

XXXVIII Congreso Argentino de Cardiología

IV Simposio TCT@CACI@SAC,

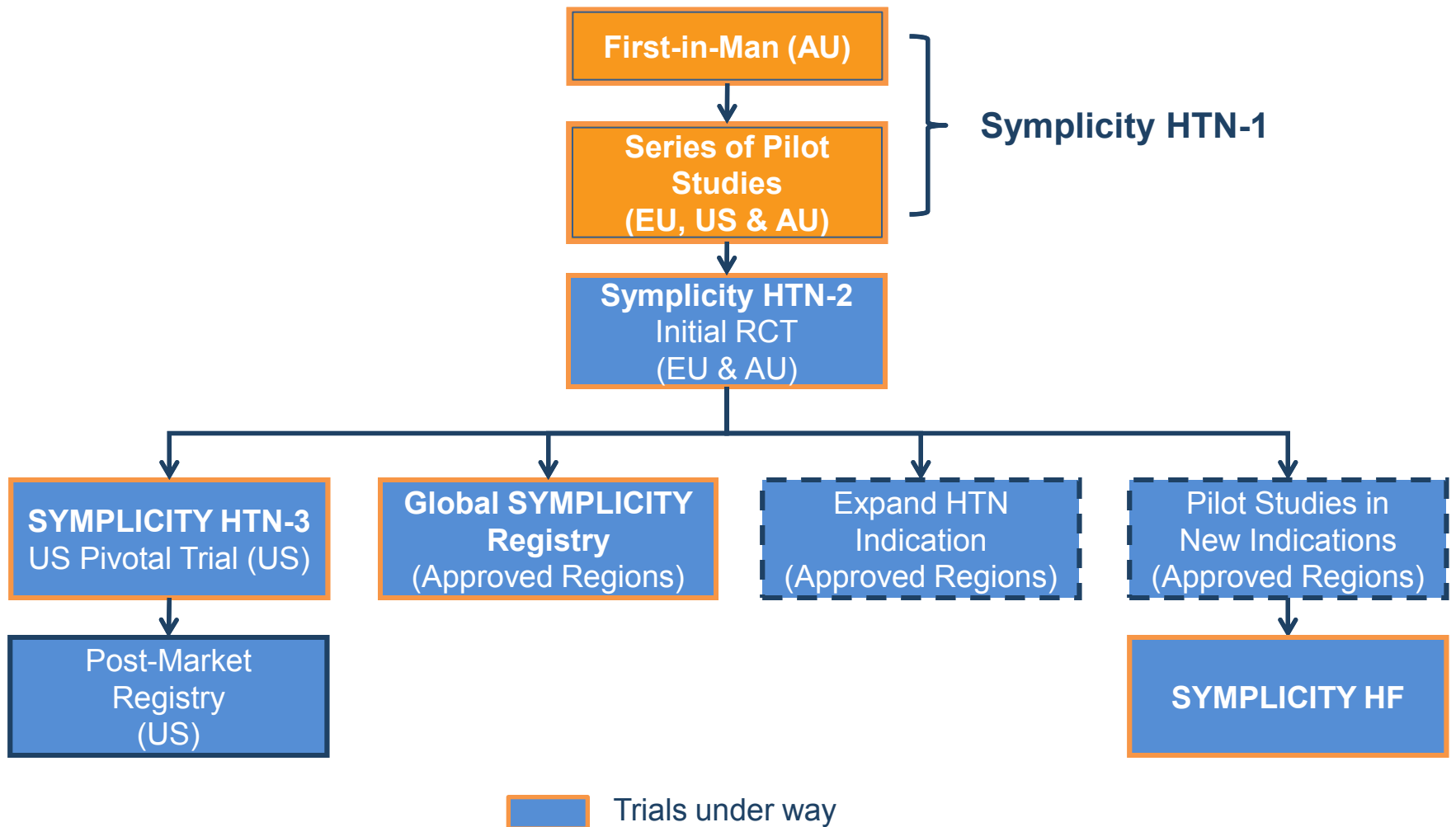
Buenos Aires - Octubre 5, 2012

Rol de la Denervacion renal por radiofrecuencia en el tratamiento de la hipertension arterial resistente



Dr. Juan Gaspar
Director Medical Training & Education
Medtronic Cardiovascular
Latin America

SYMPPLICITY Clinical Trial Program follows over 5000 patients across multiple indications



Symplicity HTN-1

THE LANCET

Volume 373, Number 9675, Pages 1275-1281, April 11-17, 2009

www.thelancet.com

Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study

Henry Krum, Markus Schminch, Rob Whitbourn, Paul A Sobczka, Jerzy Szolowski, Krzysztof Bartus, Boguslawa Kupelak, Anthony Walker, Harald Sievert, Suku Thambur, William T Abraham, Murray Esler

Lancet. 2009;373:1275-1281

Hypertension

Celebrating 30 Years, 1979 to 2009

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Catheter-Based Renal Sympathetic Denervation for Resistant Hypertension

Durability of Blood Pressure Reduction Out to 24 Months

Symplicity HTN-1 Investigators*

Hypertension. 2011;57:911-917.

Initial Cohort – Reported in the *Lancet*, 2009:

- First-in-man, non-randomized
- Cohort of 45 patients with resistant HTN (SBP ≥ 160 mmHg on ≥ 3 anti-HTN drugs, including a diuretic; eGFR ≥ 45 mL/min)
- 12-month data

Expanded Cohort* – This Report (Symplicity HTN-1):

