



Ipertensione farmaco resistente: terapia endovascolare

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AHA Scientific Statement

REPRINT

Resistant Hypertension: Diagnosis, Evaluation,
and Treatment

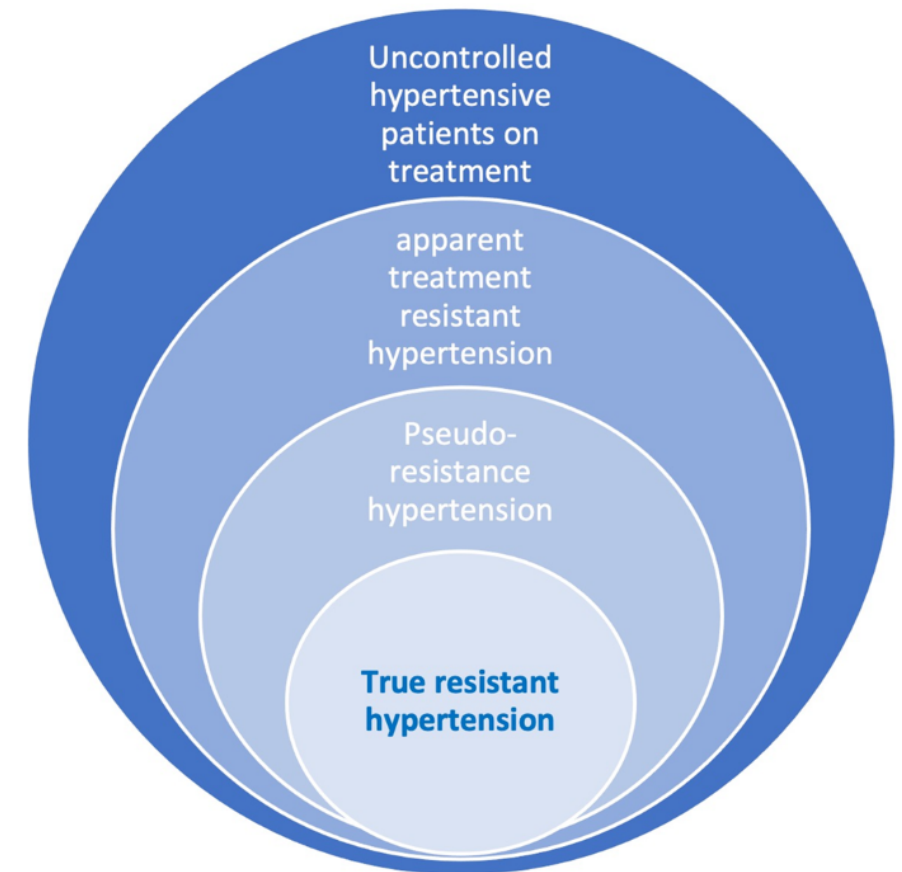
A Scientific Statement From the American Heart Association
Professional Education Committee of the Council for
High Blood Pressure Research

Resistant hypertension is defined as above-goal elevated blood in a patient despite the concurrent use of **3 antihypertensive drug classes**, including a diuretic.

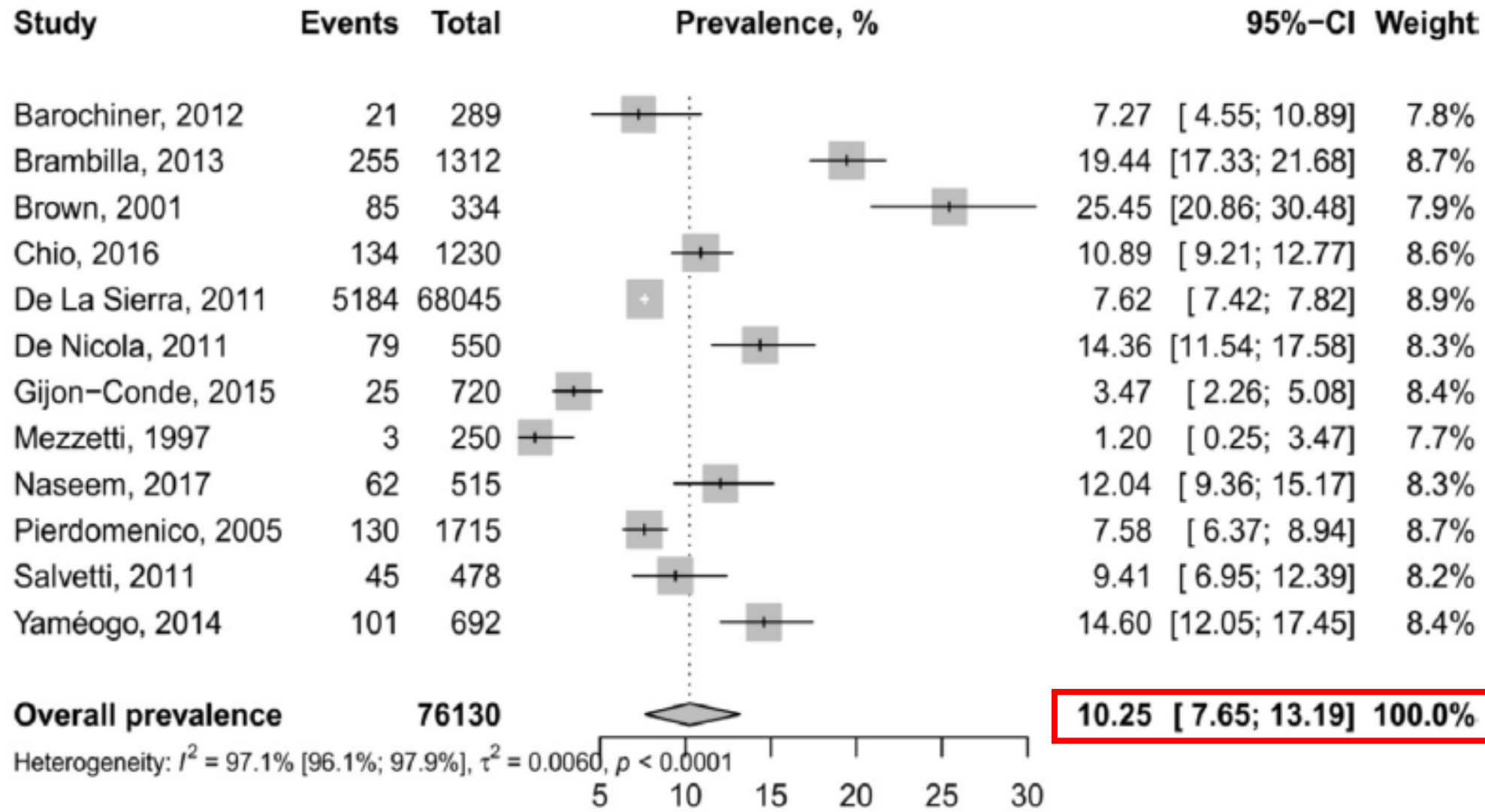
Calhoun et al. *Circulation* 2008

- **Pseudo-resistance:** falsely elevated caused by factors such as improper BP measurement technique, white coat HTN, nonadherence and undertreatment.
- **Apparent treatment resistant:** pseudoresistance cannot be excluded, that is, when medication dose, adherence, or out-of-office BP values are not documented.

