ACCADEMIA di ALTA FORMAZIONE CLINICA per MEDICI del TERRITORIO

MILANO | 2023

4 marzo

ICCS +

Il grande aiuto non farmacologico della denervazione renale nell'iperteso nefropatico: esempi real-life

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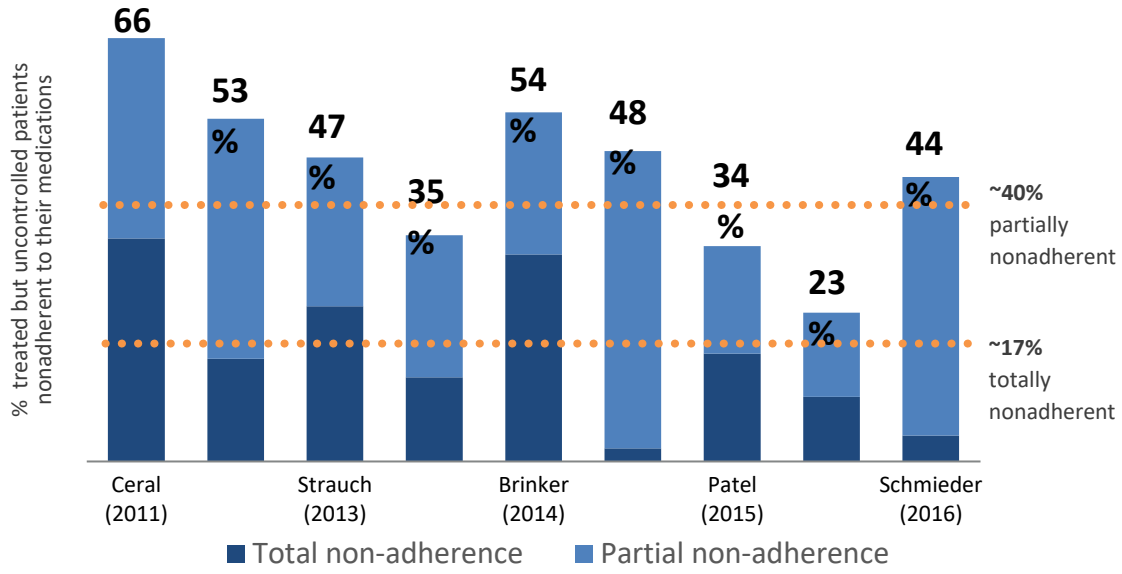
Milano

Existing treatments can fail in reaching HTN control due to non-adherence

Either unwilling or unable, studies show patients struggle to adhere to their treatment strategy



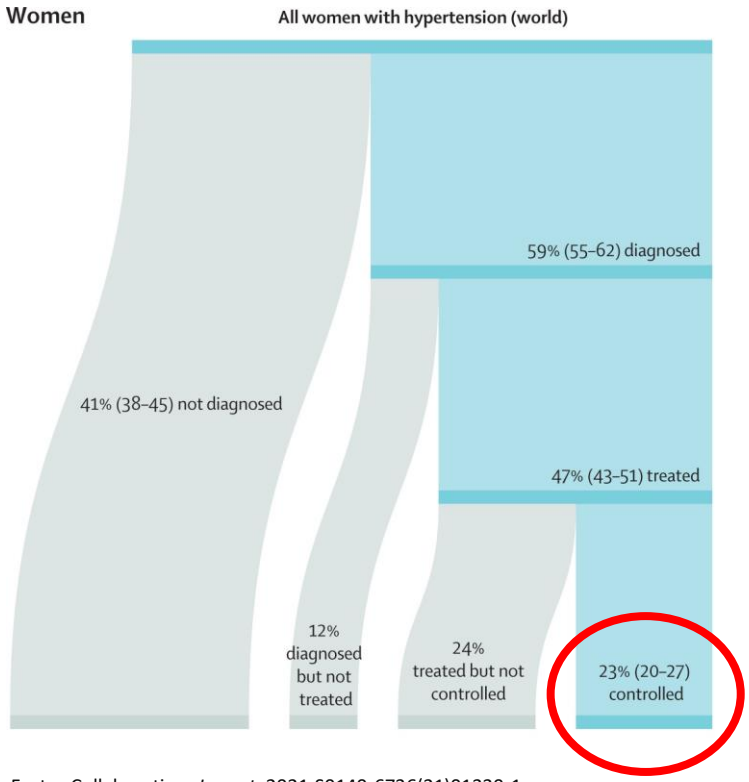
Many patients cannot tolerate polypharmacy and abandon it[2]

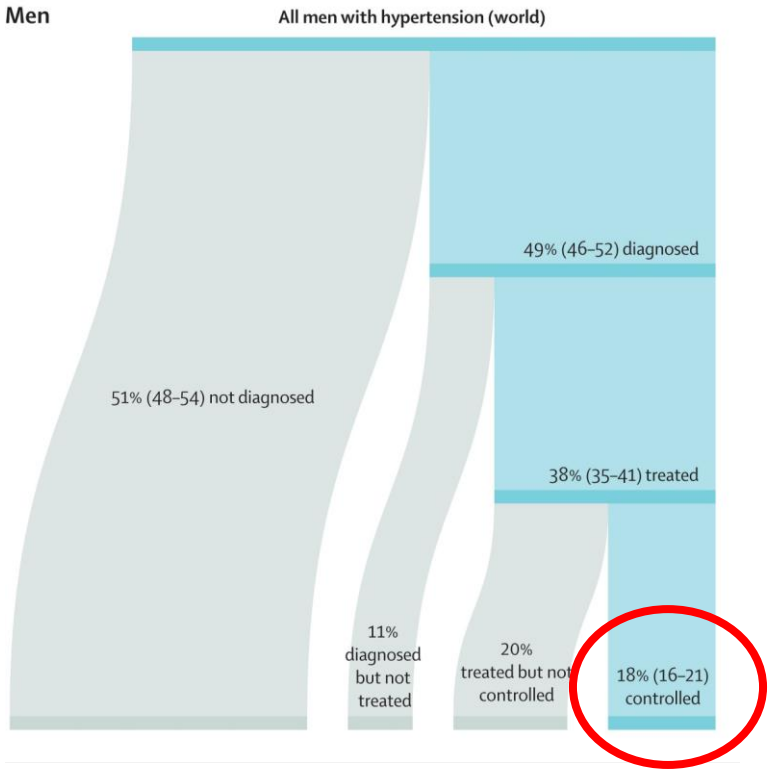
[1] Kandzari DE, et al. *Eur Heart J.* 2015;36:219-227.
[2] Berra E, et al. *Hypertension*. 2016;68:297-306.

