UPDATE

Denervazione renale: quando e per quali pazienti

Franco Rabbia

AZIENDA OSPEDALIERO-UNIVERSITARIA
Città della Salute e della Scienza di Torino

Device-based therapies for hypertension

Recommendation	Class[a]	Level[b]
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.[367,368]	III	B

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RCT = randomized controlled trial.
[a]Class of recommendation.
[b]Level of evidence.

Importanti progressi in termini di HTA (health technology assessment)

- Maggiori conoscenze di anatomia dell'innervazione renale
- Sviluppo di devices di seconda generazione
- Conduzione di studi clinici controllati più rigorosi
- Primi dati di follow up a medio termine

SISTEMA SIMPATICO E RENE

Conoscenze anatomiche e sviluppo di nuovi devices

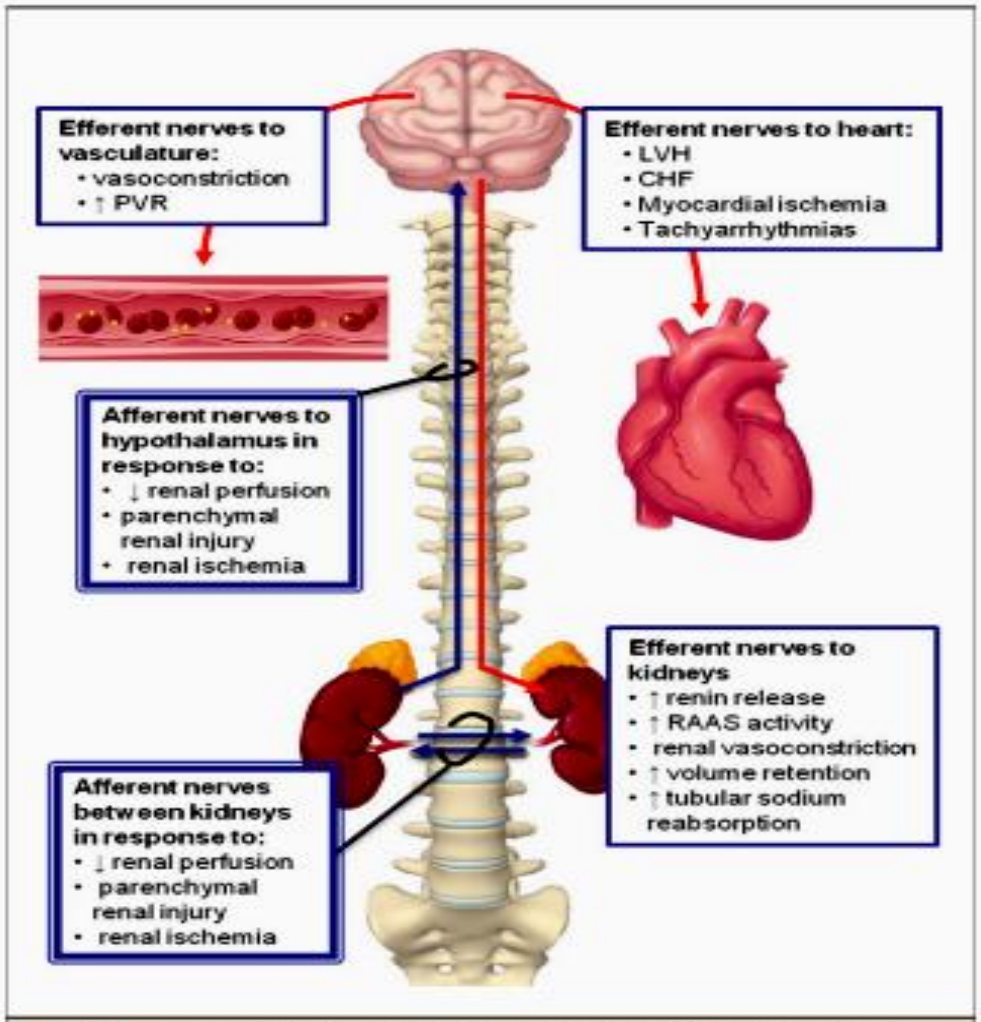

Figure 1. Pathways of Sympathetic Activity Leading to Hypertension

↑ = increased; ↓ = decreased; CHF = chronic heart failure; LVH = left ventricular hypertrophy; PVR = peripheral vascular resistance; RAAS = renin-angiotensin-aldosterone system.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. XX, NO. X, 2013
MONTH 2013:xxx

DENERVAZIONE RENALE

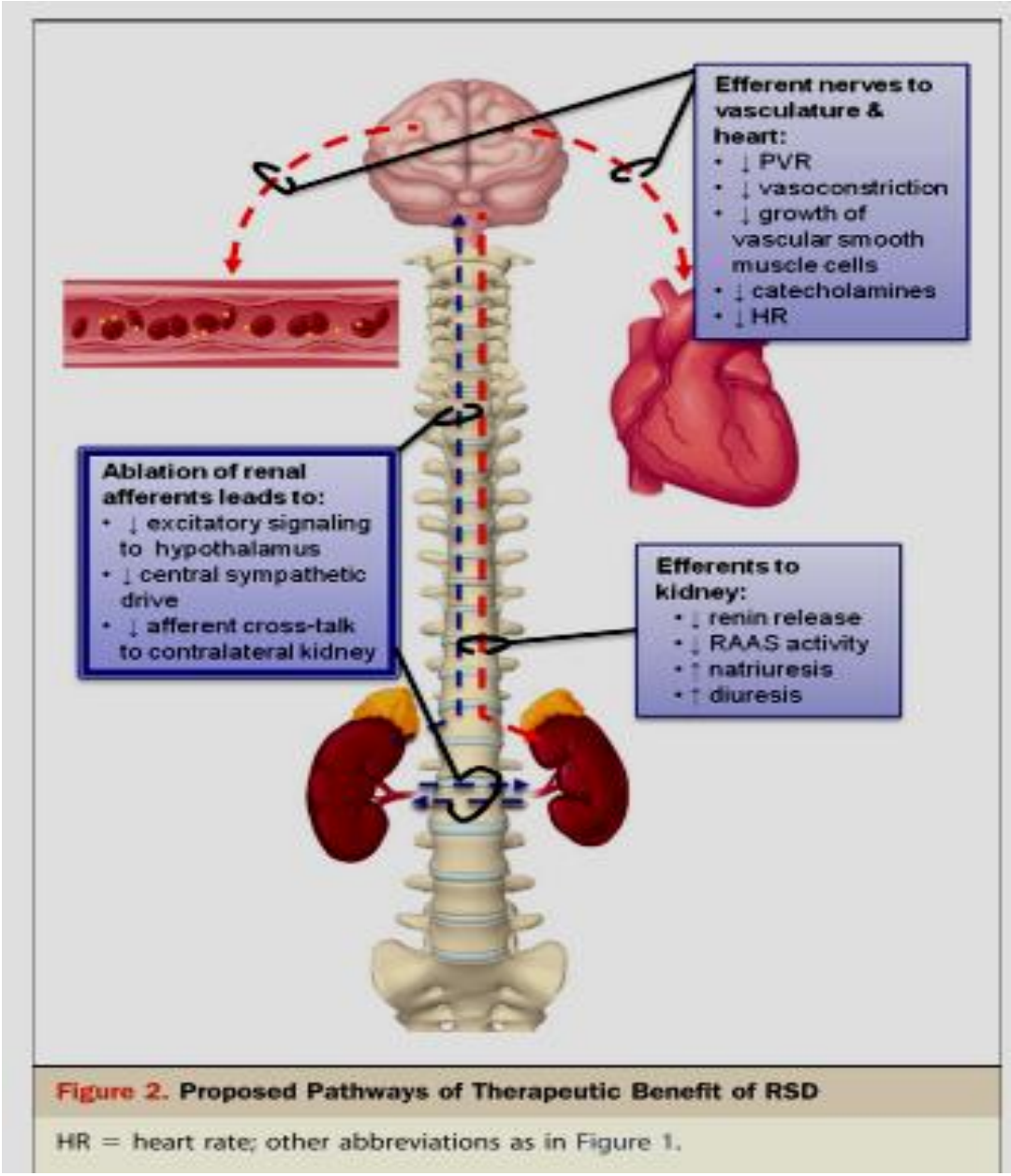

Figure 2. Proposed Pathways of Therapeutic Benefit of RSD

HR = heart rate; other abbreviations as in Figure 1.

