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Palacio de Ferias y Congresos de Málaga
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HTA Refractaria: Denervación simpática o intensificación del tratamiento antihipertensivo con antagonistas de la aldosterona y otros fármacos antihipertensivos

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Definiciones de HTA R

EUROPA		ESTADOS UNIDOS	
ESH 2007	BHS 2011	JNC 7 2003	AHA 2008
PA≥140/90 mm Hg a pesar de tratamiento con 3 fármacos (incluido un diurético) en dosis adecuadas y tras exclusión de HTA falsa como bata blanca y uso de manguito adecuado en brazos obesos	Quien no esté con PA controlada, <140/90 mm Hg a pesar del tratamiento óptimo, a la dosis mejor tolerada con tratamiento de tercera línea.	No conseguir objetivo de PA en paciente con buena adherencia a dosis plenas de un régimen de 3 fármacos que incluye un diurético	PA que permanece sobre el nivel objetivo, a pesar de usar 3 antihipertensivos de diferentes clases, (idealmente, uno de ellos diurético) y todos a dosis óptimas . Todo paciente con más de cuatro fármacos

HABLAMOS DE HTA REFRACTARIA NO CONTROLADA

Datos epidemiológicos prevalencia (NHANES):

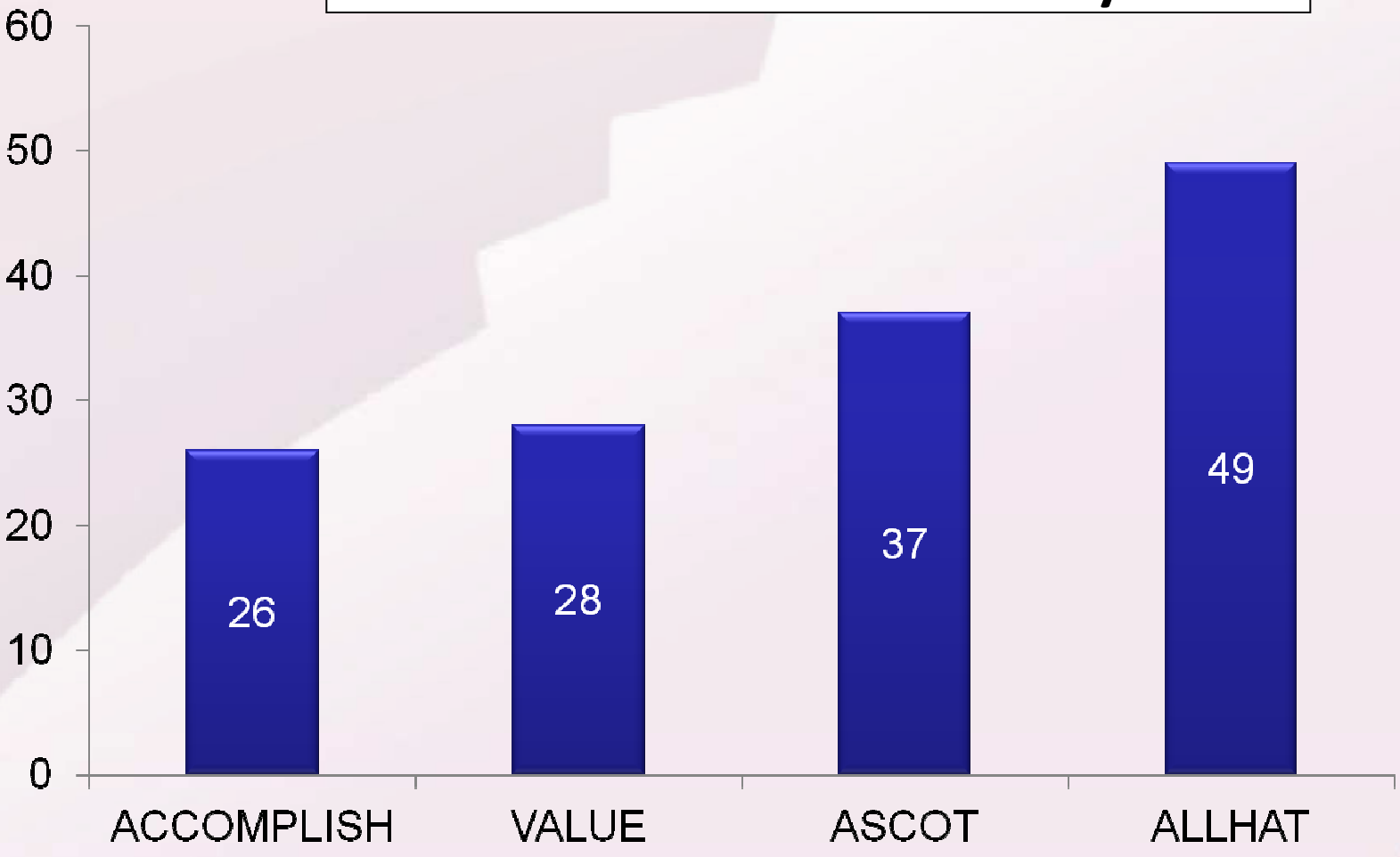
- Incremento progresivo de la prevalencia de HTAR Prevalencia 1988 - 1994: **5.5%** de todos los hipertensos;
- 1999 -2004: **8.5%**,
- 2005 - 2008: **12.8%**
- (Egan BM, Zhao Y, Axon RN, Brzezinski WA, Ferdinand KC. Uncontrolled and apparent treatment resistant hypertension in the United States, 1988–2008. *Circulation*. 2011;124:1046 –1058)

Datos epidemiológicos prevalencia (España)

Registro CARDIORISC, 68.000 pacientes con MAPA: **14,8%** de prevalencia de HTAR en los hipertensos tratados

(de la Sierra A, Segura J, Banegas JR, Gorostidi M, de la Cruz JJ, Amario P, Oliveras A, Ruilope LM. Clinical features of 8295 patients with resistant hypertension classified on the basis of ambulatory blood pressure monitoring. *Hypertension*. 2011;57:898 –902)

Prevalencia: ensayos



Resumen

- Conciliando los resultados de los diferentes diseños de los estudios observacionales y los ensayos clínicos, la prevalencia de la HTAR puede estimarse entre un **15% y un 30%** de los pacientes hipertensos tratados.

Prognostic Value of Ambulatory Blood Pressure Monitoring in Refractory Hypertension

A Prospective Study

Josep Redon, Carlos Campos, Maria L. Narciso, Jose L. Rodicio, Jose M. Pascual, Luis M. Ruilope

Abstract—The objective of this study was to establish whether ambulatory blood pressure offers a better estimate of cardiovascular risk than does its clinical blood pressure counterpart in refractory hypertension. This prospective study assessed the incidence of cardiovascular events over time during an average follow-up of 49 months (range, 6 to 96). Patients were referred to specialized hypertension clinics (86 essential hypertension patients who had diastolic blood pressure >100 mm Hg during antihypertensive treatment that included three or more antihypertensive drugs, one being a diuretic). Twenty-four-hour ambulatory blood pressure monitoring (ABPM) was performed at the time of entrance. End-organ damage was monitored yearly, and the incidence of cardiovascular events was recorded. Patients were divided into tertiles of average diastolic blood pressure during activity according to the ABPM, with the lowest tertile <88 mm Hg (LT, n=29), the middle tertile 88 to 97 mm Hg (MT, n=29), and the highest tertile >97 mm Hg (HT, n=28). While significant differences in systolic and diastolic ambulatory blood pressures were observed among groups, no differences were observed at either the beginning or at the time of the last evaluation for office blood pressure. During the last evaluation, a progression in the end-organ damage score was observed for the HT group but not for the two other groups. Twenty-one of the patients had a new cardiovascular event; the incidence of events was significantly lower for the LT group (2.2 per 100 patient-years) than it was for the MT group (9.5 per 100 patient-years) or for the HT group (13.6 per 100 patient-years). The probability of event-free survival was also significantly different when comparing the LT group with the other two groups (LT versus MT log-rank, $P<.04$; LT versus HT log-rank, $P<.006$). The HT group was an independent risk factor for the incidence of cardiovascular events (relative risk, 6.20; 95% confidence interval, 1.38 to 28.1, $P<.02$). Higher values of ambulatory blood pressure result in a worse prognosis in patients with refractory hypertension, supporting the recommendation that ABPM is useful in stratifying the cardiovascular risk in patients with refractory hypertension. (***Hypertension***. 1998;31:712-718.)