Global Hypertension Control Rates are Low

Less Than 25% of HTN Patients are Controlled Worldwide

Hypertension Treatment Cascade in 2019

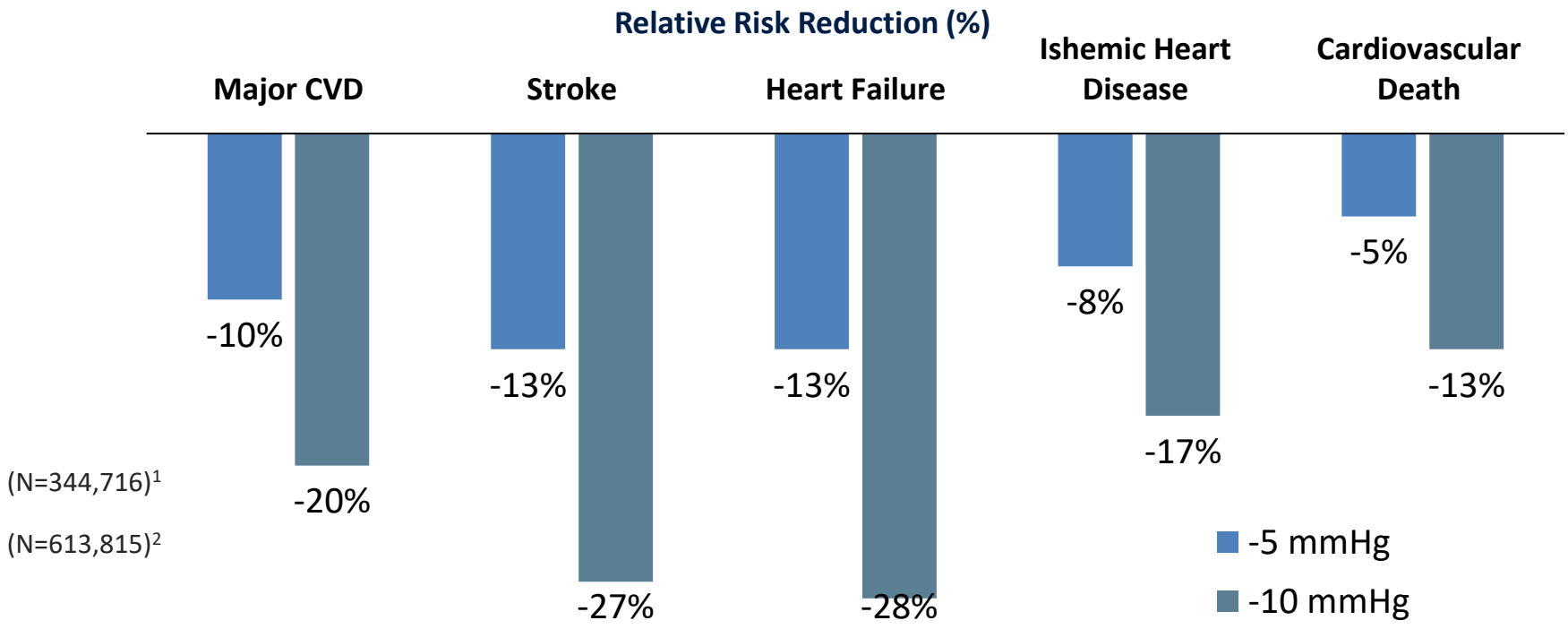




NCD Risk Factor Collaboration. *Lancet.* 2021;S0140-6736(21)01330-1

Relative Risk Reduction Proportional to Decrease in OSBP

Irrespective of Baseline BP or CVD History in 2 Meta-Analyses



[1] Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2021;397(10285):1625-36
[2] Ettehad D, et al. *Lancet*. 2016;387(10022):957-67

European Society of Hypertension position paper on renal denervation 2018

POSITION PAPER

Italian Society of Arterial Hypertension (SIIA) Position Paper on the Role of Renal Denervation in the Management of the Difficult-to-Treat Hypertensive Patient

Consensus Document

European Society of Hypertension position paper on renal denervation 2021

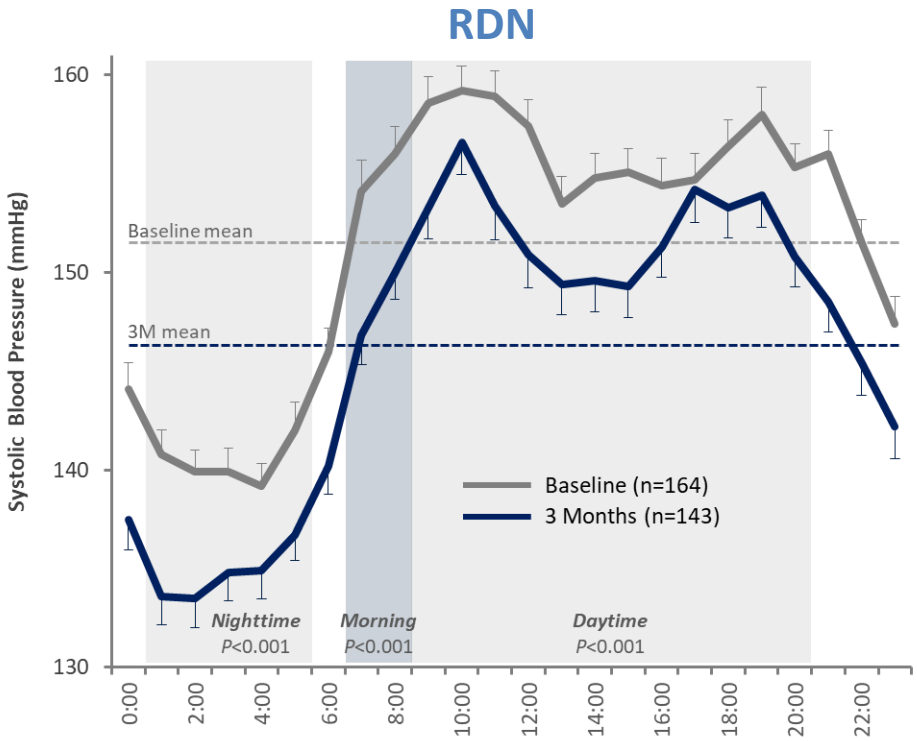
This ESH Position Paper 2021 with updated proposed recommendations was deemed necessary after the publication of a set of new pivotal sham-controlled randomized clinical trials (RCTs), which provided important information about the efficacy and safety of endovascular device-based renal denervation (RDN) for hypertension treatment. RDN is effective in reducing or interrupting the sympathetic signals to the kidneys and decreasing whole body sympathetic activity. Five independent, fully completed, sham-controlled RCTs provide conclusive evidence that RDN lowers ambulatory and office blood pressure (BP) to a significantly greater extent than sham treatment. BP-lowering efficacy is evident both in patients with and without concomitant antihypertensive medication. The average decrease of 10 mmHg in office BP is estimated to lower the incidence of cardiovascular events by 25–30%, based on meta-analyses of RCTs using pharmacological treatment. Neither peri-procedural, nor short-term or long-term adverse events or safety signals (available up to 3 years) have been observed. Implementing RDN as an innovative third option in the armamentarium of antihypertensive treatment requires a structured process that ensures the appropriate performance of the endovascular RDN procedure and adequate selection of hypertensive patients. The latter should also incorporate patients' perspective and preference that needs to be respected in a shared decision-making process.

