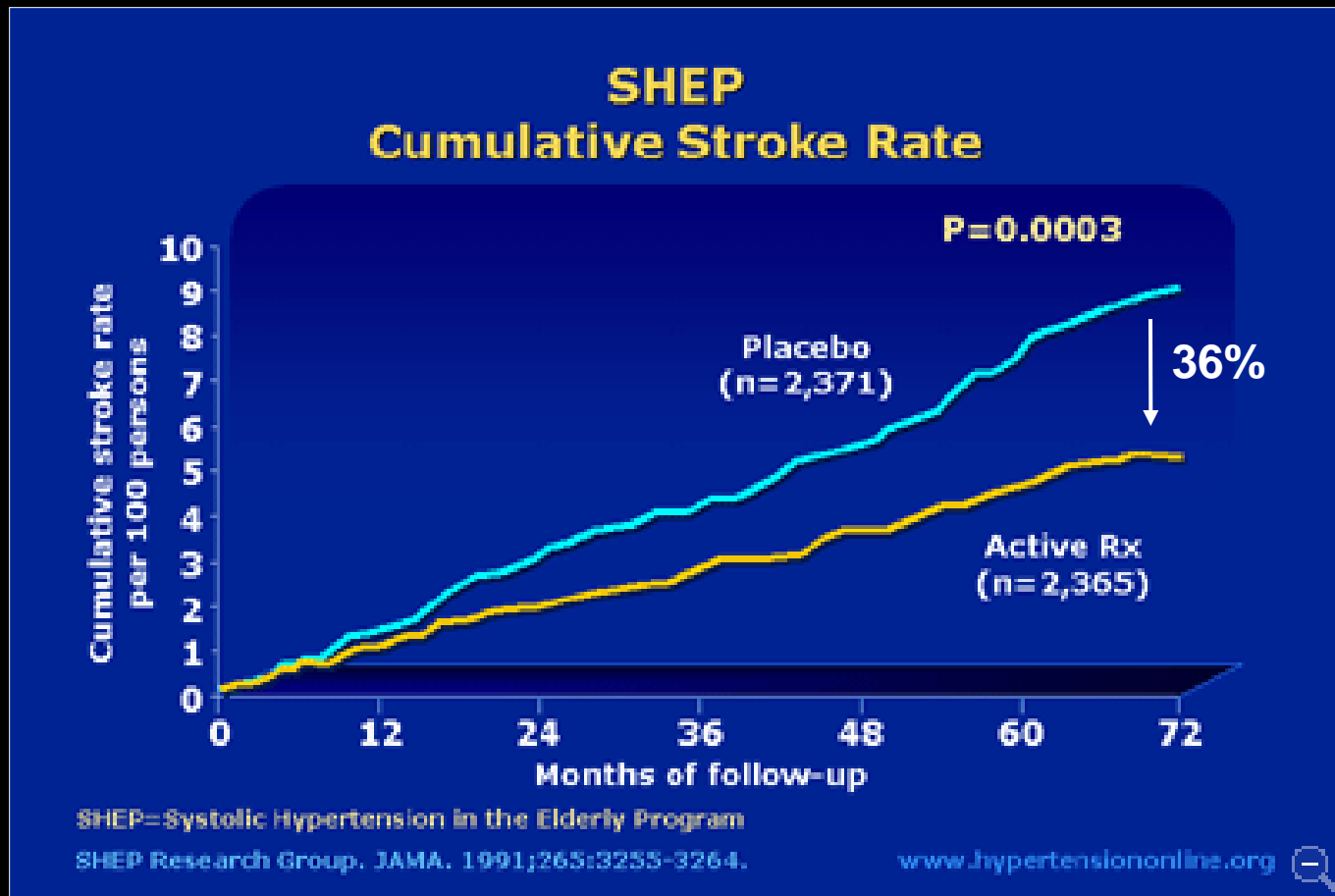
The SHEP pilot study demonstrated the feasibility of undertaking trials in older people with ISH, including ability to recruit participants. It also established ability of drug therapy to reduce blood pressure among persons with ISH.<sup>22</sup> For SHEP, ISH was defined as systolic blood pressure (SBP) greater than 160 mm Hg and diastolic blood pressure (DBP) less than 90 mm Hg, based on the average of four measurements at two baseline visits.<sup>1,30</sup>