Alsharari R et al. J Hum Hypertens. 2022

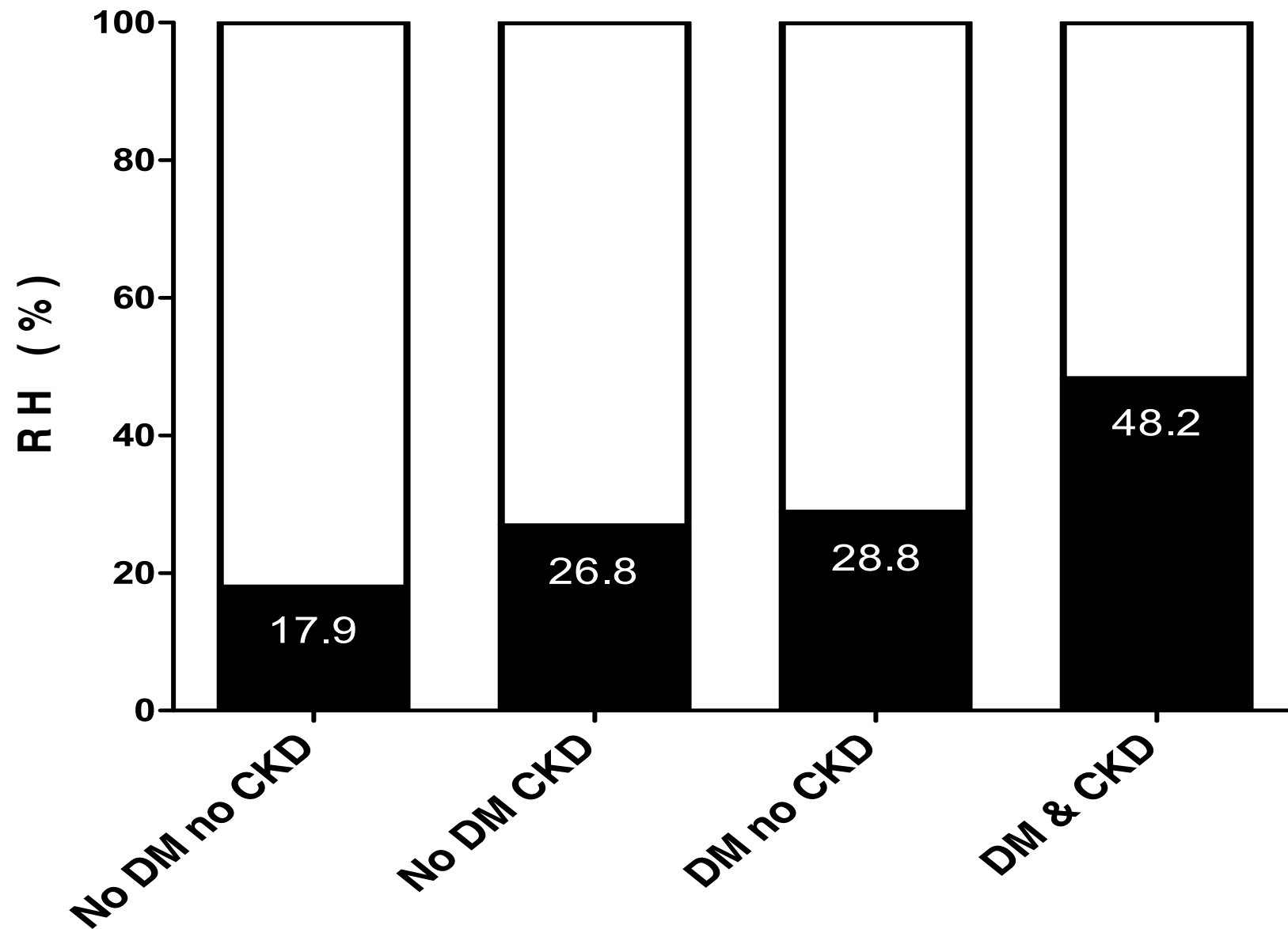


The prevalence of true resistant HTN

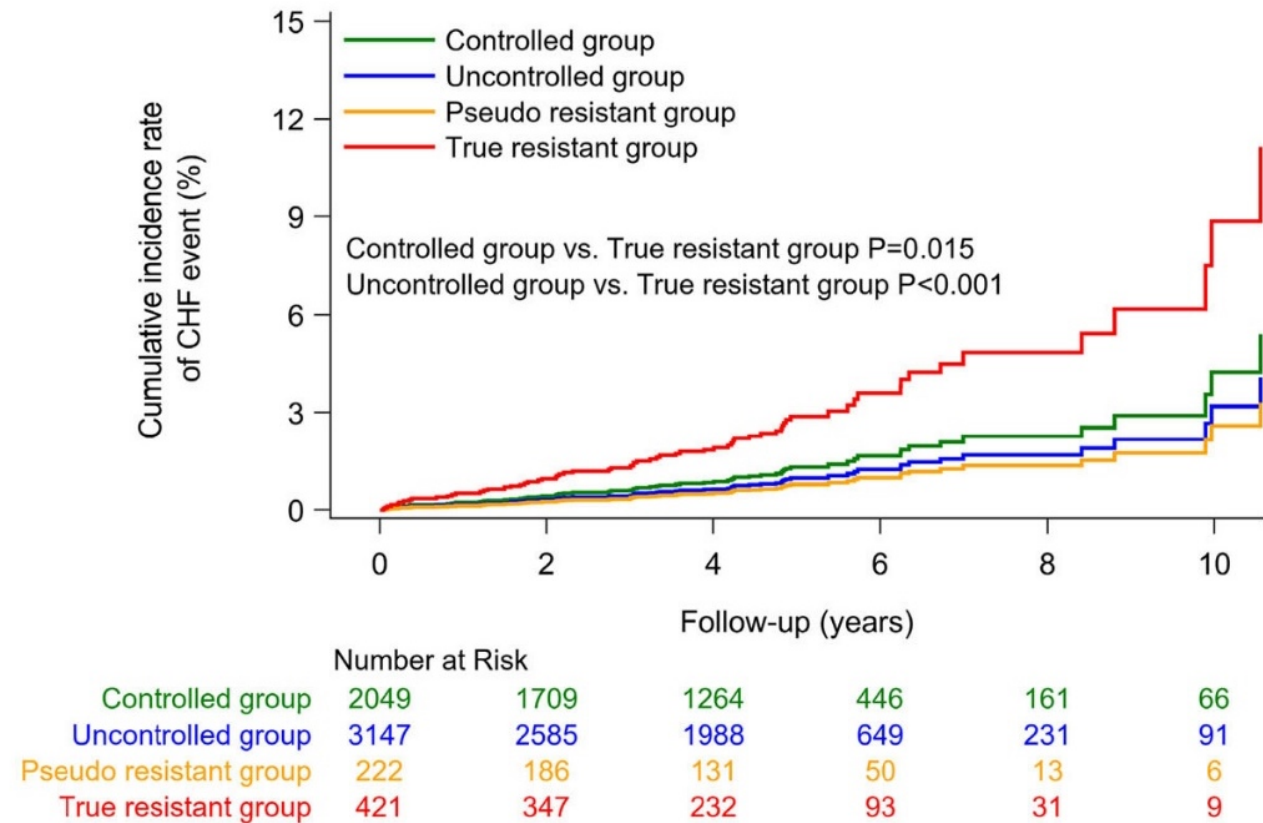
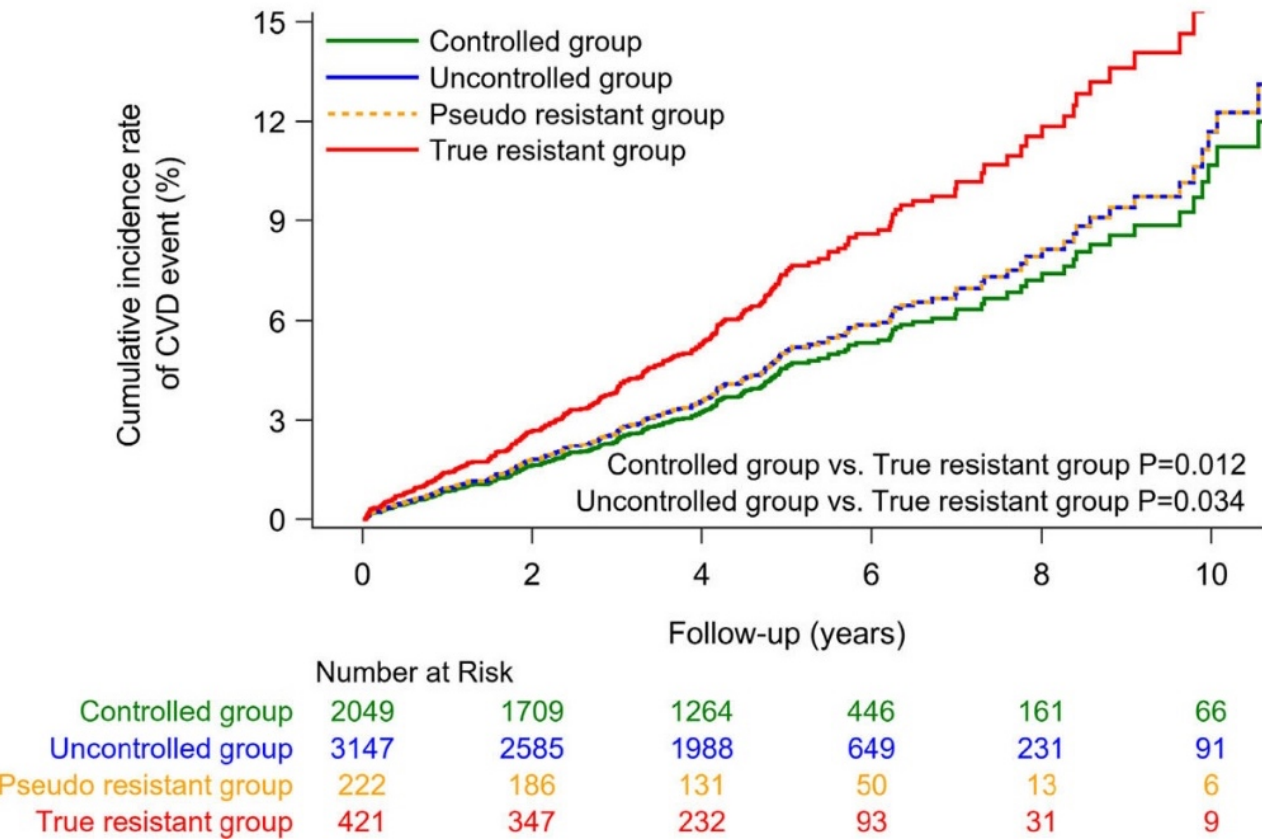


Noubiap JJ et al. Heart. 2019





Prognosis of resistant hypertension in hypertensive patients



Daugherty SL et al. Circulation. 2012



ESH Guidelines for the management of arterial hypertension



Mancia G. et al. *J Hypertens* 2023

BP-lowering therapy in true resistant hypertension^a

If eGFR ≥ 30 ml/min/1.73 m²

Patients not controlled with
ACEi or ARB + CCB + T/TL Diuretic^b

Add
I) **Spironolactone^d** (preferred)
or other **MRA^d**
or
II) **BB^e** or **Alpha1-blocker**
or
III) **Centrally acting agent**
or consider
Renal Denervation
If eGFR > 40 ml/min/1.73 m²

If eGFR < 30 ml/min/1.73 m²
(not on dialysis)

Patients not controlled with
ACEi or ARB + CCB + Loop Diuretic^b

Add^c
I) **Chlorthalidone** (preferred)
or other **T/TL Diuretic**
or
II) **BB^e** or **Alpha-1 Blocker**
or
III) **Centrally acting agent**

Documento di consenso della Società Italiana di Cardiologia Interventistica (GISE) e della Società Italiana dell'Ipertensione arteriosa (SIIA) sul ruolo della denervazione renale nella gestione dell'ipertensione arteriosa difficile da trattare

Eugenio Stabile¹, Maria Lorenza Muiasan², Flavio Luciano Ribichini³, Giuseppe Sangiorgi⁴, Stefano Taddei⁵, Francesco Versaci⁶, Bruno Villari⁷, Alessandra Bacca⁵, Daniela Benedetto⁴, Vincenzo Fioretti^{1,8}, Gaetano Liccardo⁹, Eugenio Laurenzano⁷, Massimiliano Scappaticci⁶, Francesco Saia¹⁰, Giuseppe Tarantini¹¹, Guido Grassi¹², Giovanni Esposito⁸