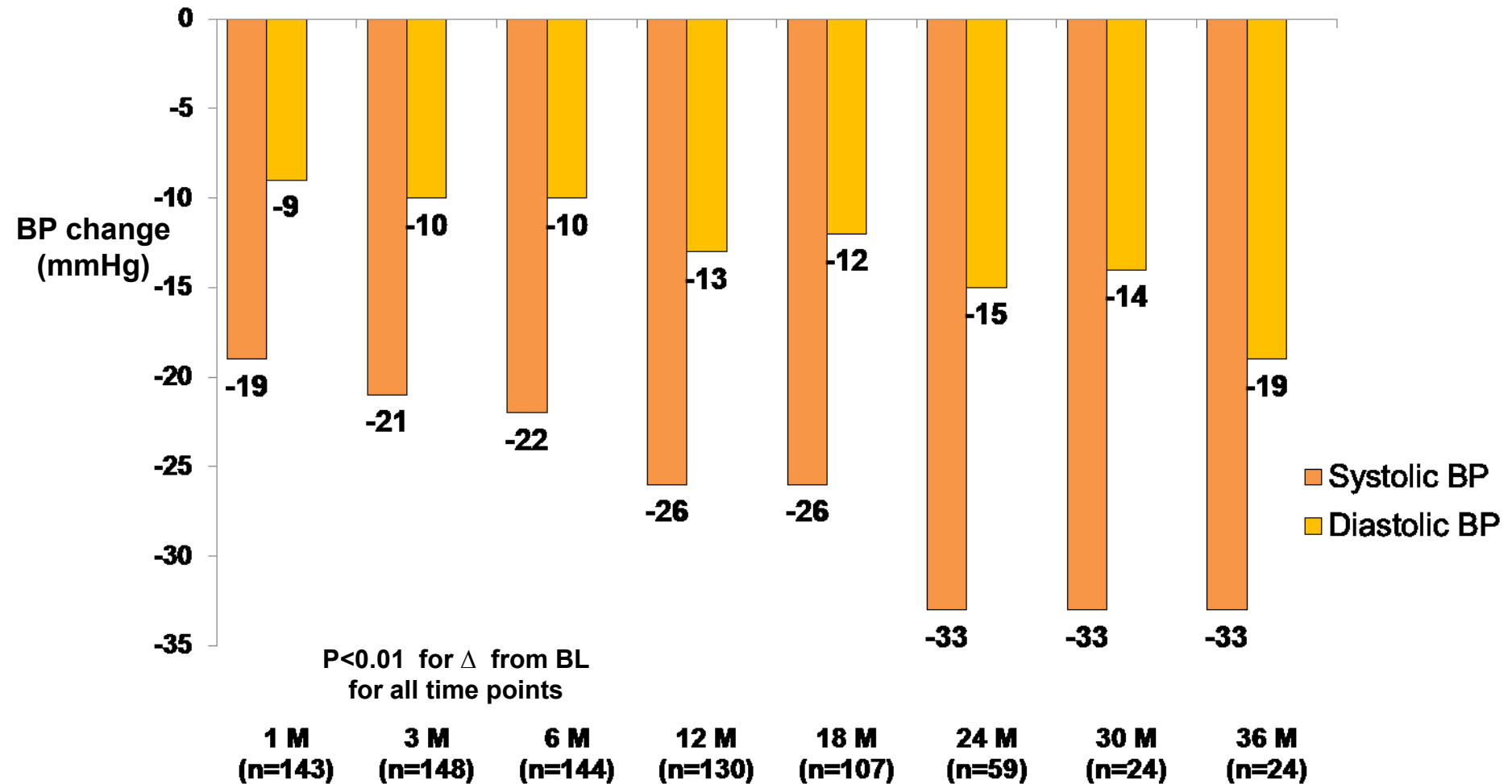
- Expanded cohort of patients (n=153)
- 36-month follow-up

*Expanded results presented at the *American College of Cardiology Annual Meeting 2012* (Krum, H.)

Baseline Patient Characteristics (n=153)

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)	5.1 ± 1.4
	Diuretic (%)	95%
	Aldosterone blocker(%)	22%
	ACE/ARB (%)	91%
	Direct Renin Inhibitor	14%
	Beta-blocker (%)	82%
	Calcium channel blocker (%)	75%
	Centrally acting sympatholytic (%)	33%
	Vasodilator (%)	19%
Alpha-1 blocker	19%	

Symplicity HTN-1: BP Reductions through 3 years



Symplicity HTN-2

THE LANCET

Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial

Symplicity HTN-2 Investigators*

Lancet. 2010;376:1903-1909.

- **Purpose:** To demonstrate the effectiveness of catheter-based renal denervation for reducing blood pressure in patients with uncontrolled hypertension in a prospective, randomized, controlled, clinical trial
- **Patients:** 106 patients randomized 1:1 to treatment with renal denervation vs. control
- **Clinical Sites:** 24 centers in Europe, Australia, & New Zealand (67% were designated hypertension centers of excellence)

Symplicity HTN-2 Trial

- Treatment-resistant HTN population
- BL OBP 178/97 mmHg
- 49 RDN, 51 Control
- Age 58 years
- BMI 31 kg/m²
- 40% with Diabetes
- eGFR 77*
- Avg # meds 5.2
- RDN and Control groups generally well-matched

Inclusion Criteria:

- Office SBP \geq 160 mmHg (\geq 150 mmHg with type II diabetes mellitus)
- Stable drug regimen of 3+ more anti-HTN medications
- Age 18-85 years