Secondary objectives included assessment of the relationship of antihypertensive treatment to (1) multiple cardiovascular morbidity and mortality end points, including cardiac end points; (2) cause-specific and all-cause mortality; (3) multi-infarct dementia, clinical depression, and deterioration of cognitive function; (4) possible adverse effects; (5) hospitalizations and intermediate or skilled nursing facility admissions; (6) falls and fractures; and (7) multiple indexes of quality of life.<sup>1,30</sup>

The SHEP protocol also stipulated two other questions for investigation as subgroup hypotheses: (1) Would treatment of ISH reduce the frequency of total stroke (fatal and nonfatal) similar-

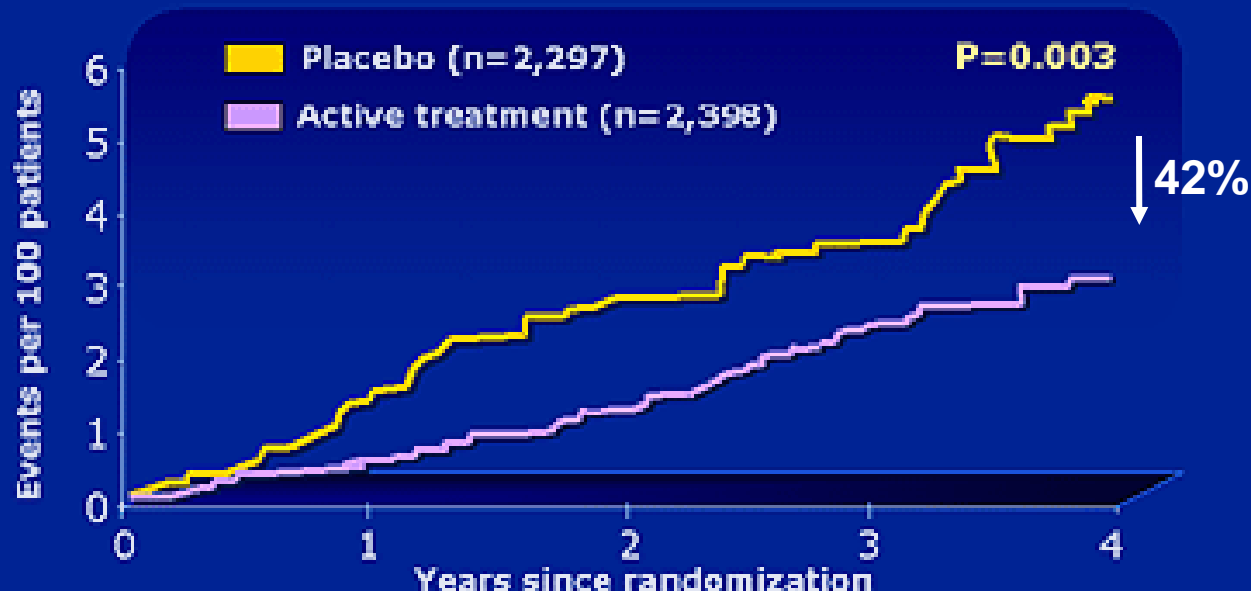


# SHEP – Redução em 35% do risco de AVC com a clorotalidona



# SYST-EUR – Redução em 42% do risco de AVC com a nitrendipina

## Syst-Eur Primary Endpoint Fatal and Nonfatal Stroke



Syst-Eur=Systolic Hypertension in Europe Trial  
Staessen JA, et al. Lancet. 1997;350:757-764.  
Reprinted with permission from Elsevier Science.