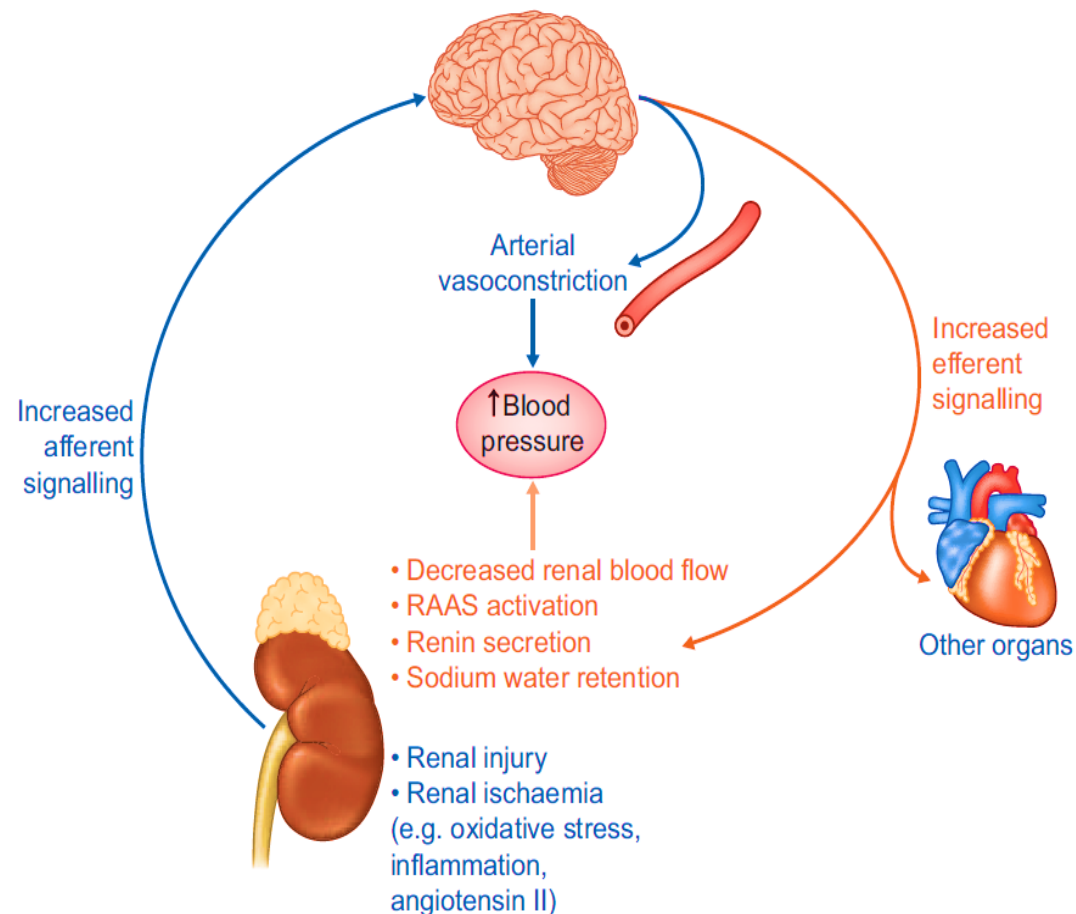
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Minerva Cardiology and Angiology 2024 Mar 27
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GUIDELINES

Italian Society of Interventional Cardiology (GISE) and Italian Society of Arterial Hypertension (SIIA) Position Paper on the role of renal denervation in the management of the difficult-to-treat hypertension

Eugenio STABILE¹, Maria L. MUIESAN², Flavio L. RIBICHINI³, Giuseppe SANGIORGI⁴, Stefano TADDEI⁵, Francesco VERSACI⁶, Bruno VILLARI⁷, Alessandra BACCA⁵, Daniela BENEDETTO⁴, Vincenzo FIORETTI^{1,8}, Eugenio LAURENZANO⁷, Massimiliano SCAPATICCI⁶, Francesco SAIA⁹, Giuseppe TARANTINI¹⁰, Guido GRASSI¹¹, Giovanni ESPOSITO^{8 *}

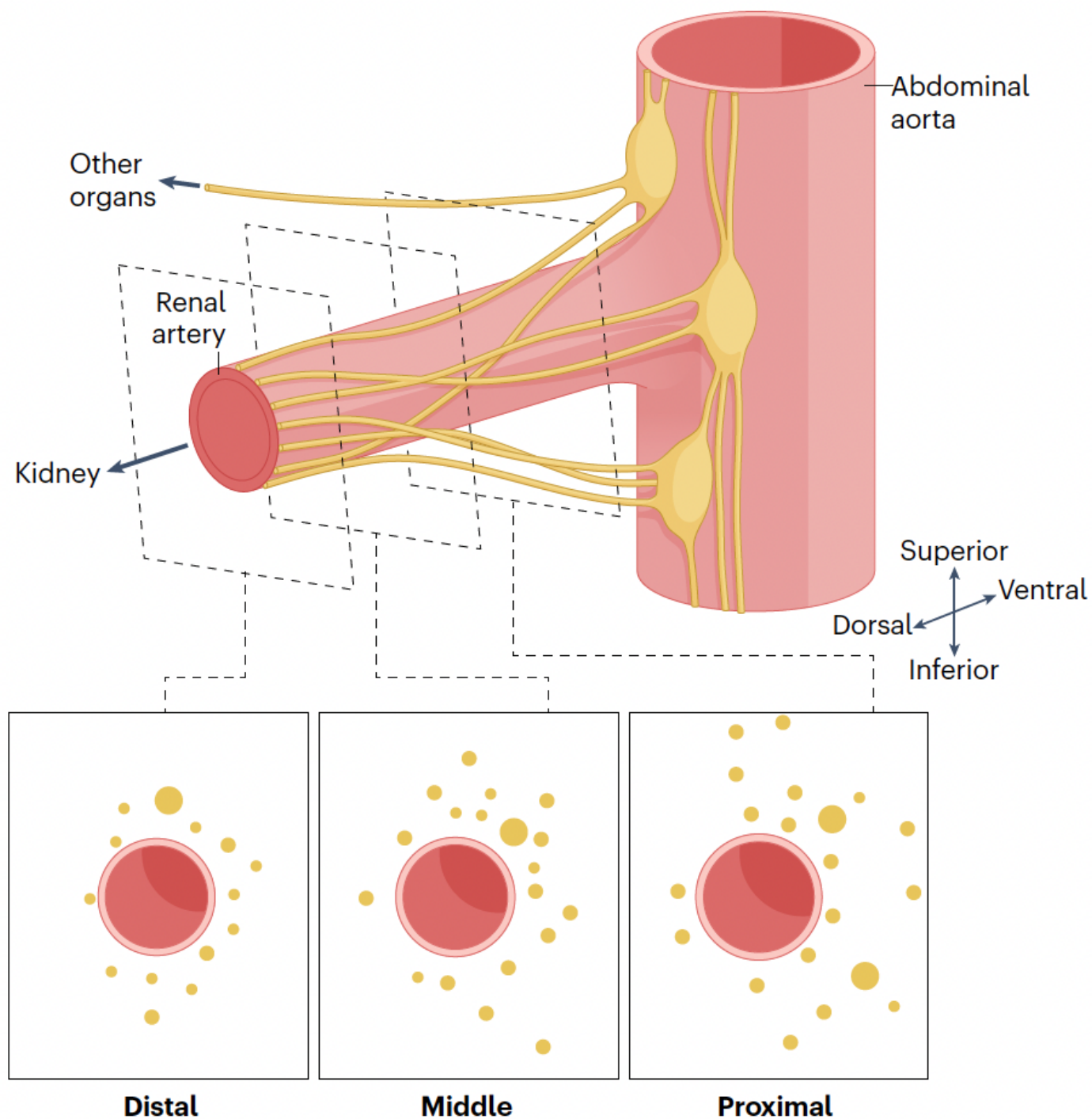


Stabile E et al. Documento di consenso GISE e SIIA sul ruolo della denervazione renale nella gestione dell'ipertensione arteriosa difficile da trattare. G Ital Cardiol (Rome). 2023



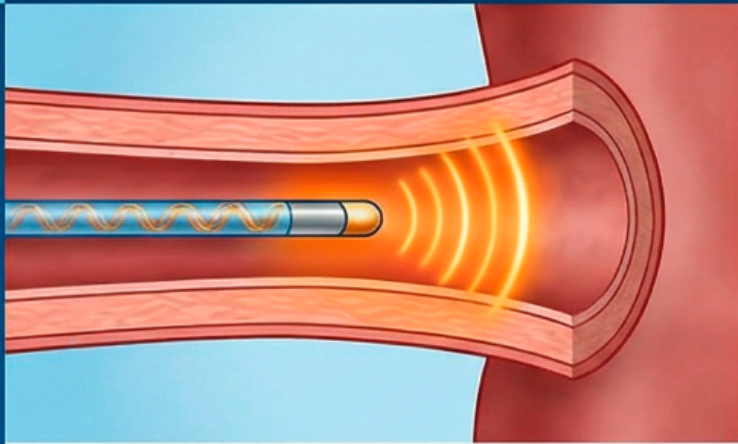
Distribution and density of renal sympathetic nerves allows a Catheter-Based Approach

Fisher NDL and Kirtane AJ. *Nature Rev Cardiol* 2025



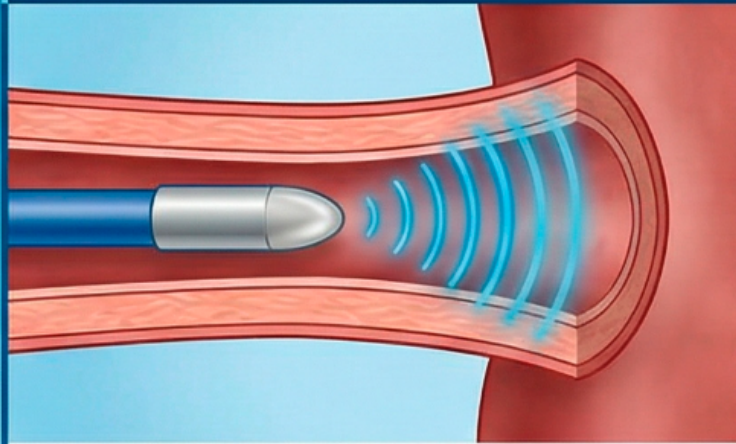
RENAL DENERVATION PLATFORMS

RADIOFREQUENCY (RF) ABLATION



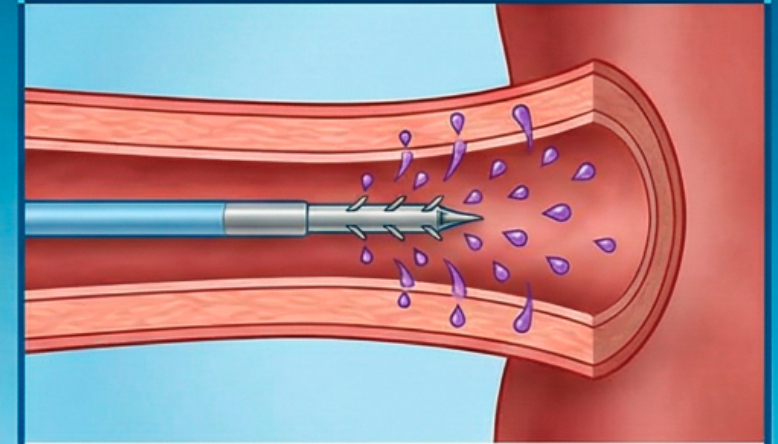
 Catheter-based electrodes deliver heat energy to disrupt nerves.
Example: Symplicity Spyral™.