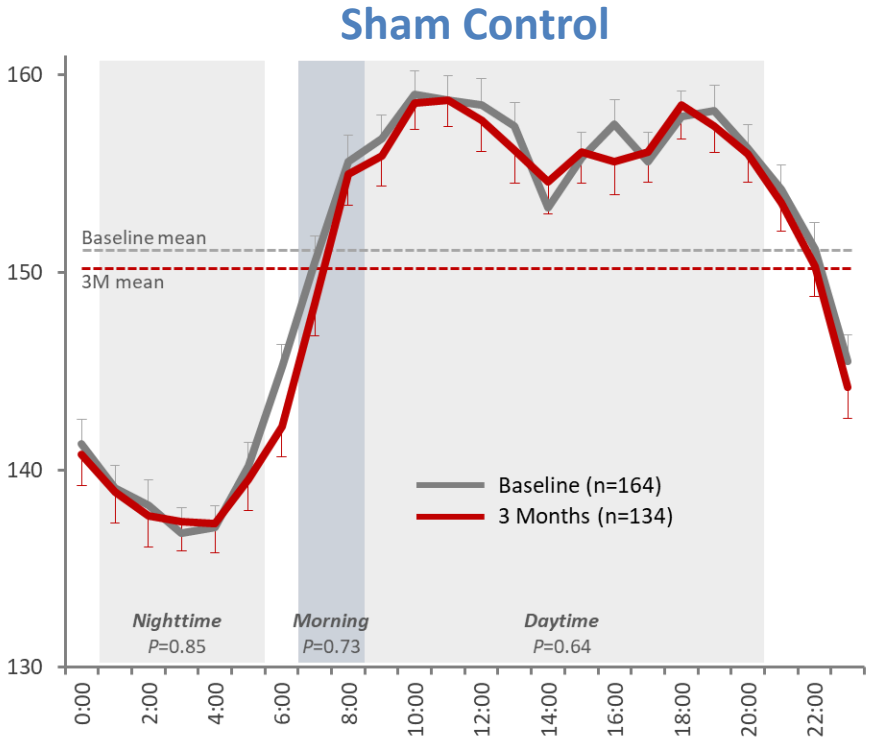
Keywords: hypertension, position paper, renal

Office BP

RDN Demonstrated "Always On" Effect on 24-hr BP Lowering[1]

24-Hr Systolic Blood Pressure in OFF MED Pivotal Trial





The nighttime / early morning period is associated with increased risk for stroke and cardiovascular events[2,3]

[1] Böhm M, et al. *Lancet*. 2020;395:1444-51 [2] Amodeo C, *Blood Pressure Monit*, 2014 [3] Boggia J, *Lancet*, 2007.

TITOLO

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)

Emanuele Barbato[1], MD, PhD; Michel Azizi[2,3], MD; Roland E. Schmieder[4], MD; Lucas Lauder[5], MD; Michael Böhm[5], MD; Sofie Brouwers[6], MD , PhD; Rosa Maria Bruno[2,7], MD, PhD; Dariusz Dudek[8], MD, PhD; Thomas Kahan[9], MD, PhD; David E. Kandzari[10], MD; Thomas F. Lüscher[11], MD; Gianfranco Parati[12], MD; Atul Pathak[13], MD, PhD; Flavio L. Ribichini[14], MD; Markus P. Schlaich[15], MD; Andrew S.P. Sharp[16], MD; Isabella Sudano[17], MD, PhD; Massimo Volpe[18], MD; Costas Tsioufis[19], MD; William Wijns[20,21], MD, PhD; Felix Mahfoud[5]*, MD, MA

2023;18-online publish-ahead-of-print February 2023

La dichiarazione di consenso clinico del consiglio ESC sull'HTN / EAPCI riconosce l'RDN come un trattamento HTN sicuro ed efficace e identifica i pazienti che possono trarne beneficio [1]

Renal Denervation in the Management of Hypertension in Adults.

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"Questo è un terzo pilastro degli approcci antipertensivi oltre alle modifiche dello stile di vita e ai farmaci per abbassare la pressione sanguigna …"
Prof. Felix Mahfoud

ESC European Society of Cardiology

EAPCI

RDN è un trattamento sicuro ed efficace per controllare la pressione arteriosa

Patient considerations

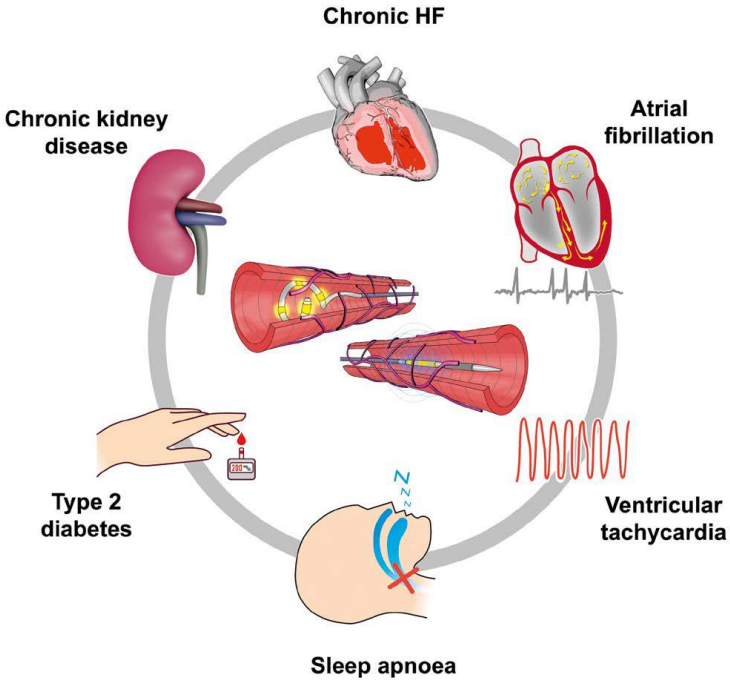
- **Ipertensione resistente non controllata** (office BP ≥140/≥90 mmHg confermata da 24-hour ABPM ≥130 mmHg or sistolica diurnal BP ≥135 mmHg) **trattato con ≥3 meds** e eGFR ≥40 ml/min/1.73 m2
- Pazienti intolleranti ai farmaci.La preferenza del paziente integrata in un processo decisionale condiviso.
- Rischio cardiovascolare globale a favore di RDN

