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# Renal Denervation for moderate and resistant hypertension?

# Con: weigh risks vs benefits and consider new additions to the toolkit

## Judith Hsia, MD Research Professor of Medicine, Univ of Colorado 20ct2022

## Hypertension control: Room for improvement

>120 million US adults with BP systolic >130 and/or diastolic > 80



No major adverse effect of COVID on BP control



Egan BM. Hypertension Control Among US Adults, 2009 to 2012 Through 2017 to 2020, and the Impact of COVID-19. Hypert 2022;79:1981-1983 Heart Disease and Stroke Statistics – 2022 Update. <u>www.ahajournals.org/doi/10.1161/CIR.000000000001052</u> Fabiana GAM. Hypert Res 2022;45:364

## Meta-analysis of randomized denervation trials

Study and Year	Catheter	RDN	N Sham	Medic RDN	ations Sham	Weight (%)			М	ean difference [95% CI]
Ambulatory systolic blood press	sure reduction									
SYMPLICITY HTN-3, 2014	Symplicity Flex	329	162	5.1	5.2	18.1				-1.96 [ -4.98, 1.06]
ReSET, 2016	Symplicity Flex	35	33	4.1	4.2	3.3		H		► -1.10 [ -8.17, 5.97]
SPYRAL HTN OFF MED, 2020	Spyral	156	150	0	0	34.1		⊢	-	-3.60 [ -5.80, -1.40]
Desch et al, 2014	Symplicity Flex	32	35	4.4	4.3	7.3				-3.50 [ -8.27, 1.27]
SPYRAL HTN ON MED, 2018	Spyral	36	36	2.2	2.3	6.9			-	-7.00 [-11.90, -2.10]
RADIANCE-HTN SOLO, 2018	Paradise	74	72	0	0	19.6		<b>⊢</b>	-	-4.10 [ -7.00, -1.20]
RADIANCE-HTN TRIO, 2021	Paradise	69	67	3	3	10.8				-4.20 [ -8.10, -0.30]
Random effects model for change	in ambulatory systolic	blood p	ressure (p <	: 0.0001)	)			-		-3.61 [-4.89, -2.33]
Q = 3.67, df = 6, p for heterogeneit	y = 0.72; l <sup>2</sup> = 0.0%									
Ambulatory diastolic blood pres	sure reduction									
SYMPLICITY HTN-3, 2014	Symplicity Flex	329	162	5.1	5.2	19.6				-1.00 [ -2.81, 0.81]
ReSET, 2016	Symplicity Flex	35	33	4.1	4.2	5.6				0.90 [ -2.88, 4.68]
SPYRAL HTN OFF MED, 2020	Spyral	156	150	0	0	28.1		н	ні	-2.90 [ -4.30, -1.50]
Desch et al, 2014	Symplicity Flex	32	35	4.4	4.3	12.4		۲		-0.70 [ -3.12, 1.72]
SPYRAL HTN ON MED, 2018	Spyral	36	36	2.2	2.3	6.5				-4.30 [ -7.80, -0.80]
RADIANCE-HTN SOLO, 2018	Paradise	74	72	0	0	16.9		F	-	-1.80 [ -3.80, 0.20]
RADIANCE-HTN TRIO, 2021	Paradise	69	67	3	3	11.0				-2.00 [ -4.60, 0.60]
Random effects model for change	in ambulatory diastoli	c blood p	pressure (p •	< 0.0001	)				•	-1.85 [-2.78, -0.92]
Q = 7.79, df = 6, p for heterogeneit	$y = 0.25; I^2 = 18.6\%$									
						Г	1	1	1	٦
						-15	5 –10	-5	0	5



Ahmad Y et al. JACC CV Interv 2021 doi:10.1016/j.jcin.2021.09.020

Denervation better < Change in blood pressure (mmHg) > Placebo better

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Q = 3.67, df = 6, p for beterogeneit	$v = 0.72$ ; $l^2 = 0.0\%$	0.000 p	000010 (p		/		-0.01 [-4.03, -2.05]
	, = 0.12, 1 = 0.070						
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Q = 7.79, df = 6, p for heterogeneit	y = 0.25; l <sup>2</sup> = 18.6%						
						Г	
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Denervation better < Change in blood pressure (mmHg) > Placebo better

#### **Balance the magnitude of BP reduction vs costs**





## Markov model using meta-analysis efficacy

Table 2. Initial CVD risk and base case results of the cost-effectiveness analysis of RDN compared with SoC in 1,000 TRH participants

	Tota	al (discounted)		Incremen	ntal (discount	ted)			Initial 10-year
Treatment arm	Cost	Life year gained	QALY gained	Cost	Life year gained	QALY gained	ICER: \$/ life year gained	ICER: \$/ QALY gained	CVD risk for RDN to be cost-effective
Base case: lifet	time horizon								
SoC	\$26,273,976	11630.8	11216.9	\$8,696,568	175.6	184.5	\$ 49,519	\$ 47,130	13.2%
RDN	\$34,970,545	11806.4	11401.5						
Scenario analy	sis: 20-year time	e horizon							
SoC	\$28,538,954	10285.9	9845.3	\$8,200,761	165.3	179.8	\$ 49,618	\$ 45,624	24.3%
RDN	\$36,739,714	10451.2	10025.1						
Sensitivity analysis: RDN procedure repeated every 10 years									
SoC	\$41,940,529	8562.6	7960.1	\$9,861,892	197.3	211.3	\$49,859	\$47,333	61.1%
RDN	\$51,802,421	8759.9	8171.4						

Abbreviations: CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; RDN, renal denervation; SoC, standard treatment of care; TRH, treatment-resistant hypertension.