ULTRASOUND ABLATION



 Focuses acoustic energy to thermally ablate nerves from within the artery.
Example: Paradise® System.

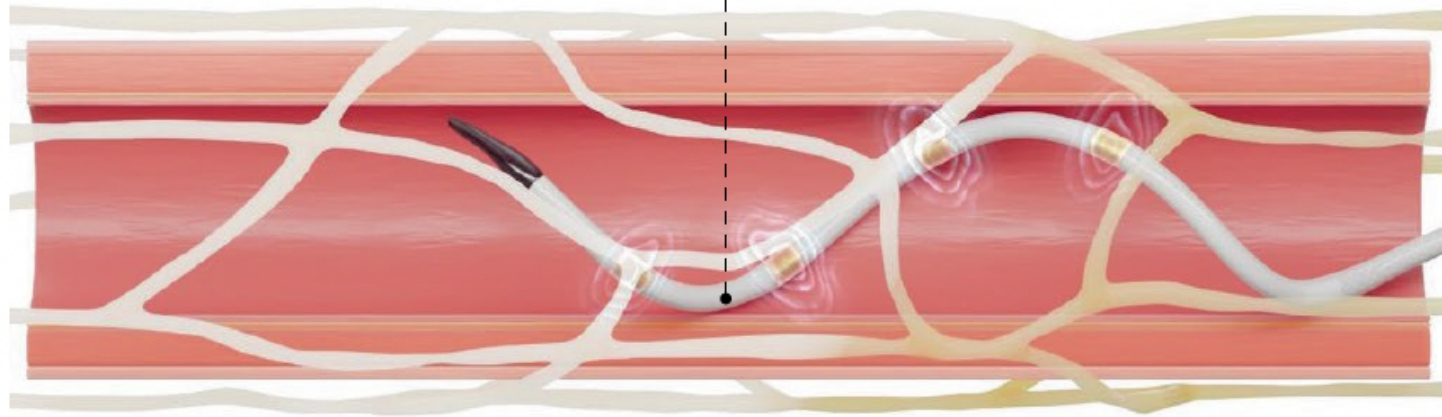
CHEMICAL ABLATION



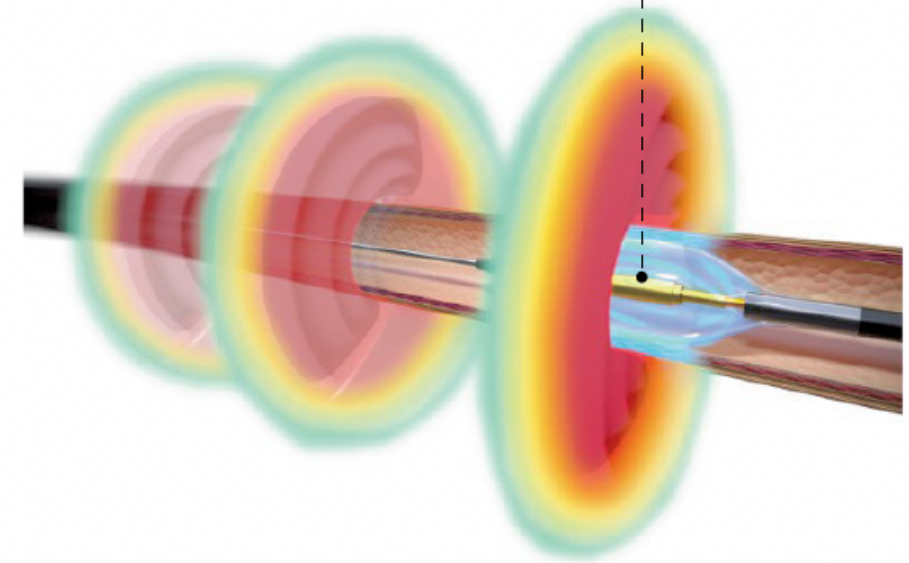
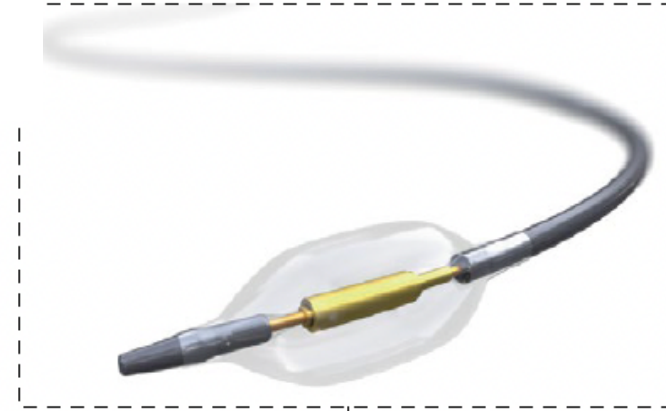
 Injection of neurotoxic agents (e.g., alcohol) directly into the perivascular space to destroy nerves. (Investigational)

FDA-approved devices for renal denervation

**Symlicity Spyral
(SPYRAL HTN Trials)**



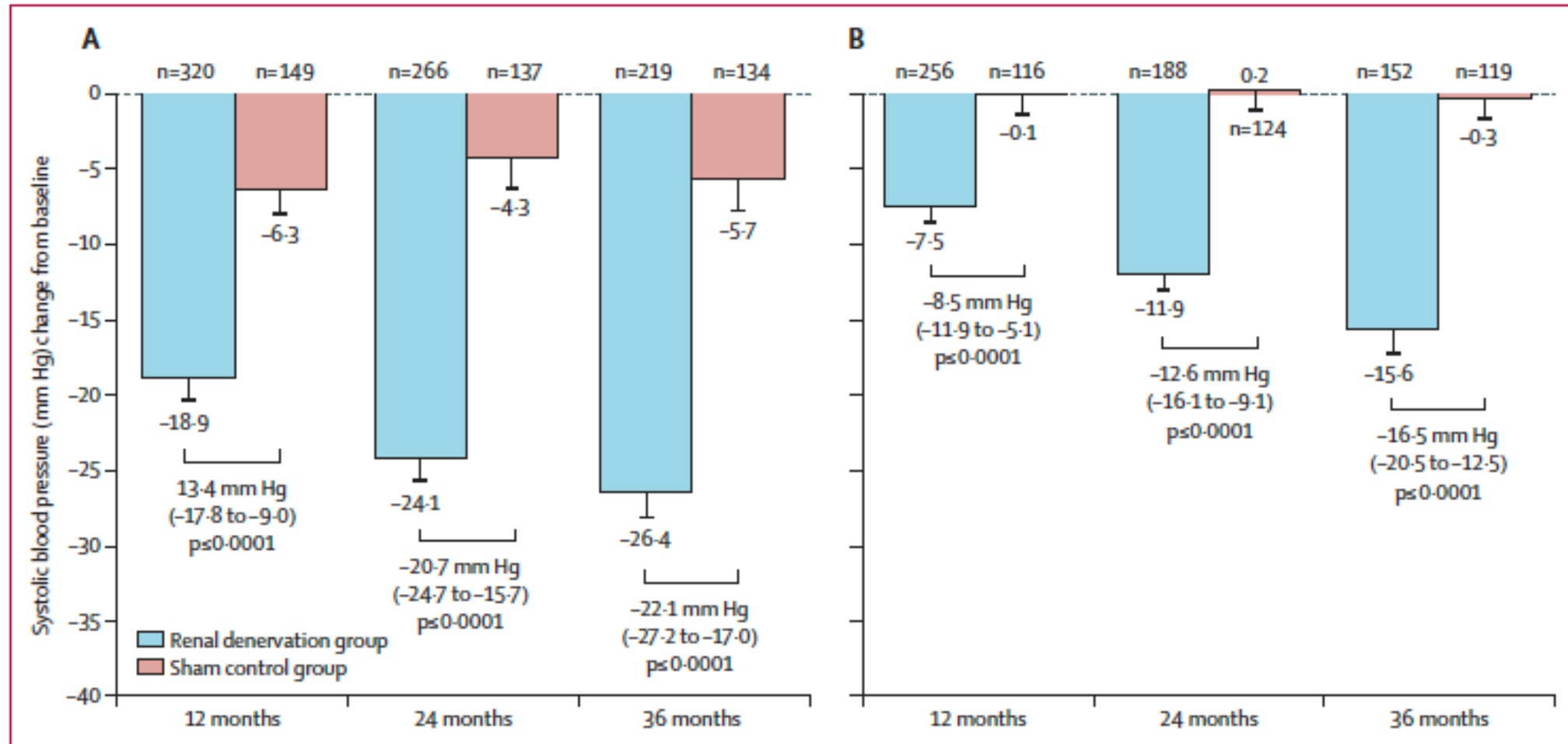
**Paradise Ultrasound
(RADIANCE Trials)**



Fisher NDL and Kirtane AJ. *Nature Rev Cardiol* 2025

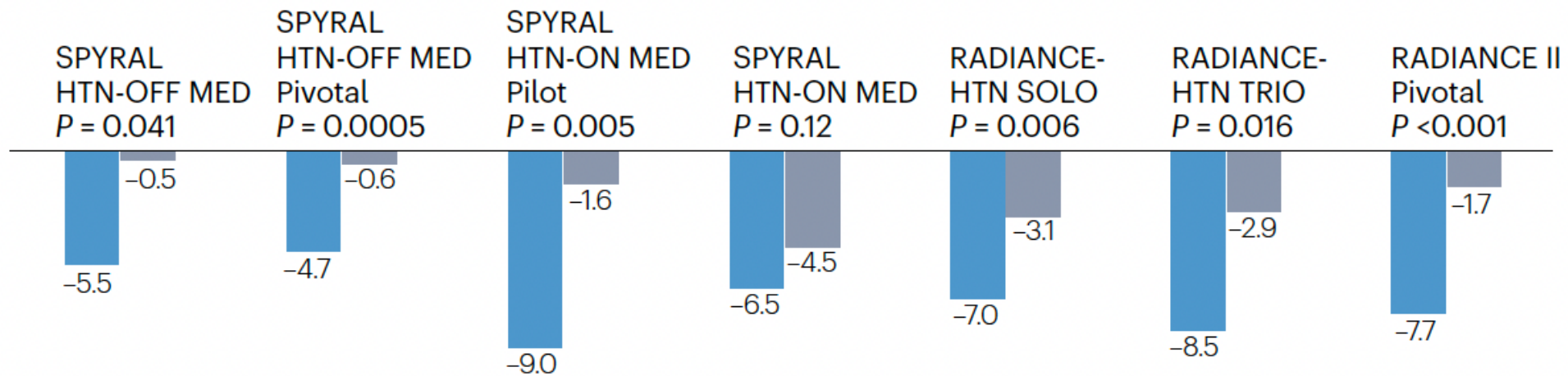
Long-term outcomes after catheter-based renal artery denervation for resistant hypertension: final follow-up of the randomised SYMPPLICITY HTN-3 Trial