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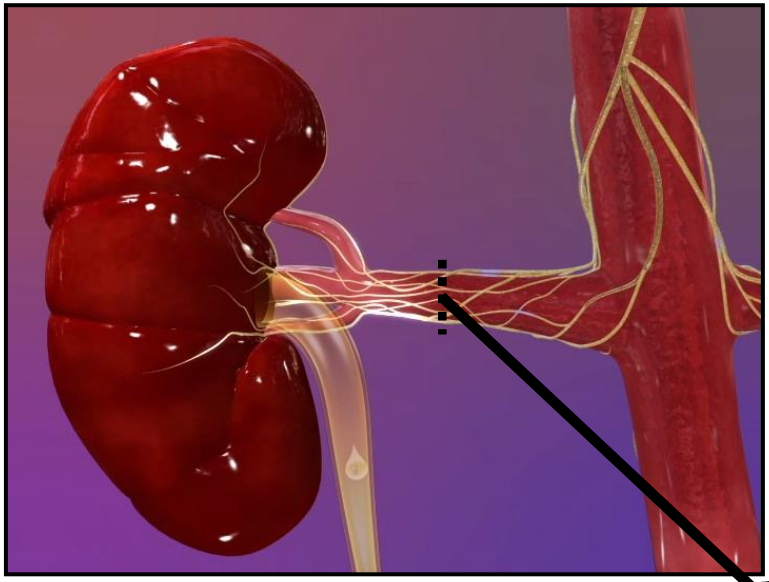
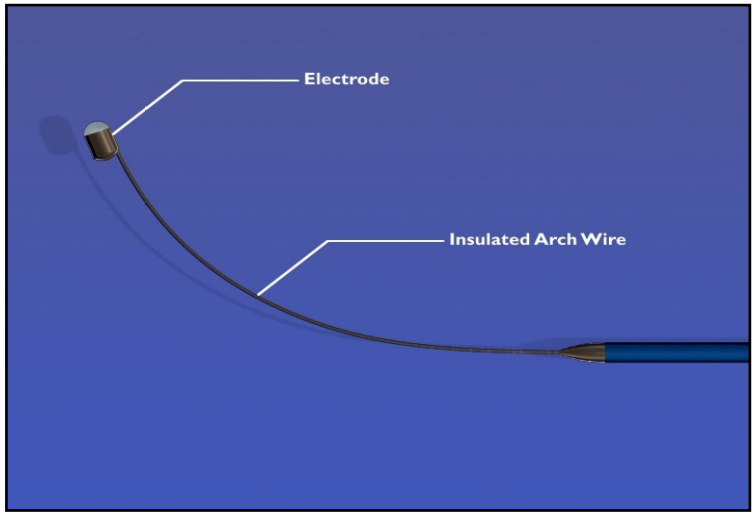
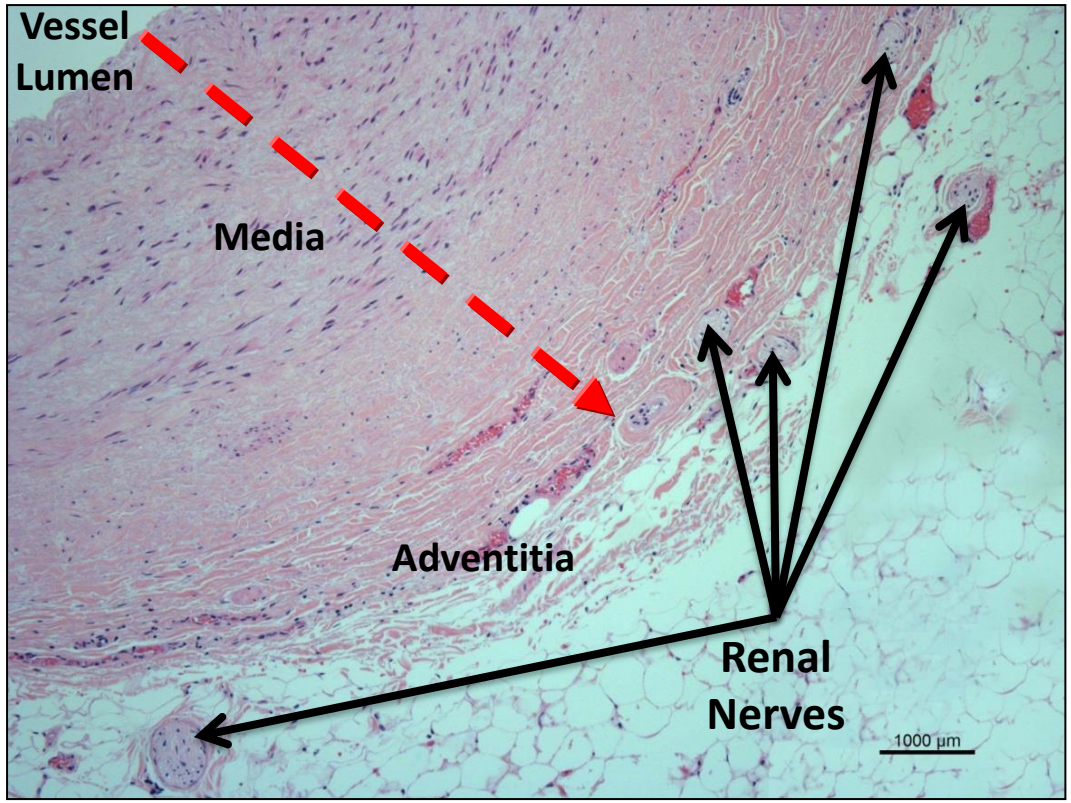
MONTH 2013:xxx

Renal Nerves as a Therapeutic Target

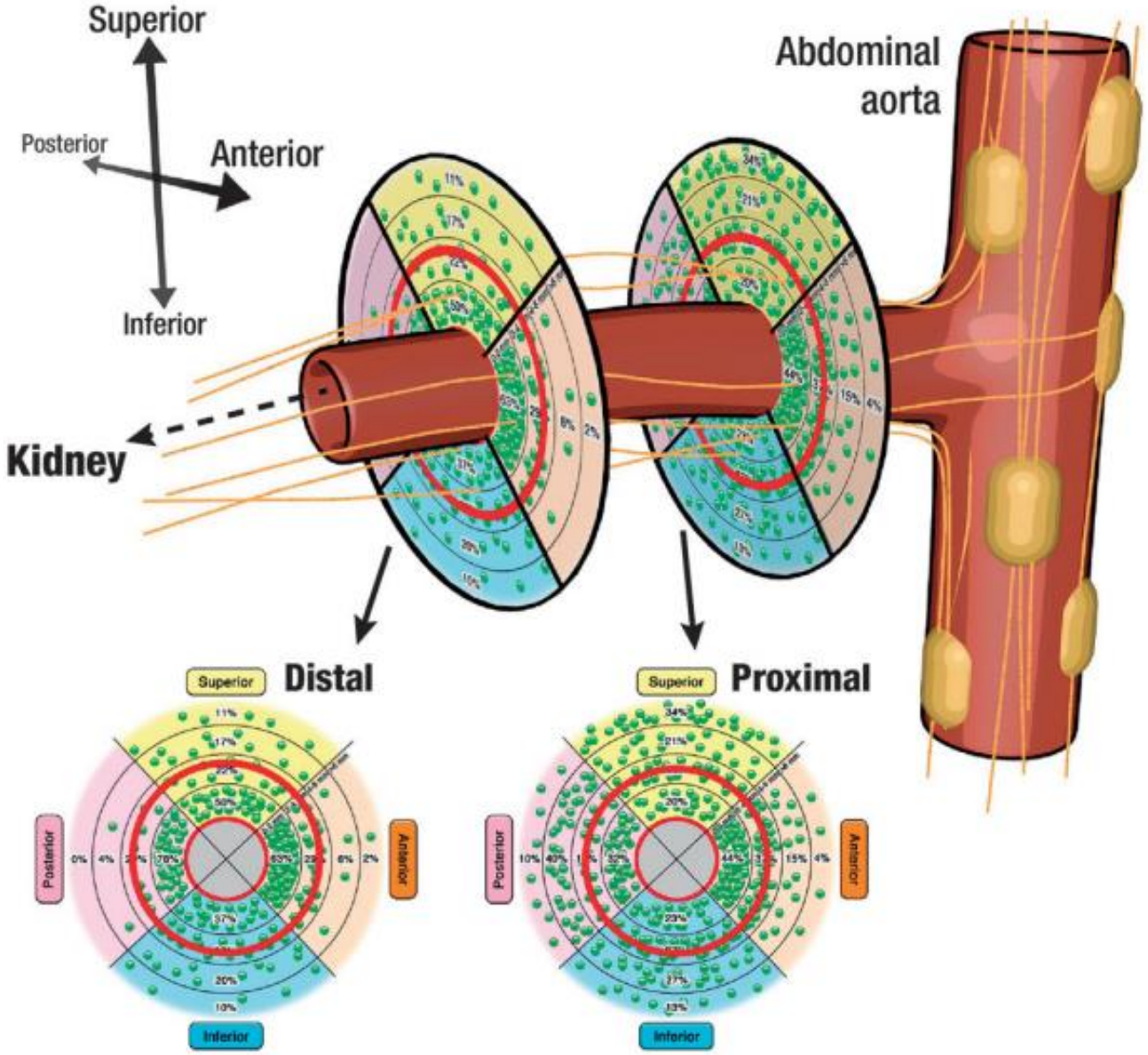




Arise from T10-L1
Follow the renal artery to the kidney
Primarily lie within the adventitia