Team Multidisciplinare

1. Mahfoud et al. ESC 2022.

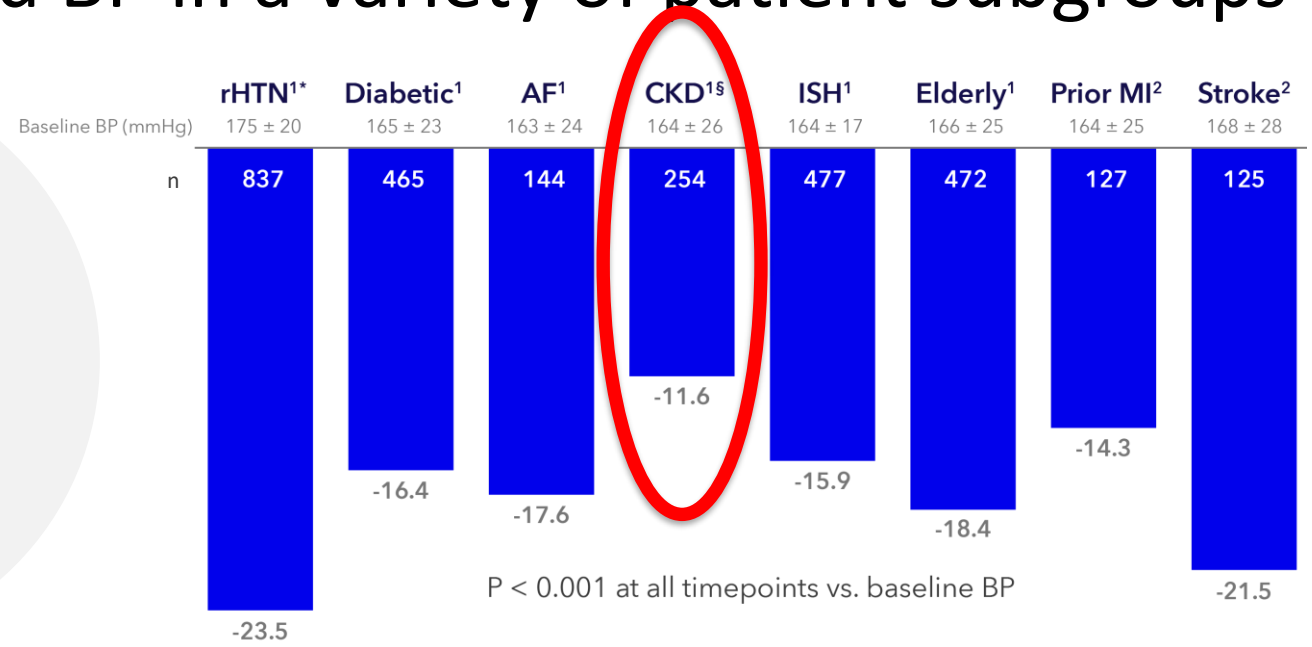
RDN

effetti secondari su altri distretti



RDN reduced BP in a variety of patient subgroups

Significant BP reductions across high-risk subgroups

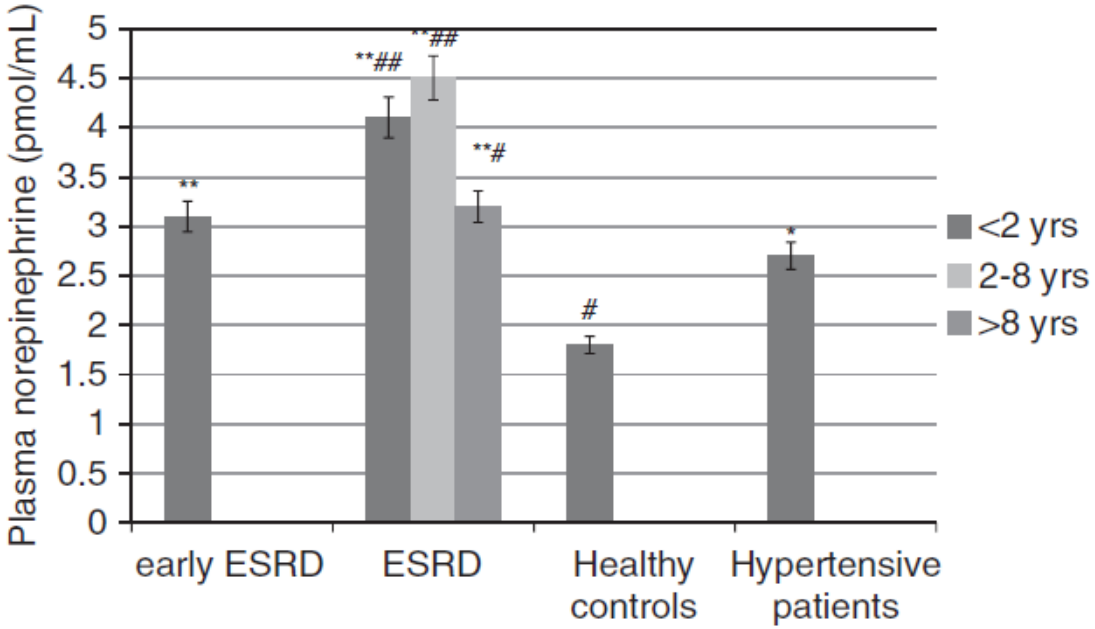


1. Mahfoud F, et al. J Am Coll Cardiol. 2020;75:2879-2888.
2. Mahfoud et al, ESH 2022.

- * Resistant hypertension defined as OSBP>150 mmHg, ≥3 anti-hypertensive medications.
- § CKD defined as eGFR <60ml/min/1.73m2

