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TŘETÍ INTERNÍ KLINIKA VFN 1.LFUK

KOMPLEXNÍ KARDIO VASKULÁRNÍ CENTRUM VFN Praha

INVAZÍVNÍ LÉČBA U REZISTENTNÍ HYPERTENZE

Rezistentní hypertenze

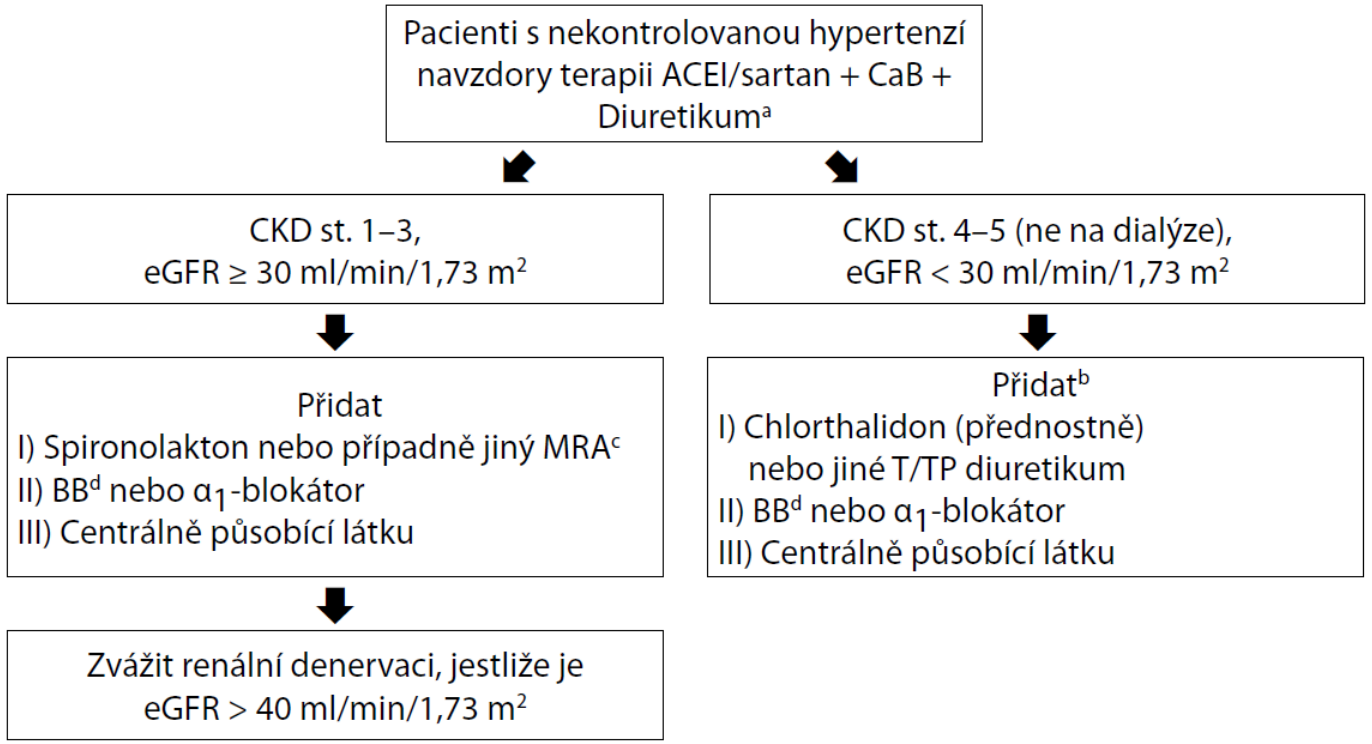
- TK >140/90 mm Hg navzdory terapii 3 antihypertenzívy (blokátor RAAS, Ca blokátor a diuretikum) v maximální tolerované dávce

Typ hypertenze	TK < 140/90 mmHg	Počet léků
kontrolovaná hypertenze	ano	1–3
nekontrolovaná hypertenze	ne	1–2
rezistentní hypertenze	ne	> 3
kontrolovaná rezistentní hypertenze	ano	≥ 4
refrakterní hypertenze	ne	> 5*

* *Při současné terapii dlouhodobě působícím thiazidovým diuretikem (chlortalidon nebo indapamid) a blokátory mineralokortikoidního receptoru (spironolakton nebo eplerenon).*

Přístupy

- **Renální denervace**
- Renovaskulární hypertenze
- Primární hyperaldosteronismus



Doporučení a stanoviska	Třída doporučení	Úroveň důkazů
RDN může být zvážena jako terapeutická možnost u pacientů s eGFR > 40 ml/min/1,73m², u nichž se nedaří kompenzovat TK antihypertenzní terapií nebo je léčba doprovázena závažnými vedlejšími příznaky nebo zhoršením kvality života	II	B
RDN může být zvážena jako dodatečná léčebná možnost u pacientů s rezistentní hypertenzí a eGFR > 40 ml/min/1,73m²	II	B
Výběr pacientů by měl být prováděn na základě sdíleného rozhodovacího procesu po poskytnutí kompletních informací pacientovi	I	C
RDN by měla být prováděna jen ve specializovaných centrech s dostatečnou zkušeností za účelem zajištění správného výběru vhodných pacientů a provedení vlastního denervačního výkonu	I	C

- Antihypertenzní efekt
- Výběr pacientů
- Požadavky na centrum

Renální denervace

Main indications (2022 ESC/EAPCI clinical consensus statement & 2023 ESH hypertension guidelines):
– Uncontrolled hypertension confirmed by ABPM
– ≥3 antihypertensives or <3 drugs, if treatment elicits serious side effects
– eGFR ≥40 ml/min/1.73 m²

Centre qualifications:
– Multidisciplinary hypertension team including hypertension specialists & specifically trained interventionalists

FDA-approved systems:

Paradise (US, 7 Fr, CE-marked)

Symplicity Spyral (RF, 6 Fr, CE-marked)

Catheter systems under investigation:

Netrod (RF, 8 Fr, CE-marked)

Iberis (RF, 6 Fr, CE-marked)