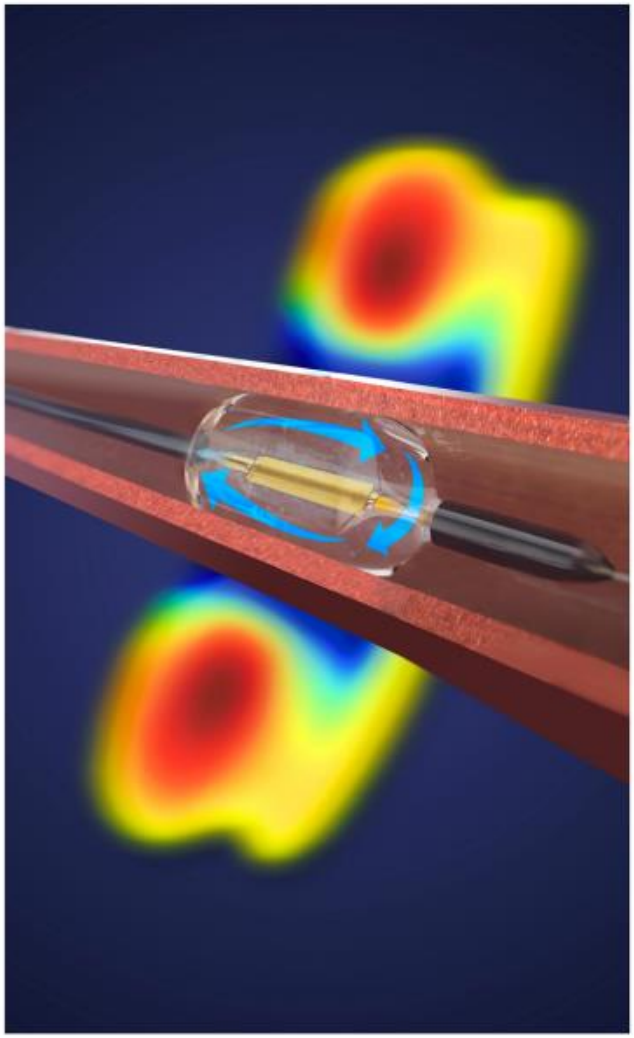
Anatomia dell'innervazione delle arterie renali



Curr Cardiol Rep. 2019

Sviluppo di devices di seconda generazione

Fig. 2 Second-generation radiofrequency-based renal denervation device



Second generation US

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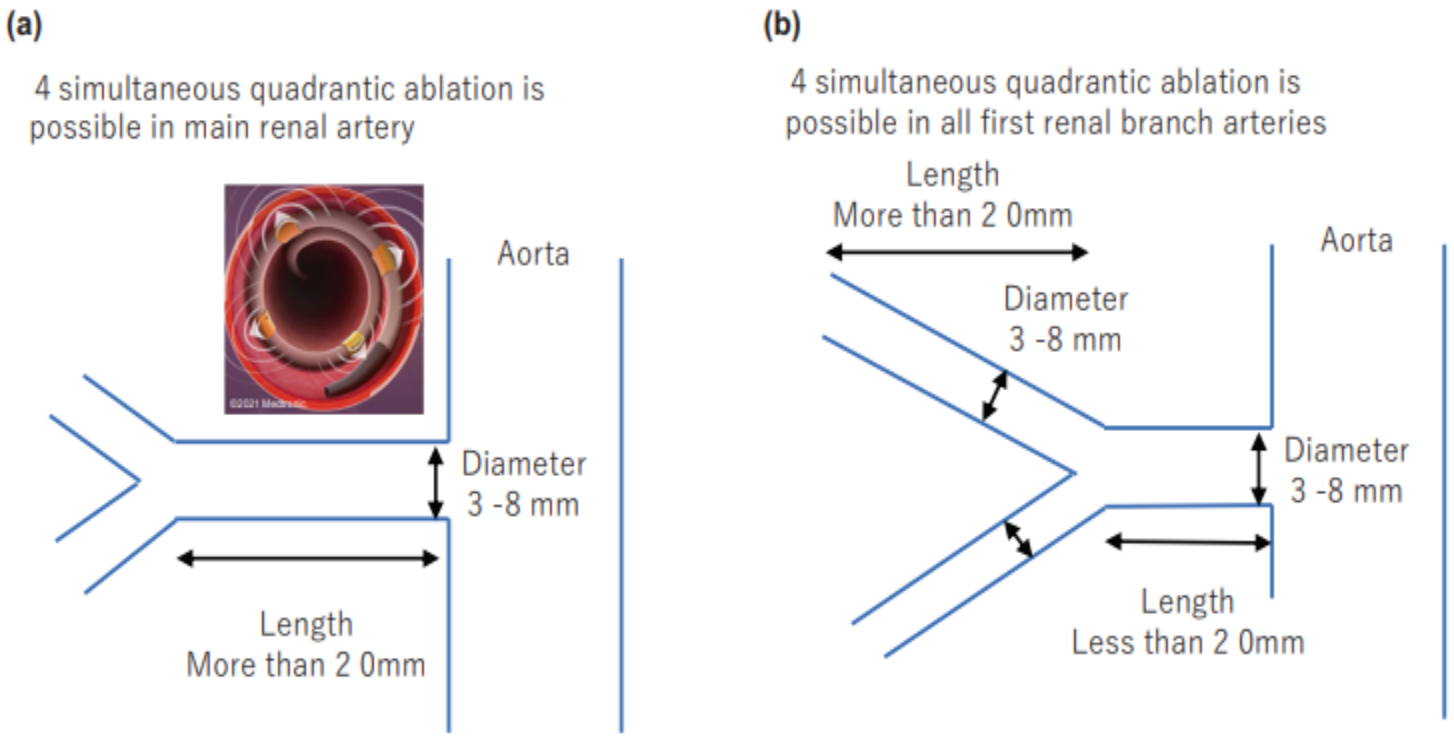
Devices a RF di seconda generazione



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Procedure di breve durata

Table 5 Specific considerations related to the RDN device

	Symplicity Spyral RF catheter system	Paradise US catheter system
Anatomical eligibility criteria	Treatment of all accessible arteries with a diameter of 3-8 mm	Treatment of accessible main renal arteries with a diameter of 3-8 mm
Access	Femoral access (6 Fr)	Femoral access (7 Fr)
Wiring	Consider use of extra-support wires or buddy wires in tortuous anatomy	Consider use of extra-support wires or buddy wires in tortuous anatomy
Ablation sites	Main renal artery and branches	Main renal artery, 2-3 ablations per artery. The selection of catheter size and ablation site required preprocedural planning with CT/MRA in trials. Final sizing can be done during the renal angiogram before the procedure
Arterial wall contact	Ensure appropriate contact of the RF electrodes and the vessel wall Ensure energy delivery (for at least 45 sec, ideally 60 sec)	Ensure complete occlusion of the renal artery after balloon inflation
Duration	Simultaneous ablation at 4 points (for at least 45 sec, ideally 60 sec)	7 seconds per ablation

CT: computed tomography; MRA: magnetic resonance angiography; RF: radiofrequency; US: ultrasound

Eur heart J 2023

Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

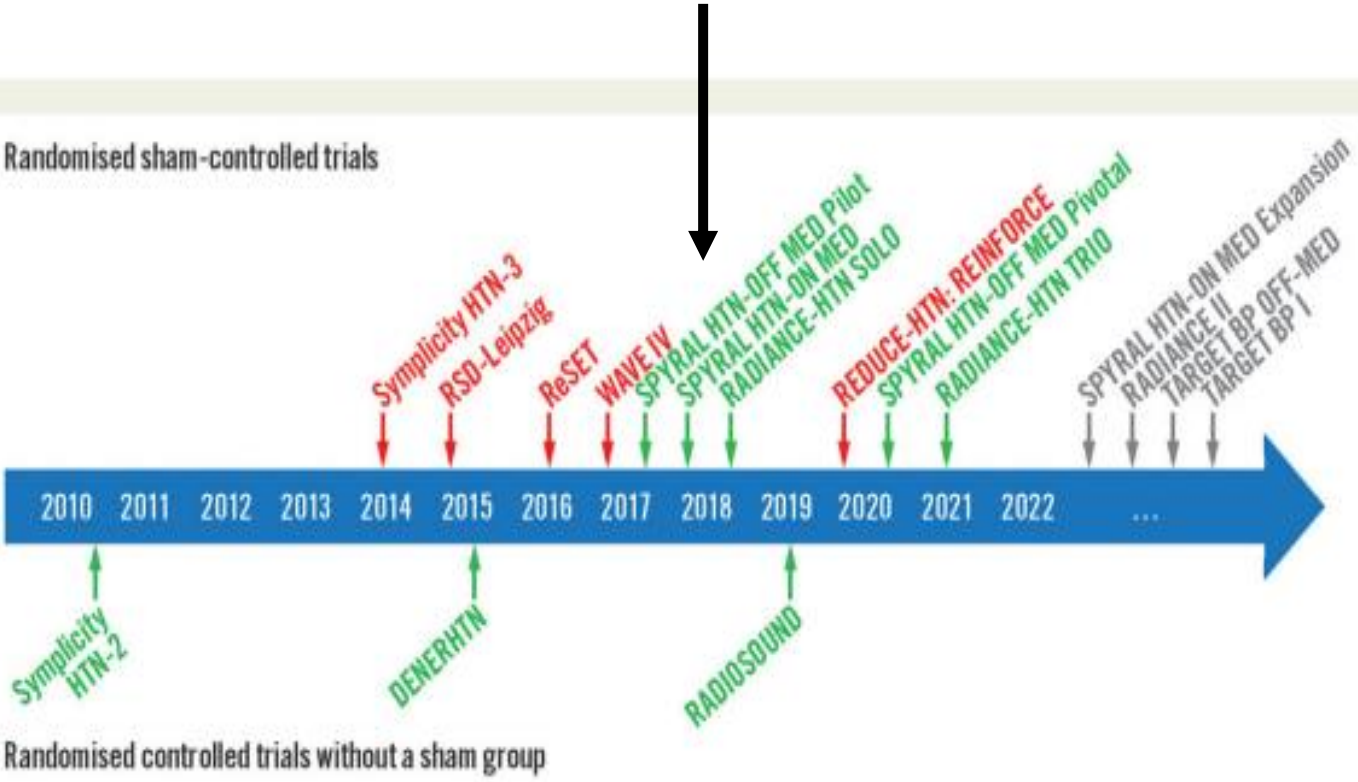

Figure 1 Landmark RDN trials. Overview of important randomised controlled trials with (top) and without (bottom) an invasive sham-control group. Green indicates that the trial met its primary efficacy outcome; red indicates that the trial did not meet its primary efficacy outcome.