Renal Denervation in CKD Patients

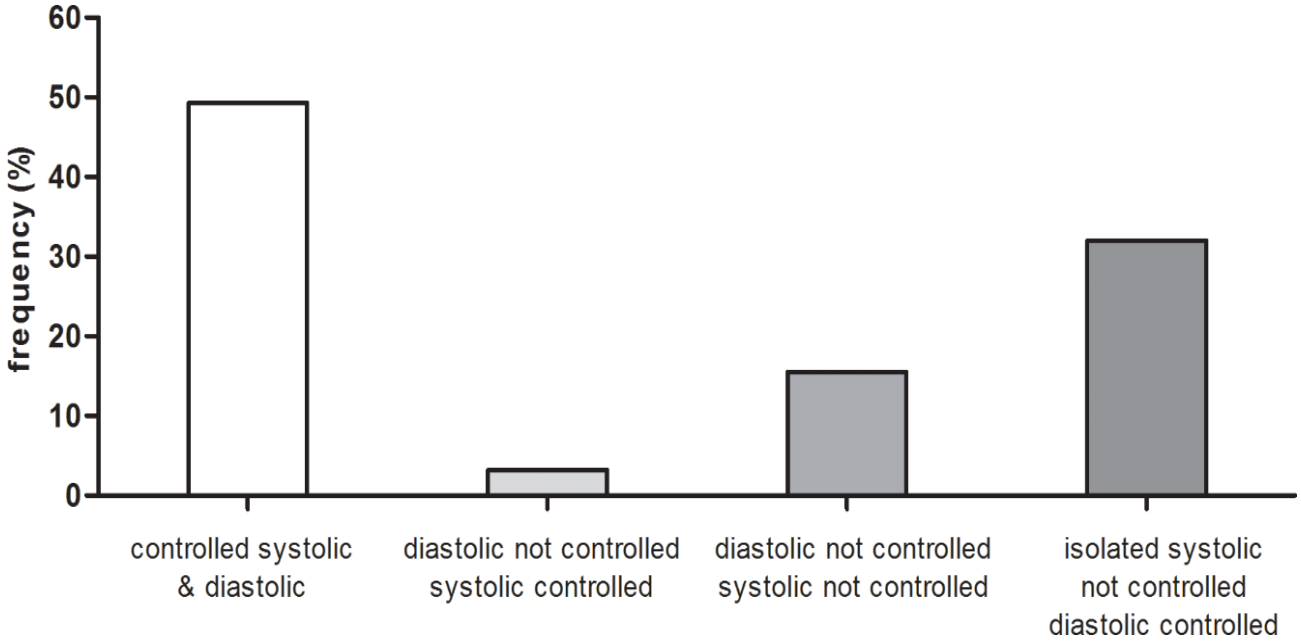
CKD is Associated with Increased Sympathetic Activity



Masuo K, et al. Hypertension Research (2010) 33, 521–528

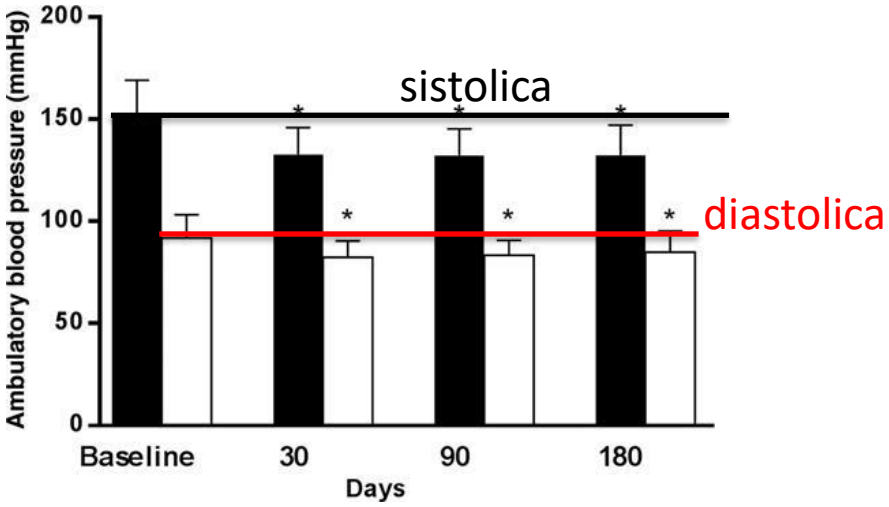
Blood Pressure Control in Chronic Kidney Disease

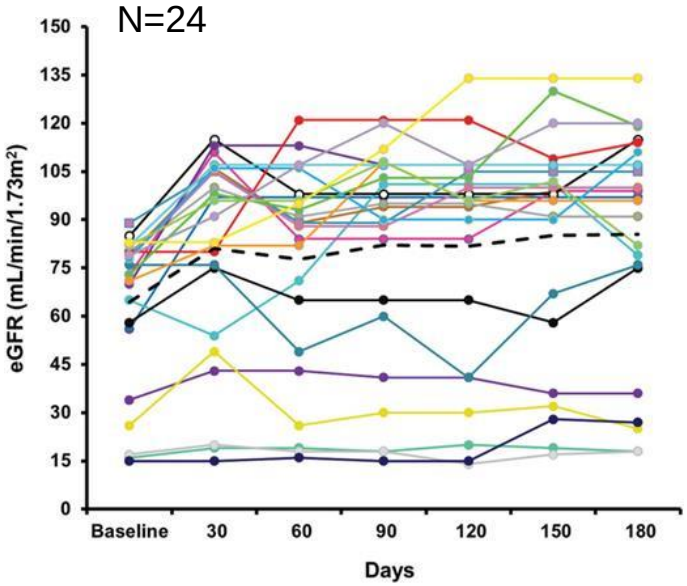
ANALYSIS FROM THE GERMAN CHRONIC KIDNEY DISEASE (GCKD) STUDY



Schnieder M, et al. PLoS One. 2018 Aug 20;13(8):e0202604.