[www.hypertensiononline.org](http://www.hypertensiononline.org)

# **Factores de resistência ao tratamento**

**Idade avançada**

**Pressão sistólica basal muito elevada**

**Hipertrofia ventricular esquerda**

**Sexo feminino**

**Obesidade**

**Diabetes**

**Doença renal crónica**

**Ingestão elevada de sal**

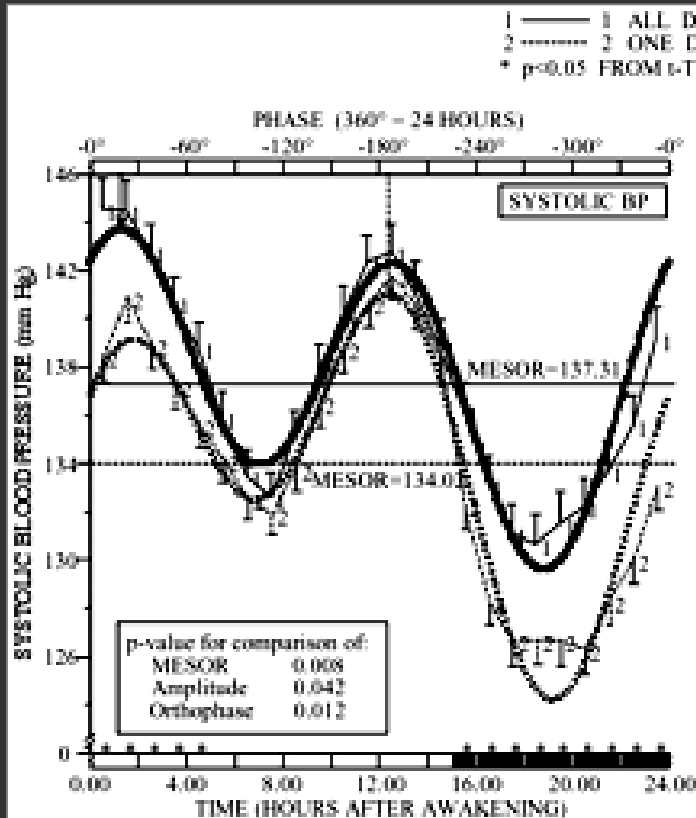
**Raça negra**



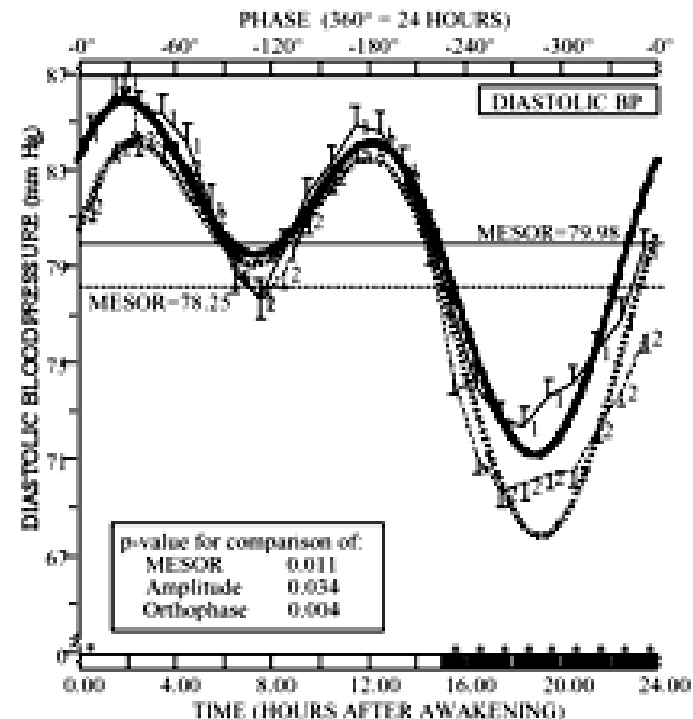
# Cronoterapia da Hipertensão

# Redução acrescida da PA com a administração de $\geq 1$ anti-hipertensor à noite

## PA Sistólica



## PA Diastólica



# Cronoterapia da Hipertensão

**Tiazida + IECA/ARA II**



**Dihidropiridina**



# Cronoterapia da Hipertensão





## Efficacy of Low-Dose Spironolactone in Subjects With Resistant Hypertension

Mari Konishi Nishizaka, Mohammad Amin Zaman, and David A. Calhoun

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**Background:** Previous reports have demonstrated the antihypertensive efficacy of high doses of spironolactone in subjects with primary aldosteronism and, to a lesser degree, subjects with resistant hypertension.

