

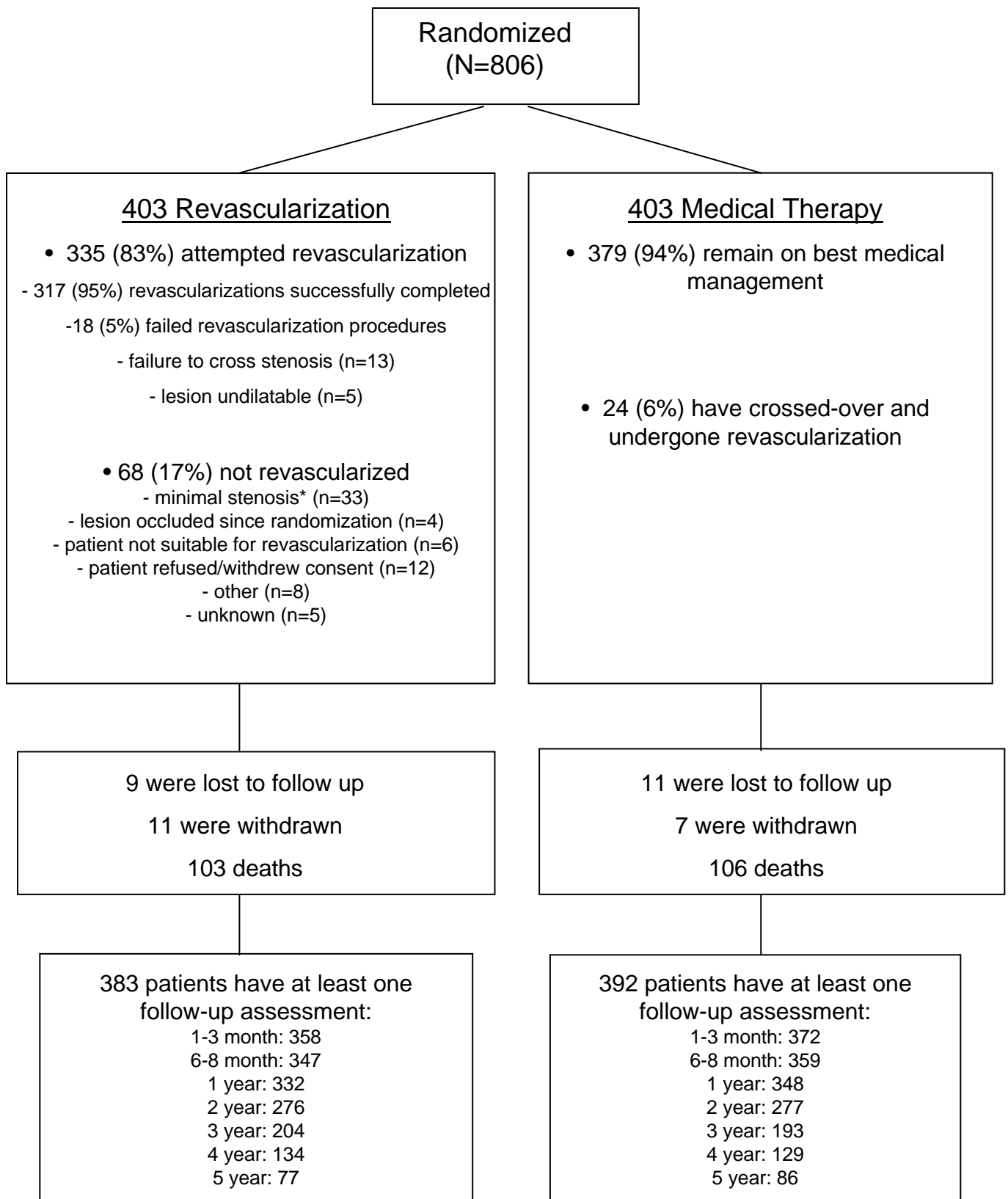
Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The ASTRAL Investigators. Revascularization versus medical therapy for renal-artery stenosis. N Engl J Med 2009;361:1953-62.