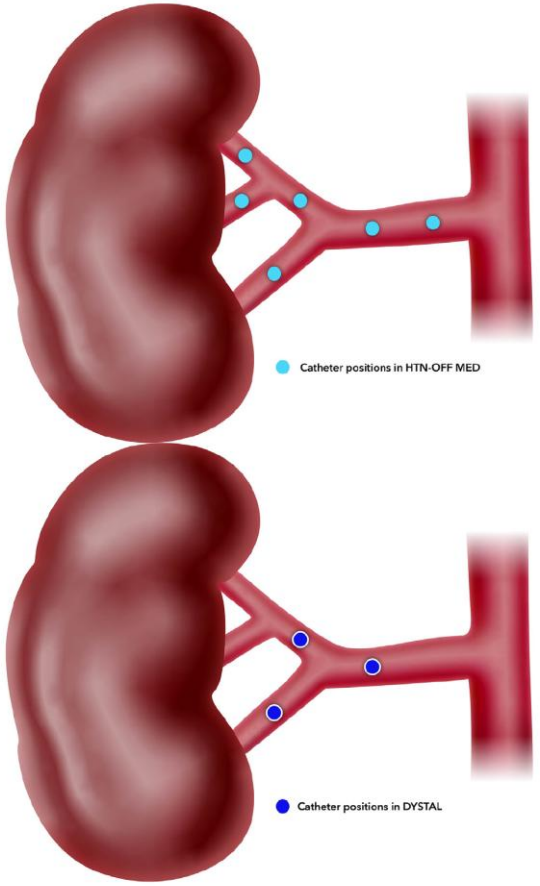
SyMapCath (mapping & RF, 6-7 Fr, not CE-marked)

Peregrine (alcohol-mediated, 7 Fr, CE-marked)

Procedural considerations:
– Safe arterial access & closure (e.g., US-guided puncture, use of closure devices)
– Adequate analgesia & sedation
– Start treatment distally and then move proximally
– Standard operating procedures (SOPs) are needed for each device

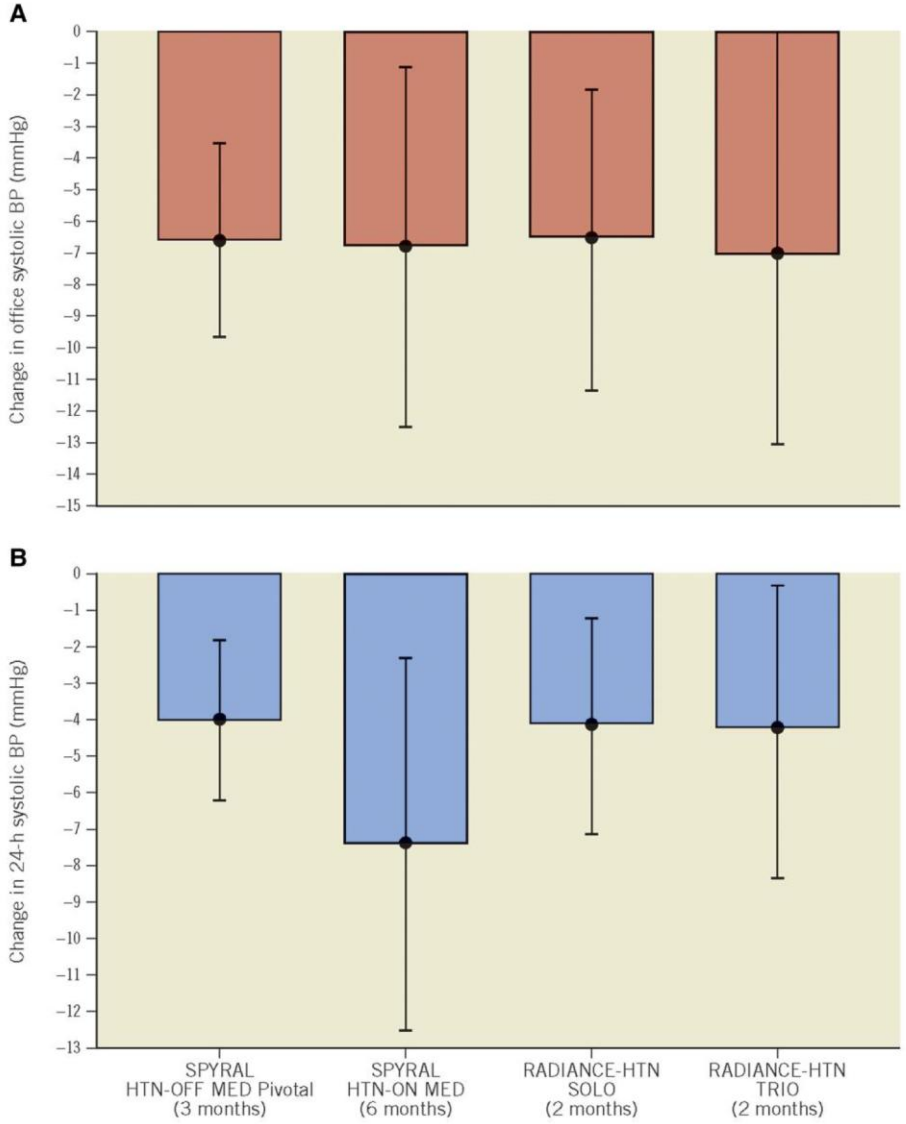
Lauder L et al. EuroIntervention 2024;20:e467-e478.

Kompletní vs. částečná denervace



Sharp ASP et al. Cardiovasc Revasc Med 2024.

Antihypertenzní efekt – krátkodobý efekt



Barbato E, et al. Eur Heart J 2023;44:1313-1330.

Antihypertenzní efekt – dlouhodobý efekt I

SPYRAL On Med – 80 pacientů (36 měsíců)