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Pronóstico de la HTA Resistente

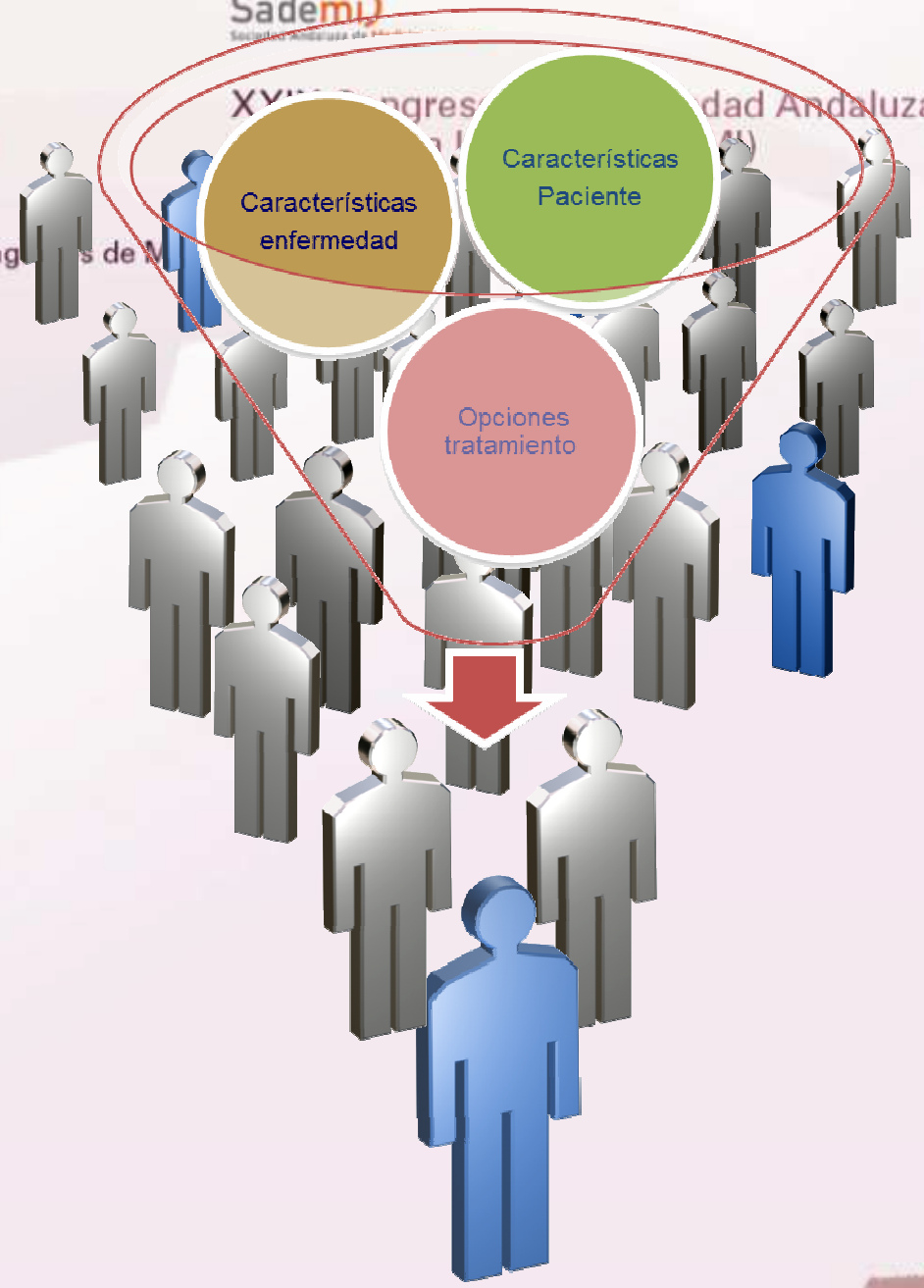
- Incremento del 50% del RCV durante el seguimiento de 5 años (sobretodo debido al desarrollo de enfermedad renal crónica) con respecto a los hipertensos controlados con 2 o 3 fármacos

- Comparados con todos los sujetos con tratamiento antihipertensivo de novo, el RCV en los resistentes se incrementa el doble

Interés en la HTAR: Por su prevalencia, aumento de incidencia y mal pronostico

No todos los pacientes con HTA Resistente están mal controlados (AHA).

No todos los pacientes con HTA mal controlada son resistentes.



Algoritmo para el diagnóstico de la HTA R

Dgco: PA> 140/90 mmHg, tto ¿3 fármacos, uno diu, a dosis plenas? ¿PseudoHTA?

¿HTA bata blanca? **SÍ** → AMPA, medidas ambulatorias

NO

¿Adherencia a tto? **NO** → Preguntar E adv, MEMS, contaje…

SÍ

¿Sustancias presoras (AINES…)? **SÍ** → Suspender o reducir, aumentar tto antihipertensivo

NO

¿Obesidad, S.mtb? **SÍ** → Recomendar dieta, ejercicio

NO

¿HTA secundaria? **SÍ** → DGCO y TTO:
Enf parenquimatosa renal
Enf. Renovascular Hiperaldosteronismo
Enf. Tiroides Sdr. Cushing
Feocromocitoma Coartación de aorta
SAOS

NO

Optimizar, intensificar tto

Adaptado de: Moser M and Setaro J. N Engl J Med 2006;355:385-392

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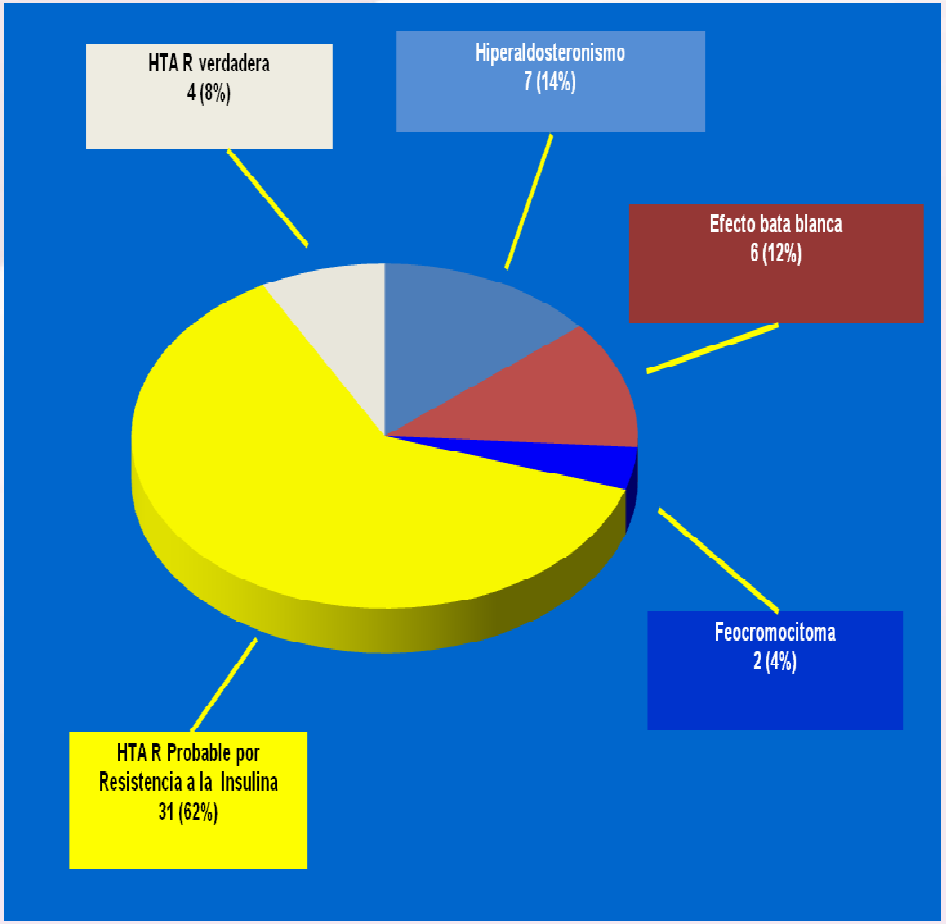
- 50 hipertensos consecutivos remitidos a nuestra Unidad de Hipertensión
- PA > 140/90 con tres fármacos incluido un diurético
- Edad media: 52±8 años
- PAS media: 168±16 mmHg
- PAD media: 101±10 mmHg



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Tratamiento Farmacológico

Diuréticos

- Si hay poca alteración renal: se utilizará **clortalidona** en lugar de hidroclorotiazida, por su mayor vida media (poca evidencia en HTAR) (titular hasta 50mg si es necesario).
- Si la tasa de **filtrado glomerular es < 30 mL/min** por m^2, las tiazidas son menos eficaces que los **diuréticos de asa** (furosemida 3/día, torasemida 1/día).
- A una dosis dada de diurético en los pacientes hipertensos estables, las pérdidas urinarias de sodio y potasio ocurren fundamentalmente durante los primeros 10-14 días.
- La hipokaliemia es frecuente en la HTAR, debido en parte a unos niveles inadecuadamente altos de aldosterona.