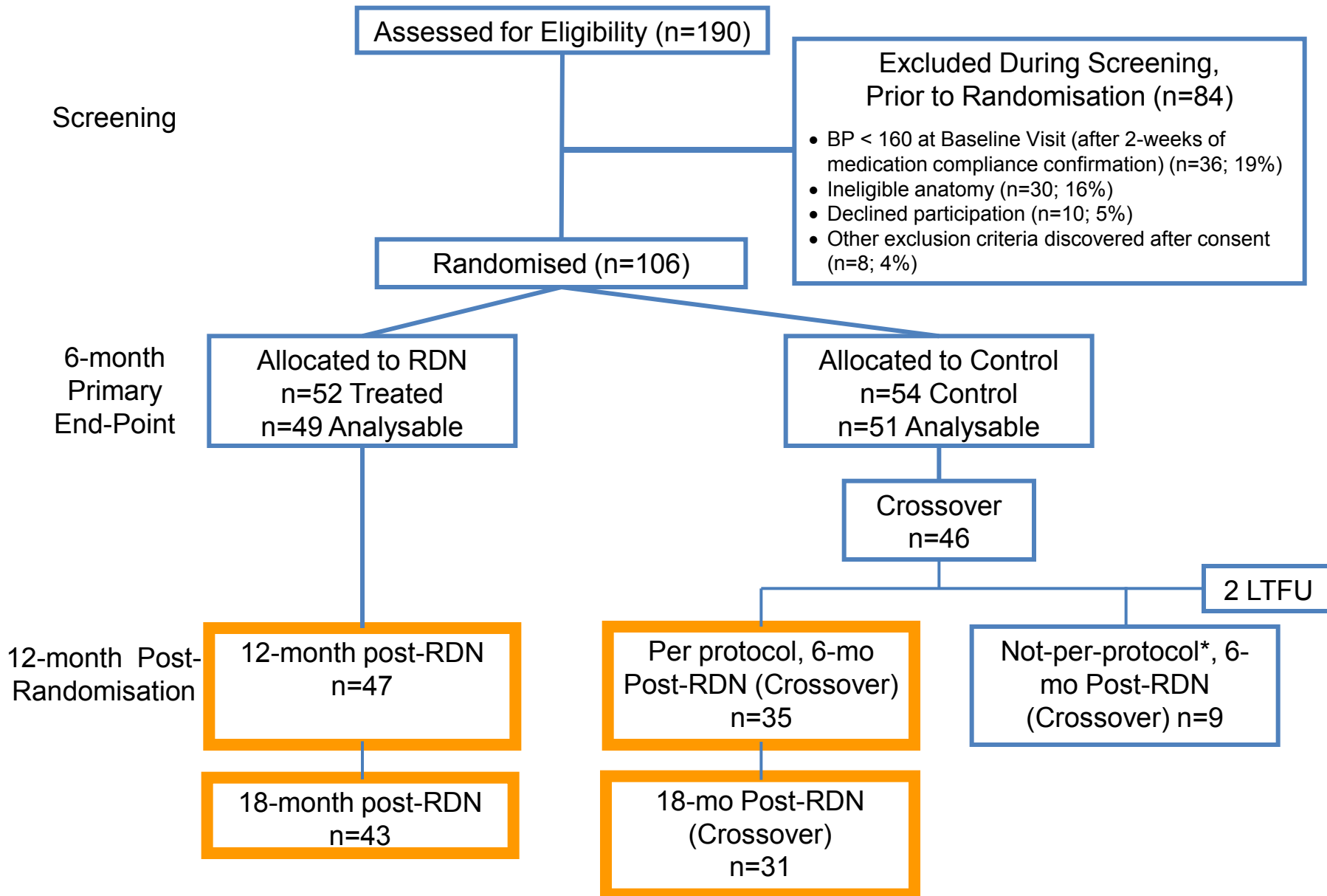
Exclusion Criteria:

- Hemodynamically or anatomically significant renal artery abnormalities or prior renal artery intervention
- eGFR $<$ 45 mL/min/1.73m² (MDRD formula)
- Type 1 diabetes mellitus
- Contraindication to MRI
- Stenotic valvular heart disease for which reduction of BP would be hazardous
- MI, unstable angina, or CVA in the prior 6 months

*MDRD, ml/min/1.73m²

Symplicity HTN-2 Investigators. *Lancet*. 2010;376:1903-1909.

Symplificity HTN-2: Patient disposition



* Crossed-over with ineligible BP (<160 mmHg)

RDN and Control Populations Well-matched, Severe Treatment Resistant Hypertensives

	RDN (n = 52)	Control (n = 54)	p-Value
Baseline systolic BP (mmHg)	178 ± 18	178 ± 16	0.97
Baseline diastolic BP (mmHg)	97 ± 16	98 ± 17	0.80
Number anti-HTN medications	5.2 ± 1.5	5.3 ± 1.8	0.75
Age	58 ± 12	58 ± 12	0.97
Gender (female) (%)	35%	50%	0.12
Race (Caucasian) (%)	98%	96%	>0.99
BMI (kg/m ²)	31 ± 5	31 ± 5	0.77
Type 2 diabetes	40%	28%	0.22
Coronary artery disease	19%	7%	0.09
Hypercholesterolemia	52%	52%	>0.99
eGFR (MDRD, ml/min/1.73m ²)	77 ± 19	86 ± 20	0.013
Serum creatinine (mg/dL)	1.0 ± 0.3	0.9 ± 0.2	0.003
Urine alb/creat ratio (mg/g)*	128 ± 363	109 ± 254	0.64
Cystatin C (mg/L)†	0.9 ± 0.2	0.8 ± 0.2	0.16
Heart rate (bpm)	75 ± 15	71 ± 15	0.23

