Scuola di Specializzazione in Malattie dell'Apparato Cardiovascolare
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Anno Accademico 2013-2014

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Progetto Formazione Avanzata in Cardiologia nel Web 2014
Scuola di Specializzazione in Malattie dell'Apparato Cardiovascolare

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Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) Trial

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Background (1/2)

90s

- Uncontrolled studies suggested that renal artery angioplasty or stenting resulted in significant reductions in SBP and in the stabilization of chronic kidney disease

2000

- Three randomized trials of renal artery PTA failed to show a benefit with respect to BP

2005

- ASPIRE II Trial

2009

- STAR and ASTRAl trial

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Background (2/2)

ASPIRE 2

- Prospective, non ramdomized study of 208 patients on 9-mont restenosis of a stent after failed PTRA
- Extremely favorable compared to PTRA alone and significant reduction in BP at 9 and 24 months
- No significant changes in serum creatinine levels at 9 mo. follow-up

STAR

- Multicenter, randomized study of 140 patients on progression of renal disease (creat > 20%) with omt alone vs stenting + omt
- Only 72% received a stent (stenosis <50%). No difference in BP control or overall mortality between the groups. Higher complication rates in the stent group

ASTRAL

- Multicenter, prospective randomized study on renal function comparing renal stenting with omt vs omt alone →Trend in favour of the stenting group at 34 mo., but no differences in BP or adverse renal or CV events. 5 serious complications

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Methods: Inclusion Criteria

- Severe renal artery stenosis (> 80% or 60-80% with a systolic gradient of at least 20 mmHg; all angiograms were centrally analyzed with the use of a validated QVA program) and…
- SBP > 155 mmHg or higher while taking two or more antihypertensive agents (no longer specified)

- Severe renal artery stenosis and…
- Chronic kidney disease with GFR less than 60 ml/min/ 1.73m^2 of BSA (MDRD).

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Methods: Exclusion Criteria

- Fibromuscolar dysplasia
- Chronic kidney disease other than ischemic nephropathy or associated with cretinine > 4 mg/dl
- Kidney length < 7 cm
- Lesion that coul not be treated with a single stent

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Methods: Randomization and Interventions

- 1:1 ratio
- medical therapy alone or stenting plus medical therapy

- Both treatment groups received antiplatelets therapy and other protocol-driven medical therapies
- to control BP, glucose and lipid levels

- Medications:
- Candesartan +/- hydoclorothiazide
- and the combination agent amlodipine-atorvastatin

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Methods: Study Endpoints

Primary Endpoint

- The occurence of a major cardiovascular or renal event
- A composite of death from cardiovascular or renal causes, stroke, myocardial infarction, hospitalization for CHF, progressive renal insufficency, or the need for permanent renal replacement therapy

Secondary Endpoints

- Individual components of the primary endpoint.