Tratamiento : ESH/ESC-2007

- En ningún ensayo clínico se ha demostrado cuál sería la elección óptima de un 4º o 5º fármaco antihipertensivo
- Evidencias basadas en estudios observacionales recientes, apoyan el uso de **espironolactona** añadida a los esquemas múltiples de tratamiento, como buena opción para conseguir un descenso de la PA

(1) Calhoun DA. J Clin Hypertens 2007; 9(suppl 1): 19-24 y
(2) Zannad F. J Hypertens 2007; 25: 747-50

Management of resistant arterial hypertension: role of spironolactone versus double blockade of the renin–angiotensin–aldosterone system

Beatriz Alvarez-Alvarez[a], María Abad-Cardiel[b], Arturo Fernandez-Cruz[b] and Nieves Martell-Claros[b]

Background Currently there is no consensus regarding which add-on therapy to use in resistant hypertension. This study was designed to compare two treatment options, spironolactone (SPR) versus dual blockade of the renin–angiotensin–aldosterone system (RAAS).

Methods Forty-two patients with true resistant hypertension were included in the study. An open-label prospective crossover design was used to add a second RAAS blocker to previous treatment and then SPR following 1 month of wash-out. BP was measured in the office and by ambulatory blood pressure monitoring (ABPM). Changes in laboratory tests were also studied for both treatments. The predictive values of aldosterone–renin ratio (ARR) and serum potassium of determining the antihypertensive response were analyzed for both arms.

Results Following the first stage of dual blockade, SBP dropped significantly both in office (reduction of 12.9 ± 19.2 mmHg)) and by ABPM (reduction of 7.1 ± 13.4 mmHg). Office DBP was unchanged but was significantly reduced as measured by ABPM (3.4 ± 6.2 mmHg). On SPR treatment, office BP was reduced 32.2 ± 20.6/10.9 ± 11.6 mmHg. By ABPM the reduction was 20.8 ± 14.6/8.8 ± 7.3 mmHg ($P<0.001$). The BP control was achieved by 25.6% of patients in dual blockade and 53.8% in SPR with office blood pressure. By ABPM, 20.5% were controlled on dual blockade and up to 56.4% with SPR. Serum potassium was a weak inverse predictor of the blood pressure-lowering effect of SPR.

Conclusion SPR has a greater antihypertensive effect than dual blockade of the RAAS in resistant hypertension. SPR at daily doses of 25–50 mg shows a potent antihypertensive effect when added to prior regimes of single RAAS axis blockade in patients with resistant arterial hypertension.
J Hypertens 28:2329–2335

Journal of Hypertension 2010, 28:2329–2335

Keywords: ambulatory blood pressure monitoring, potassium, renin–aldosterone ratio, renin–aldosterone axis dual blockade, resistant arterial hypertension, spironolactone

Abbreviations: ABPM, ambulatory blood pressure monitoring; ACE-I, angiotensin-converting enzyme inhibitor; AHT, arterial hypertension; ARB, angiotensin receptor blockade; ARR, aldosterone–renin ratio; LVH, left ventricular hypertrophy; LVM, left ventricular mass; PAC, plasma aldosterone concentration; RAAS, renin–angiotensin–aldosterone system; RAH, resistant arterial hypertension; SPR, spironolactone

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See editorial comment on page 2194

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Role of spironolactone versus double blockade of the RAAS in resistant hypertension

Forty-two patients with true resistant hypertension were included in the study. An open-label prospective crossover design was used to add a second RAAS blocker to previous treatment and then SPR following 1 month of wash-out.

Table 2 Changes in blood pressure with dual blockade and spironolactone plus single blockade

	Office BP		ABPM 24 h		ABPM day		ABPM night	
	SBP	DBP	SBP	DBP	SBP	DBP	SBP	DBP
Baseline	158.4 ± 15.3	80.4 ± 11.4	141.0 ± 14.4	77.7 ± 9.1	142.1 ± 16.0	79.9 ± 9.2	136.5 ± 18.7	73.9 ± 16.7
Dual blockade	145.5 ± 29.3	78.2 ± 13.9	133.9 ± 14.8	74.3 ± 8.1	136.0 ± 14.6	77.4 ± 9.2	129.4 ± 17.2	69.2 ± 9.5
SPR + SB	126.2 ± 19.0	69.5 ± 11.7	120.2 ± 15.4	68.9 ± 9.7	122.1 ± 15.9	71.4 ± 10.1	117.1 ± 17.1	64.8 ± 10.7

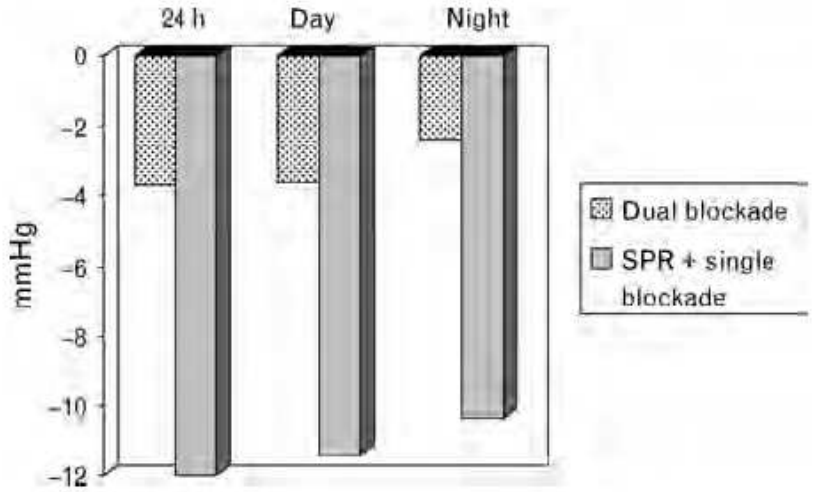
ABPM, ambulatory blood pressure monitoring; SPR + SB, spironolactone plus double blockade; SPR, spironolactone.

-32,2/10,9 mmHg

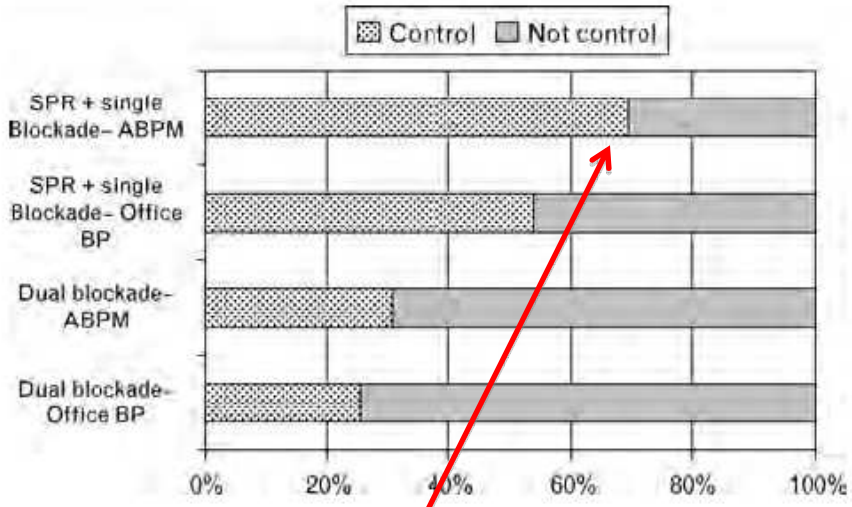
-20/8,8

Alvarez B et al. J Hypertens 2010; 28: 2329-2335.