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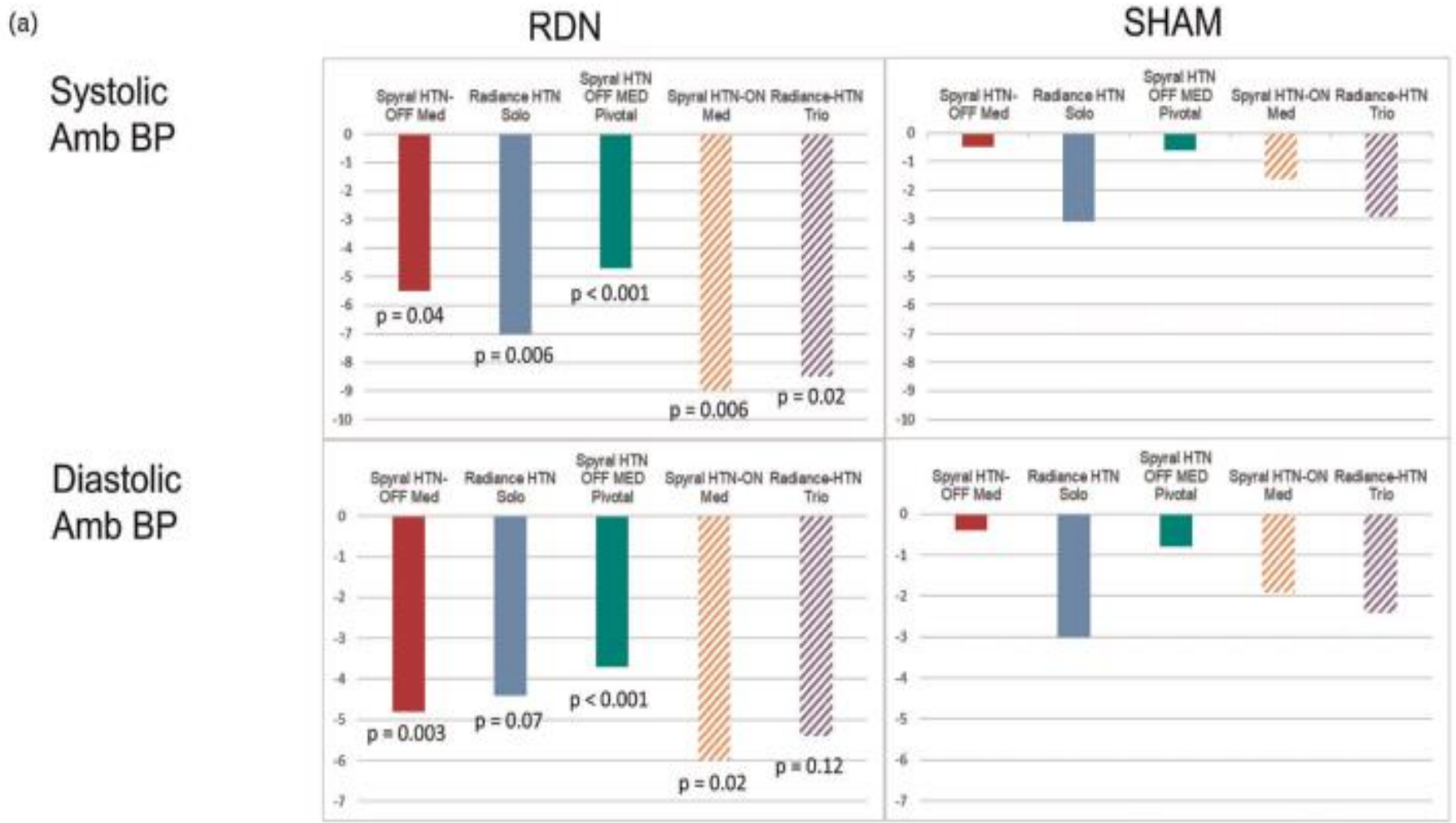
Variazioni PA 24h negli RCT di seconda generazione con gruppo di controllo SHAM



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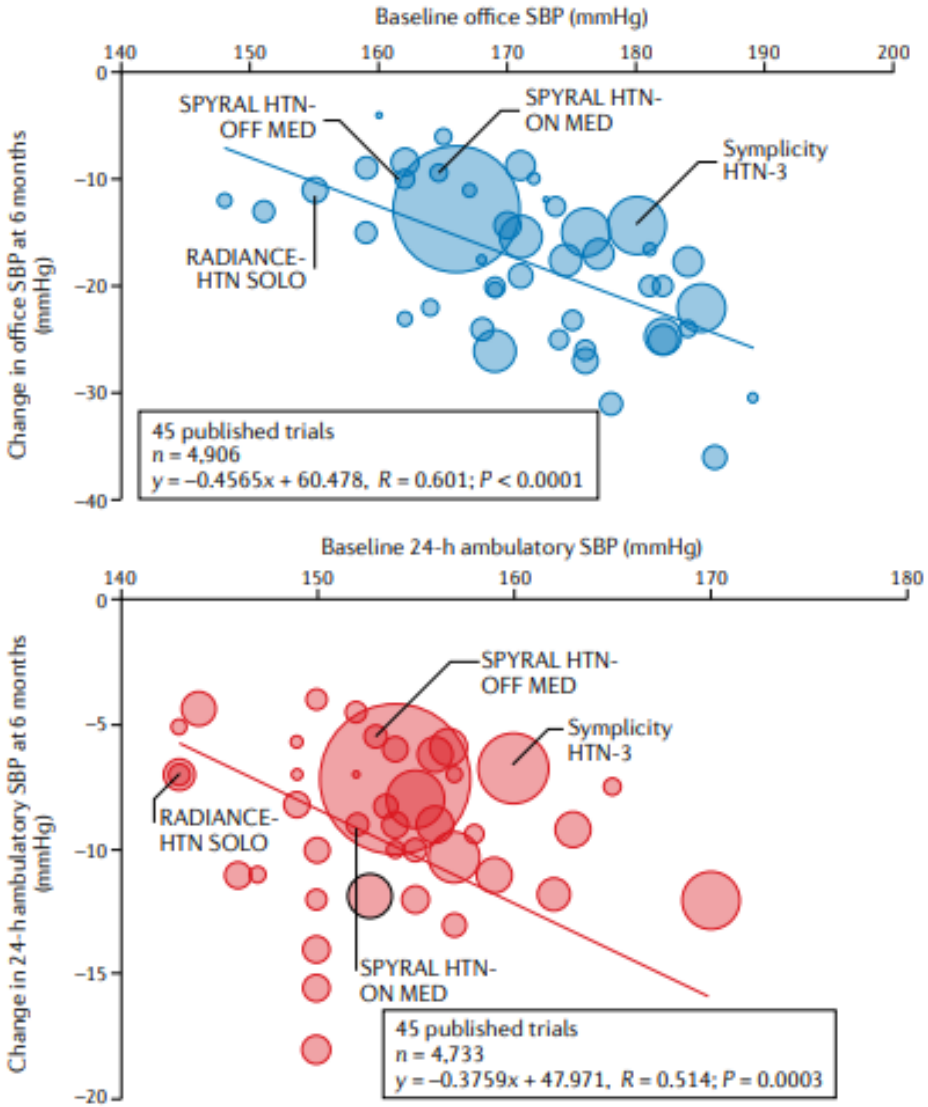
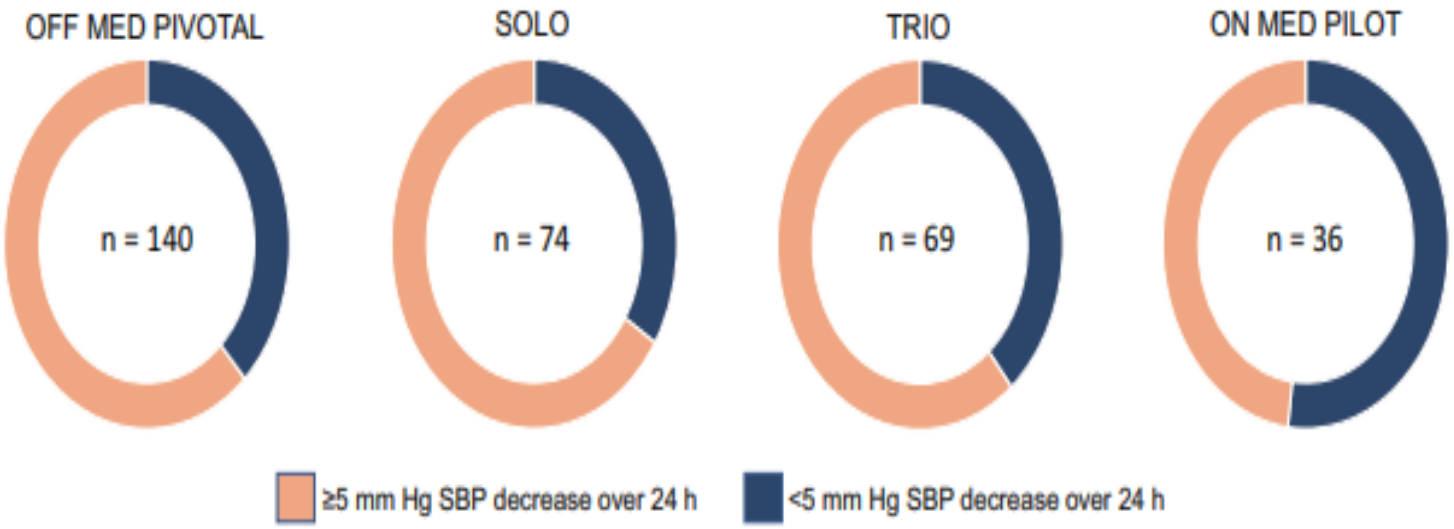
Change in systolic blood pressure with renal sympathetic denervation