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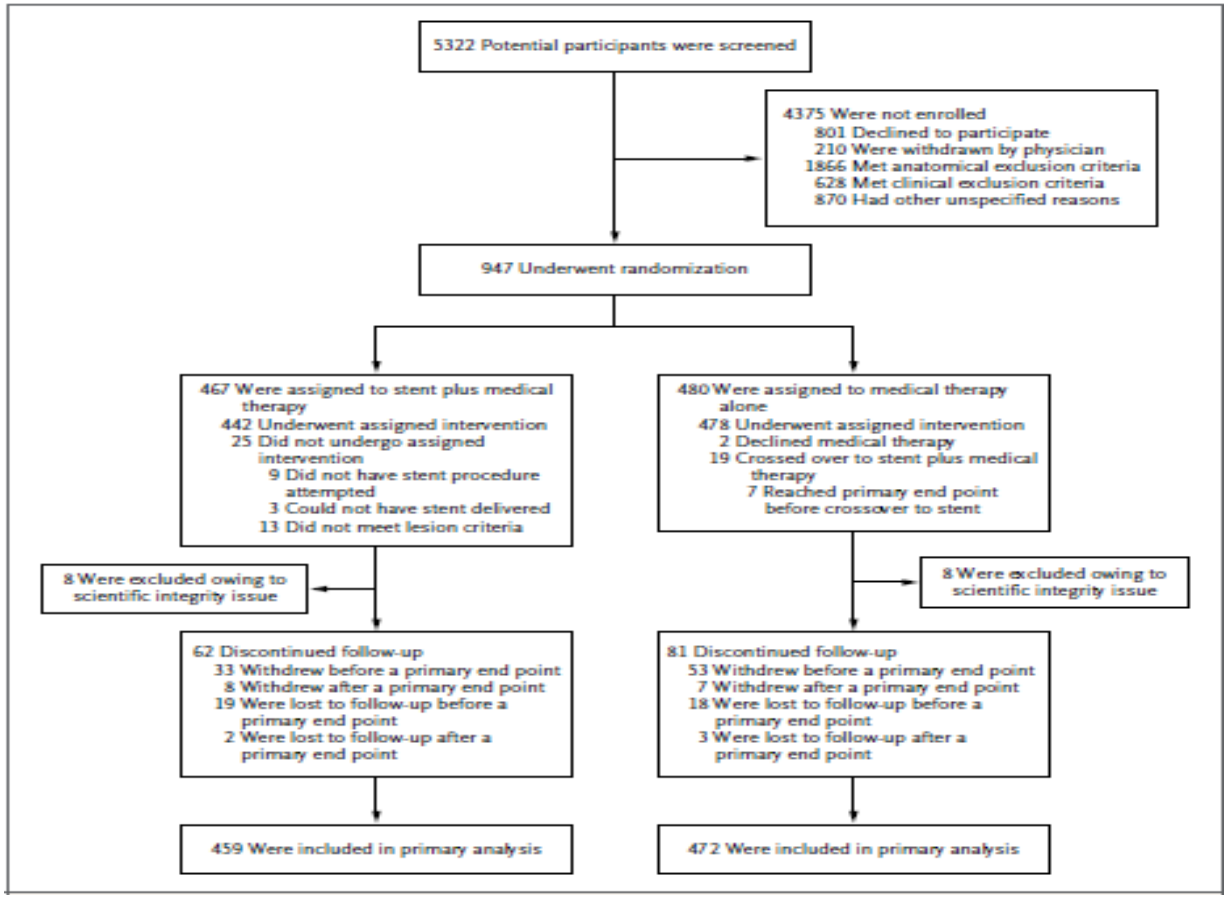
Methods: Screening and Randomization



Baseline Characteristics of Study Population

Table 1. Baseline Characteristics of the Study Population, According to Treatment Group.*

Characteristic	Stenting plus Medical Therapy (N=459)	Medical Therapy Only (N=472)
Age (yr)	69.3±9.4	69.0±9.0
Male sex (%)	51.0	48.9
Race (%)†		
Black	7.0	7.0
Other	93.0	93.0
Body-mass index‡	28.2±5.3	28.7±5.7
Systolic blood pressure (mm Hg)	149.9±23.2	150.4±23.0
Blood pressure at target level (%)§	29.2	25.3
Estimated GFR (ml/min/1.73 m²)¶	58.0±23.4	57.4±21.7
Stage ≥3 chronic kidney disease (%)	49.6	50.4
Method of identification of stenosis (%)		
Angiography	68.4	68.6
Duplex ultrasonography	25.5	24.2
Computed tomographic angiography	4.4	5.3
Magnetic resonance angiography	1.7	1.9
Medical history and risk factors (%)		
Diabetes	32.4	34.3
Prior myocardial infarction	26.5	30.2
History of heart failure	12.0	15.1
Smoking in past yr	28.0	32.2
Hyperlipidemia	89.4	90.0
Angiographic findings‖		
% Stenosis, as assessed by core laboratory	67.3±11.4	66.9±11.9
% Stenosis, as assessed by investigator	72.5±14.6	74.3±13.1
Global ischemia (%)**	20.0	16.2
Bilateral disease (%)††	22.0	18.1

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Results: Incidence of the Clinical Endpoints

Table 2. Clinical End Points.*

End Point	Stenting plus Medical Therapy (N=459)	Medical Therapy Only (N=472)	Hazard Ratio (95% CI)	P Value
	no. (%)			
Primary end point: death from cardiovascular or renal causes, stroke, myocardial infarction, hospitalization for congestive heart failure, progressive renal insufficiency, or permanent renal-replacement therapy†	161 (35.1)	169 (35.8)	0.94 (0.76–1.17)	0.58
Components of primary end point‡				
Death from cardiovascular or renal causes	20 (4.4)	20 (4.2)		
Stroke	12 (2.6)	16 (3.4)		
Myocardial infarction	30 (6.5)	27 (5.7)		
Hospitalization for congestive heart failure	27 (5.9)	26 (5.5)		
Progressive renal insufficiency	68 (14.8)	77 (16.3)		
Permanent renal-replacement therapy	4 (0.9)	3 (0.6)		
Secondary clinical end points§				
Death from any cause	63 (13.7)	76 (16.1)	0.80 (0.58–1.12)	0.20
Death from cardiovascular causes	41 (8.9)	45 (9.5)	0.89 (0.58–1.36)	0.60
Death from renal causes	2 (0.4)	1 (0.2)	1.89 (0.17–20.85)	0.60
Stroke	16 (3.5)	23 (4.9)	0.68 (0.36–1.28)	0.23
Myocardial infarction	40 (8.7)	37 (7.8)	1.09 (0.70–1.71)	0.70
Hospitalization for congestive heart failure	39 (8.5)	39 (8.3)	1.00 (0.64–1.56)	0.99
Progressive renal insufficiency	77 (16.8)	89 (18.9)	0.86 (0.64–1.17)	0.34
Permanent renal-replacement therapy	16 (3.5)	8 (1.7)	1.98 (0.85–4.62)	0.11