Role of spironolactone versus double blockade of the RAAS in resistant hypertension



Difference in pulse pressure reduction (measured by ambulatory blood pressure monitoring) between dual blockade and spironolactone. ABPM, ambulatory blood pressure monitoring.



Percentage of hypertensive patients controlled by dual blockade and spironolactone (in office and by ambulatory blood pressure monitoring). ABPM, ambulatory blood pressure monitoring.

Control 68% en 2 meses

Alvarez B et al. J Hypertens 2010; 28: 2329-2335.

Efficacy of Spironolactone Therapy in Patients With True Resistant Hypertension

Fabio de Souza, Elizabeth Muxfeldt, Roberto Fiszman, Gil Salles

Abstract—The role of spironolactone in resistant hypertension management is unclear. The aim of this prospective trial was to evaluate the antihypertensive effect of spironolactone in patients with true resistant hypertension diagnosed by ambulatory blood pressure monitoring. A total of 175 patients had clinical and complementary exams obtained at baseline and received spironolactone in doses of 25 to 100 mg/d. A second ambulatory blood pressure monitoring was performed after a median interval of 7 months. Paired Student *t* test was used to assess differences in blood pressure before and during spironolactone administration, and multivariate analysis adjusted for age, sex, and number of antihypertensive drugs to assess the predictors of blood pressure fall. There were mean reductions of 16 and 9 mm Hg, respectively, in 24-hour systolic and diastolic blood pressures (95% CIs: 13 to 18 and 7 to 10 mm Hg; $P<0.001$). Office systolic blood pressure and diastolic blood pressure also decreased (14 and 7 mm Hg). Controlled ambulatory blood pressure was reached in 48% of patients. Factors associated with better response were higher waist circumference, lower aortic pulse wave velocity, and lower serum potassium. No association with plasma aldosterone or aldosterone:renin ratio was found. Adverse effects were observed in 13 patients (7.4%). A third ambulatory blood pressure monitoring performed in 78 patients after a median of 15 months confirmed the persistence of the spironolactone effect. In conclusion, spironolactone administration to true resistant hypertensive patients is safe and effective in decreasing blood pressure, especially in those with abdominal obesity and lower arterial stiffness. Its addition to an antihypertensive regimen as the fourth or fifth drug is recommended. (***Hypertension*. 2010;55:147-152.**)

-16/9
ABPM24h

Control:48% en 7 meses

Antagonismo Aldosterónico:

- Adición de dosis bajas (desde 12,5 a 50 mg diarios) de Espironolactona a terapia múltiple previa –media de 4 fármacos-: disminuyen la PAS 25 mmHg y la PAD 12 mmHg. Efecto similar en raza blanca y negra (1)

- Adición de 25mg de Espironolactona como 4º fármaco en el Brazo de PA del ASCOT produjo disminuciones de22/10 mmHg. Especialmente eficaz en pacientes mayores y obesos (2)

- Resultado eficaz con 25-50 mg de Espironolactona (3)

(1) Nishizaka et al. AmJ Hypertens, 2003; 16:925
(2) Chapman et al. Hypertension 2007; 49:839
(3) Lane DA et al. J Hypertens 2007; 25:891-94

Effectiveness of the selective aldosterone blocker, eplerenone, in patients with resistant hypertension

After receiving eplerenone (at a dose of 50 to 100 mg/day, titrated to achieve BP < 140/90 mmHg) on top of a three-drug regimen for 12 weeks, office BP was reduced by 18/8mmHg, and 24-hour mean BP decreased by 12/6mmHg ($P < .001$).

Again, these effects were independent of baseline plasma aldosterone and PRA levels.

Calhoun DA et al. J Am Soc Hypertens 2008; 2: 462-468.

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Denervación Renal

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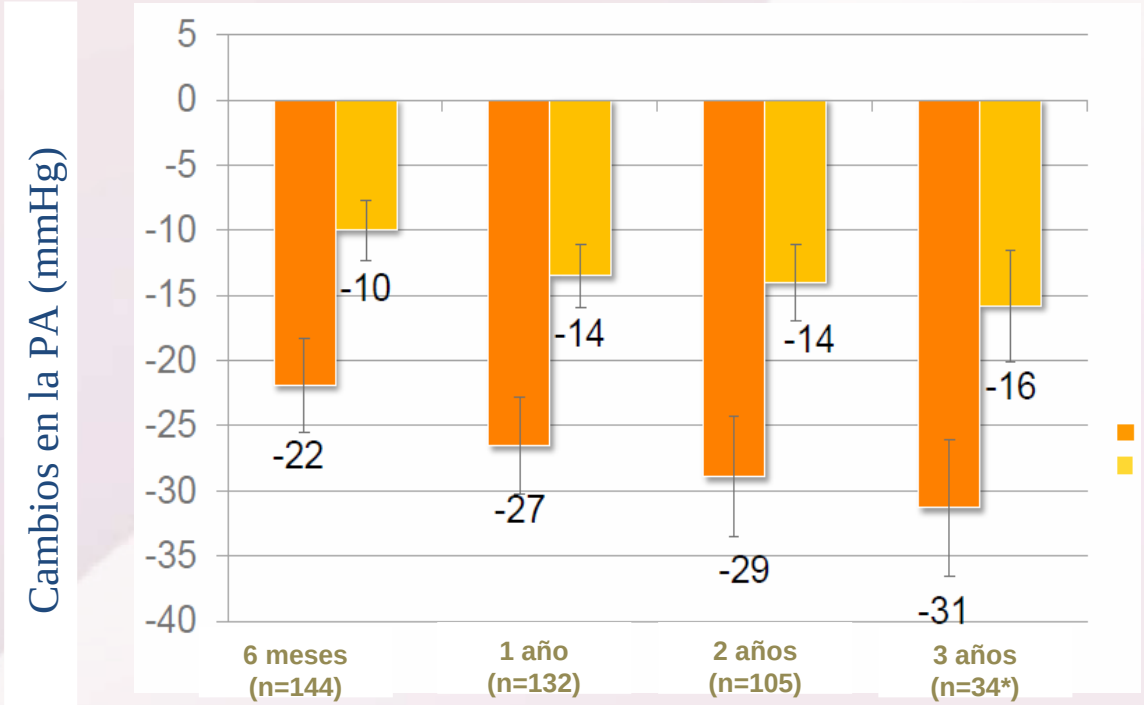
6.14.2 Renal denervation

Ya está incluido en las guías

through the femoral artery [617–621]. The rationale for renal denervation lays in the importance of sympathetic influences on renal vascular resistance, renin release and sodium re-absorption, the increased sympathetic tone to the kidney and other organs displayed by hypertensive patients [622–624], and the pressor effect of renal afferent fibres, documented in experimental animals [625,626]. The procedure has been shown to induce a marked reduction in

At present, the renal denervation method is promising, but in need of additional data from properly designed long-term comparison trials to conclusively establish its safety and persistent efficacy vs. the best possible drug treatments. Understanding what makes renal denervation effective or ineffective (patient characteristics or failure to achieve renal sympathectomy) will also be important to avoid the procedure in individuals unlikely to respond. A position paper of the ESH on renal denervation should be consulted for more details [631].