The Pivotal Setback

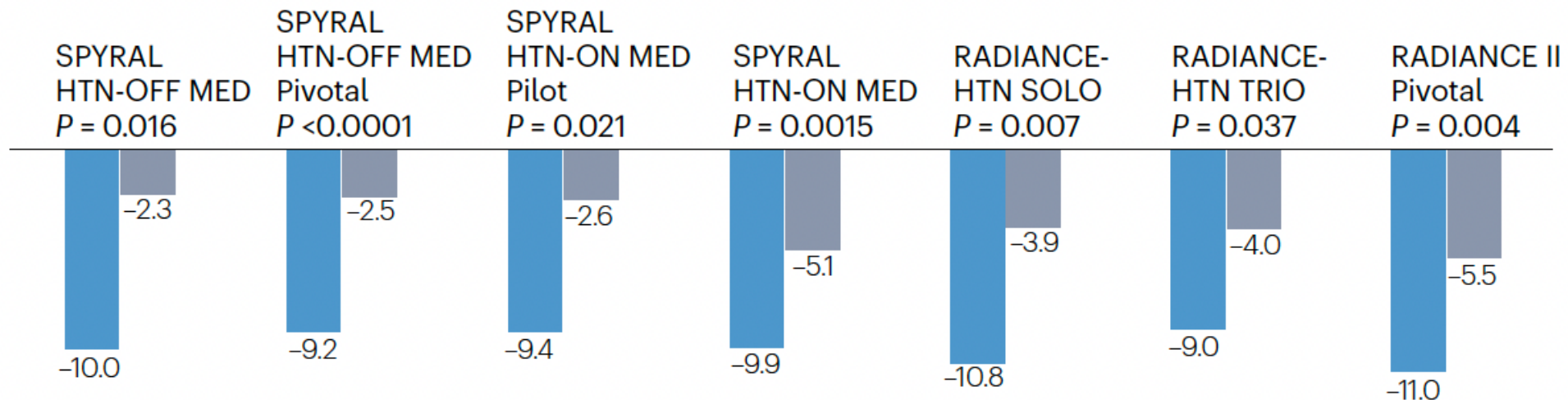


BP-lowering efficacy of RDN in shamcontrolled trials

a 24-h ambulatory BP (mmHg)



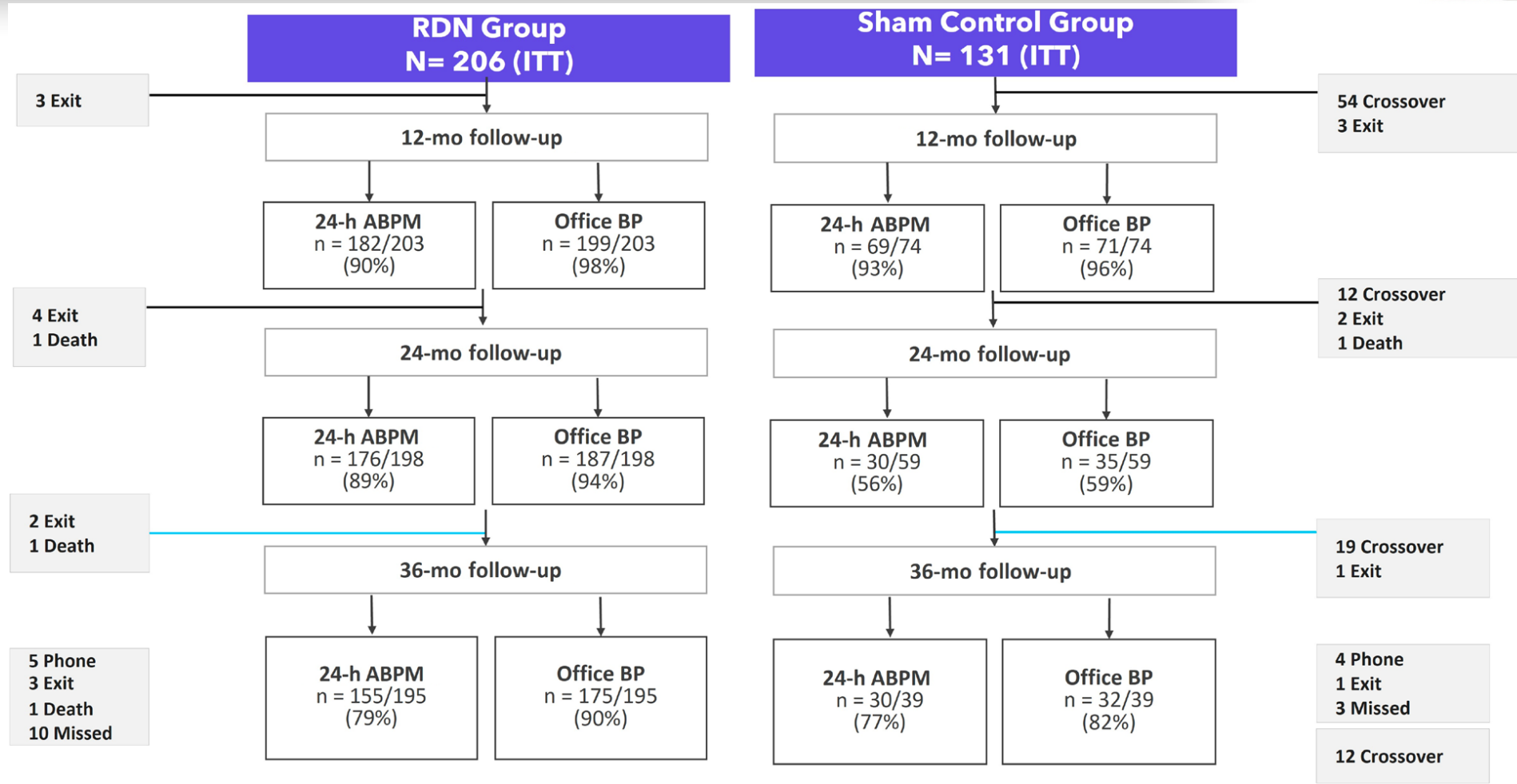
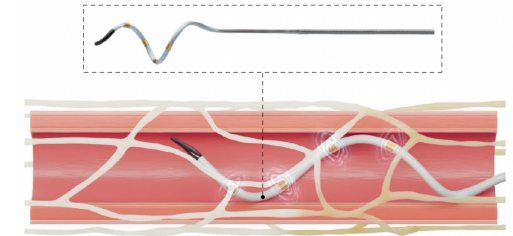
b Office BP (mmHg)