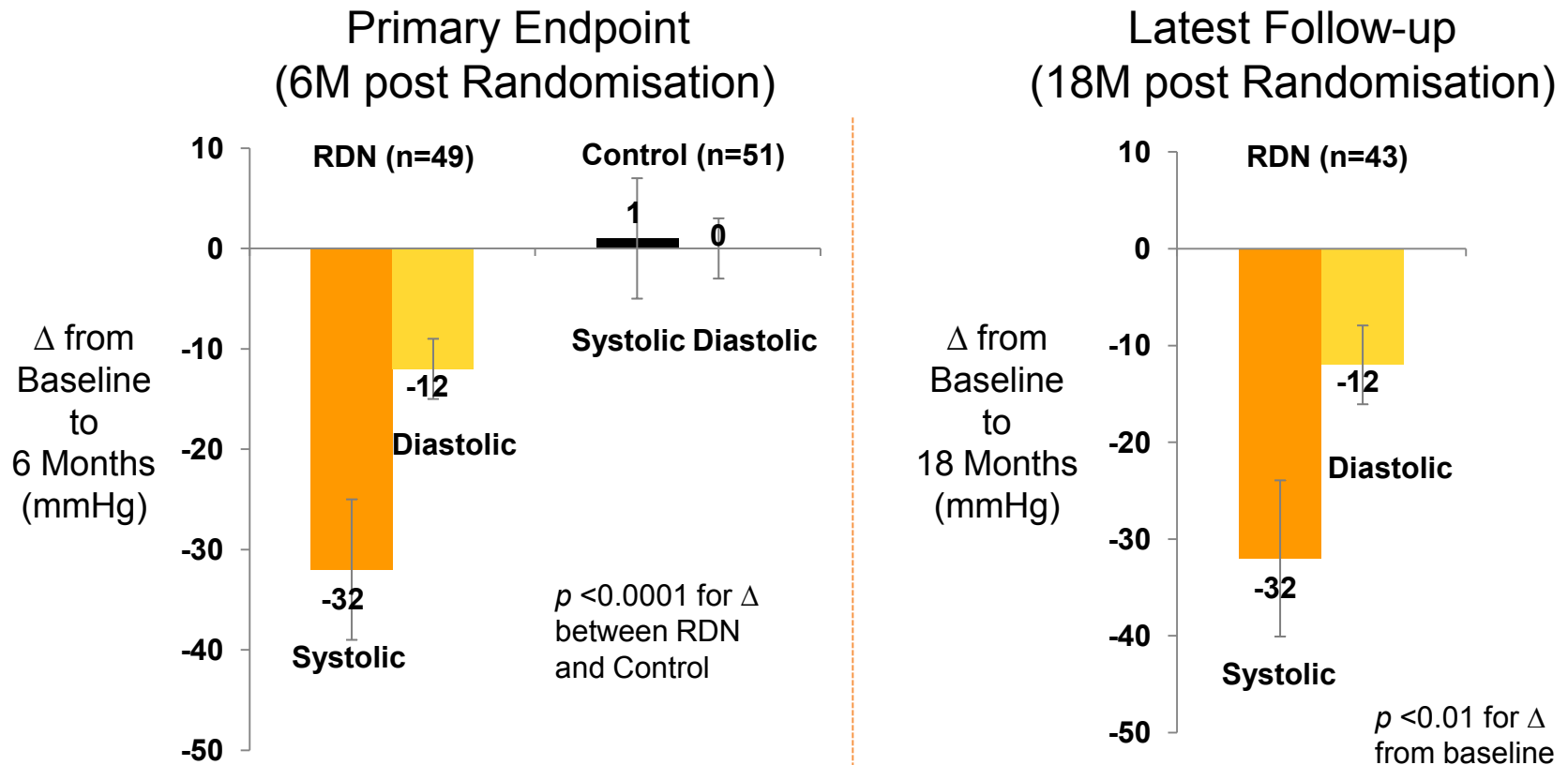
* n = 42 for RDN and n = 43 for Control. Wilcoxon rank-sum test for two independent samples used for between-group comparisons of UACR.

† n = 39 for RDN and n = 42 for Control.

Procedural Safety in an Expanded Cohort of Treated Patients

- One renal artery dissection from injection of contrast into renal artery wall during dye angiography. The lesion was stented without further consequences
- One hospitalization prolonged in a crossover patient due to hypotension following the RDN procedure. IV fluids administered, anti-hypertensive medications decreased and patient discharge without further incident
- No radiofrequency-related renal artery stenosis or aneurysm occurred in either Randomised group
- Minor adverse events (full cohort)
 - 1 femoral artery pseudoaneurysm treated with manual compression
 - 1 postprocedural drop in BP resulting in a reduction in medication
 - 1 urinary tract infection
 - 1 prolonged hospitalisation for evaluation of paraesthesias
 - 1 back pain treated with pain medications and resolved after 1 month

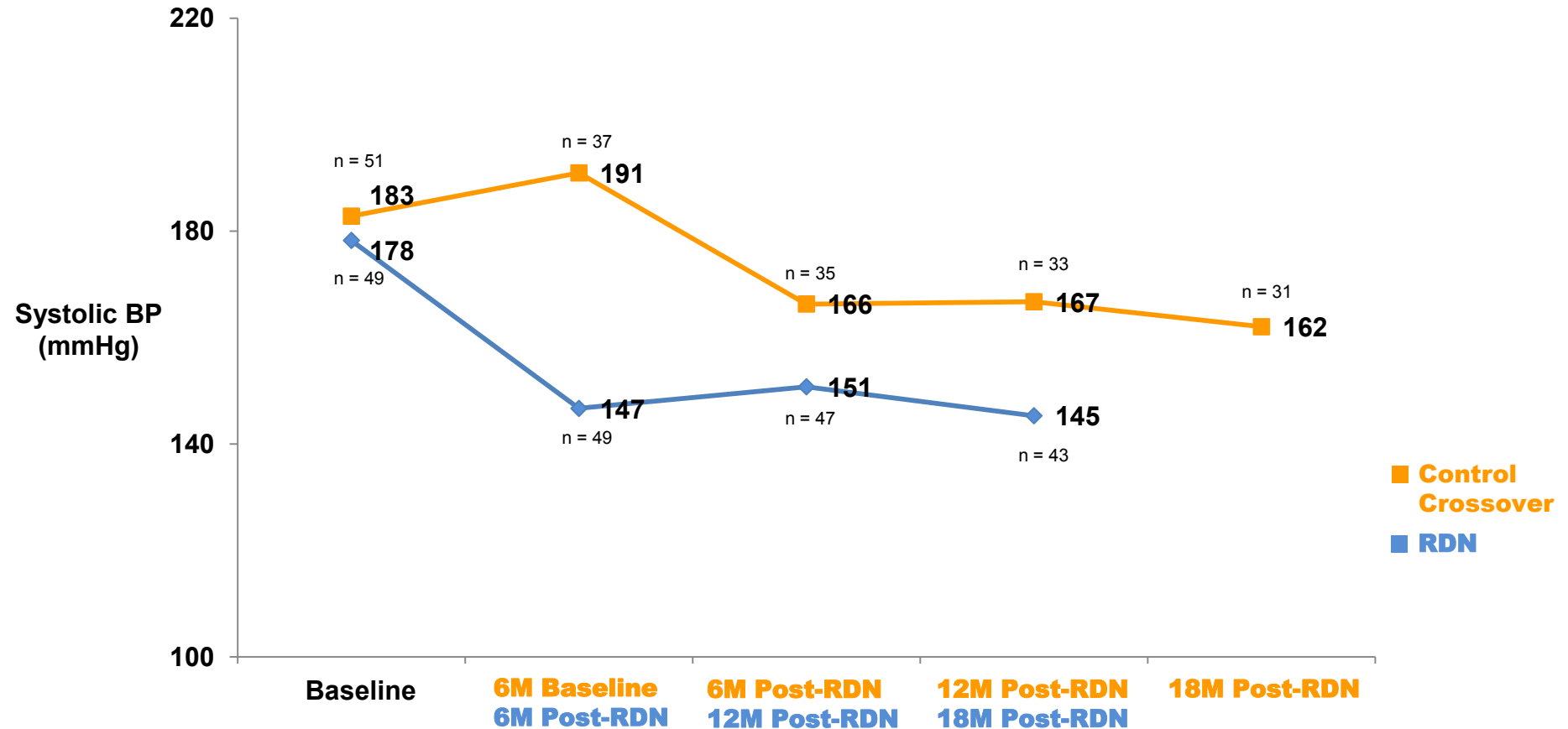
Symplicity HTN-2: RDN Superior to Medical Management, Reductions Sustained to 18M