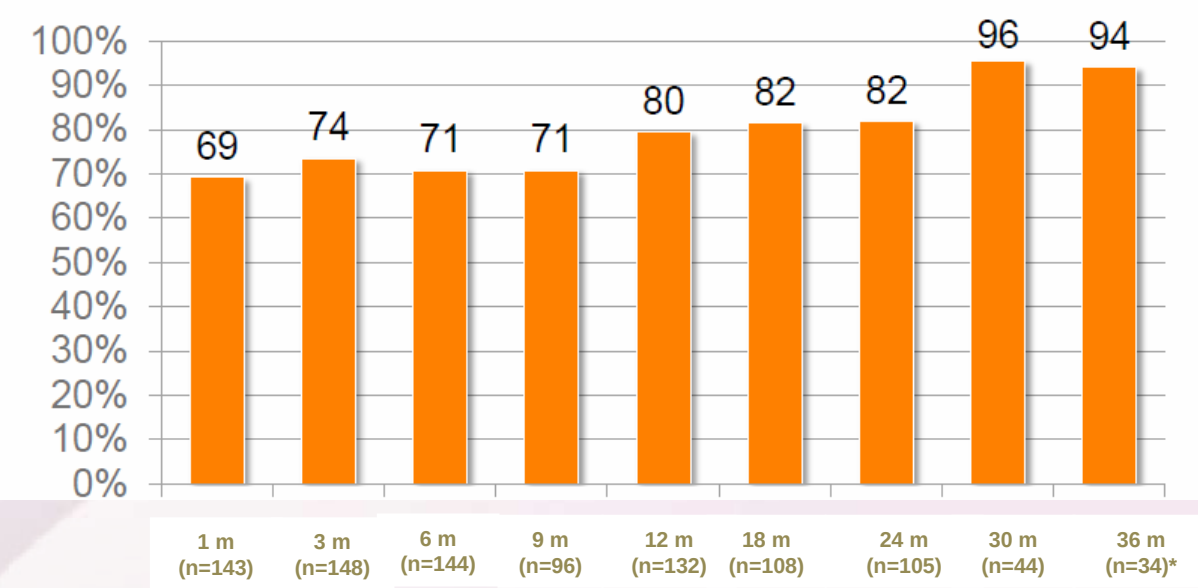
Reducciones de PA significativas y sostenidas en el tiempo



p <0.01 for Δ from baseline for all time points.
+ Number of patients represents data available at time of data-lock.

Resultados ampliados presentados en el TCT 2012 (Schlaich M).

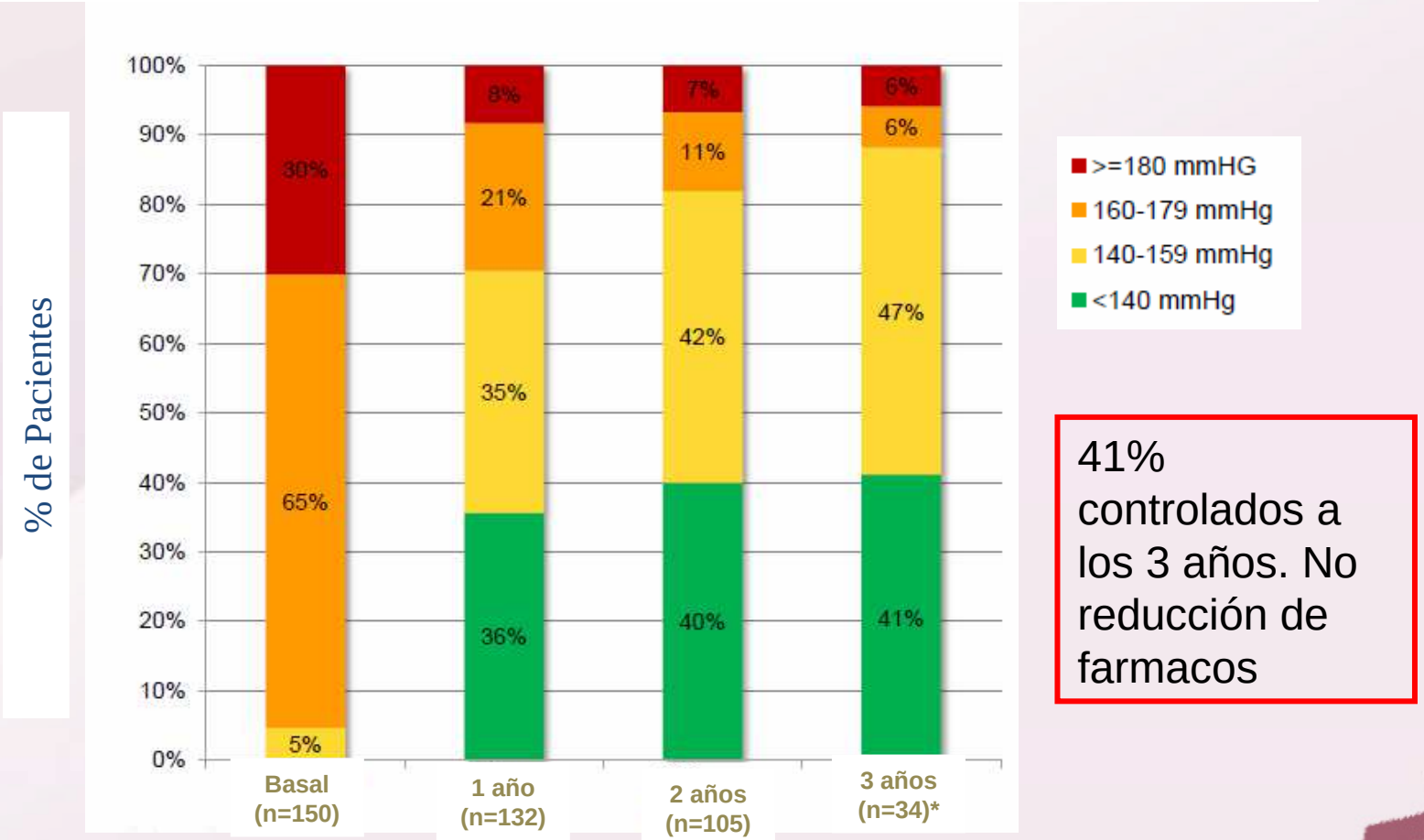
La tasa de respondedores no disminuye con el tiempo



Respondedor = Paciente con una reducción de PA sistólica en consulta de ≥10 mmHg
*Número de pacientes con seguimiento en ese momento

Resultados ampliados presentados en el TCT 2012 (Schlaich M).

Tras la RDN se consigue reducir el riesgo de sufrir eventos cardiovasculares



41% controlados a los 3 años. No reducción de farmacos

Lewington S et al. The Lancet 2002;360:1903-1913.
Resultados ampliados presentados en el TCT 2012 (Schlaich M).

Características basales Symplicity HTN-1

Demographics	Age (years)	57 ± 11
	Gender (% female)	39%
	Race (% non-Caucasian)	5%
Co-morbidities	Diabetes Mellitus II (%)	31%
	CAD (%)	22%
	Hyperlipidemia (%)	68%
	eGFR (mL/min/1.73m^2)	83 ± 20
Blood Pressure	**Baseline BP (mmHg)**	**176/98 ± 17/15**
	Number of anti-HTN meds (mean)	**5.0 ± 1.4**
	ACE/ARB (%)	90%
	Beta-blocker (%)	82%
	Calcium channel blocker (%)	75%
	Vasodilator (%)	19%
	Diuretic (%)	95%
	Spironolactone (%)	21%

Sievert et al. European Society of Cardiology. 2010.

	Espironolactona	Denervacion renal
TAS consulta	-22 a -32 mmHg	-31 mmHg
TAD consulta	-9 a -12	-16 mmHg
Controlados	48-68%	41%
Tiempo hasta control	4-7 meses	1mes a 3 años
TAS inicial	158-160	176
Nº fármacos	4-4,2	5-5,4

21% de los DNR tomaban espironolactona

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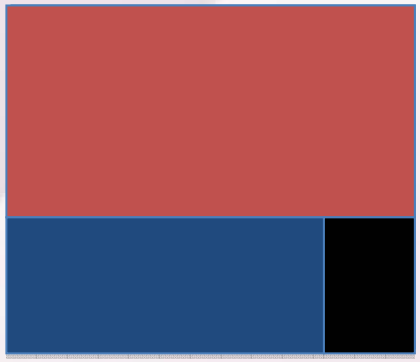
Respuesta 1.- intensificación del tto y si no control DNR.