Fisher NDL and Kirtane AJ. *Nature Rev Cardiol* 2025

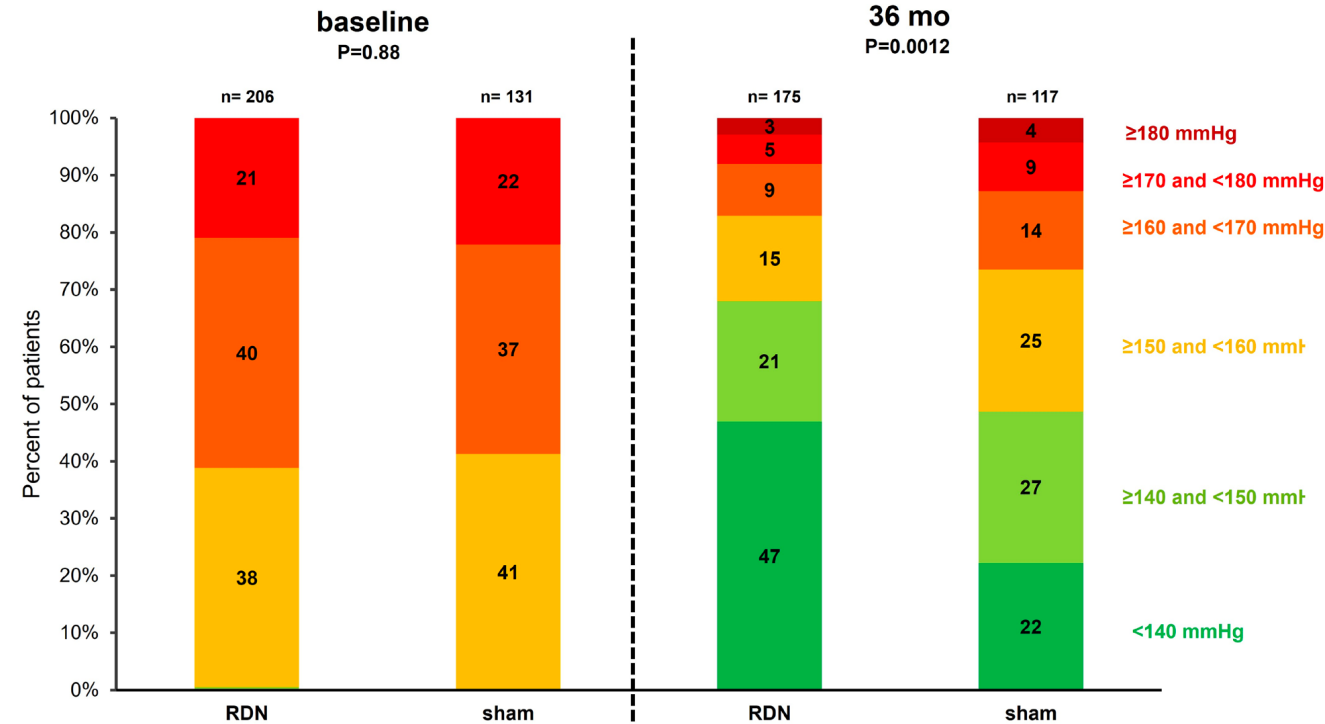
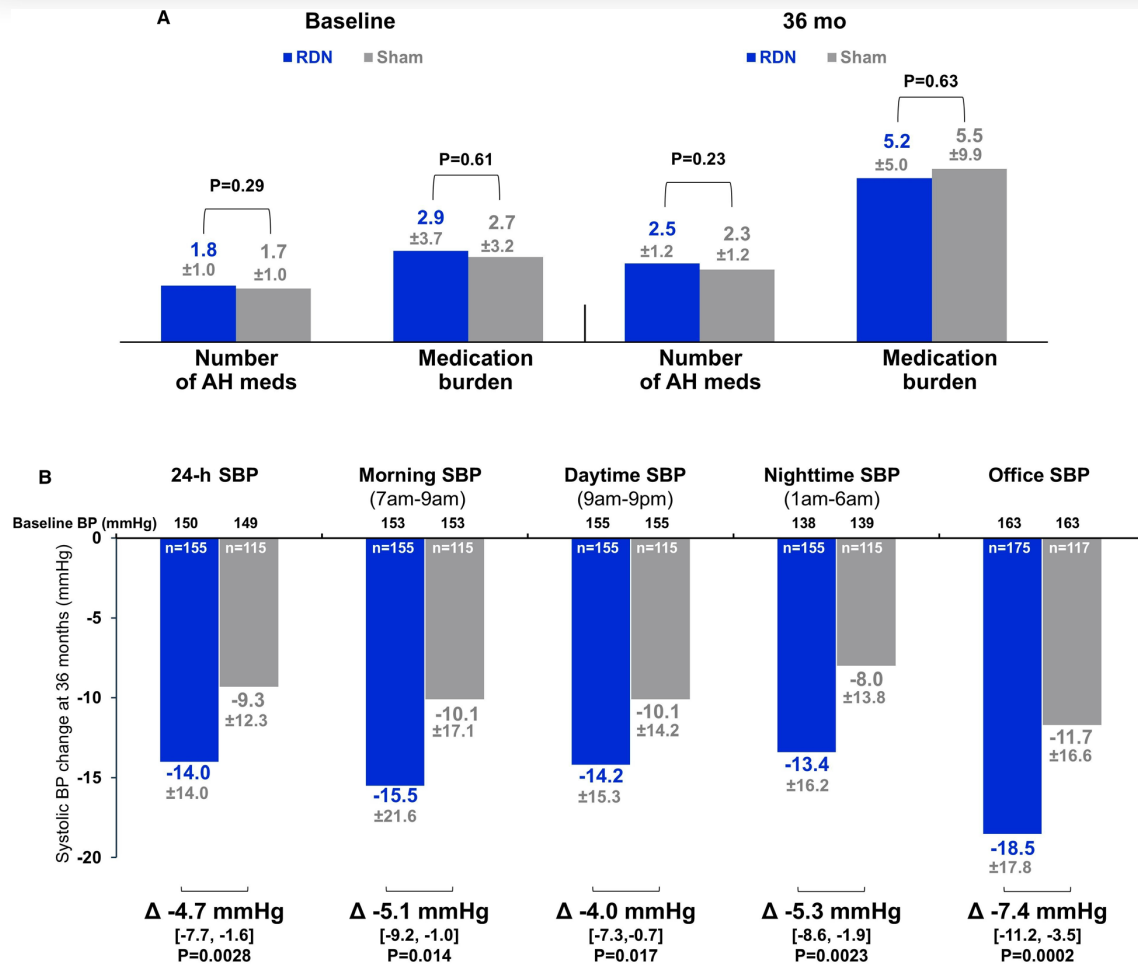
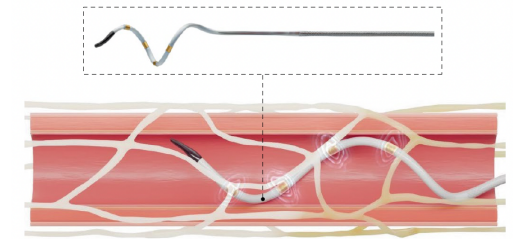


Three-Year Durability of Radiofrequency Renal Denervation: SPYRAL HTN-ON MED

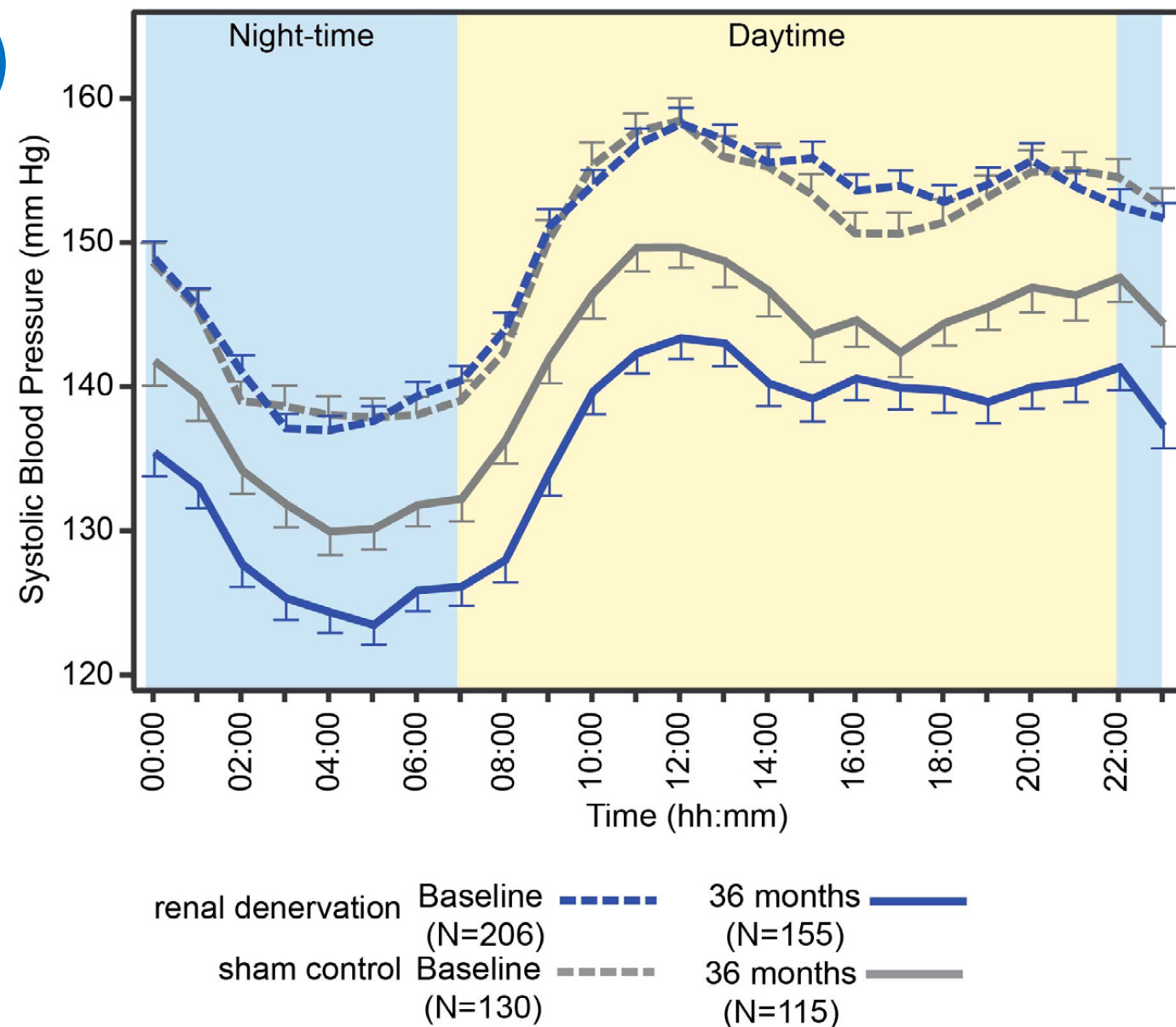
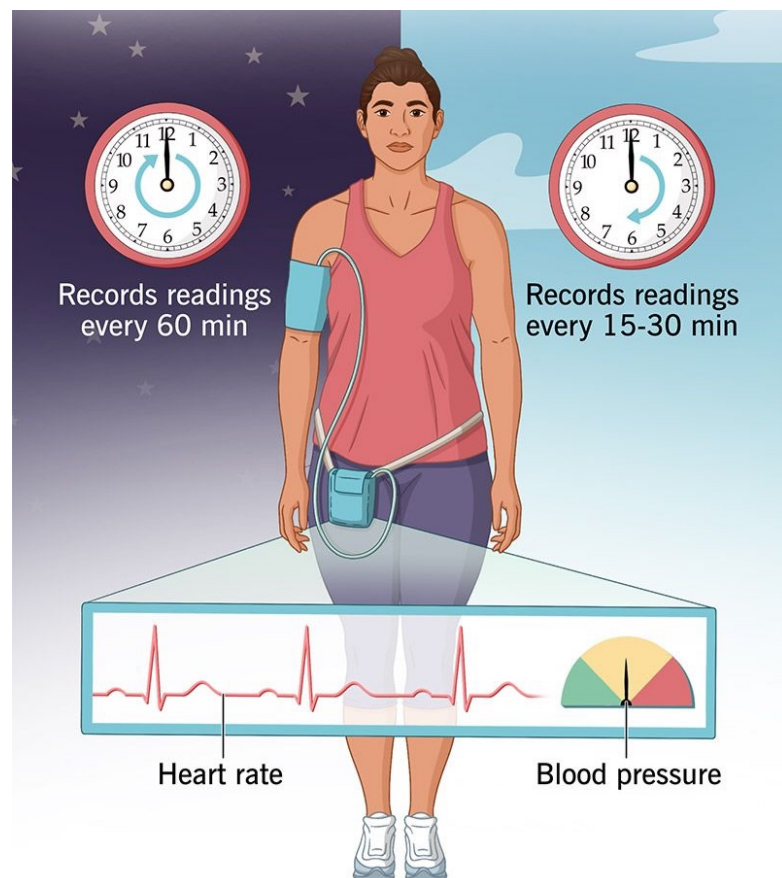


Kandzari DE et al. *J Am Heart Assoc.* 2026

Three-Year Durability of Radiofrequency Renal Denervation: SPYRAL HTN-ON MED



Long term efficacy during 24 Hours (SPYRAL-HTN ON MED)



Kandzari DE et al. *J Am Heart Assoc.* 2026



Complications

Preventive measures/management strategies

Access-site vascular complication, i.e., haematoma, pseudoaneurysm, fistula, bleeding, etc.