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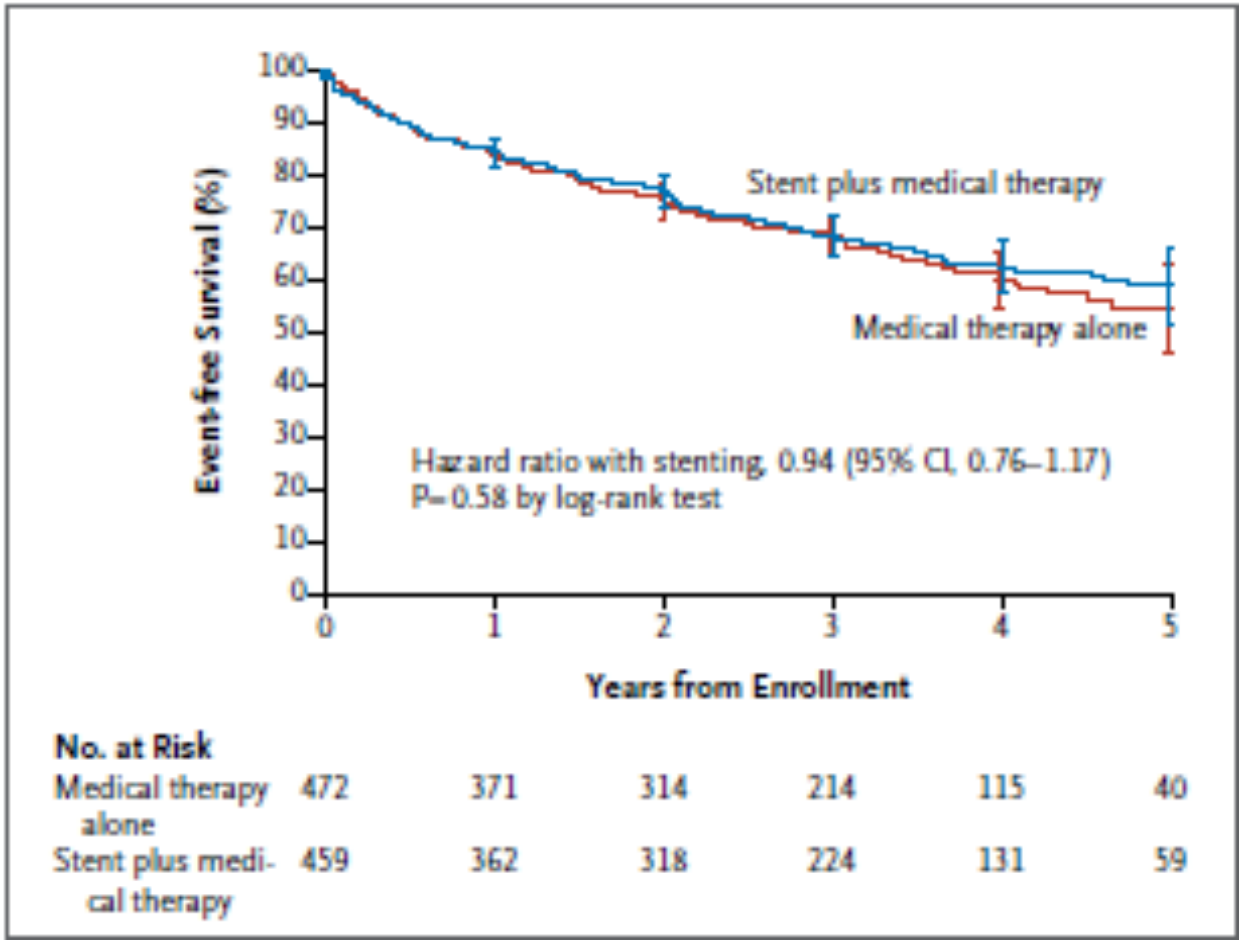
Results: Event-free Survival