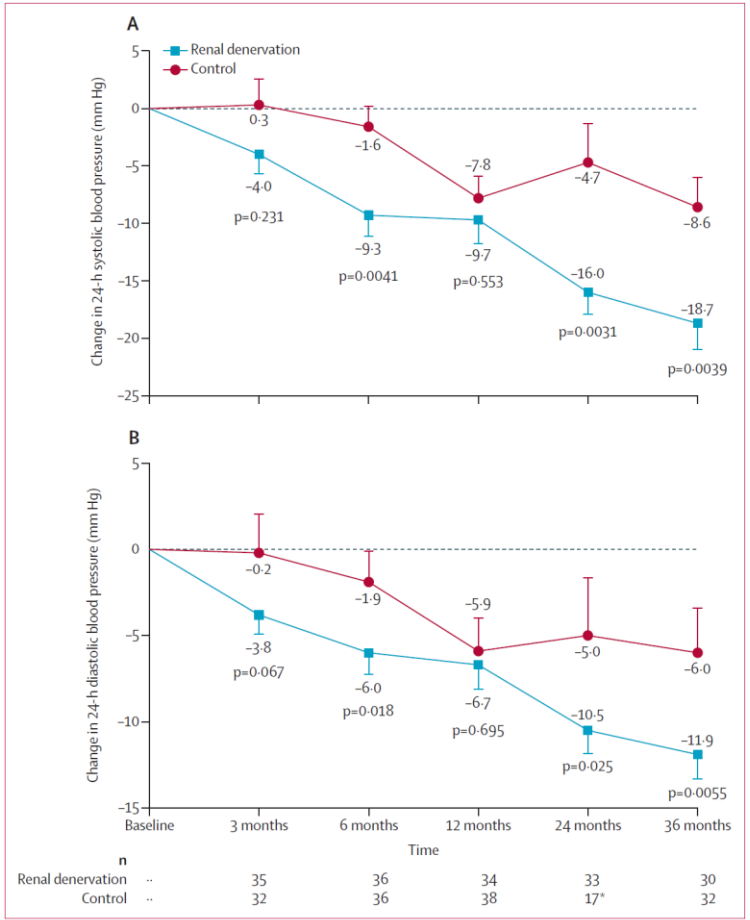


Figure 1: **Change in 24-h systolic blood pressure (A) and diastolic blood pressure (B) from baseline up to 36 months**

Mean sham control measurements at 36 months include 13 imputed crossover patients' blood pressure values from the most recent measurements before the renal denervation procedure. Error bars represent the SE. *Only safety event follow-up was originally required for patients in the sham control group after 12 months, and not all patients reconsented before 24-month follow-up.

	Renal denervation group	Sham control group	p value*
Baseline	2·13 (1·40)†	1·98 (1·14)‡	0·59
3 months	1·84 (1·37)†	2·05 (1·10)‡	0·044
6 months	2·13 (1·40)†	2·21 (1·05)‡	0·17
12 months	2·53 (0·89)†	2·81 (0·99)‡	0·09
24 months	2·97 (1·21)§	2·95 (1·16)¶	0·74
36 months	3·03 (1·20)‖	3·05 (1·43)**	0·76

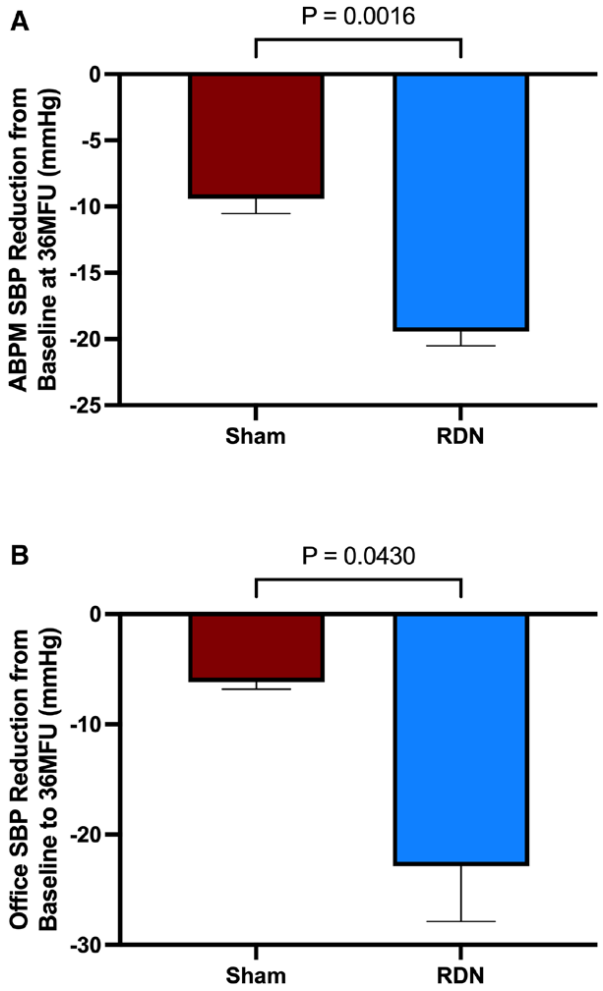
Data are mean (SD), unless otherwise indicated. *From ANCOVA. †n=38. ‡n=42. §n=36. ¶n=41. ‖n=35. **n=39.

***Table 2:* Number of antihypertensive medications from baseline to 36 months**

Mahfoud F, et al. Lancet 2022;399:1401-1410.

Antihypertenzní efekt – dlouhodobý efekt II

Metaanalýza 4 studií – doba sledování až 9 let



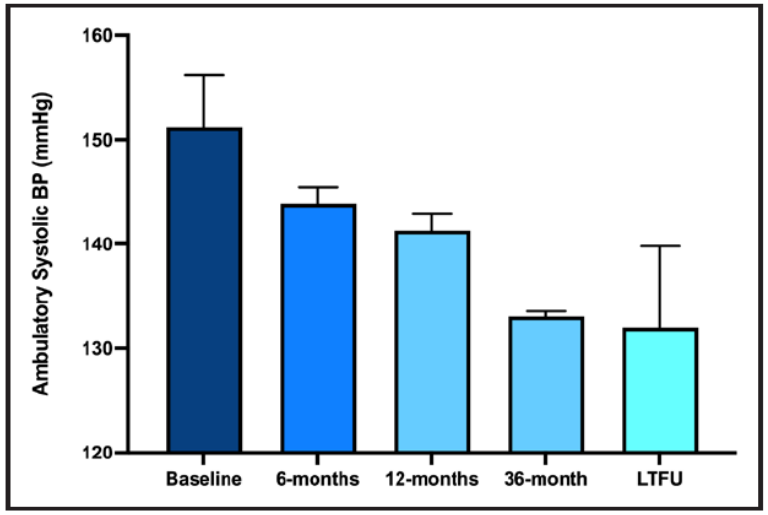


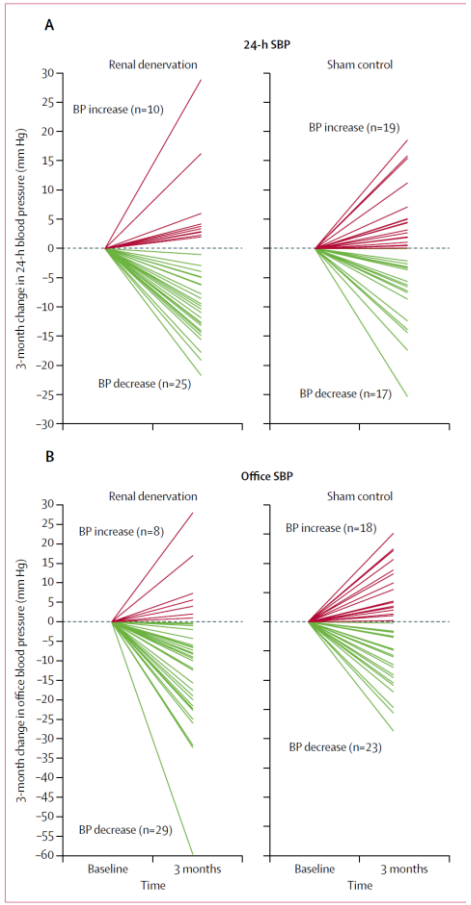
Figure 3. Pooled data from available active participants across available time points from Bhatt et al[7] and Mahfoud et al[8] from baseline to 36 months.