#### AHRQ report 2016: Renal denervation in Medicare population

Adverse effects were uncommon but potentially serious



#### AHRQ Report 2016: Renal denervation in Medicare population Adverse effects were uncommon but potentially serious

	Renal denervation	Control	Control group management	Study			
n/N (%)							
Access site							
Pseudoaneurysm at puncture site	2/9 (22) 1/52 (2) 1/52 (2)	NR NR NR	Antihypertensive medication " Unspecified	Schneider 2015 Rosa 2015 Symplicity 2010			
Groin hematoma	1/46 (2) 4/9 (44)	0/53 NR	Antihypertensive medication	Azizi 2015 Fadi Elmula 2014			
AV fistula	1/52 (2)	NR	Antihypertensive medication	Rosa 2015			
Vascular complication requiring treatment	1/352 (0.3)	0/171	Sham procedure	Bhatt 2014			
Vascular complication	1/355 (0.3)	0/69	Sham procedure	Bhatt 2014			
Renal artery events							
Renal artery dissection	1/52 (2) NR	NR 1/35 (3)	Antihypertensive medication Unspecified	Rosa 2015 Symplicity 2010			
Renal artery stenosis	1/332 (0.3)	0/165	Sham procedure	Bhatt 2014			
Renal artery reintervention	2/355 (0.6)	0/69	Sham procedure	Bhatt 2014			
Progression of atherosclerotic lesion	1/43 (2.3)	NR	Unspecified	Symplicity 2010			

NR not reported



#### AHRQ Report 2016: Renal denervation in Medicare population Adverse effects were uncommon but potentially serious

	Renal denervation	Control	Control group mgmt	Study
	n/N (%)			
Embolic event				
Embolic event resulting in end-organ damage	1/352 (0.3)	0/171	Sham procedure	Bhatt 2014
Significant embolic event resulting in end-organ damage	1/355 (0.3)	0/69	Sham procedure	Bhatt 2014
Renal function				
50% increase in serum creatinine	1/22 (5) 5/352 (1)	0/19 1/171 (1)	Antihypertensive med Sham procedure	Kario 2015 Bhatt 2014
Worsening of renal function	NR	1/54 (2)	Antihypertensive med	Rosa 2015
New onset end-stage renal disease	1/355 (0.3)	0/70	Sham procedure	Bhatt 2014
Acute renal failure	1/69 (1)	MR	Unspecified	Symplicity 2010
BP-related event				
Hypertensive crisis/emergency	3/46 (7) 9/352 (3) 17/355 (5)	3/53 (6) 9/171 (5) 4/69 (6)	Antihypertensive med Sham procedure "	Azizi 2015 Bhatt 2014 Bhatt 2014
Syncope	0	1/53 (2)	Antihypertensive med	Azizi 2015
Post-procedural drop in BP resulting in reduction in anti- hypertensive drugs	1/52 (2)	NR	Unspecified	Symplicity 2010
Symptomatic hypotension	1/9 (11)	4/10 (40)	Antihypertensive med	Fado Elmula 2014

CPC

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## **AHRQ conclusion**

- Further research is needed to
  - identify optimal candidates for renal denervation
  - refine next generation renal denervation technology
  - develop methods for assessing completeness of renal denervation procedure
  - demonstrate efficacy of renal denervation in reducing BP and improving clinical endpoints



#### Therapeutic toolkit





Kario. Hyperten 2022;79:00–00. DOI: 10.1161/HYPERTENSIONAHA.122.19414

## **Digital therapeutic: HERB-DH1**

Randomized, open label comparison of digital app + lifestyle modification vs lifestyle modification alone N=390

- 12 weeks
- 1° endpoint: ABPM





## **Digital therapeutic: HERB-DH1**



Kario K et al. Eur Heart J. 2021;42:4111

## **Cognitive behavioral therapy for hypertension**

Meta-analysis 15 trials, 2195 subjects

Mean reduction of systolic BP - 8.7 mm Hg (95% CI: - 10.7 to - 6.7)

Mean reduction of diastolic BP - 5.8 mm Hg (95% CI: - 7.8 to - 3.8)





## Fully automated digital cognitive behavioral therapy

CBT well suited to automated, digital delivery

- Highly structured
- Time limited, eg 12-20 sessions
- Developed or in development for
  - Anxiety
  - Depression
  - Insomnia
  - Type 2 diabetes

Future possibility for hypertension toolkit





J Med Internet Res. 2019; 21: e14754 JAMA Psych 2022;79(6):538-549 Clin Cardiol 2022;45:850-856

## Conclusion

- Renal denervation appears to provide modest BP reduction
- Considering the cost and adverse event profile, risks and benefits of alternative complementary therapies should be considered