Nature 2020

Numero di pazienti «responders» negli RCT di seconda generazione



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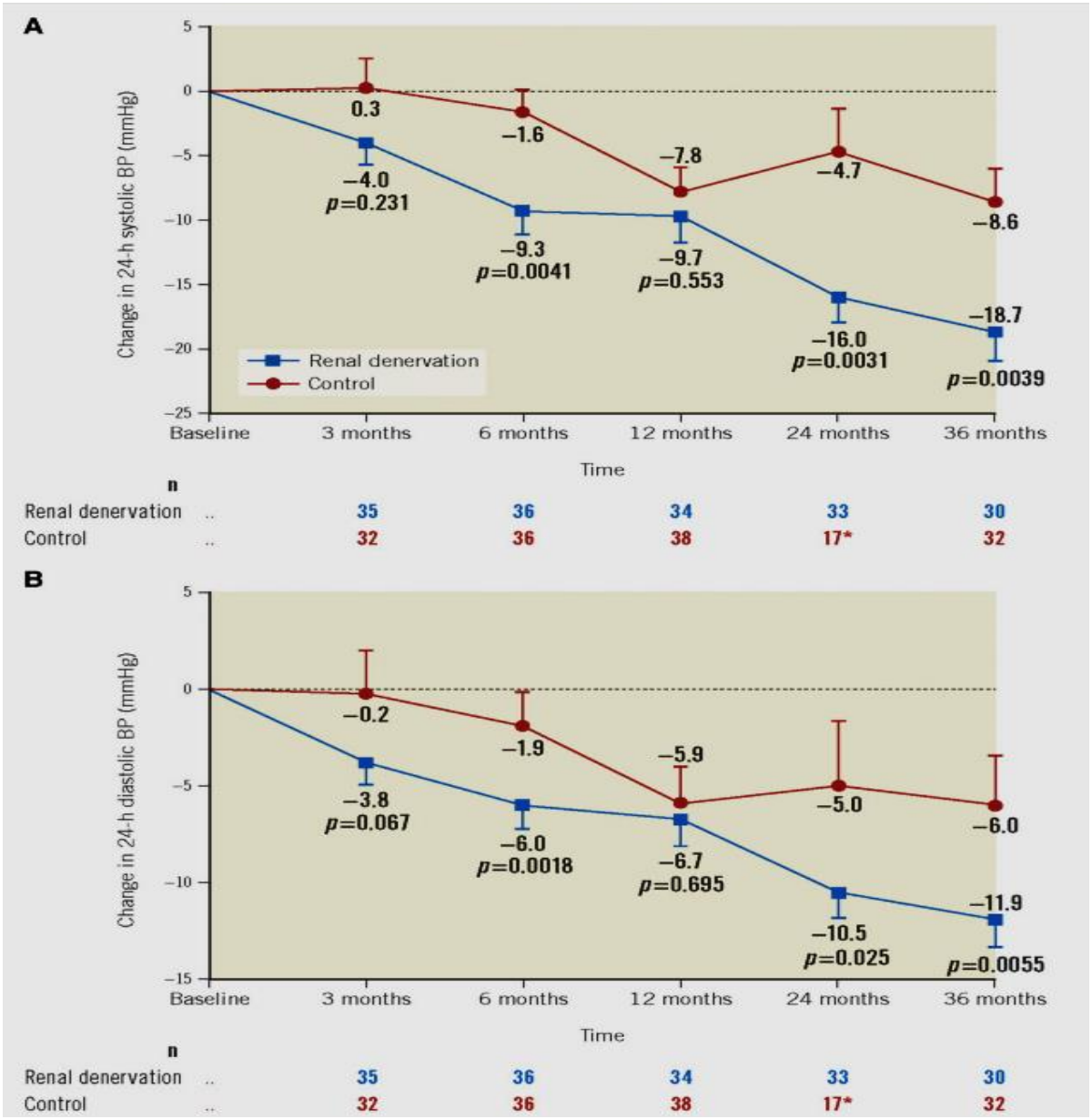

Calo pressorio medio nello **SPYRAL HTN-ON MED trial**

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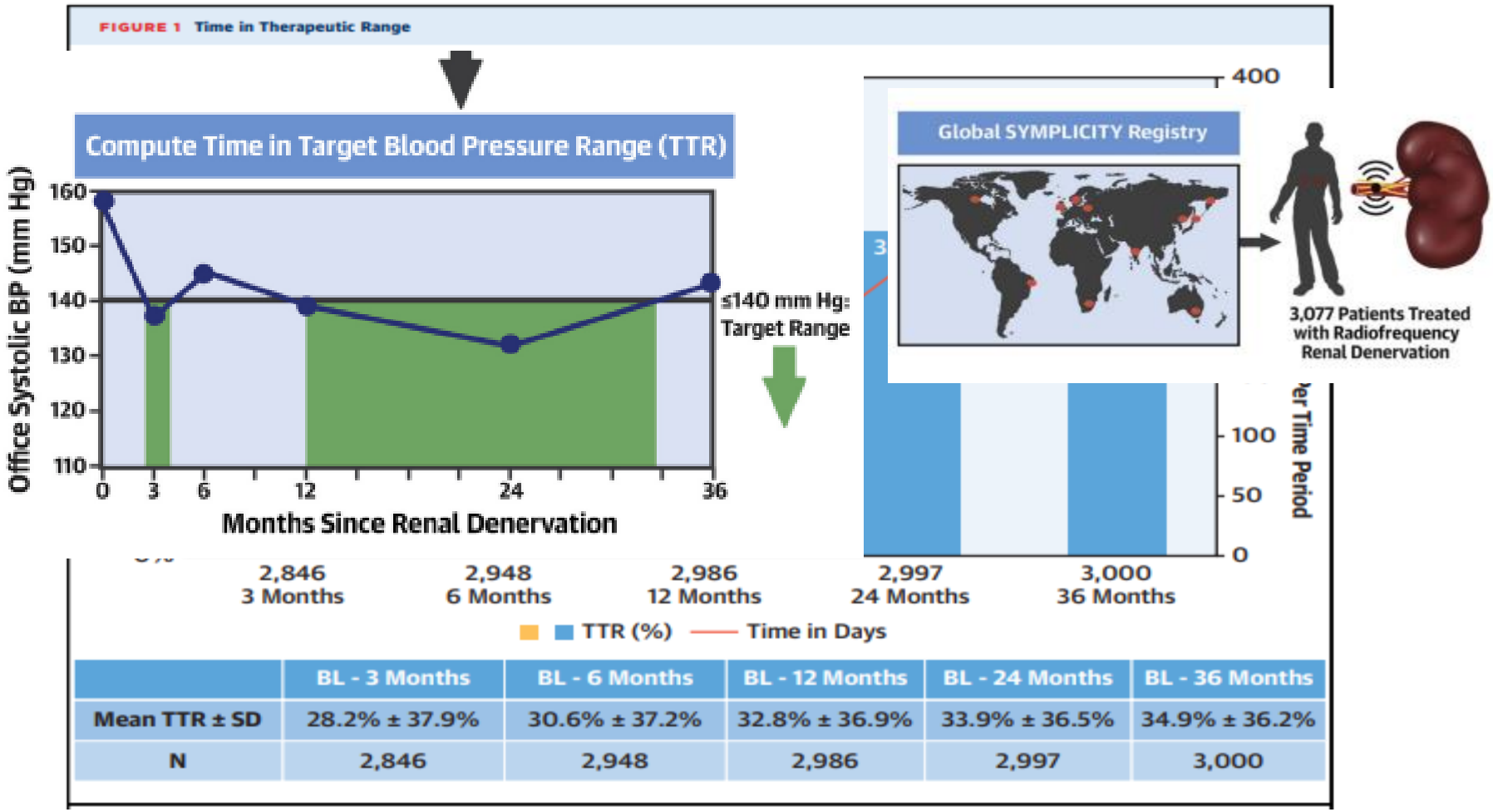
La Denervazione renale è efficace nel ridurre gli eventi cardio-cerebrovascolari?