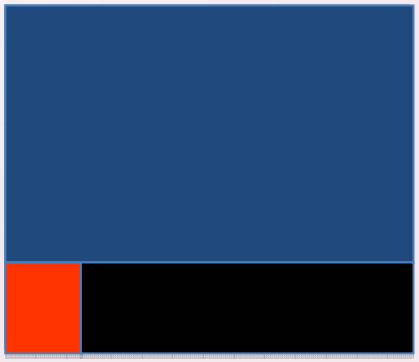
HTA como patología multifactorial. Diferentes vías reguladoras

Sistema nervioso simpático

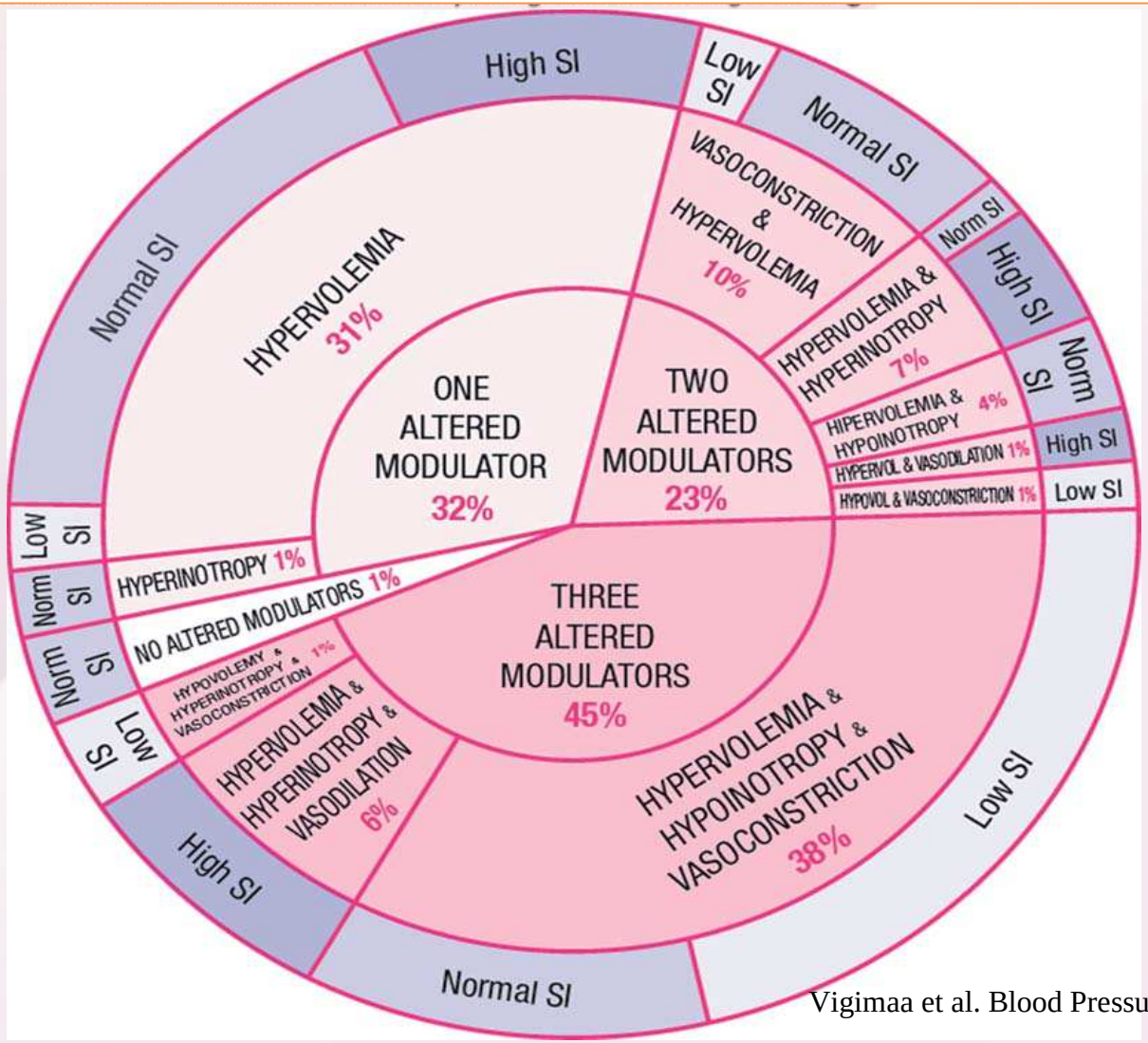
Sistema renina-angiotensina

Sistema sensi/resistencia a la sal





NUEVOS MÉTODOS DE EVALUACIÓN HEMODINÁMICA



Vigimaa et al. Blood Pressure, 2013; Early Online: 1–9

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Respuesta 1.- intensificación del tto y si no control DNR.
Respuesta 2.- Intolerancias a espiro y eplerenona y no resultado con 4 fármacos (forzando diureticos): DNR
Respuesta 3.- Sospecha alta de aumento de actividad simpática (aumento +++ vc).

Ventajas con DNR no demostrados con tto farmacologico

Renal denervation in moderate to severe CKD.

Hering D, **Mahfoud F**, **Walton AS**, Krum H, Lambert GW, Lambert EA, Sobotka PA, Böhm M, Cremers B, Esler MD, Schlaich MP.

Neurovascular Hypertension & Kidney Disease Laboratory, Baker IDI Heart & Diabetes Institute, Melbourne, Australia.

Abstract

Sympathetic activation contributes to the progression of CKD and is associated with adverse cardiovascular outcomes. Ablation of renal sympathetic nerves reduces sympathetic nerve activity and BP in patients with resistant hypertension and preserved renal function, but whether this approach is safe and effective in patients with an estimated GFR (eGFR) < 45 ml/min per 1.73 m(2) is unknown. We performed bilateral renal denervation in 15 patients with resistant hypertension and stage 3-4 CKD (mean eGFR, 31 ml/min per 1.73 m(2)). We used CO(2) angiography in six patients to minimize exposure to contrast agents. Estimated GFR remained unchanged after the procedure, irrespective of the use of CO(2) angiography. Mean baseline BP ± SD was 174 ± 22/91 ± 16 mmHg despite the use of 5.6 ± 1.3 antihypertensive drugs. Mean changes in office systolic and diastolic BP at 1, 3, 6, and 12 months were -34/-14, -25/-11, -32/-15, and -33/-19 mmHg, respectively. Night-time ambulatory BP significantly decreased (P<0.05), restoring a more physiologic dipping pattern. In conclusion, this study suggests a favorable short-term safety profile and beneficial BP effects of catheter-based renal nerve ablation in patients with stage 3-4 CKD and resistant hypertension.

J Am Soc Nephrol. **2012** Jul;23(7):1250-7.

DENERVACION RENAL Y APNEA DEL SUEÑO

Effects of Renal Sympathetic Denervation on Blood Pressure, Sleep Apnea Course, and Glycemic Control in Patients With Resistant Hypertension and Sleep Apnea

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See Editorial Commentary, pp 542–543

Abstract—Percutaneous renal sympathetic denervation by radiofrequency energy has been reported to reduce blood pressure (BP) by the reduction of renal sympathetic efferent and afferent signaling. We evaluated the effects of this procedure on BP and sleep apnea severity in patients with resistant hypertension and sleep apnea. We studied 10 patients with refractory hypertension and sleep apnea (7 men and 3 women; median age: 49.5 years) who underwent renal denervation and completed 3-month and 6-month follow-up evaluations, including polysomnography and selected blood chemistries, and BP measurements. Antihypertensive regimens were not changed during the 6 months of follow-up. Three and 6 months after the denervation, decreases in office systolic and diastolic BPs were observed (median: −34/−13 mm Hg for systolic and diastolic BPs at 6 months; both $P<0.01$). Significant decreases were also observed in plasma glucose concentration 2 hours after glucose administration (median: 7.0 versus 6.4 mmol/L; $P=0.05$) and in hemoglobin A1C level (median: 6.1% versus 5.6%; $P<0.05$) at 6 months, as well as a decrease in apnea-hypopnea index at 6 months after renal denervation (median: 16.3 versus 4.5 events per hour; $P=0.059$). In conclusion, catheter-based renal sympathetic denervation lowered BP in patients with refractory hypertension and obstructive sleep apnea, which was accompanied by improvement of sleep apnea severity. Interestingly, there are also accompanying improvements in glucose tolerance. Renal sympathetic denervation may conceivably be a potentially useful option for patients with comorbid refractory hypertension, glucose intolerance, and obstructive sleep apnea, although further studies are needed to confirm these proof-of-concept data. (***Hypertension*****. 2011;58:559-565.)**

