RENAL ARTERY STENOSIS [RAS]- TRIALS

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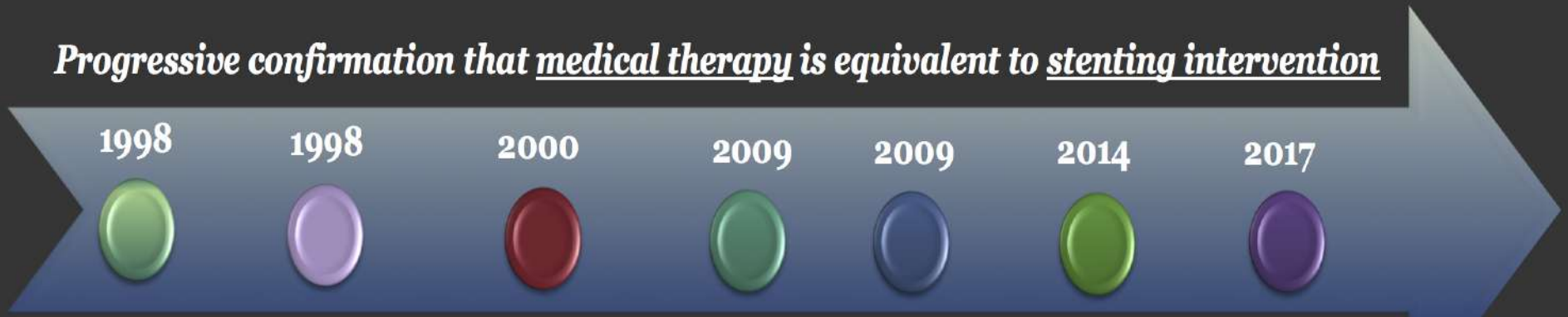
Landmark Trials in Renal Artery Stenosis

Progressive confirmation that <u>medical therapy</u> is equivalent to <u>stenting intervention</u>



EMMA

No difference in BP in angioplasty group at 6 mo.

Scottish and Newcastle

- Lower BP in those with bilateral RAS
- No difference in CV events or death

Dutch RAS

- No difference in systolic or diastolic fBP after angioplasty [12 mo.]
- No difference in anti-HTN meds or worsening kidney function

STAR

No difference in decrease in CrCl [24 mo.]

ASTRAL

No difference in kidney outcomes, BP, CV events

[34 mo]

CORAL

No difference in primary composite outcome including kidney outcomes, CV events, and death

[43 mo.]

ACC/AHA RAS Guidelines

Medical mgmt recommended.

If worsening clinically, consider revascularization

@DoctorGates @Landmark_Neph

Feature	ASTRAL (2009)[3]	CORAL (2014)[8]
Design	Multicentre RCT (UK-based)	Multicentre, international RCT
Sample size	806 patients	947 patients
Inclusion criteria	RAS with clinical uncertainty about the benefit of revascularisation	RAS with hypertension or reduced renal function
Key exclusions	Patients where stenting was clearly indicated	Serum creatinine >4.0 mg/dL; rapidly progressive disease
Stenosis severity	≥50% (uncertain in many cases, no haemodynamic criteria)	≥60% + haemodynamic significance (pressure gradient ≥20 mmHg)
Baseline renal function	Mean eGFR ~40 mL/min/1.73m²	Median eGFR ~57 mL/min/1.73m²
Intervention	Medical therapy ± stenting	Medical therapy ± stenting
Primary endpoint	Change in renal function over time	Composite of MI, stroke, hospitalisation for CHF, death, and renal outcomes
Follow-up duration	Median 34 months	Median 43 months
Main outcome	No change in renal function, BP, or mortality	No change in composite cardiovascular/renal outcomes
Blood pressure change	~2 mmHg lower in the stent group (not statistically significant)	~2 mmHg lower in the stent group (statistically significant)
Complication rate	~3% serious stent-related complications	0.9% stent-related complications
Conclusion	Stenting adds no benefit to medical therapy in patients with atherosclerotic RAS	Stenting does not improve outcomes over medical therapy in stable atherosclerotic RAS
Controversies	Included patients at low risk or with late-stage disease, lack of haemodynamic criteria, 'equipoise' bias	Underpowered for subgroups, underrepresentation of high-risk patients, modest BP benefit