Cardiovascular Risk Reduction After Renal Denervation According to Time in Therapeutic Systolic Blood Pressure Range



	BL - 3 Months	BL - 6 Months	BL - 12 Months	BL - 24 Months	BL - 36 Months
Mean TTR ± SD	28.2% ± 37.9%	30.6% ± 37.2%	32.8% ± 36.9%	33.9% ± 36.5%	34.9% ± 36.2%
N	2,846	2,948	2,986	2,997	3,000

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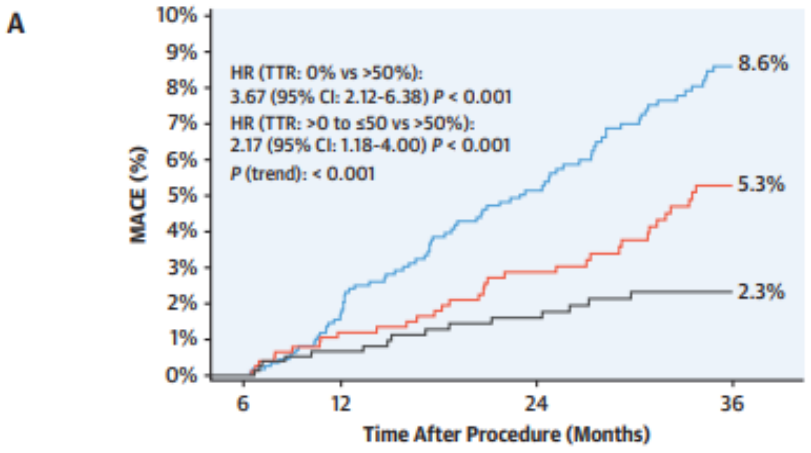
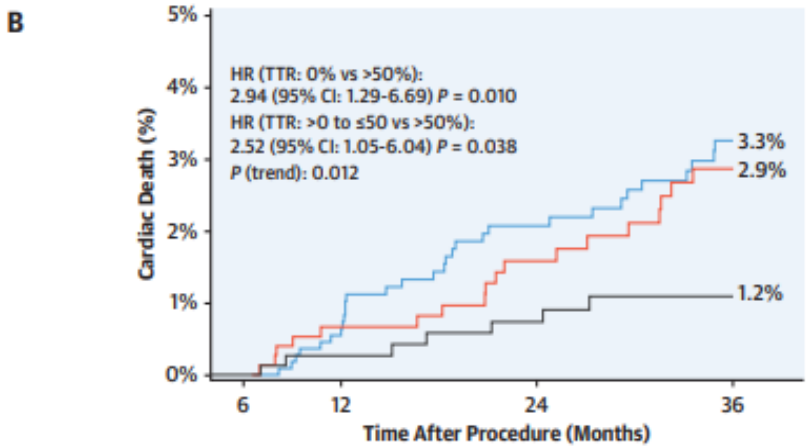
FIGURE 2 Kaplan-Meier Estimates of Cardiovascular Events Based on TTR



At Risk				
TTR: 0%	1,152	1,049	853	568
TTR: >0% to ≤50%	782	717	609	408
TTR: >50%	775	720	597	438

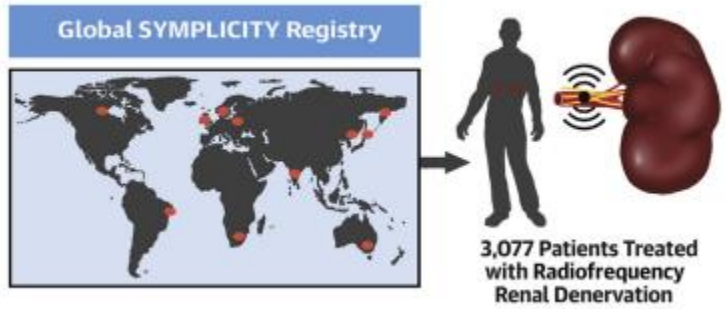


At Risk				
TTR: 0%	1,152	1,061	879	598
TTR: >0% to ≤50%	782	721	618	422
TTR: >50%	775	723	600	442

Kaplan-Meier event rates from 6 to 36 months are plotted based on combined time in therapeutic range (TTR) (maximum of office or 24-hour ambulatory blood pressure) from baseline through 6 months. HRs with 95% CIs comparing patients with 0% TTR or >0 to ≤50% TTR vs >50% TTR are listed. A higher TTR through 6 months was associated with a significant reduction in **(A)** major adverse cardiac events (MACE), **(B)** cardiovascular death, **(C)** myocardial infarction (MI), and **(D)** stroke from 6 to 36 months.

Cardiovascular Risk Reduction After Renal Denervation According to Time in Therapeutic Systolic Blood Pressure Range

Felix Mahfoud, MD,[a] Giuseppe Mancia, MD, PhD,[b] Roland E. Schmieder, MD,[c] Luis Ruilope, MD, PhD,[d,e] Krzysztof Narkiewicz, MD, PhD,[f] Markus Schlaich, MD,[g] Bryan Williams, MD,[h] Flavio Ribichini, MD,[i] Joachim Weil, MD,[j] Hsien-Li Kao, MD,[k] Oriol Rodriguez-Leor, MD, PhD,[l] Elias Noory, MD,[m] Tiong Kiam Ong, MD,[n] Thierry Unterseeh, MD,[o] Pedro de Araújo Gonçalves, MD,[p] Andreas Zirlik, MD,[q] Khaled Almerri, MD,[r] Faisal Sharif, MD, PhD,[s] Lucas Lauder, MD,[a] Marianne Wanten, MS,[t] Martin Fahy, MS,[t] Michael Böhm, MD[a]



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Sicurezza della procedura di denervazione

Event	RADIANCE-HTN SOLO (n = 64)[24]	SPYRAL HTN-OFF MED (n = 166)[25]	SPYRAL HTN-ON MED (n = 38)[27]	RADIANCE-HTN TRIO (n = 69)[26]
Periprocedural (denervation day and ≤30 d after)				
Death	0	0	0	1 (1%)
Acute kidney injury	0	0	0	0
Embolic event	0	0	0	0
Femoral vascular injury	0	0	0	1 (1%)
Renal artery stenosis	0	0	0	0
Pain >2 d post procedure	8 (11%)	NR	NR	12 (17%)
Hypertensive emergency	0	0	0	0
HF hospitalization	0	0	0	0
Postprocedural (1-6 mo after denervation)				
New RAS (>50%)	0	0	0	0
Scr doubling	0	0	0	1 (1%)
Hypertensive emergency	0	1 (1%)	0	0
Heart failure hospitalization	0	0	0	0
Stroke, TIA	0	0	0	0
AMI	0	0	0	1 (1%)
Coronary intervention	0	0	0	0
Renal angioplasty/stent	0	0	0	0
New orthostasis	0	0	0	0

Abbreviations: AMI, acute myocardial infarction; NR, not reported; RAS, renal artery stenosis; Scr, serum creatinine; TIA, transient ischemic attack.

Eventi avversi negli RCT di seconda generazione

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European Society of Hypertension position paper on renal denervation 2021

- **Sulla base dei risultati di numerosi RCT-SHAM, la RDN rappresenta una opzione evidence based per il trattamento dell'ipertensione, *in aggiunta* alle modifiche dello stile di vita ed alla terapia farmacologica**
- **La RDN espande le opzioni terapeutiche a disposizione per il raggiungimento del target terapeutico.**
- **La RDN è da considerarsi una procedura sicura in base a dati disponibili di follow up.**
- **La RDN è una strategia terapeutica alternativa o additiva, non competitiva**
- **SI raccomanda di strutturare uno specifico percorso clinico alla RDN**
- **La decisione di effettuare un trattamento con RDN deve essere condivisa tenendo conto dello stadio di ipertensione, delle comorbidità e della preferenza del paziente**

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Criteri di esclusione RDN

Clinici

- **Ipertensione secondaria**
- **Filtrato glomerulare < 45 ml/min**
- **Non condivisione completa della procedura con il paziente**

Anatomici:

- **Diametri arteria renale < 3 mm->8 mm**
- **Presenza di stenosi arterie renali >50%**
- **Presenza di arterie polari di < 3 mm di calibro**
- **Importante patologia ATS a carico dell'aorta addominale sotto renale**
- **Presenza di protesi aortica sottorenale**

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Linee Guida ESH 2023 e Denervazione Renale

Recommendations and statements	CoR	LoE
RDN can be considered as a treatment option in patients with an eGFR >40 ml/min/1.73m^2 who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	IIb	B
RDN can be considered as an additional treatment option in patients with true resistant hypertension if eGFR is >40 ml/min/1.73m^2.	IIb	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
RDN should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

European Society of Hypertension position paper on renal denervation 2021
Linee Guida ESH 2023

Questioni aperte

- **Non esistono, al momento, predittori della risposta pressoria alla denervazione**
- **Non esistono markers della riuscita della procedura**
- **Non esistono RCT che confrontino le differenti tecnologie di ablazione**
- **Necessità di RCT in pazienti con comorbidità**
- **Pochi dati ancora sulla sicurezza della RDN in pazienti con GFR <45 ml/min**