Key Words: drug resistance ■ hypertension ■ obstructive sleep apnea ■ renal sympathetic denervation ■ blood pressure ■ glycemic control

Renal Sympathetic Denervation Reduces Left Ventricular Hypertrophy and Improves Cardiac Function in Patients With Resistant Hypertension

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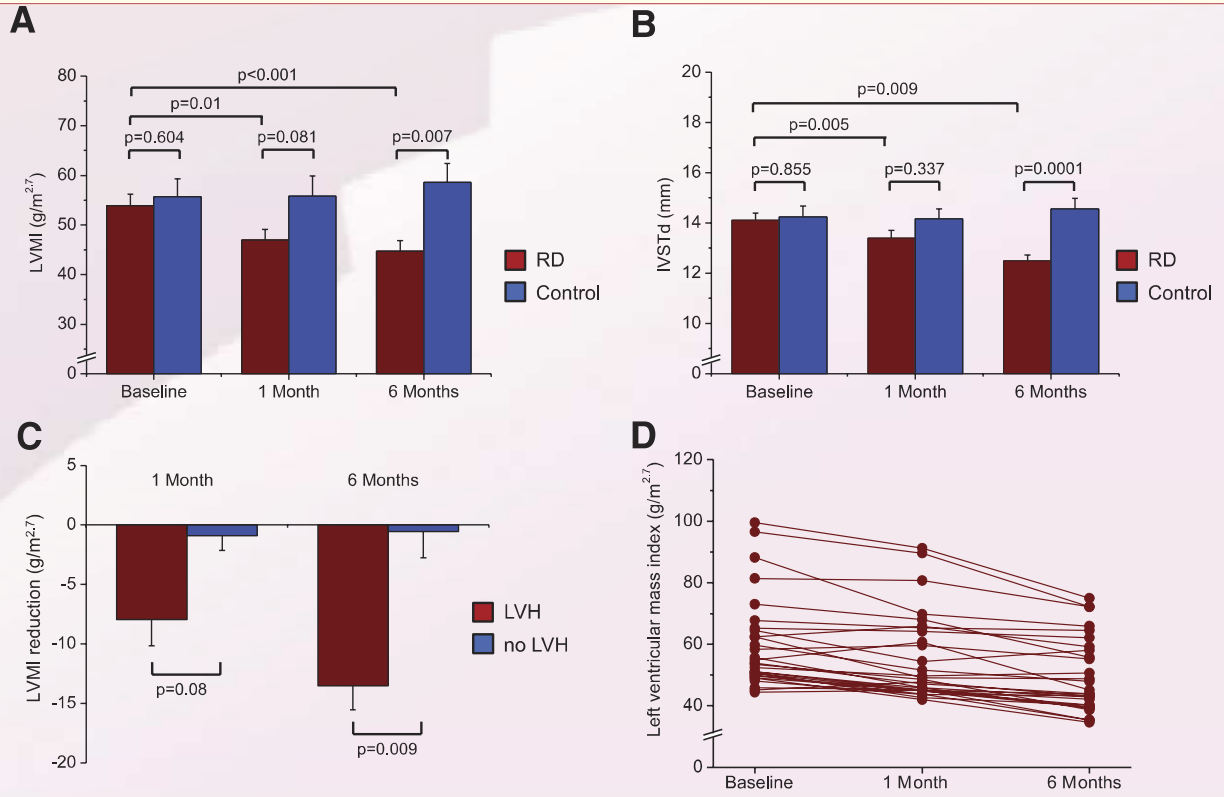

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March 6, 2012:901–9

New BP-lowering drugs (nitric oxide donors, vasopressin antagonists, neutral endopeptidase inhibitors, aldosterone synthase inhibitors, etc.) are all undergoing early stages of investigation

At present, the renal denervation method is promising, but in need of additional data from properly designed longterm comparison trials to conclusively establish its safety and persistent efficacy vs. the best possible drug treatments.

Understanding what makes renal denervation effective or ineffective (patient characteristics or failure to achieve renal sympathectomy) will also be important to avoid the procedure in individuals unlikely to respond.

ESH-ESC 2013

SEMI
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA

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Sociedad Andaluza de Medicina Interna

XXXIV Congreso Nacional de la Sociedad Española de Medicina Interna (SEMI)

XXIX Congreso de la Sociedad Andaluza de Medicina Interna (SADEMI)

21-23 Noviembre 2013 Palacio de Ferias y Congresos de Málaga. Málaga

GRACIAS POR SU ATENCIÓN

Tablas de estratificación del riesgo CV de la ESH-ESC

	BP (mm Hg)				
Other risk factors OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD, or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Considerar RDN?

HT=hypertension. SBP=systolic blood pressure. DBP=Diastolic blood pressure. MS=metabolic syndrome. OD=subclinical organ damage. CV=cardiovascular.
Mancia G, et al. *Eur Heart J*. 2007;28:1462-1536.

Seguridad en el procedimiento a 30 meses

- 0-12 meses tras el procedimiento
  - 9 eventos hipertensivos que requirieron hospitalización
  - 2 eventos hipotensivos que requirieron hospitalización

- 12-30 meses tras el procedimiento
  - 3 eventos hipertensivos que requirieron hospitalización
  - 1 insuficiencia renal aguda leve y transitoria
  - 2 muertes consideradas no relacionadas con el dispositivo o la terapia

- Sin cambios significativos en el eGFR comparado con los valores antes del procedimiento y sin eventos vasculares renales reportados

45 ensayos en marcha…

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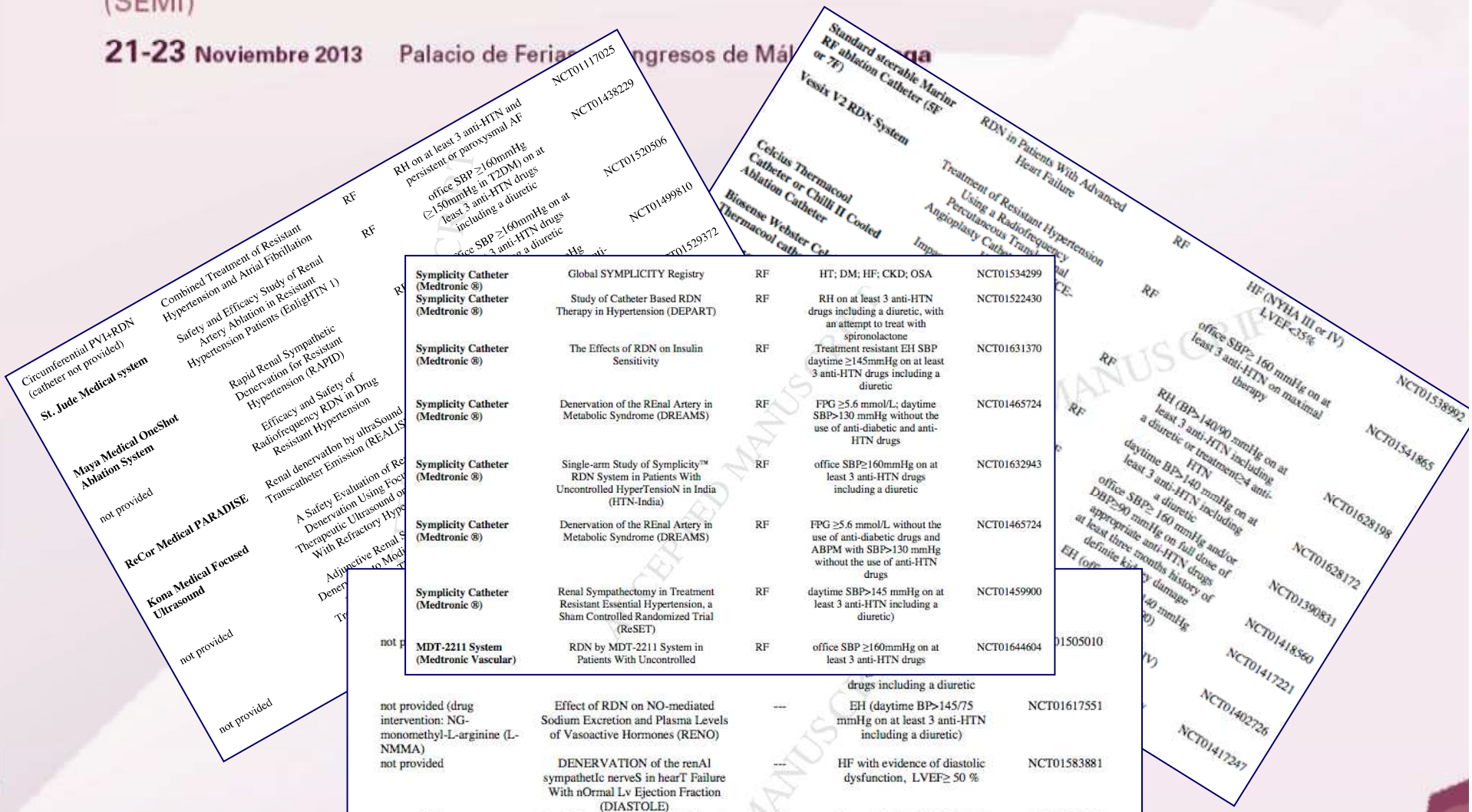