Long-term follow-up (LTFU) and baseline data are collected and pooled from Sesa-Ashton et al,[12] Vogt et al,[13] Al Ghorani et al,[14] and Zeijin et al[16] at LTFU. One-way ANOVA indicated significant trend across time points (P=0.0015). BP indicates blood pressure.

Sesa-Ashton G, et al. Hypertension 2024.

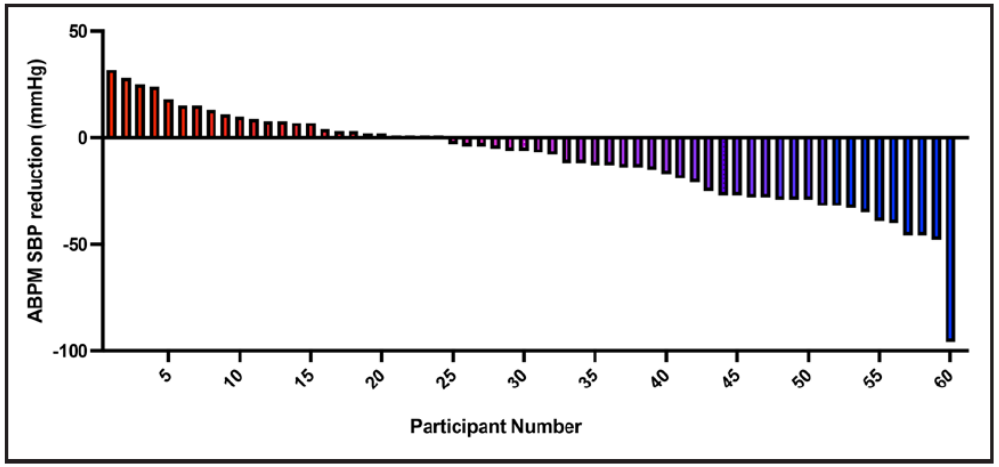
Predikce efektu?

SPYRAL OFF MED



Sesa-Ashton G, et al. Hypertension 2023;80:811-819.

Dlouhodobá data z Austrálie

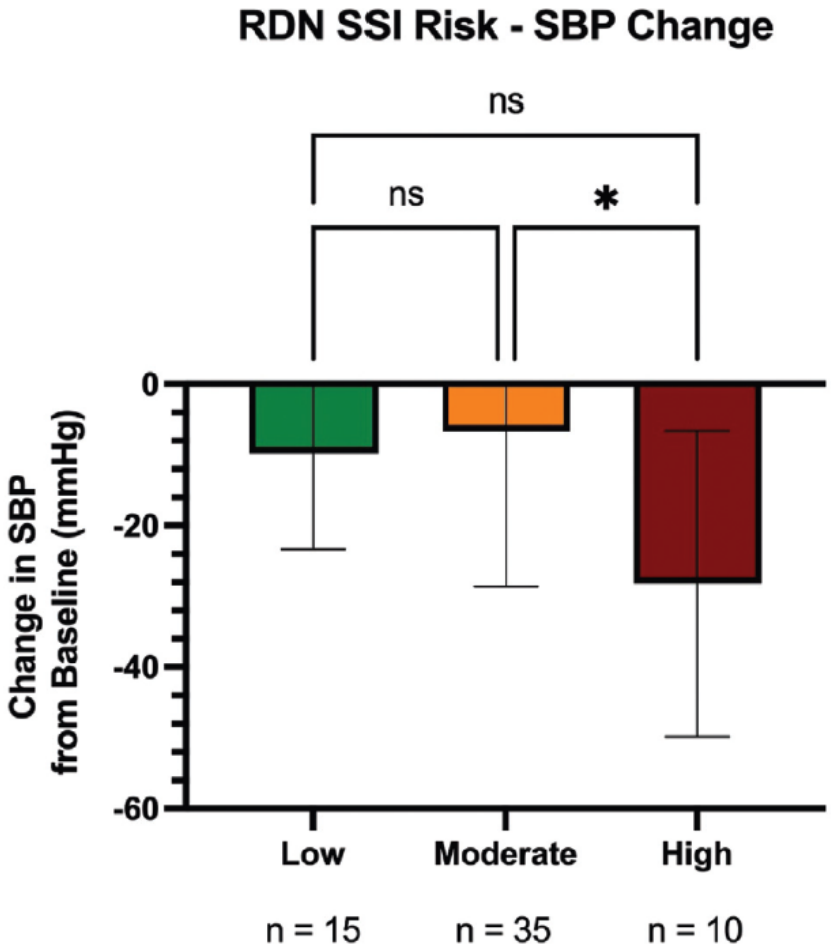


Sesa-Ashton G, et al. Hypertension 2023;80:811-819.

Prediktor efektu I

Salt Sensitivity Risk (Castiglioni et al, Hypertension 2012):

- nízký: SF ≤ 70/min + dipper pro MAP
- vysoký: SF > 70/min + nondipper pro MAP



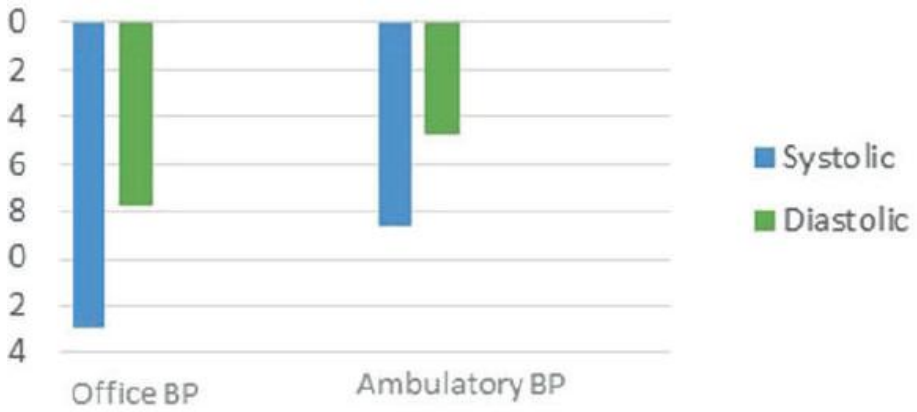
Sesa-Ashton G, et al. J Hypertens 2024;42:922-927.