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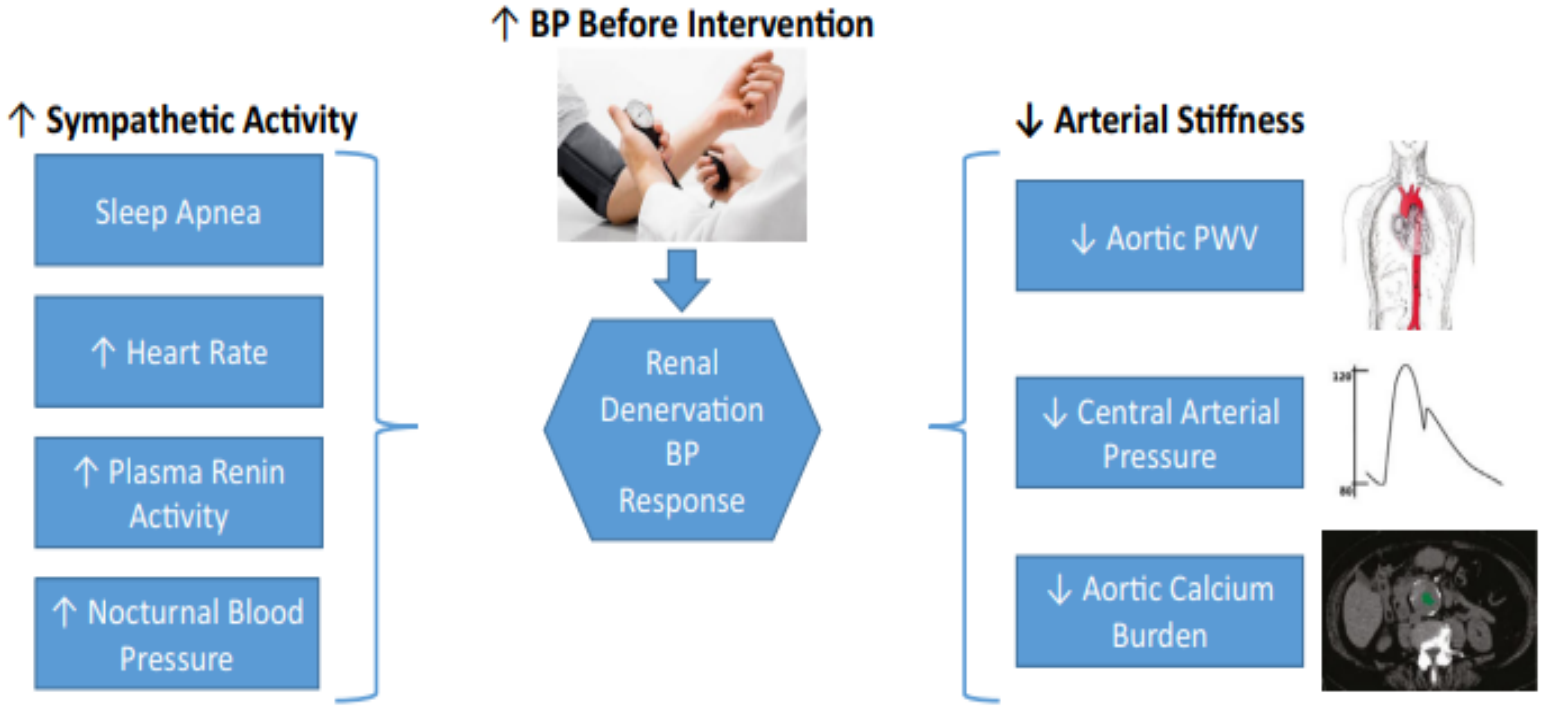
Possibili predittori di risposta clinica



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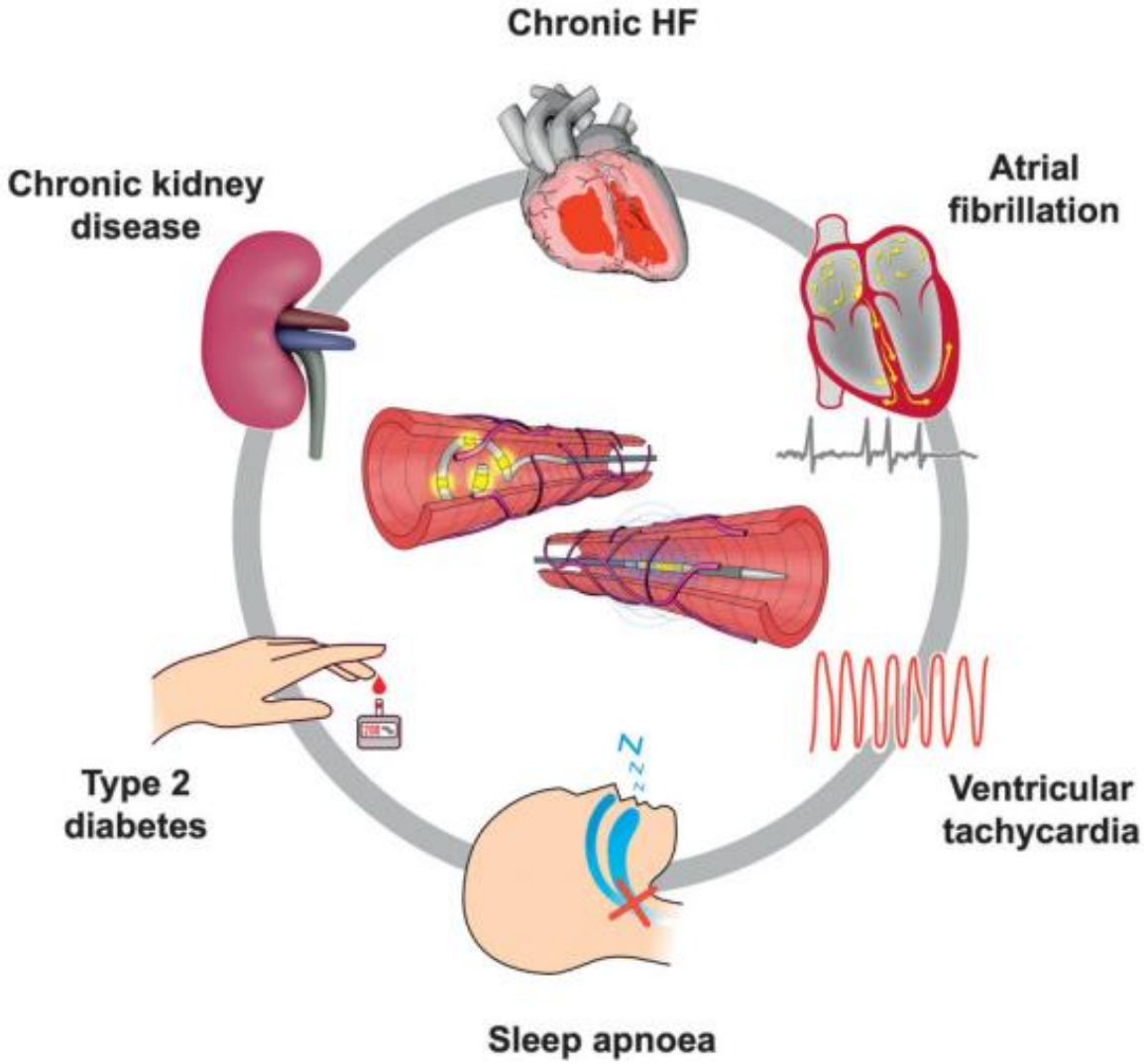
Possibili future indicazioni della denervazione renale



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PROTOCOLLO OPERATIVO

Valutazione eleggibilità del paziente iperteso

SI'

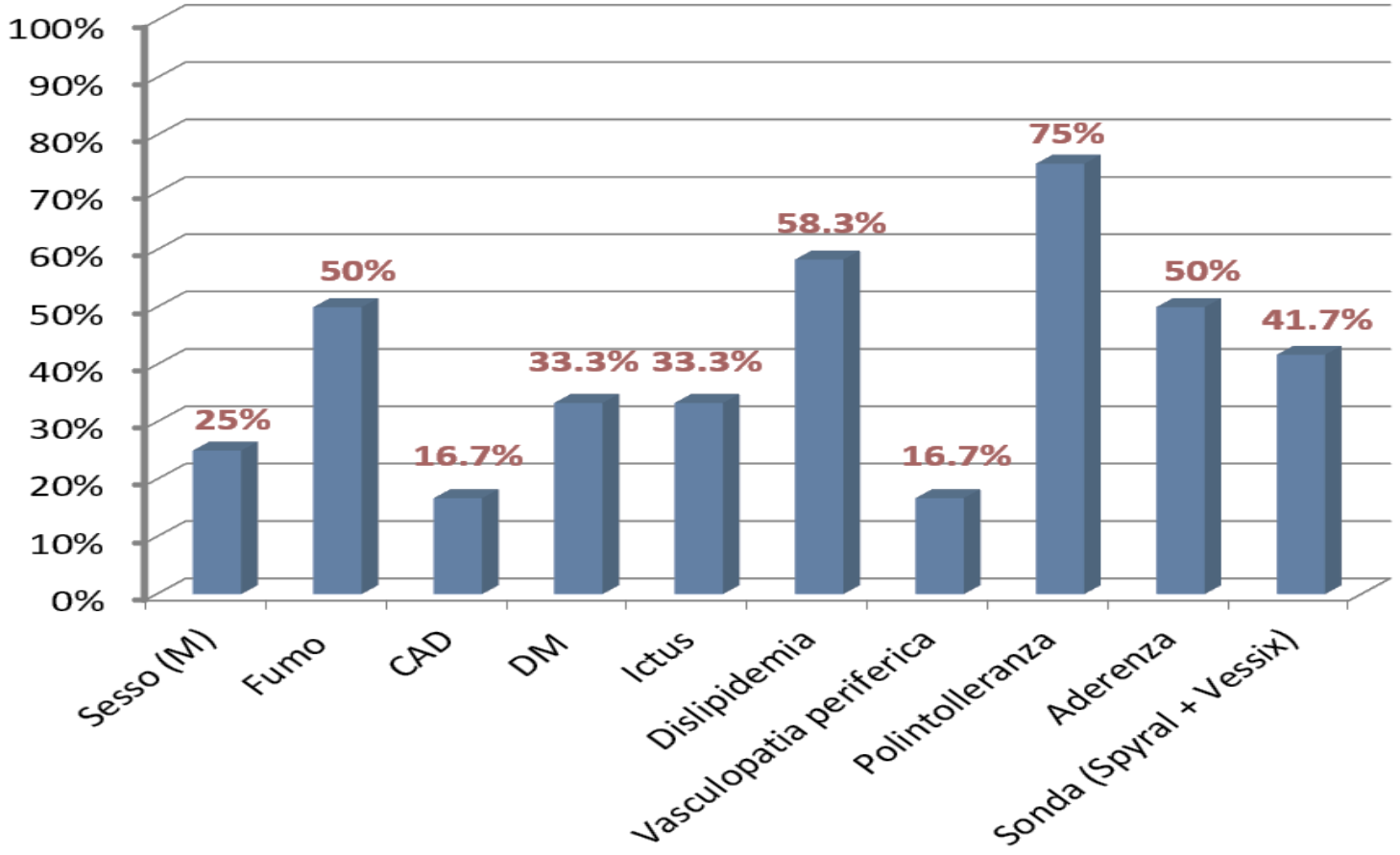
- **Resistente - Non aderente - Polintollerante** → NO
- **Ipertensione essenziale** → NO
- **GFR > 45 ml/min** → NO
- **ABPM 24 ore (PA 24 ore** >130/80) → NO
- **Consenso informato** → NO
- **ANGIO TC-** RMN renale (lunghezza e larghezza arteria renale, escludere controindicazioni anatomiche → NO
- EcocardiogrammaTT, pulse wave velocity, pressione centrale aortica, OBP (HMOD pre intervento) → NO