Effects of Renal Denervation with RF Ablation on Blood Pressure and Renal Function in Patients with Chronic Kidney Disease and Resistant Hypertension

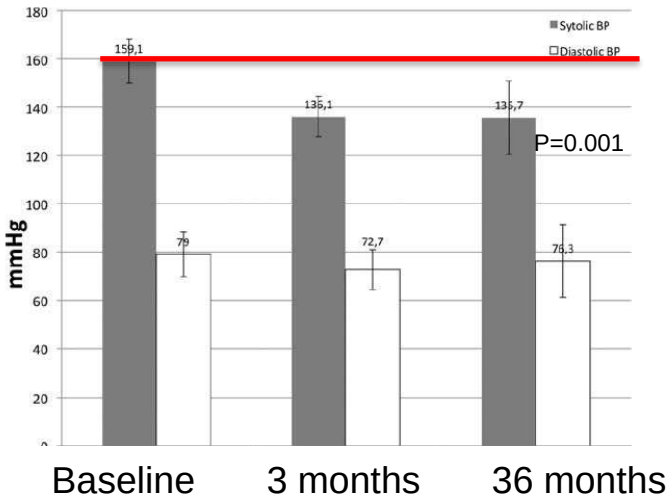




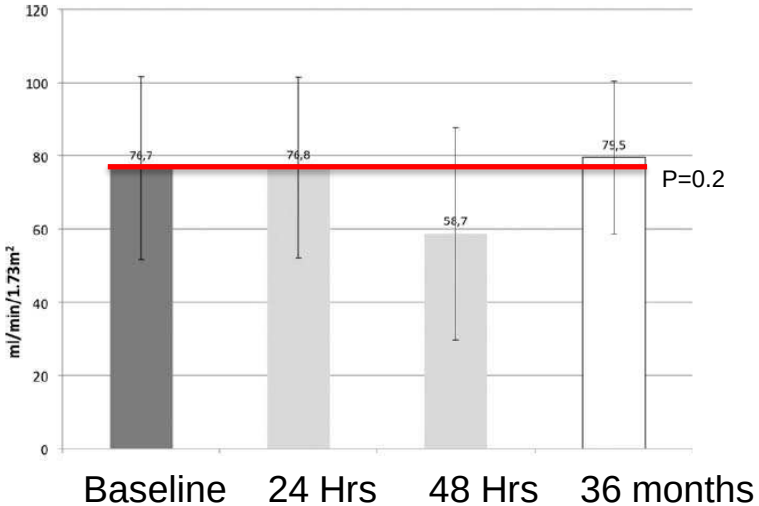
Kiuchi M, et al. Eur Heart J. 2013 Jul;34(28):2114-21.

Long-Term Verification of Functional and Structural Renal Damage After Renal Sympathetic Denervation

Systolic and Diastolic BP



eGFR



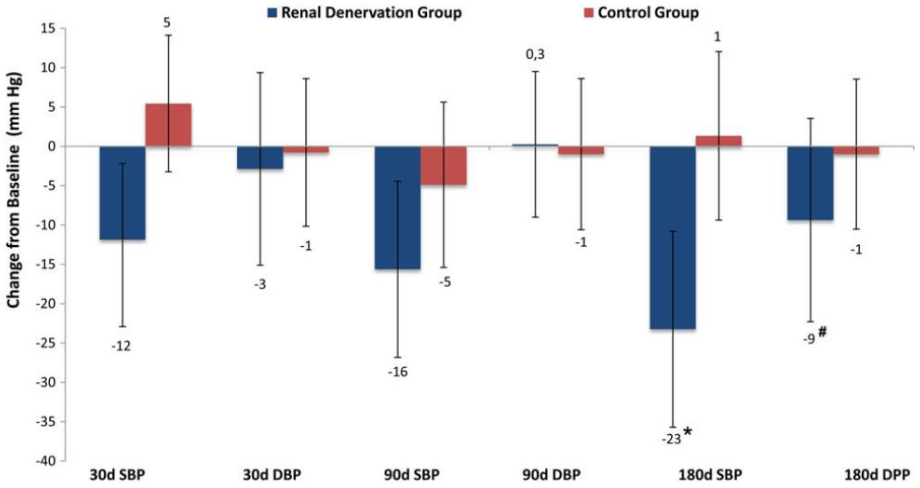
N=62 baseline, n=47 at 3 years

Dörr O, et al. Catheterization and Cardiovascular Interventions 87:1298–1303 (2016)

Impact of Sympathetic Renal Denervation: a Randomized Study in Patients after Renal Transplantation (ISAR-denerve)

	Denervation group		Control group			
	Baseline	Mean change	Baseline	Mean change	Difference in mean change (95% CI)	P-value
eGFR, mL/min/1.73 m^2	39.9 (10.5)	−2.15 (2.8)	42.0 (9.9)	−1.37 (2.8)	3.52 (−5.1–12.14)	0.39
Serum creatinine, mg/dL	1.8 (0.4)	−0.1 (0.6)	1.9 (0.5)	−0.07 (0.6)	−0.04 (−0.19–0.12)	0.62
Proteinuria, mg/dL	133.4 (226.9)	−94.6 (153.7)	73.5 (85.8)	−32.5 (62.9)	−62.1 (−180.5–56.4)	0.31

6-Month Change in 24-hr mean SBP

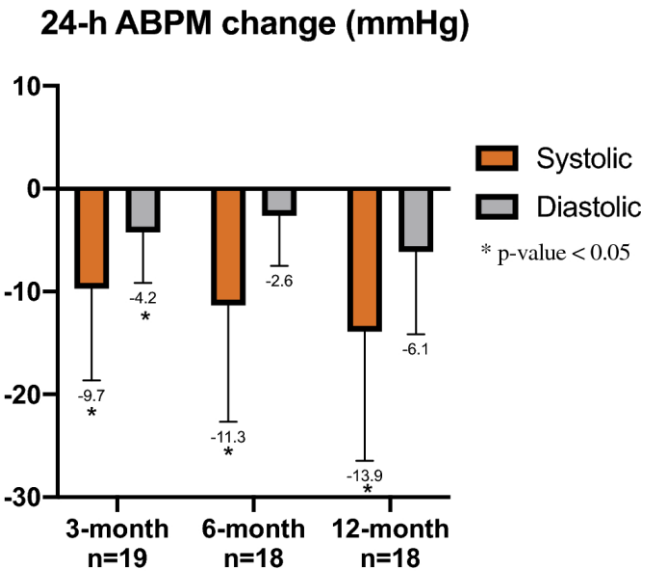


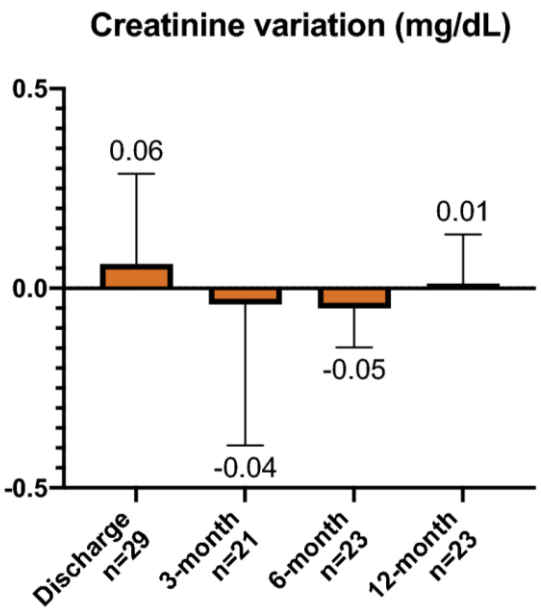
- Single Center prospective Randomized trial
- Post renal transplant hypertension
- N=8 RDN; N=9 Medical Treatment
- 6-month follow up

Schneider S, et al. Nephrol Dial Transplant (2015) 30: 1928–1936

Sicurezza ed efficacia di RDN per l'ipertensione resistente incontrollata in una popolazione ad alto rischio con malattia renale cronica.