**Methods:** In current analysis, we examined the antihypertensive benefit of adding low-dose spironolactone to multidrug regimens that included a diuretic and an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) in subjects with resistant hypertension with and without primary aldosteronism. Subjects referred for resistant hypertension were evaluated with an early morning plasma renin activity, 24-h urinary aldosterone and sodium during a high dietary salt ingestion. The diagnosis of primary aldosteronism was confirmed with a renin activity  $<1.0$  ng/mL/h, urinary aldosterone  $>12$   $\mu$ g/24 h and urinary sodium  $>200$  mEq/24 h. After biochemical evaluation, spironolactone (12.5 to 25 mg/d) was added to each subject's antihypertensive regimen. If blood pressure (BP) remained uncontrolled, the dose of spirono-

lactone was titrated up to 50 mg/d. Follow-up BP was determined at 6 weeks, 3 months, and 6 months.

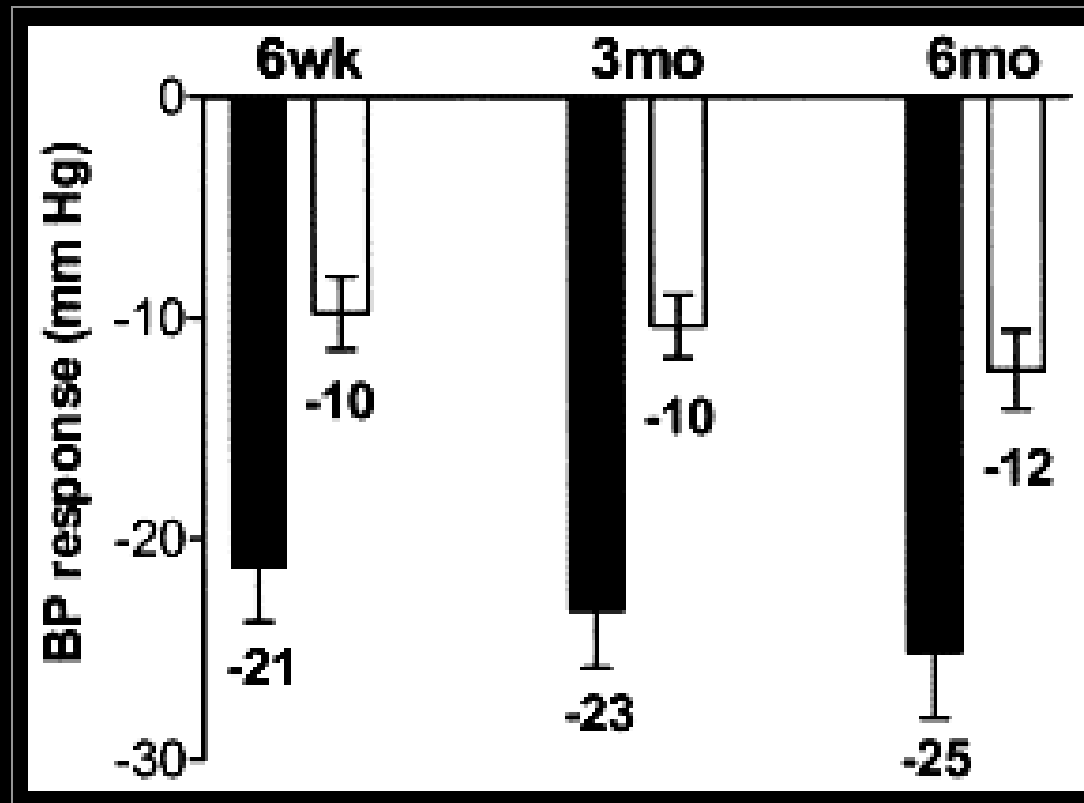
**Results:** A total number of 76 subjects were included in the analysis, 34 of whom had biochemical primary aldosteronism. Low-dose spironolactone was associated with an additional mean decrease in BP of  $21 \pm 21/10 \pm 14$  mm Hg at 6 weeks and  $25 \pm 20/12 \pm 12$  mm Hg at 6-month follow-up. The BP reduction was similar in subjects with and without primary aldosteronism and was additive to the use of ACE inhibitors, ARBs, and diuretics.

**Conclusions:** We conclude that low-dose spironolactone provides significant additive BP reduction in African American and white subjects with resistant hypertension with and without primary aldosteronism. Am J Hypertens 2003;16:925-930 © 2003 American Journal of Hypertension, Ltd.