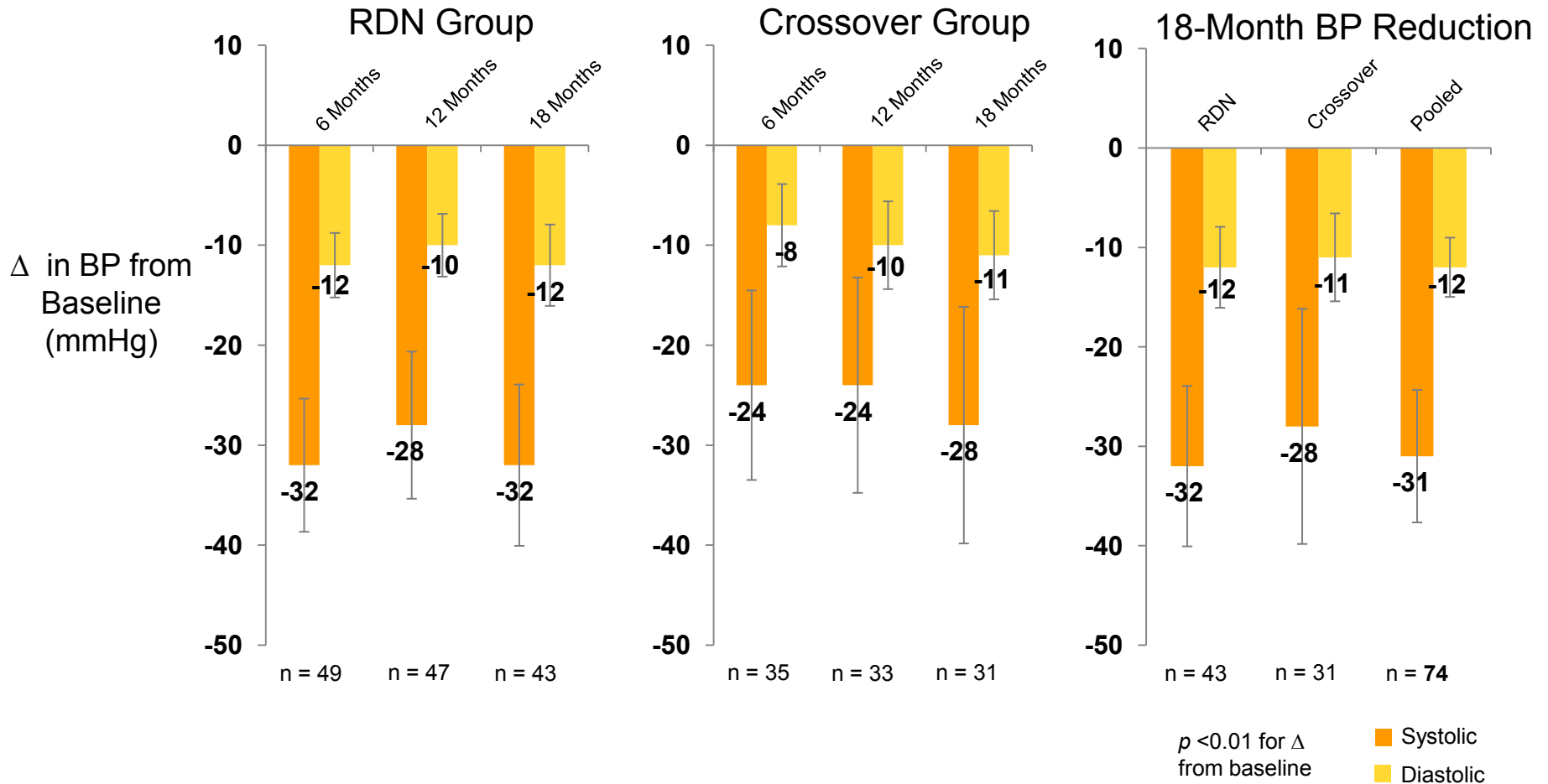
Primary Endpoint:

- >80% of RDN patients had ≥ 10 mmHg reduction in SBP
- 5 patients had ≤ 5 mmHg reduction in SBP