No. at Risk						
Medical therapy alone	472	371	314	214	115	40
Stent plus medical therapy	459	362	318	224	131	59

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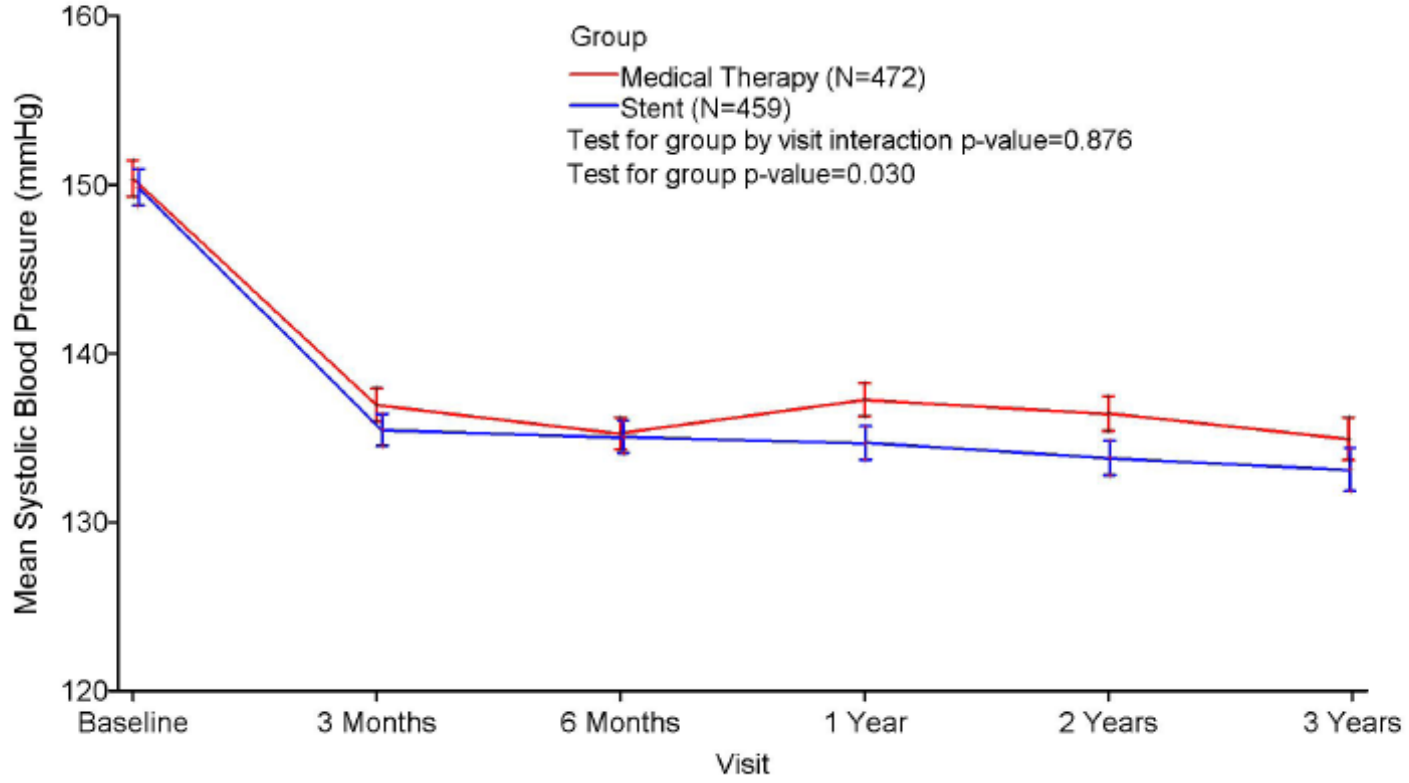
Results: Systolic BP levels

H. Systolic blood pressure over time

Figure S7. CORAL study systolic blood pressure in mmHg.



Potential Limitations

- Renal artery stenosis of 60% or more (debate about the severity of stenosis that is necessary to justify intervention).
- Exclusion of fibromuscolar dysplasia.
- Some patient not enrolled because of the preference of their physician.

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Conclusions

- Contemporary renal stenting provides no incremental benefit when added to a background of high quality multifactorial medical therapy.

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Towards the Future…. Ongoing Trials

STRETCH

- Aims to examine the clinical impact of renal artery stenting on heart failure outcomes

RADAR

- The primary endpoint is change in GFR at 1 years (only patients with 70% stenosis)

METRAS

- The primary endpoint is change in GFR at 2 years assessed quantitatively by renal scintigraphy

FORMULA-PTX

- Paclitaxel coated stent

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Grazie per la Vostra Attenzione!

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