**Key Words:** Resistant hypertension, spironolactone, aldosterone, renin, ethnicity.

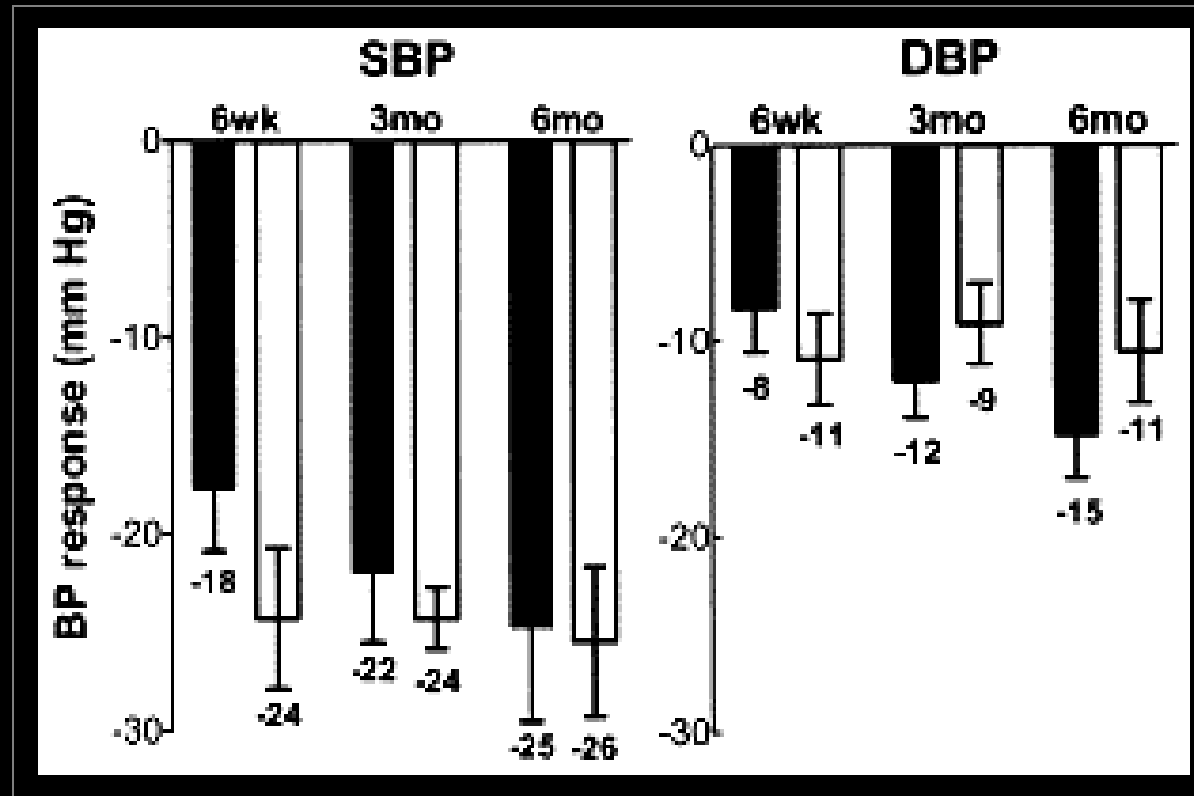


# Redução da PA sistólica e diastólica em indivíduos com Hipertensão Resistente



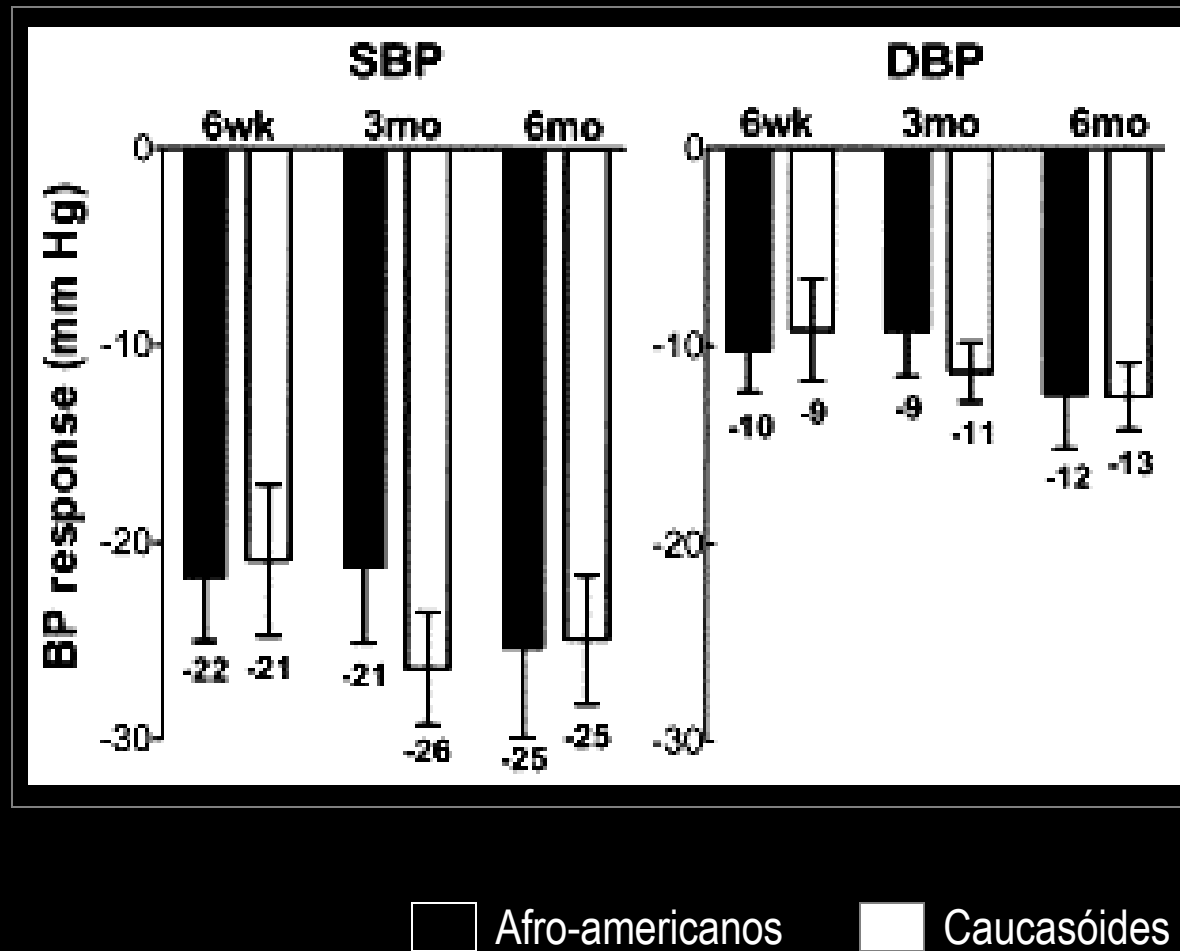
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# Redução da PA sistólica e diastólica em indivíduos com e sem aldosteronismo primário



Com aldosteronismo primário      Sem aldosteronismo primário

# Redução da PA sistólica e diastólica em Afro-americanos e caucasóides com Hipertensão Resistente



# The Role of Spironolactone in the Treatment of Patients With Refractory Hypertension

James Ouzan, Catherine Pérault, A. Michael Lincoff, Evelyne Carré, and Michel Mertes

**Background:** Hypertension is resistant to pharmacologic therapy in 5% to 10% of patients. The current study tested whether addition of spironolactone to the treatment of patients with refractory hypertension would lead to adequate blood pressure (BP) control.

**Methods:** Among 520 patients who were referred for treatment of hypertension to one medical clinic from 1997 to 1999, a total of 25 patients who met the inclusion criteria of refractory hypertension were prospectively included in this study. The inclusion criteria were as follows: 1) hypertension of  $\geq 6$  months without any apparent cause; 2) clinical BP measurement and mean 24-h ambulatory BP monitoring  $> 140/90$  mm Hg despite treatment with at least two antihypertensive drugs; 3) no prior therapy with spironolactone; and 4) no renal insufficiency. Spironolactone was added to the previous regimen at a dosage of 1 mg/kg/day while any angiotensin converting enzyme inhibitor was suppressed. Serum potassium and creatinine levels were checked before the introduction of spironolactone and 1 month later.