US-guided puncture, vascular closure device, blood pressure control

Contrast-induced acute kidney injury

Adequate (preprocedural) hydration, minimal contrast volume (or diluted contrast)

Vascular complications, i.e., renal artery spasm, dissections, distal perforation, intracapsular renal haematoma, renal artery stenosis/dissections, aortic dissection, embolisation

Non-selective abdominal aorta angiogram, no-touch technique to selectively engage the renal artery, avoidance of hydrophilic guidewires, proper RDN technique, intra-arterial injection of a vasodilator, availability of adequately sized stents on site in case of acute renal artery complication which cannot be reversed by prolonged renal artery ballooning

Safety

Mahfoud F et al. Effects of renal denervation on kidney function and long-term outcomes: 3-year follow-up from the Global SYMPPLICITY Registry. Eur Heart J. 2019

Table 4 Safety results using Kaplan–Meier time-to-event analysis

	6 months (number at risk ^a : 2237)	1 year (number at risk ^a : 2112)	2 years (number at risk ^a : 1917)	3 years (number at risk ^a : 1345)
Death	0.5 (10)	1.3 (28)	2.8 (54)	4.1 (59)
Cardiovascular events				
Cardiovascular death	0.3 (6)	0.8 (16)	1.5 (28)	2.0 (29)
Stroke	0.7 (15)	1.3 (27)	2.1 (41)	3.2 (47)
Hospitalization for new onset heart failure	0.7 (16)	1.1 (24)	2.0 (38)	3.2 (46)
Hospitalization for atrial fibrillation	0.7 (15)	1.5 (32)	2.4 (46)	3.0 (45)
Hospitalization for hypertensive crisis/hypertensive emergency	0.8 (17)	1.1 (24)	1.8 (36)	2.6 (40)
Myocardial infarction	0.7 (16)	1.1 (23)	1.6 (31)	2.2 (33)
Renal events				
New onset end-stage renal disease	0.2 (4)	0.4 (9)	1.0 (19)	1.6 (23)
Serum creatinine elevation >50% mg/dL	0.4 (9)	0.9 (19)	1.2 (24)	1.5 (24)
New artery stenosis (>70% diameter stenosis)	0.05 (1)	0.1 (3)	0.2 (4)	0.3 (4)
Post-procedural events				
Non-cardiovascular death	0.1 (2)	0.3 (7)	1.0 (19)	1.6 (22)
Renal artery reintervention	0.2 (5)	0.4 (8)	0.4 (9)	0.6 (10)

Data are presented as Kaplan–Meier estimate % (number of events).

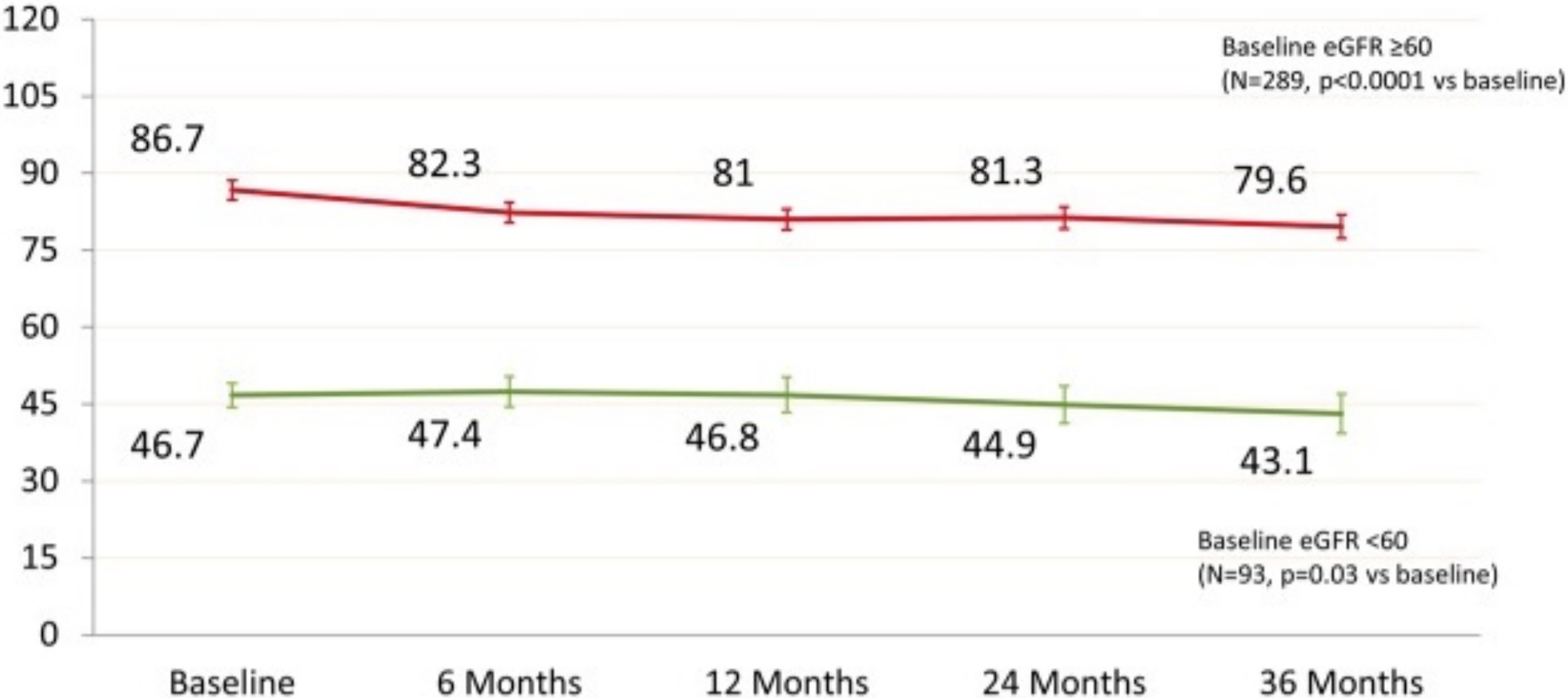
^aNumber at risk at the start of each new follow-up period.



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Stage 1	Stage 2	Stage 3A	Stage 3B	Stage 4	Stage 5
GFR ≥ 90	89 $\geq$ GFR ≥ 60	59 $\geq$ GFR ≥ 40	44 $\geq$ GFR ≥ 30	29 $\geq$ GFR ≥ 15	GFR < 15
					
Normal or high function	Mildly decreased function	Mild to moderately decreased function	Severely decreased function	Kidney failure	

Effects of renal denervation on kidney function (the Global SYMPPLICITY Registry)

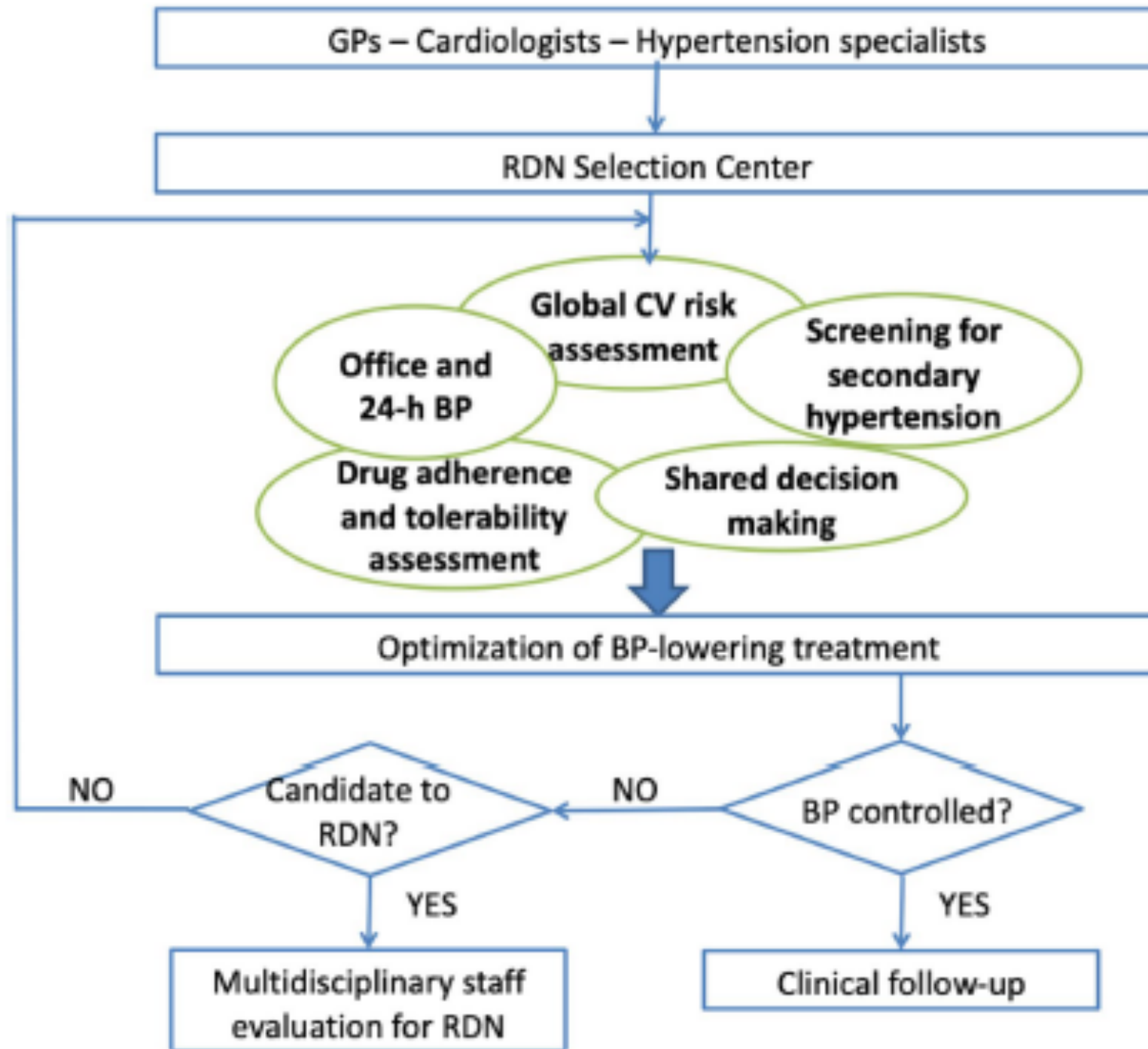


Mahfoud F et al. Eur Heart J. 2019



Which patient is candidate for RADN?