INTERVENTO DI DENERVAZIONE RENALE
- Radiologia interventistica/emodinamica -

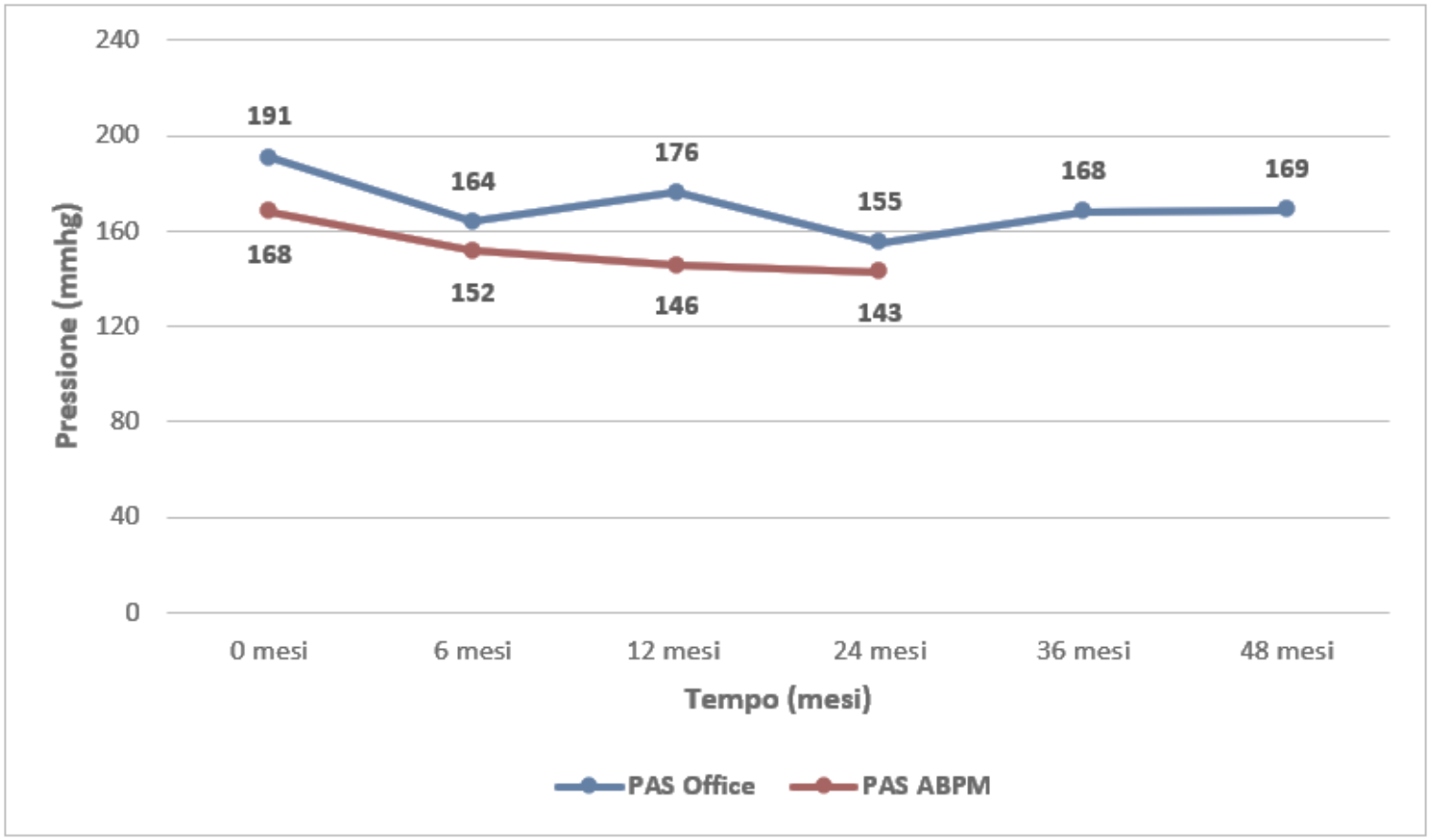
Consensus document: "European Society of Hypertension position paper on renal denervation 2021"

Caratteristiche della popolazione

N. 15 pazienti

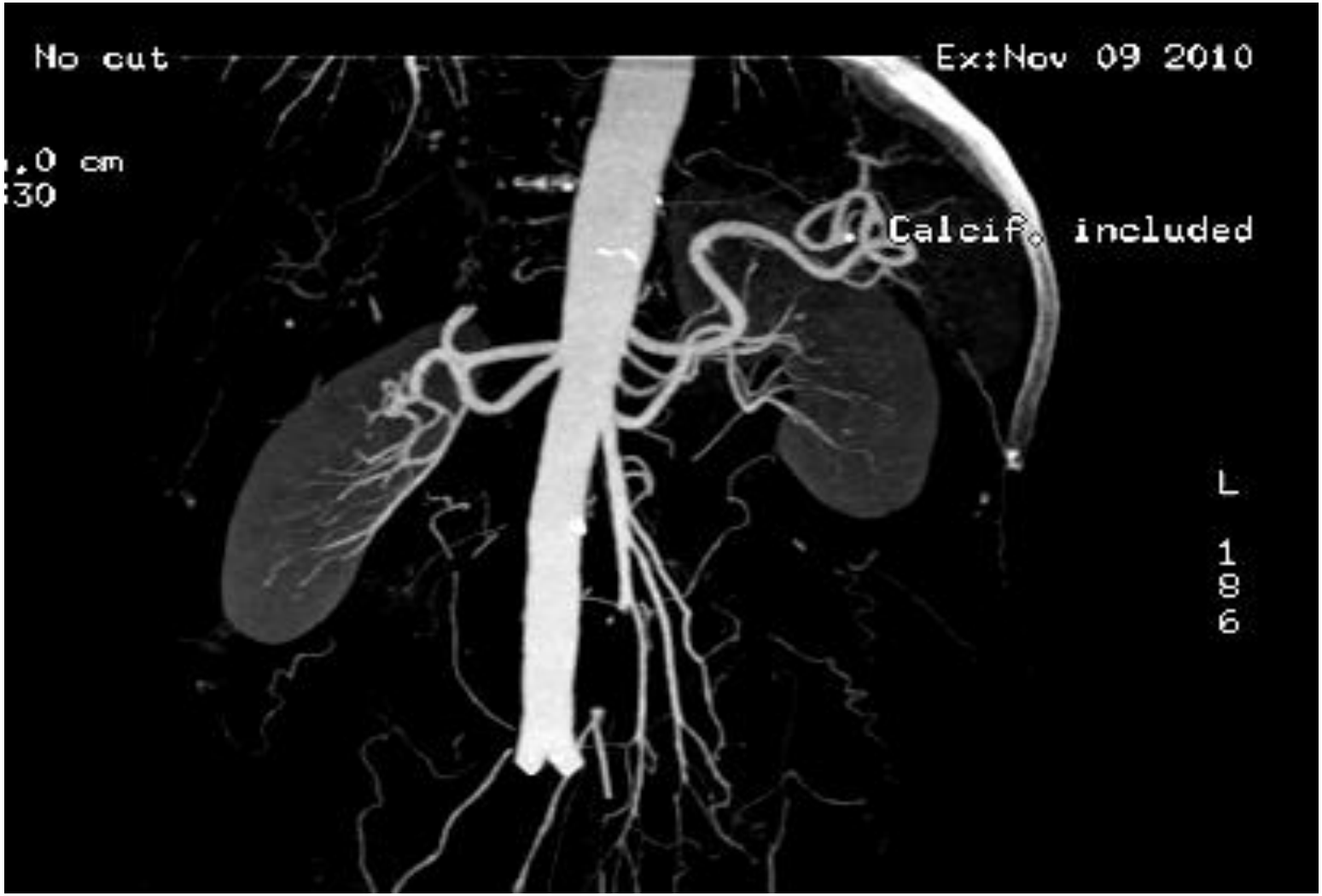


Andamento della PAS Office e ABPM nel corso di 48 mesi di follow-up:



14% PAO <140/90 mmHg

Pz. Con 3 arterie renali a sx (esclusa da denervazione)



Gruppo “resistenti”

Dr. Marco Pappaccogli

Dr.ssa Chiara Fasano

Dr.ssa Elisabetta Eula

Dr.ssa Lara Ponsa

Dr.ssa Martina Mangeruga

Dr Denis Rossato SCU Radiologia Interventistica