Circumferential PVI+RDN (catheter not provided)	Combined Treatment of Resistant Hypertension and Atrial Fibrillation	RF	RH on at least 3 anti-HTN and persistent or paroxysmal AF	NCT01117025
St. Jude Medical system	Safety and Efficacy Study of Renal Artery Ablation in Resistant Hypertension Patients (EnligHTN 1)	RF	office SBP ≥160mmHg (≥150mmHg in T2DM) on at least 3 anti-HTN drugs including a diuretic	NCT01438229
Maya Medical OneShot Ablation System	Rapid Renal Sympathetic Denervation for Resistant Hypertension (RAPID)		office SBP ≥160mmHg on at least 3 anti-HTN drugs including a diuretic	NCT01520506
not provided	Efficacy and Safety of Radiofrequency RDN in Drug Resistant Hypertension			NCT01499810
ReCor Medical PARADISE	Renal denervation by ultraSound Transcatheter Emission (REALIS			NCT01529372
Kona Medical Focused Ultrasound	A Safety Evaluation of Re Denervation Using Focu Therapeutic Ultrasound or With Refractory Hype			
not provided	Adjunctive Renal S to Mod			
not provided				
Standard steerable Marinr RF ablation Catheter (5F or 7F)	**Vessix V2 RDN System**	**Celcius Thermacool Catheter or Chilli II Cooled Ablation Catheter**	**Biosense Webster Cel Thermacool cath**	
RDN in Patients With Advanced Heart Failure	Treatment of Resistant Hypertension Using a Radiofrequency Percutaneous Transl Angioplasty Cathe	Impa		
RF	RF	RF	RF	RF
HF (NYHA III or IV) LVEF<35%	office SBP≥ 160 mmHg on at least 3 anti-HTN on maximal therapy	RH (BP>140/90 mmHg on at least 3 anti-HTN including a diuretic or treatment≥4 anti-HTN	daytime BP>140 mmHg on at least 3 anti-HTN including a diuretic	office SBP≥ 160 mmHg and/or DBP≥90 mmHg on full dose of appropriate anti-HTN drugs at least three months history of definite kid damage
NCT01538992	NCT01541865	NCT01628198	NCT01628172	NCT01390831
EH (off	140 mmHg			
NCT01418560	NCT01417221	NCT01402726	NCT01417247	

Symplicity Catheter (Medtronic ®)	Global SYMPLICITY Registry	RF	HT; DM; HF; CKD; OSA	NCT01534299
Symplicity Catheter (Medtronic ®)	Study of Catheter Based RDN Therapy in Hypertension (DEPART)	RF	RH on at least 3 anti-HTN drugs including a diuretic, with an attempt to treat with spironolactone	NCT01522430
Symplicity Catheter (Medtronic ®)	The Effects of RDN on Insulin Sensitivity	RF	Treatment resistant EH SBP daytime ≥145mmHg on at least 3 anti-HTN drugs including a diuretic	NCT01631370
Symplicity Catheter (Medtronic ®)	Denervation of the REnal Artery in Metabolic Syndrome (DREAMS)	RF	FPG ≥5.6 mmol/L; daytime SBP>130 mmHg without the use of anti-diabetic and anti-HTN drugs	NCT01465724
Symplicity Catheter (Medtronic ®)	Single-arm Study of Symplicity™ RDN System in Patients With Uncontrolled HyperTensioN in India (HTN-India)	RF	office SBP≥160mmHg on at least 3 anti-HTN drugs including a diuretic	NCT01632943
Symplicity Catheter (Medtronic ®)	Denervation of the REnal Artery in Metabolic Syndrome (DREAMS)	RF	FPG ≥5.6 mmol/L without the use of anti-diabetic drugs and ABPM with SBP>130 mmHg without the use of anti-HTN drugs	NCT01465724
Symplicity Catheter (Medtronic ®)	Renal Sympathectomy in Treatment Resistant Essential Hypertension, a Sham Controlled Randomized Trial (ReSET)	RF	daytime SBP>145 mmHg on at least 3 anti-HTN including a diuretic)	NCT01459900
MDT-2211 System (Medtronic Vascular)	RDN by MDT-2211 System in Patients With Uncontrolled	RF	office SBP ≥160mmHg on at least 3 anti-HTN drugs	NCT01644604
not p				01505010
			drugs including a diuretic	
not provided (drug intervention: NG-monomethyl-L-arginine (L-NMMA)	Effect of RDN on NO-mediated Sodium Excretion and Plasma Levels of Vasoactive Hormones (RENO)	---	EH (daytime BP>145/75 mmHg on at least 3 anti-HTN including a diuretic)	NCT01617551
not provided	DENERVATION of the renAl sympathetIc nerveS in hearT Failure With nOrmal Lv Ejection Fraction (DIASTOLE)	---	HF with evidence of diastolic dysfunction, LVEF≥ 50 %	NCT01583881
not provided	Renal Artery Denervation in Chronic Heart Failure (REACH-Pilot) STUDY COMPLETED	RF	Congestive HF(NYHA III/IV)	NCT01584700

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Salzburg, Austria; and Cologne and Homburg/Saar, Germany

- Treatment-resistant HTN population
- 46 RDN, 18 Control
- Evaulated BP and cardiac structure and function via echo at baseline, 1 mo & 6 mo
- RDN Group:
  - 180.7 18.3/95.8 10.1 mmHg
  - Mean age 63 years
  - BMI 28.6 kg/m²
  - 46% with Diabetes
  - 4.7 mean anti-htn meds
  - Incidence LVH 63% by echo

Table 1 Patient Characteristics at Baseline

	Renal Denervation (n = 46)	Control (n = 18)	p Value
Age, yrs	63.1 ± 10.2	63.0 ± 15.3	0.977
Male	31 (67%)	11 (61%)	0.771
BMI, kg/m^2	28.6 ± 3.4	28.1 ± 3.8	0.595
Coronary artery disease	20 (44%)	7 (39%)	0.785
Atrial fibrillation	7 (15%)	2 (11%)	1.000
Stroke	8 (17%)	4 (22%)	0.726
Type 2 diabetes	21 (46%)	7 (39%)	0.781
Hypercholesterolaemia	32 (70%)	10 (56%)	0.382
Smoking	14 (30%)	3 (17%)	0.086
Number of antihypertensive drugs	4.7 ± 0.5	4.8 ± 2.5	0.979
Patients receiving (drug class)			
ACE inhibitors/ARBs	45 (98%)	18 (100%)	1.000
Direct renin inhibitors	17 (37%)	5 (28%)	0.770
Beta-blockers	45 (98%)	16 (89%)	0.189
Calcium-channel blockers	40 (87%)	13 (72%)	0.267
Diuretics	46 (100%)	18 (100%)	1.000
Oral sympatholytics	23 (50%)	7 (39%)	0.579

Values are mean ± SD or n (%). Statistical differences between groups, where applicable, are indicated in the far-right column.

Brandt et al. *J Am Coll Cardiol.* 2012;59:901–9