- Baseline eGFR: 47±27 ml/min
- Baseline 24-hour mean SBP: 155±21 mmHg
- BP reduction at 1 year among patients with eGFR<45 mL/min was similar to patients with higher eGFR.

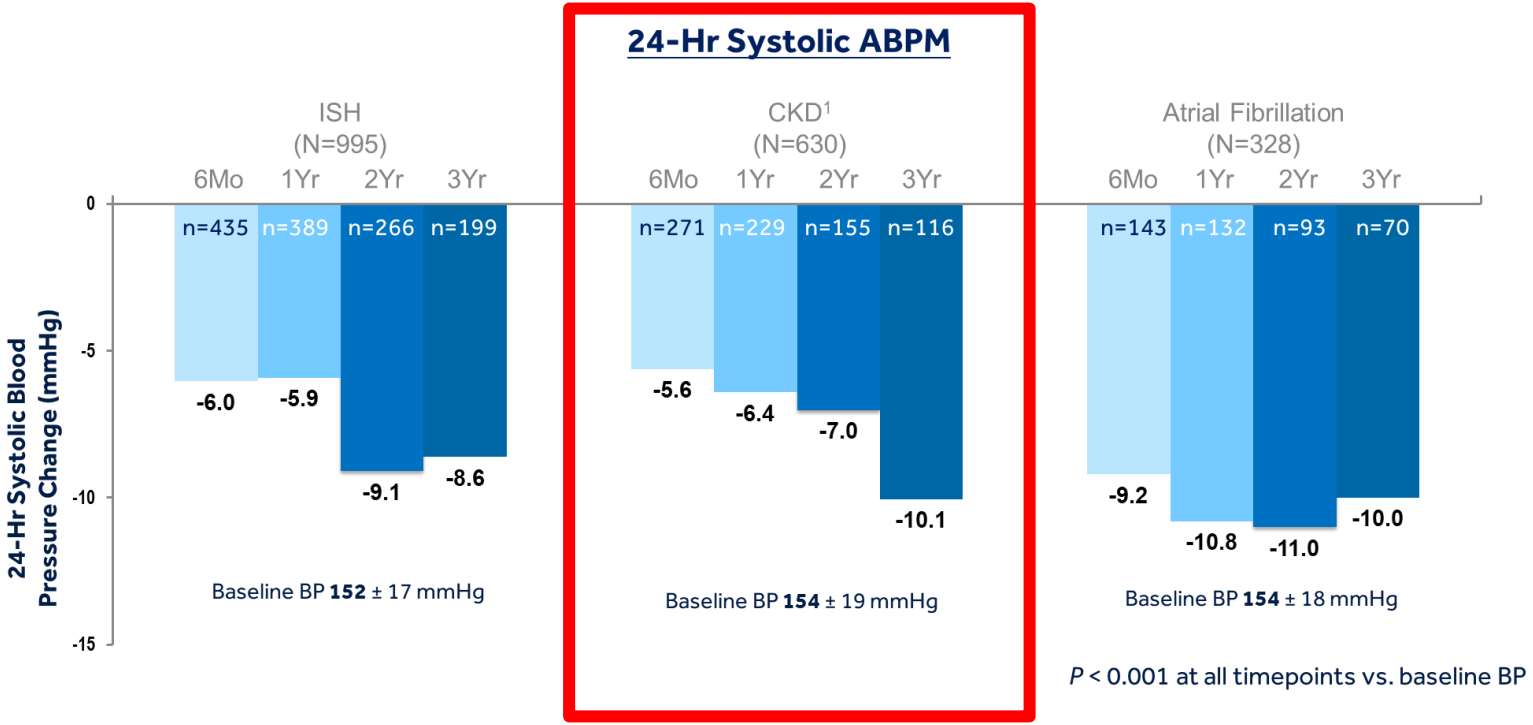




-13.9 mm Hg in 24-hour SBP – 1y

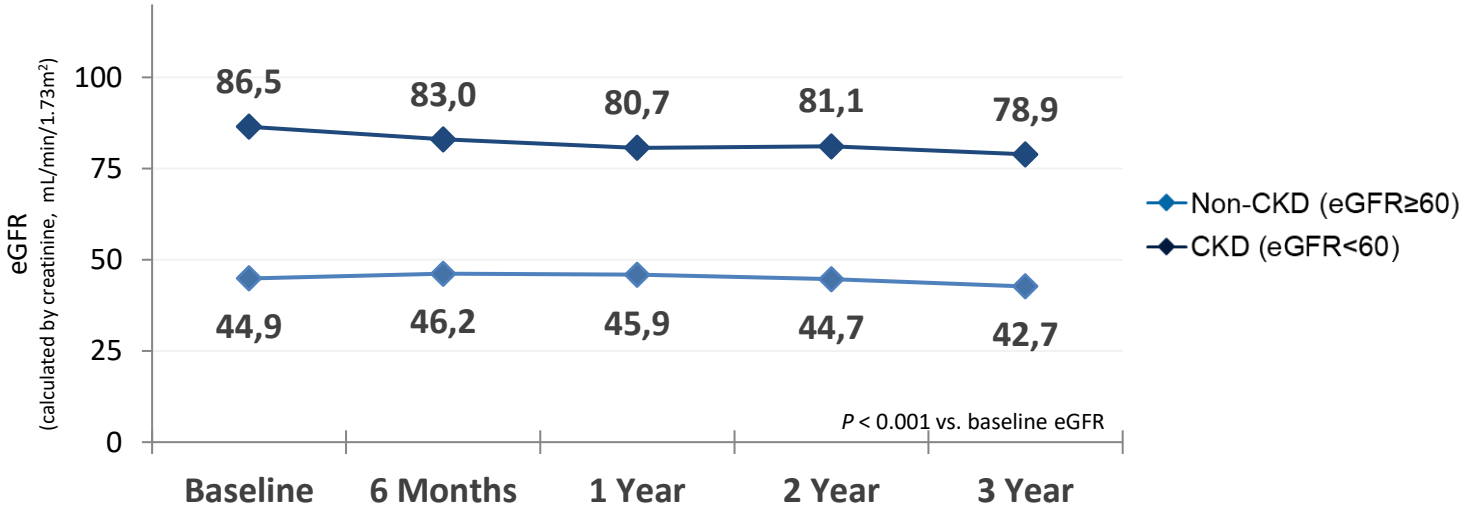
Marin F, et al., *J Nephrol*.2021 Jan 22. doi: 10.1007/s40620-021-00966-7.