Prediktor efektu II

Obsah Na v kůži

Sodium-MRI prior to radiofrequency based renal denervation (RDN) was performed

Change of 24-h ambulatory and office blood pressure (BP) 6 months after RDN (mmHg)



Univariate analysis of responders versus non-responders at 6 months based on the median of the change of 24-h systolic ABP

	Baseline		
	Responder (n= 27)	Non-Responder (n= 26)	P-value*
Baseline characteristics			
Gender (m/f)	17/10	23/3	**0.027**
Na-MRI			
Sodium in skin (AU)	19.7±3.3	22.2±5.1	**0.040**
Baseline ABP			
Nighttime heart rate (bpm)	65.3±12.8	58.9±8.0	**0.047**
Laboratory values			
LDL-cholesterol (mg/dl)	150.6±39.1	114.7±37.0	**<0.001**
Antihypertensive medication			
Aldosterone-antagonist, n (%)	7 (25.9)	1 (3.8)	**0.032**

*p = adjusted for baseline 24-h systolic BP

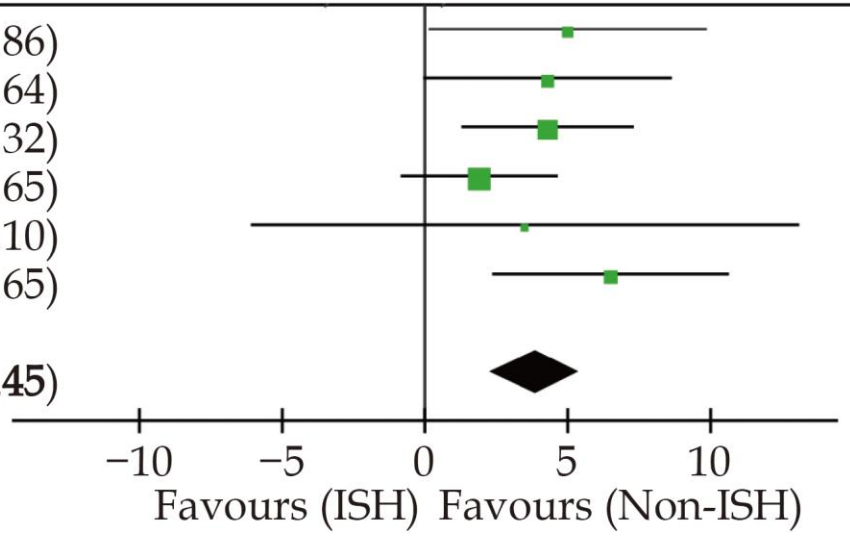
Guenes-Altan M et al. Hypertens Res 2024;47:361-371.

Výraznější efekt u systolicko-diastolické hypertenze ve srovnání s izolovanou systolickou hypertenzí

Study or Subgroup	ISH Mean	ISH SD	ISH Total	Non-ISH Mean	Non-ISH SD	Non-ISH Total	Weight	Mean difference IV, Fixed, 95% CI
Ewen, *et al.*[15]	−8	8	63	−13	18	63	10.4%	5.00 (0.14−9.86)
Fengler, *et al.*[16]	−5	11.5	40	−9.3	10.5	69	13.1%	4.30 (−0.04−8.64)
Mahfoud, *et al.*[17]	−4	12.2	125	−8.3	16.3	225	27.0%	4.30 (1.28−7.32)
Mahfoud, *et al.*[17]	−7.3	17.9	288	−9.2	17.9	373	32.5%	1.90 (−0.85−4.65)
Chernin, *et al.*[18]	−5	11.6	20	−8.5	18.1	19	2.7%	3.50 (−6.10−13.10)
Fengler, *et al.*[19]	−5.3	11.7	61	−11.8	11.5	59	14.3%	6.50 (2.35−10.65)
Total (95% CI)			**597**			**808**	**100.0%**	**3.89 (2.32−5.45)**

Heterogeneity: Chi² = 3.84, df = 5 (P = 0.57); I^2 = 0

Test for overall effect: Z = 4.85 (P < 0.00001)



Li L, et al. J Geriatr Cardiol 2023;20:121-129.