**Results:** After 1 month of therapy with spironolactone, 23 patients had a clinical BP  $< 140/90$  mm Hg. Ambulatory BP monitoring when compared before and 1 month after initiation of spironolactone decreased significantly (systolic BP from  $152 \pm 2$  mm Hg to  $128 \pm 2$  mm Hg,  $P < .001$ ; and diastolic BP from  $86 \pm 2$  mm Hg to  $76 \pm 2$  mm Hg,  $P < .013$ ). By 3 months after the introduction of spironolactone, the mean number of antihypertensive drugs required per patient was significantly reduced (from  $3.2 \pm 0.2$  to  $2.1 \pm 0.2$ ,  $P < .001$ ). No patient required discontinuation of spironolactone due to adverse renal effects.

**Conclusion:** Spironolactone is a safe, effective therapy for patients with refractory hypertension. Am J Hypertens 2002;15:333-339 © 2002 American Journal of Hypertension, Ltd.

**Key Words:** Refractory hypertension, spironolactone, ambulatory blood pressure monitoring.

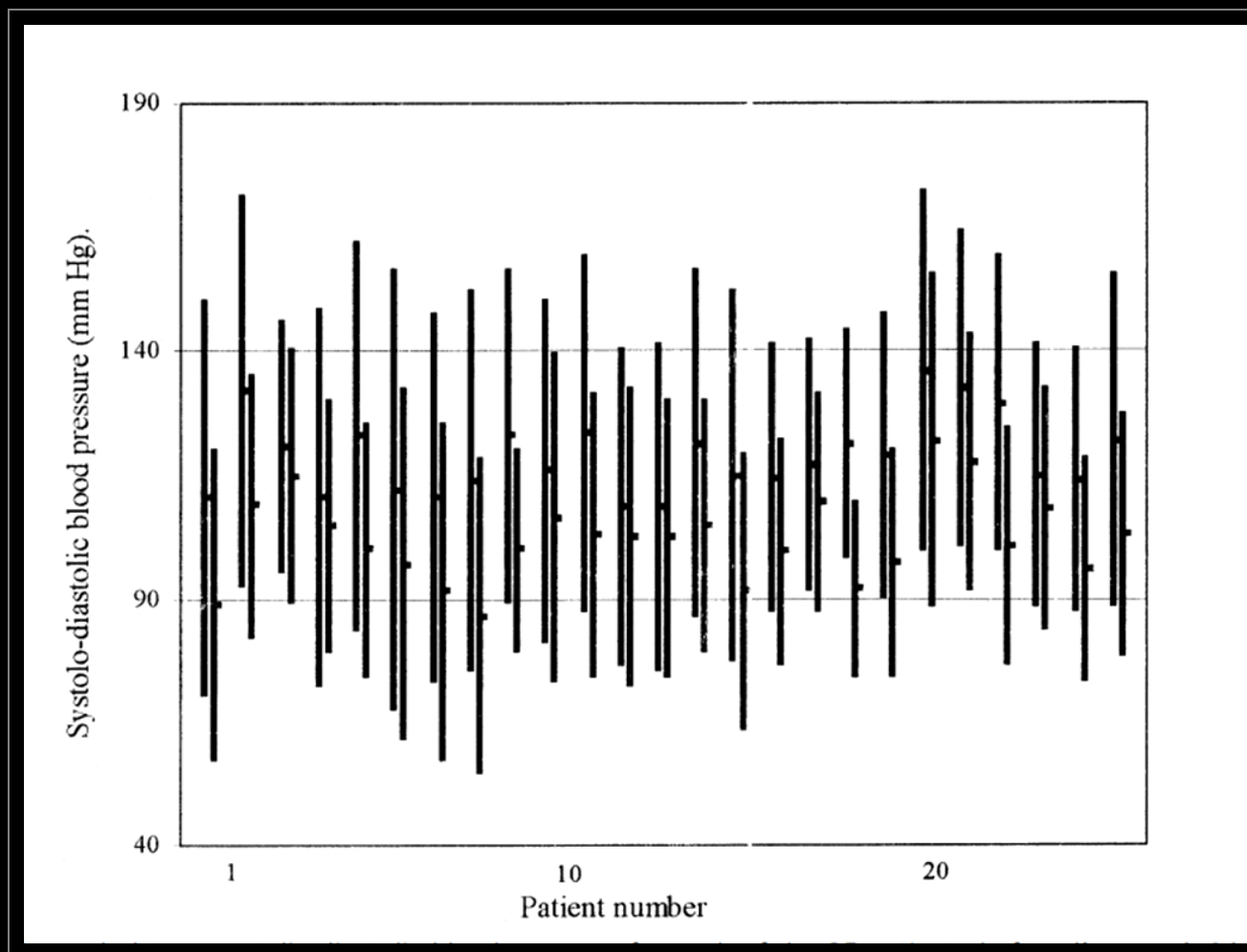
# Características da população

**Table 1.** Patient characteristics

Patient No.	Age (y)	HT Duration (y)	Before Spironolactone												After Spironolactone											
			Clinical BP		ABPM		Antihypertensive Drugs								Clinical BP		ABPM		Antihypertensive Drugs							
			Systolic	Diastolic	Systolic	Diastolic	$\alpha^-$	$\beta^-$	A C E <sup>-</sup>	D	Ca <sup>-</sup>	L	R	A R <sup>-</sup>	Systolic	Diastolic	Systolic	Diastolic	$\alpha^-$	$\beta^-$	D	Ca <sup>-</sup>	R	S		
1	75	10	230	110	150	71		x	x				x	140	90	120	58		x			x				
2	51	10	170	100	171	93		x	x	x				140	90	135	83		x			x				
3	62	18	180	110	146	96	x	x			x		x	145	90	140	90		x		x	x				
4	70	15	160	90	148	73					x		x	130	80	130	80			x		x				
5	58	12	160	100	162	84		x	x					130	80	125	75		x			x				
6	78	10	180	100	156	68		x			x		x	140	90	132	62		x		x	x				