Global SYMPLICITY Registry: 24-hour mean SBP drops in high-risk groups



Mahfoud F, et al. J Am Coll Cardiol. 2020;75:2879-2888.

Stable Renal Function Through 3 Yrs Even in Patients with Reduced eGFR

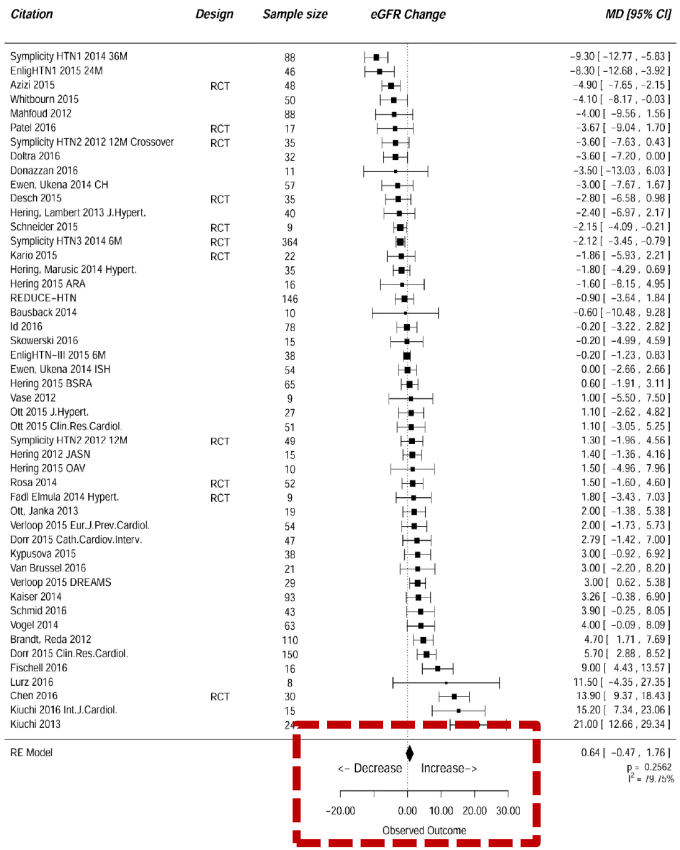


Non-CKD	**N=1,926**	**1,128**	**1,100**	**804**	**637**
CKD	**N=657**	**395**	**359**	**274**	**208**

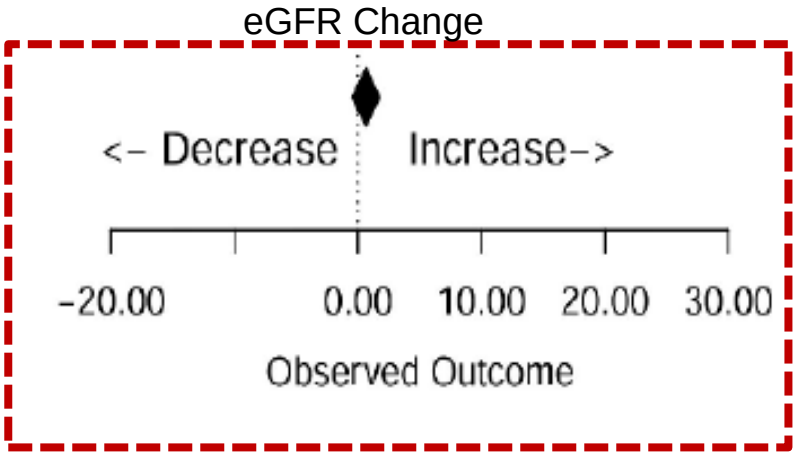
Goncalves P. PCR e-Course, 2020.

*$P < 0.001$ vs. baseline eGFR

Renal Safety of Catheter-Based Renal Denervation



META ANALYSIS OF 52 STUDIES OF RENAL DENERVATION

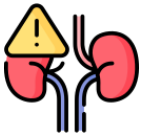


Sanders MA, *Nephrol Dial Transplant* (2017) 32: 1440–1447.

Punti chiave

- CKD è associata ad una aumentata attività simpatica e a ipertensione non controllata
- la RDN non è associata a riduzione della GFR anche nei pazienti con valori < 45 ml/min
- L'efficacia della RDN si mantiene anche in questo sottogruppo di pazienti a più alto rischio CV.

Caso Clinico: paziente Nefropatico



- Ragazzo, 21 anni – calciatore professionista.
- Diagnosi di Ipertensione Maligna.
- SBP 200 / DBP 110.
- Nefropatico grave.
- 2018: dopo 2 anni di Dialisi, entra in lista per trapianto di rene – il Ch. Vascolare curante travato il donatore ferma comunque intervento per valori pressori troppo alti.

Terapia Farmacologica:

•Ramipril 5 mg x 2
•Lacidipin 4 mg 1 x 2
•Carvedilol 6.25 mg x 2
•Furosemide 500 mg
•Spironolattone 25 mg
•Clonidine TTS2 / 7 days
•Minoxidil 5 mg

Follow up:

•Dimesso il giorno dopo procedura
•Nessun cambio della terapia farmacologica iniziale
•A 3 mesi dall'intervento va a target dei valori pressori con la stessa terapia 140/80
•A 6 mesi si stabilizza.
•Riesce a sottoporsi a trapianto 1 anno dopo.
•Agosto 2020 valori pressori a target con solo 1 Farmaco a bordo.

Conclusioni & take home messages

- Inizialmente considerata come «ultima opzione» nei pazienti con grave ipertensione

- I trial recenti e i consensus da essi derivati dimostrano come sia uno strumento efficace nel controllare meglio i valori pressori

- si affianca come terzo strumento dopo la correzione dello stile di vita e le terapie farmacologiche

- anche pazienti con GFR ridotte beneficiano della RDN senza un aggravamento della funzione renale

Grazie per l’attenzione!