Výběr pacientů

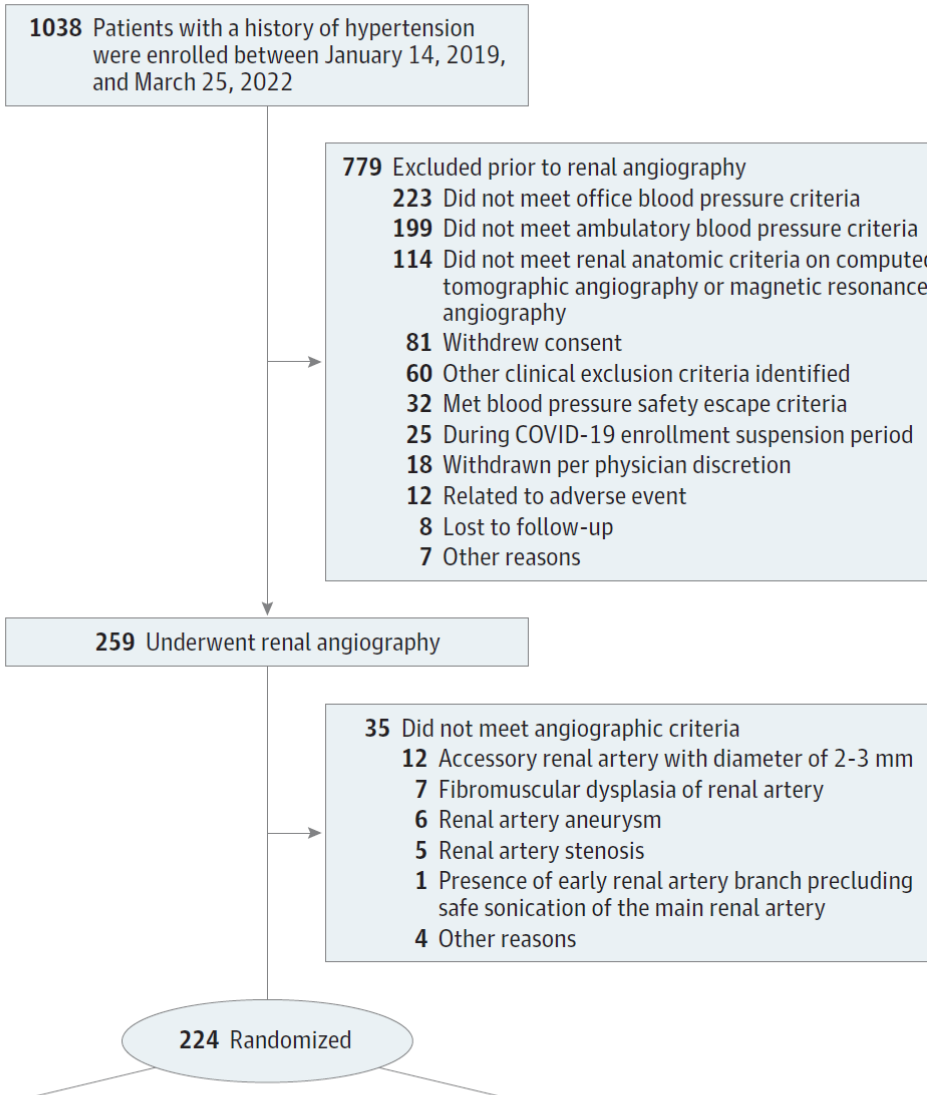
SPYRAL ON MED

Methods This randomised, single-blind, sham-controlled trial enrolled patients from 25 clinical centres in the USA, Germany, Japan, the UK, Australia, Austria, and Greece, with uncontrolled hypertension and office systolic blood pressure between 150 mm Hg and 180 mm Hg and diastolic blood pressure of 90 mm Hg or higher. Eligible patients had to have 24-h ambulatory systolic blood pressure between 140 mm Hg and less than 170 mm Hg, while taking one to three antihypertensive drugs with stable doses for at least 6 weeks. Patients underwent renal angiography and were randomly assigned (1:1) to radiofrequency renal denervation or a sham control procedure. Patients and physicians were unmasked after 12-month follow-up and sham control patients could cross over after 12-month follow-up completion. The primary endpoint was the treatment difference in mean 24-h systolic blood pressure at 6 months between the renal denervation group and the sham control group. Statistical analyses were done on the intention-to-treat population. Long-term efficacy was assessed using ambulatory and office blood pressure measurements up to 36 months. Drug surveillance was used to assess medication use. Safety events were assessed up to 36 months. This trial is registered with ClinicalTrials.gov, NCT02439775; prospectively, an additional 260 patients are currently being randomly assigned as part of the SPYRAL HTN-ON MED Expansion trial.

Findings Between July 22, 2015, and June 14, 2017, among 467 enrolled patients, 80 patients fulfilled the qualifying criteria and were randomly assigned to undergo renal denervation (n=38) or a sham control procedure (n=42). Mean

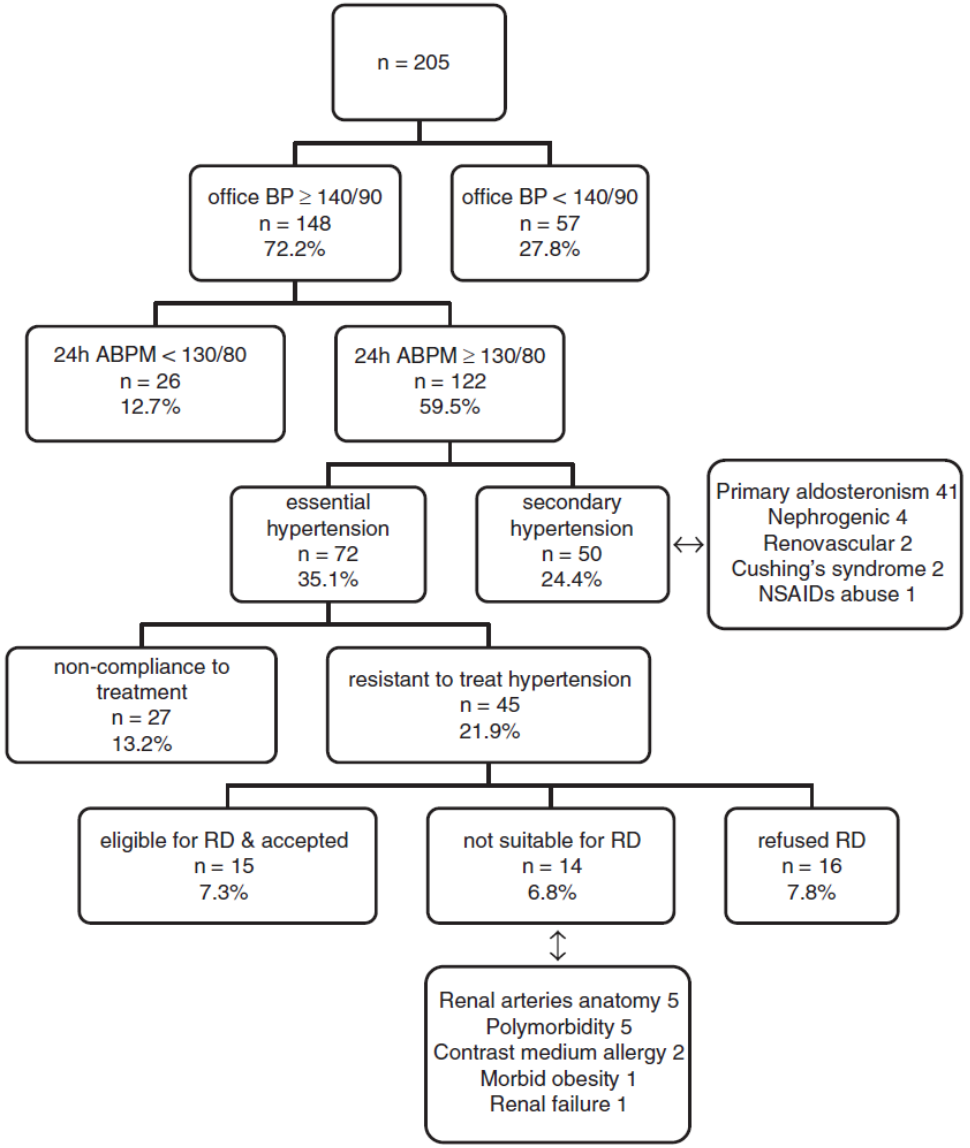
Mahfoud F, et al. Lancet 2022;399:1401-1410.