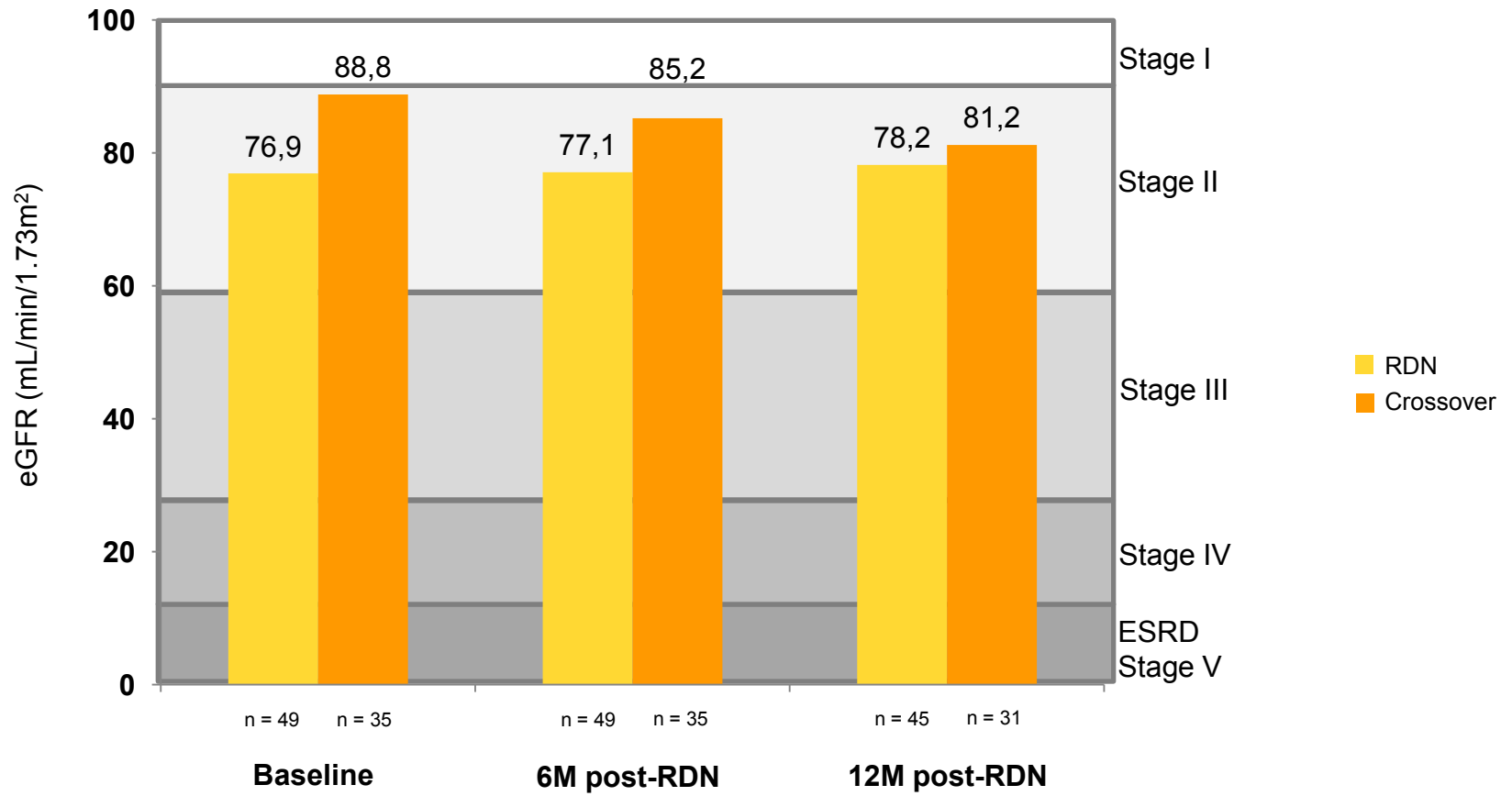
Symplivity HTN-2: Control Group Also Benefited From RDN After Crossover



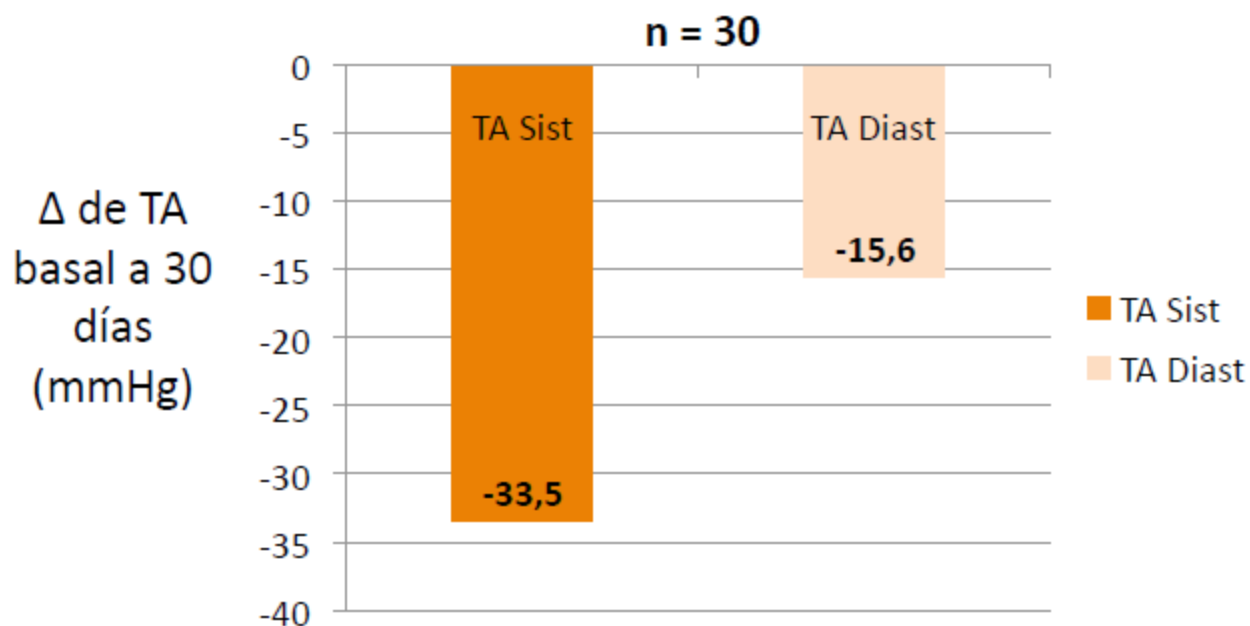
Symplicity HTN-2: BP Reduction With Symplicity™ System Sustained to 18 Months for RDN, Crossover, and Pooled Groups