Year	Trial	Design & Focus	Key findings	Impact/Controversy
2000	DRASTIC[13]	RCT, angioplasty (PTRA) versus medical therapy in hypertensive patients with RAS (N=106)	No significant improvement in BP or renal function	Small, underpowered; no stents; 44% crossover
2006	STAR[14]	RCT, stenting + medical versus medical alone in RAS with renal dysfunction (N=140)	No significant benefit in the preservation of renal function	Mild stenosis included; underpowered; didn't include high-risk patients
2009	ASTRAL[9]	RCT, stenting versus medical therapy in patients with uncertain benefit (N=806)	No benefit in BP, renal function, or mortality	Major impact on clinical practice; criticised for selection bias and inclusion of low-risk patients
2014	CORAL[8]	RCT, stenting + optimal medical therapy versus medical therapy alone in RAS with hypertension or CKD (N=947)	No difference in major CV/renal outcomes, small BP benefit	High-quality design; confirmed conservative approach; underpowered for subgroups and high-risk patients
2012 2014	HERCULES[17,18]	Single-arm, prospective study using Herculink Elite® stent in RAS with uncontrolled hypertension (N=202)	Significant SBP reduction (−22 mmHg), low complication rate	Not randomised, but included patients with severe RAS; supports the role of stenting in select patients who are hypertensive

Table 1. Clinical trails of medical treatment versus stenting for renal artery stenosis and the major drawbacks.

Renal trail	Type	Drawbacks
DRASTIC	Medical treatment versus stenting	Small sample size High cross-over rate, 44% of medical treatment group underwent renal artery angioplasty Majority of revascularization patients received balloon angioplasty only Hemodynamically significant lesions were defined by >50% rather than conventional 70% stenosis
STAR	Medical treatment versus renal artery stenting in patients with a GFR of <80 ml	Small sample size Among randomized patients, 33 had stenosis (50–70%) and 19% had <50% stenosis High complications rate
ASTRAL	Medical treatment versus renal artery stenting	Randomization bias Lack of core laboratories to adjudicate the severity of stenosis High complication rates
NITER	Medical treatment versus renal artery stenting	Small sample size

GFR: Glomerular filtration rate.

Long term outcomes after renal revascularization for atherosclerotic renovascular disease in the ASTRAL trial

Prospective randomised control trial

Multi-center study: 57 sites

806 participants with ARVD: randomised 1:1 to revascularization or medical therapy

- The initial ASTRAL study presented data with median 33.6 months follow-up
- This analysis presents extended follow-up data for a median of 56.4 months

- Mean age 70.5 years
- Mean eGFR 40ml/min/1.73m^2,
- Mean RAS 76%
- Mean BP 150/76mmHg
- 108/806 (13.4%) participants lost to follow-up by end of extended follow-up

Of the evaluable population:

18% (n=126)
1st Major Renal event

46% (n=318)
1st Major Cardiovascular event

50% (n=350) Died

There were no statistical differences between the intervention and medical treatment arms

No significant difference in the composite outcome* between the groups (HR 0.98 in revascularized group; 95% CI, 0.82-1.17; p=0.777)

- Presents the longest follow up of any ARVD trial
- These patients are high risk for cardiovascular events and mortality
- There was no significant difference between endovascular revascularization plus medical therapy compared to medical therapy alone
- Further study in high risk sub-populations (severe hypertension, heart failure, rapidly progressive renal decline) would be of value as these patient categories were not prominent in the trial

O'Keeffe et al., Circ. Cardiovasc. Interv., 2024

ARVD: Atherosclerotic Renovascular Disease; RAS: Renal Artery Stenosis

* Composite of time to the first renal, cardiovascular or mortality events, or time to >30% decline in renal function

Table 1. Optimal patients for renal intervention.	
Anatomically appropriate stenosis (demonstrated by duplex sonography or other methods)	Fibromuscular dysplasia with trans-stenotic gradient
	Atherosclerotic RAS >50% with transstenotic gradient at least 20 mm Hg (resting or hyperemic gradient)
	Atherosclerotic RAS >80% without measuring gradient
	Severe RAS to solitary functional kidney
AND	
Appropriate clinical condition	
Hypertension	Accelerated or multidrug-resistant
	End-organ damage ("malignant" hypertension)
Renal failure / chronic kidney disease	Acute renal failure/chronic kidney disease, angiotensin converting enzyme inhibitor or angiotensin receptor blocker induced
	Rapidly progressive (nonstable)
	Inevitable dialysis without intervention
Heart failure	"Flash" pulmonary edema
	Repeated admissions or poorly controlled
	Associated with nonreconstructable coronary artery disease