RADIANCE



Azizi M et al. JAMA 2023;329:651-661.

Příklad výběru pacientů pro renální denervaci

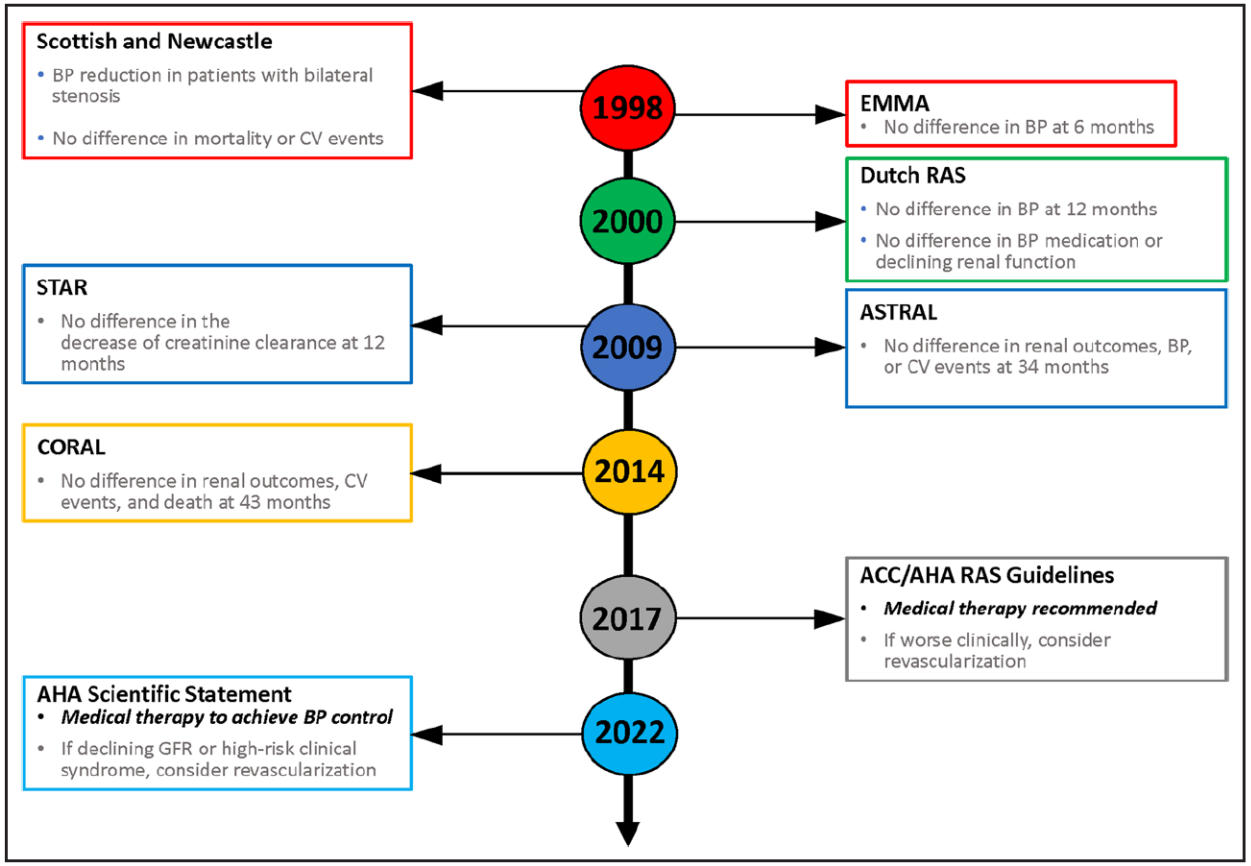


Rosa J, et al. J Hum Hypertens 2014;28:684-8.

Přístupy

- Renální denervace
- **Renovaskulární hypertenze**
- Primární hyperaldosteronismus

Renovaskulární hypertenze

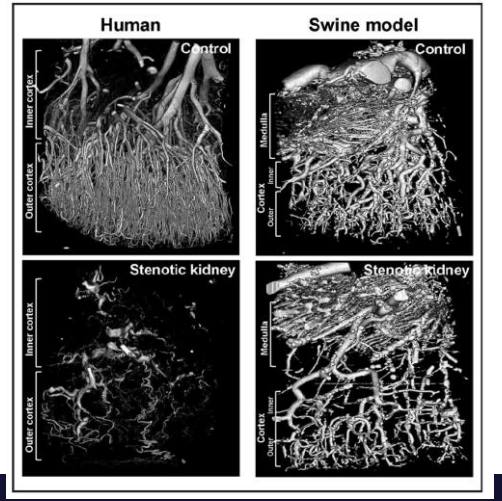


Eirin A et al. Hypertension 2024;81:206-217.

Clinical populations
Unilateral renal artery stenosis with characteristic syndromes (see below)
Fibromuscular dysplasia with hypertension*
High-risk clinical syndromes*
Rapidly progressive hypertension*
Rapidly declining estimated glomerular filtration rate*
Flash pulmonary edema*
Bilateral renal artery stenosis with progressive loss of renal functional mass
Single native kidney renal artery stenosis

Bhalla V et al. Hypertension 2022;79:e128-e143.

Příčina absence efektu invazivní léčby renovaskulární hypertenze = ischemická nefropatie



Přístupy

- Renální denervace
- Renovaskulární hypertenze
- **Primární hyperaldosteronismus**