SymPLICITY HTN-2: Renal Function Is Maintained Following RDN Therapy



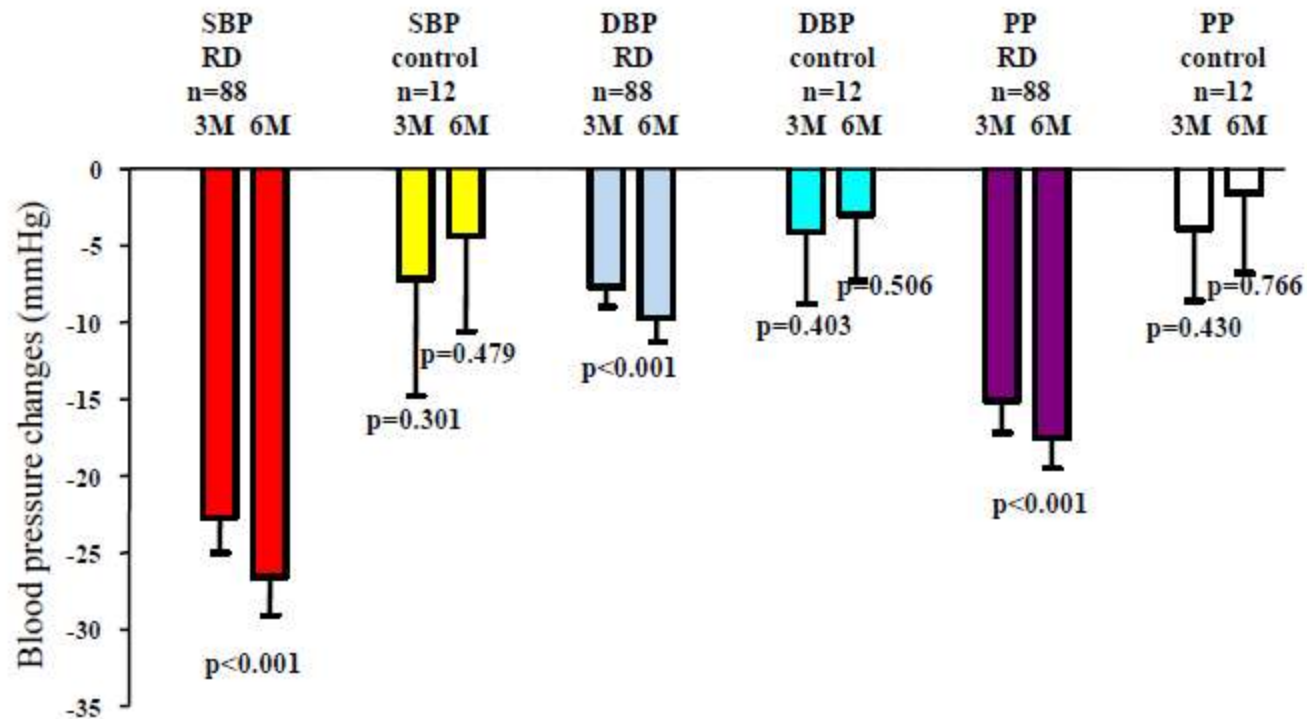
Resultado: objetivo primario



El 90% de los pacientes tuvieron reducción de ≥ 10 mmHg



Blood pressure reduction after RDN



Guidelines/Consensus Statements on Renal Denervation are Available

United Kingdom¹

Joint Societies' Statement on Renal Denervation for Resistant Hypertension

The Joint UK Societies' Consensus Statement on Renal Denervation for Resistant Hypertension.

Steering Group: Mark Caulfield¹ (Chair), Mark de Zeeuw², Trevor Cleveland³, David Collier⁴, John Deanfield⁵, Huos Gray⁶, Charles Knight⁷, Melvin Lobo⁸, Matthew Matson⁹, Jon Moss¹⁰, Neil Poulter¹¹, Iain Simpson¹², Charles Tomson¹³, Bryan Williams¹⁴.

On behalf of the British Hypertension Society¹, the British Cardiovascular Intervention Society², the British Society for Interventional Radiology³, National Institute for Clinical Outcomes Research⁴, the British Cardiovascular Society⁵, and the Renal Association⁶.

This statement was developed with the guidance and advice from patients who had undergone this procedure at Barts and The London NHR Cardiovascular Biomedical Research Unit and are members of the Patients and Public Engagement Group. The Joint UK Societies wish to express their thanks to Mr John Bold and Mr Anthony Henry.

This statement is intended to be read alongside NICE IP-422. <http://www.nice.org.uk/ip422>

Issue 1: Give an web 28th January 2012
Final version.

Any correspondence to:
Professor Mark Caulfield MRCGP
Director of the William Harvey Research Institute
Director of Barts and The London NHR Cardiovascular Biomedical Research Unit
Barts and The London School of Medicine and Dentistry, Queen Mary University of London,
Chambers Square, London EC3M 6BQ.
Tel: +44 (0)20 7547 2424, Fax: +44(0)20 7547 2422 Email: m.caulfield@qmul.ac.uk
<http://www.william-harvey.ac.uk/index.html>

Germany²

Treatment Strategies for Resistant Arterial Hypertension

Florian Mahfoud^{1,2}, Frank Hohmann³, Christian Gellera⁴, Herbert Schwikowski⁵, Michael Kretsch⁶, Josef Ritz⁷

OBJECTIVE

Summary

Resistant hypertension is one of the most frequent chronic diseases in the industrialized nations of the West and represents a major risk factor for cardiovascular morbidity and mortality.

Definition

Resistant hypertension is defined as a systolic blood pressure >160 mmHg and/or a diastolic blood pressure >100 mmHg in patients with a confirmed diagnosis of hypertension who are on a combination of at least three antihypertensive drugs at optimal doses and with adherence to therapy.

Causes

The treatment of resistant hypertension is challenging because of the high prevalence of secondary hypertension. The most common causes of secondary hypertension are obstructive sleep apnea, primary aldosteronism, renal artery stenosis, and pheochromocytoma. In addition, resistant hypertension can be caused by a white coat effect, measurement error, or non-adherence to therapy.

Diagnosis

The treatment of resistant hypertension is challenging because of the high prevalence of secondary hypertension. The most common causes of secondary hypertension are obstructive sleep apnea, primary aldosteronism, renal artery stenosis, and pheochromocytoma. In addition, resistant hypertension can be caused by a white coat effect, measurement error, or non-adherence to therapy.

Conclusion

The treatment of resistant hypertension is challenging because of the high prevalence of secondary hypertension. The most common causes of secondary hypertension are obstructive sleep apnea, primary aldosteronism, renal artery stenosis, and pheochromocytoma. In addition, resistant hypertension can be caused by a white coat effect, measurement error, or non-adherence to therapy.