Stabile E et al. *G Ital Cardiol* 2023



A) Essential Hypertensive patient uncontrolled by an association 3 drugs (including a diuretic) at maximally tolerated doses
(recommended)

Additional features

- Patient preference**
- Adverse effects with spironolactone**
- Poor drug adherence despite extensive counseling**
- Systo-diastolic hypertension**
- No extensive vascular damage**
- High/very high lifetime cardiovascular risk**

Resistant Hypertension



Prof. Eugenio Stabile, MD, PHD





A position paper of the Italian Society of Hypertension on renal denervation identifies two "ideal patients " for Renal Denervation therapy

B) Grade 1 – 2, systo-diastolic, essential hypertensive patient, untreated or uncontrolled by 1-2 BP-lowering drugs (possible)

Additional features

- Multiple intolerance to BP-lowering drugs/adverse effects**
- Poor drug adherence despite extensive counseling**
- High/very high lifetime cardiovascular risk**
- Paroxysmal atrial fibrillation and planned ablation**
- Patient preference**

Difficult To treat Hypertension



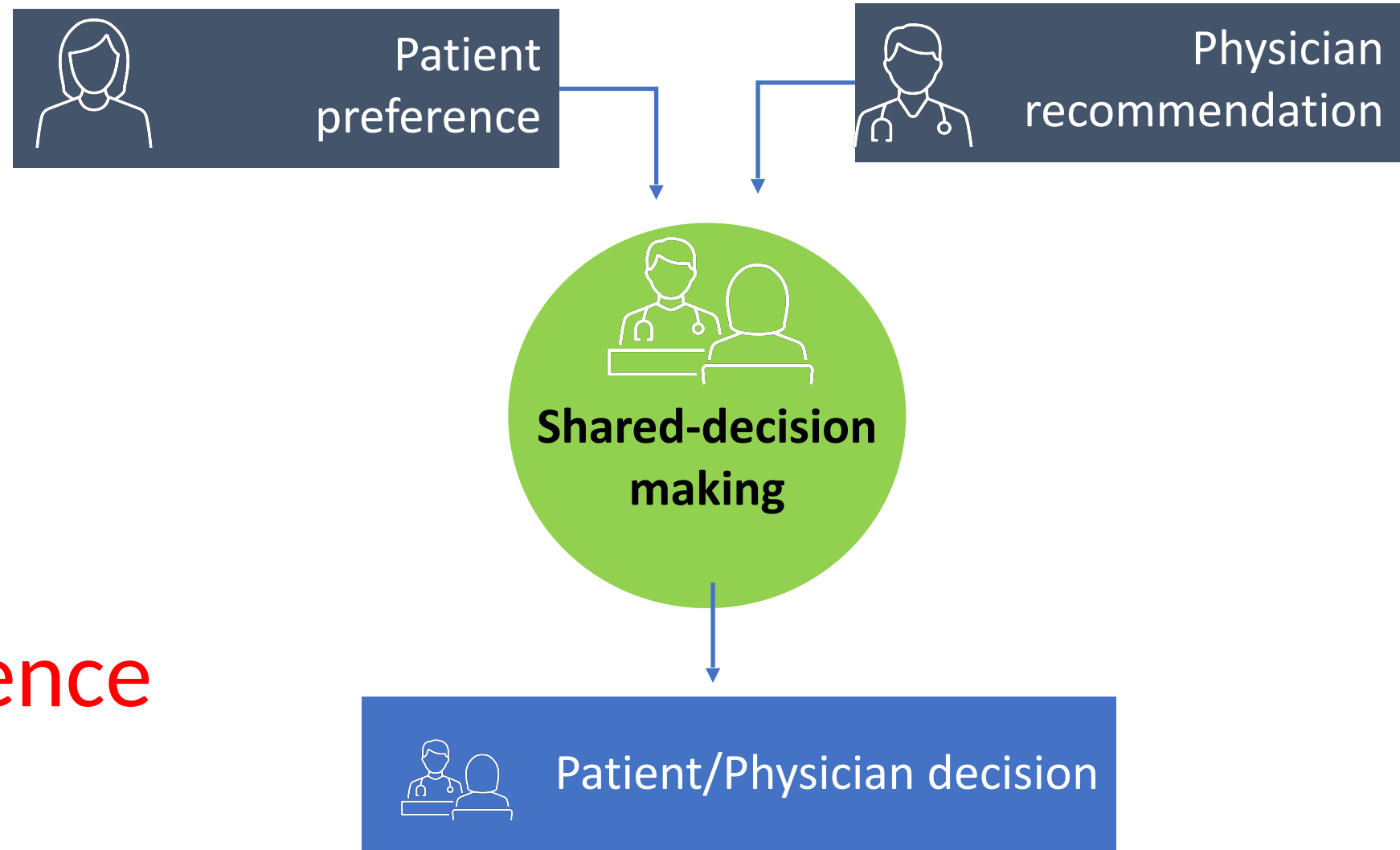
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As all the guidelines have recommended, shared decision-making is an important element in clinical planning for RDN. Patient preference data support this recommendation, which translates into the need for clinicians to take the time for risk–benefit discussions with potential candidates for RDN to allow patients to take an active role in their care



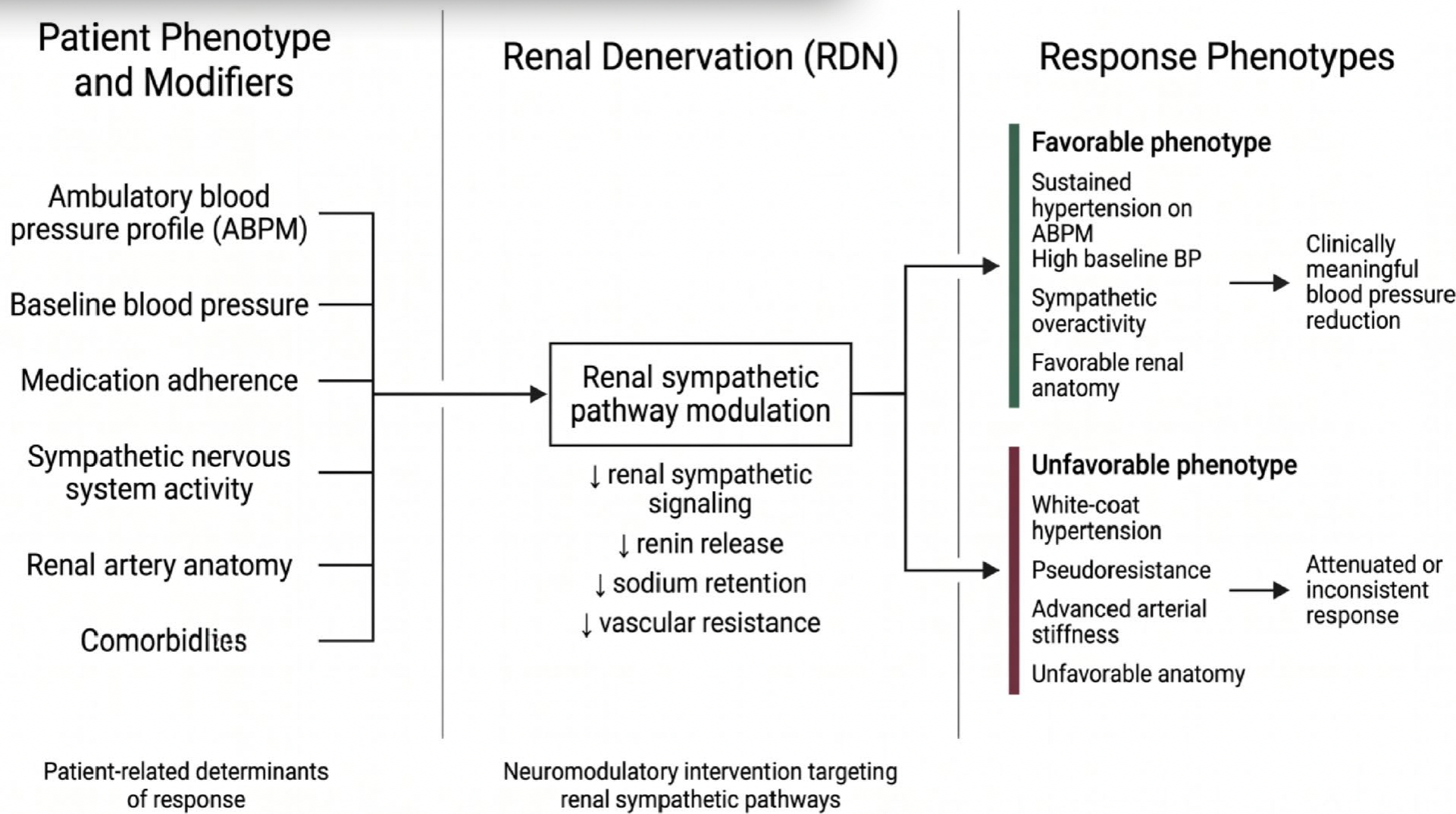
Patient preference



Phenotype-Guided Renal Denervation: the Key to Therapeutic Response



An important characteristic of the BP reductions observed with catheter-based RDN is that aggregated responses are a mean of a distribution



Minimum requirements for RDN selection centres

Hypertension Centre

- ESH Excellence Centers and/or Centers with specific SIIA certification or acknowledgement
- Dedicated outpatient service for the difficult-to-treat patients
- Medical and nurse staff with targeted education on the topic
- Equipment assess 24H BP, drug adherence and screen for main causes of secondary hypertension, including advance imaging facilities
- Coordination of the multidisciplinary team in charge of finalizing the indication to RDN

Interventional Centre

- Certified operators (interventional radiologist or cardiologist)
- Volume of renal procedures >20/year (RDN procedures >5/year)
- Agreement with regional healthcare system for reimbursement of the procedure





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