Primární hyperaldosteronismus – výsledky léčby

Francie

Variable	Preop. N (%)	Last follow-up N (%)	P (univ.)
Time since surgery, median (interquartile), d		75 [43–514]	—
Cardiovascular event	(n = 312)	(n = 282)	—
No cardiovascular event	277 (88.5)	271 (96)	—
Stroke	16 (5)	2 (0.7)	—
Myocardial infarction or ischemia	13 (4)	2 (0.7)	—
Deep veinous thrombosis	7 (2)	1 (0.4)	—
Pulmonary embolism	2 (0.5)	0	—
Other	–	7 (2.5)	—
Ambulatory blood pressure, mean (SD), mm Hg	(n = 229)	(n = 271)	—
Systolic	148 (23)	131 (15)	< 0.001
Diastolic	89 (13)	80 (12)	< 0.001
< 140/90	61 (27)	197 (76)	0.01
Nb Antihypertensive drug	(n = 350)	(n = 326)	—
0	6 (2)	156 (48)	—
1	120 (34)	91 (28)	—
2	97 (28)	46 (14)	—
3	74 (21)	20 (6)	< 0.001
4	39 (11)	11 (3)	—
5	12 (3.5)	2 (0.6)	—
6	2 (0.5)	–	—
Including antialdosterone (spironolactone or eplerenone)	198 (57)	22 (5.7)	—
Kalemia, mean (SD), mmol/L	3.5 (0.7)	4.3 (0.5)	< 0.001
< 3.6	171 (52)	7 (2.9)	—
Potassium supplementation	148 (43)	6 (3.1)	—
Complete clinical success (n = 321)	–	101 (31.5)	—
Complete biological success (n = 69)	–	51 (74)	—

Vignaud T et al. Ann Surg 2023;278:717-724.

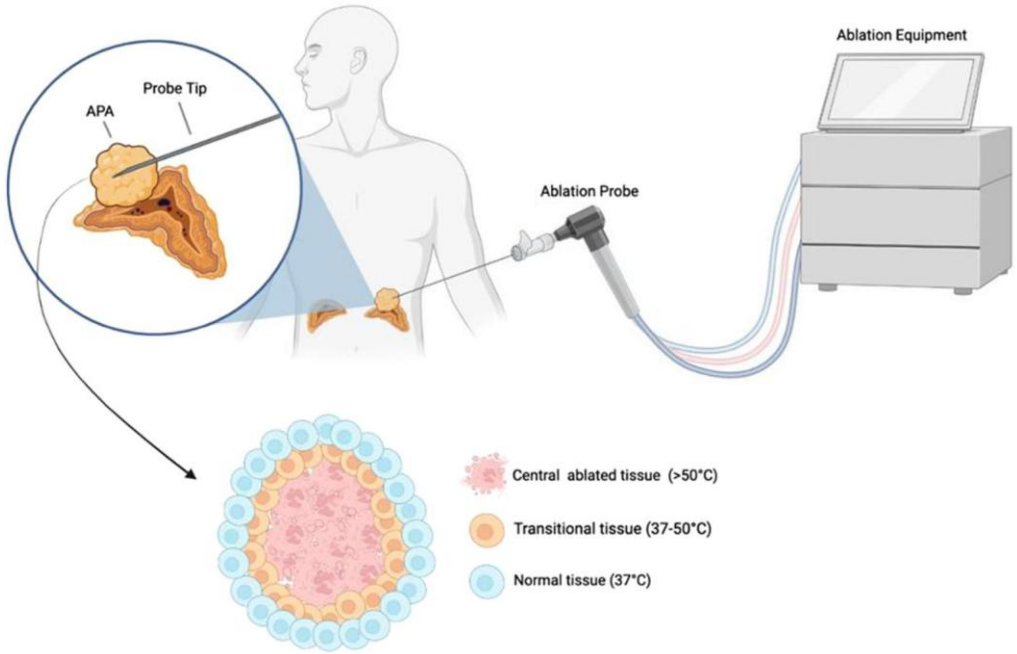
Španělsko

	PA treated by adrenalectomy ($n = 100$)	PA medically treated ($n = 168$)	HR[a] [95% CI], P value
ΔNumber of Antihypertensive drugs	-1.3 ± 1.3 [1.5 ± 1.3]	0.0 ± 1.4 [2.7 ± 1.4]	<0.0001[b]
New cases of diabetes mellitus	7.7% [$n = 5$]	3.5% [$n = 4$]	HR 2.1 [0.6–7.9], $P = 0.267$
New cases of dyslipidemia	17.4% [$n = 8$]	12.2% [$n = 10$]	HR 1.6 [0.6–0.8], $P = 0.338$
New cardiovascular events	3.9% [$n = 2$]	6.4% [$n = 7$]	HR 0.5 [0.1–2.2], $P = 0.294$
New cases of chronic kidney disease	18.0% [$n = 9$]	18.3% [$n = 21$]	HR 0.7 [0.3–1.6], $P = 0.411$
New cases of sleep apnea syndrome ($n = 128$)	3.6% [$n = 2$]	2.1% [$n = 2$]	HR 1.9 [0.3–14.0], $P = 0.524$
New cases of obesity	0% [$n = 0$]	7.6% [$n = 5$]	HR NC, $P = 0.071$
ΔSBP (mmHg) ($n = 225$)	-19.6 ± 22.5 [130.4 ± 15.7]	-17.5 ± 22.7 [132.7 ± 15.4]	0.517
ΔDBP (mmHg) ($n = 224$)	-11.8 ± 14.9 [80.2 ± 10.7]	-8.6 ± 15.2 [81.6 ± 10.9]	0.142

Araujo-Castro M, et al. Endocrine 2022;76:687-696.

Ablace uzlu nadledviny

Alternativa adrenalektomie pro ty, kteří odmítají operaci?



Mullen N et al. Endocr Rev 2024;45:125-170.

Category	Subgroup	NO. of Studies	Ablation patients	Clicinal success rate (95% CI)	I^2 (%)	*P*-value of Q-test	*P*-value of group differences
Subtype of PA	Unilateral	2	85	0.72(0.46,0.98)	86.5	0.007	0.831
	Unilateral + bilateral	2	110	0.73(0.52,0.94)	81.2	0.021	
Outcome criteria	PASO	3	162	0.78(0.66,0.89)	69.5	0.038	0.000
	Other criteria	2	72	0.51(0.40,0.63)	0.0	0.330	

Yang S et al. BMC Endocr Disord 2023;23:103.

Závěr I

- Nadále je nejefektivnější invazivní terapií rezistentní hypertenze chirurgická léčba primárního hyperaldosteronismu
- Antihypertenzní efekt renální denervace je spíše menší (v krátkodobém efektu), nelze vyloučit jeho prohloubení v delším časovém horizontu
- Zatím neznáme prediktory efektu renální denervace a tedy nezanedbatelné procento pacientů se může podrobit zcela zbytečnému invazivnímu výkonu
- Jako zvlášť nebezpečné pak vidím možnost nabídnutí renální denervace pacientům, kteří vykazují intolerance k různým skupinám antihypertenzív
- Invazivní terapie renovaskulární hypertenze je určena jen pro úzký okruh pacientů

Děkuji Vám za pozornost

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