Poland³

Stanowisko grupy ekspertów w sprawie zabiegów przeszłkowej denerwacji nerek w leczeniu nadciśnienia tętniczego w Polsce

Gathered-based renal sympathetic denervation for the treatment of resistant arterial hypertension in Poland – expert consensus statement

Adam Witkowski¹, Antoni Jankowski², Jacek Jankowski³, Bogusław Naliniński⁴, Grzegorz Opalski⁵, Olgierd Kozłowski⁶, Jacek Sadowski⁷, Dariusz Dudek⁸, Leszek Brykanski⁹, Robert J. Gł¹⁰, Maciej Jankowski¹¹, Zdzisław Gąsior¹², Jacek Kąkolka¹³, Aleksander Proch¹⁴, Maciej Nowicki¹⁵

Wskazania

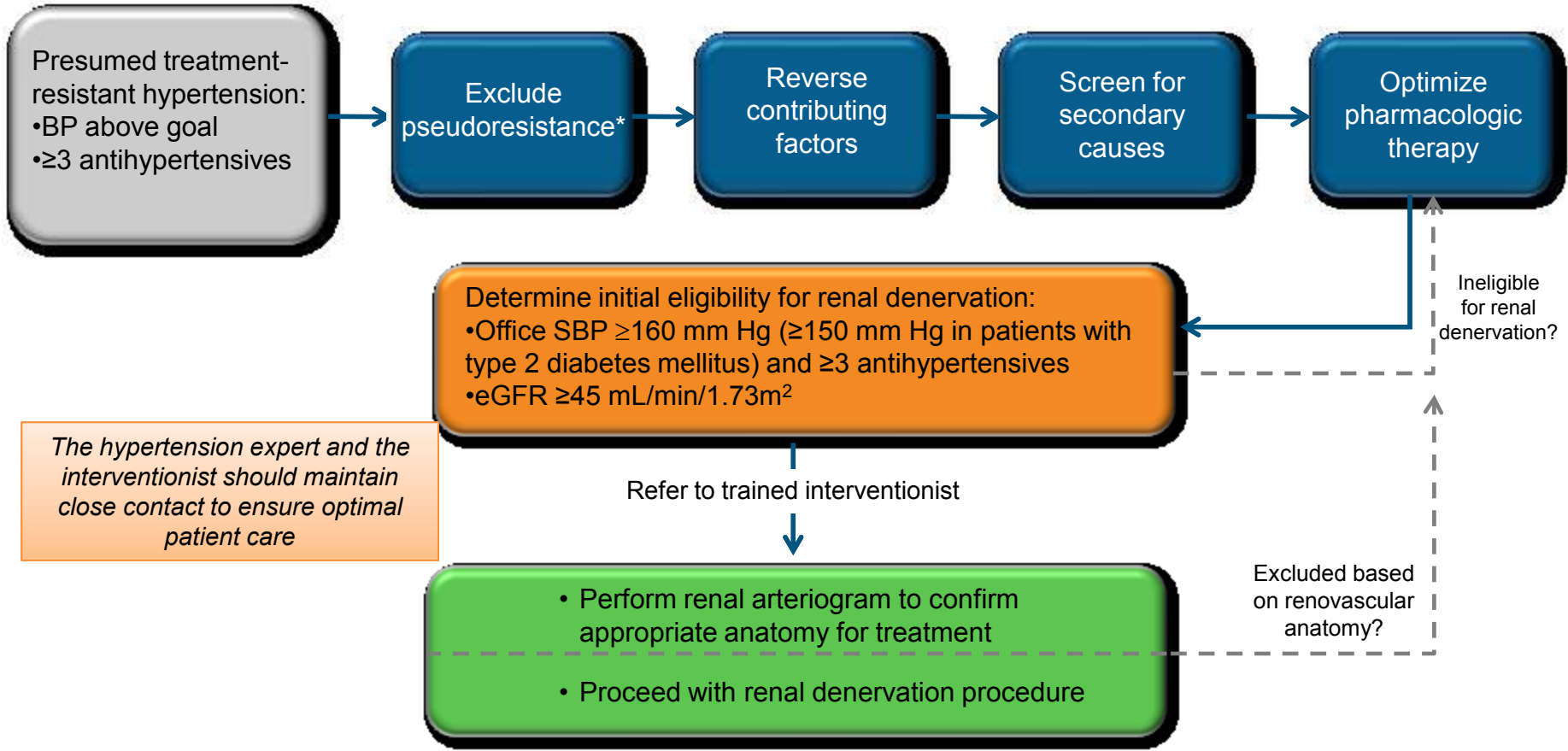
Stanowisko grupy ekspertów w sprawie zabiegów przeszłkowej denerwacji nerek w leczeniu nadciśnienia tętniczego w Polsce. Dokument ten ma charakter poglądowy i nie należy go traktować jako wytycznych. Stanowisko grupy ekspertów w sprawie zabiegów przeszłkowej denerwacji nerek w leczeniu nadciśnienia tętniczego w Polsce. Dokument ten ma charakter poglądowy i nie należy go traktować jako wytycznych.

Wskazania

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- CKD=chronic kidney disease; OSA=obstructive sleep apnea.
1. Caulfield M et al. Available at <http://www.bhsoc.org/docs/Joint-UK-Societies-Summary-on-Renal-Denervation.pdf>;
 2. Mahfoud F et al. *Dtsch Arztebl Int.* 2011;136:2418;
 3. Witkowski A et al. *Kardiologia Polska.* 2011;69:1208-1211.

Appropriate Renal Denervation Patient Selection Requires a Systematic Approach



*Work up should include 24-hour ambulatory blood pressure monitoring to exclude white-coat effect.
 Calhoun DA, et al. *Circulation*. 2008;117:e510-e526.
 Mahfoud F, et al. *Dtsch Med Wochenschr*. 2011;136:2418;doi:10.1055/s-0031-1272580.

Puntos claves para exito de un programa de RDN

- Integracion equipo multidisciplinario
- Selecccion de paciente
 - Descartar causas de HTA secundaria
 - Hipertenso Resistente
 - >160mmhg
 - FG>45 ml/mn
 - No ACV o IAM 6m
 - Etc
- Denervacion adecuada
- Seguimiento