7	82	20	170	100	147	74		x		x			x	130	90	125	58		x		x	x				
8	52	10	170	90	152	76		x	x	x				130	90	118	55		x			x				
9	68	15	170	80	156	90		x			x			125	80	120	80					x				
10	71	30	180	100	150	82		x		x	x		x	140	90	139	74		x		x	x				
11	67	30	180	100	159	88	x	x	x	x		x		130	80	131	75	x	x	x		x				
12	65	10	150	90	140	77					x			130	80	132	73			x		x				
13	75	30	170	100	141	76		x		x	x			130	80	130	75			x		x				
14	89	30	180	100	156	87	x	x	x				x	135	85	130	80					x				
15	71	23	160	90	152	78		x			x			130	80	119	64		x			x				
16	52	5	160	95	141	88		x	x	x	x			140	90	122	77					x				
17	63	10	180	100	142	92		x	x	x	x			130	80	131	88		x		x	x				
18	61	17	170	100	144	99			x	x	x			130	80	109	75		x			x				
19	54	19	170	100	147	91		x		x	x			130	90	120	75		x			x				
20	56	6	160	95	172	100		x	x	x	x			150	90	155	89			x		x				
21	51	9	157	91	164	101				x				140	70	143	92					x				
22	78	5	160	100	159	100		x			x			140	90	124	77		x			x				
23	42	2	150	80	141	89		x		x			x	135	90	132	84				x	x				
24	75	12	170	100	142	88		x	x		x			120	90	118	74		x			x				
25	61	12	160	100	155	89				x			x	140	90	127	79					x				

BP = blood pressure; ABPM = ambulatory blood pressure monitoring; HT = hypertension;  $\alpha^-$  =  $\alpha$ -blocker;  $\beta^-$  =  $\beta$ -blocker; ACE $^-$  = angiotensin converting enzyme inhibitor; D = diuretic; Ca $^-$  = calcium inhibitor; L = lonoten; R = rilmenidine; AR $^-$  = angiotensin receptor blocker; S = spironolactone.

# PA Sistólica e Diastólica de cada um dos 25 hipertensos antes e após 1 mês de tratamento com espironolactona



# **Estratégia terapêutica na HTA resistente**

- 1. Optimizar a terapêutica diurética**
  - **HCTZ 25 mg**
  - **Clorotalidona**
- 2. Fazer cronoterapia**
- 3. Associar o 4º anti-hipertensor**
- 4. Associar espironolactona**