(PDF updated June 30, 2010.)

Supplementary Appendix Figure 1: CONSORT Diagram for ASTRAL – Patient Recruitment and Follow-up



* These patients were identified as having minimal stenosis post-randomization, as patients entered into ASTRAL based on computed tomographic (CTA) or magnetic resonance angiography (MRA) (which can over-estimate renal artery stenosis), who were randomized to revascularization, were required to have 'on the table' intraarterial angiography to check the accuracy of the CTA and MRA estimates of the renal artery stenosis.

Supplementary Appendix Table 1: Medication at 1 Year Follow-up Assessment

	Revascularization (N=332)	Medical Therapy (N=348)	P value
Antihypertensive drug – no./total no. (%)			
Any	321/330 (97%)	343/345 (99%)	0.03
Diuretic	206/321 (64%)	238/343 (69%)	0.15
Calcium-channel blocker	202/321 (63%)	242/343 (71%)	0.04
Beta-blocker	148/321 (46%)	189/343 (55%)	0.02
ACE inhibitor or ARB	161/321 (50%)	146/343 (43%)	0.05
Alpha blocker	124/321 (39%)	130/343 (38%)	0.85
No. of antihypertensive drugs in class – mean (range)	2.77 (1 - 6)	2.97 (1 - 6)	0.03
Antiplatelet drug – no./total no. (%)			
Any	270/327 (83%)	268/342 (78%)	0.17
Aspirin	239/270 (89%)	245/268 (91%)	0.26
Cholesterol-lowering drug – no./total no. (%)			
Any	281/328 (86%)	299/343 (87%)	0.57
Statin	273/281 (97%)	286/299 (96%)	0.33
Warfarin – no./total no. (%)	30/324 (9%)	36/327 (11%)	0.46

* ACE denotes angiotensin-converting enzyme, and ARB angiotensin-receptor blocker.

Supplementary Appendix Table 2: Serum Creatinine and Blood Pressure over Time

	Revascularization	Medical Therapy	Mean Difference (95% Confidence Interval)	P value
Mean slope over the 5-year study period				
Reciprocal serum creatinine (liter/ μ mol/year)	-0.07 x 10 ⁻³	-0.13 x 10 ⁻³	0.06 x 10 ⁻³ (-0.002 to 0.13)	0.06
Serum creatinine (μ mol/liter/year)	7.47	10.52	-3.05 (-6.75 to 0.65)	0.11
Mean reciprocal serum creatinine (standard deviation) – liter/μmol (x 1000)				
Baseline	N=403 6.47 (2.42)	N=403 6.42 (2.29)	0.05 (-0.28 to 0.37)	0.79
1-3 month	N=349 6.19 (2.45)	N=363 6.26 (2.21)	-0.07 (-0.41 to 0.27)	0.69
6-8 month	N=336 6.40 (2.49)	N=347 6.28 (2.30)	0.12 (-0.24 to 0.48)	0.51
1 year	N=329 6.33 (2.54)	N=343 6.28 (2.39)	0.05 (-0.32 to 0.43)	0.78
2 year	N=263 6.53 (2.68)	N=272 6.07 (2.35)	0.45 (0.03 to 0.88)	0.04
3 year	N=191 6.46 (2.76)	N=183 5.96 (2.50)	0.51 (-0.03 to 1.04)	0.06
4 year	N=127 6.42 (2.86)	N=119 6.14 (2.74)	0.28 (-0.42 to 0.99)	0.43
5 year	N=72 5.96 (2.93)	N=61 6.69 (2.61)	-0.74 (-1.70 to 0.22)	0.13
Mean serum creatinine (standard deviation) – μmol/liter				
Baseline	N=403 179.21 (75.79)	N=403 178.24 (74.51)	0.97 (-9.42 to 11.37)	0.85
1-3 month	N=349 191.72 (91.03)	N=363 183.33 (80.22)	8.39 (-4.22 to 21.00)	0.19
6-8 month	N=336 190.15 (111.48)	N=347 187.20 (96.46)	2.95 (-12.70 to 18.60)	0.71

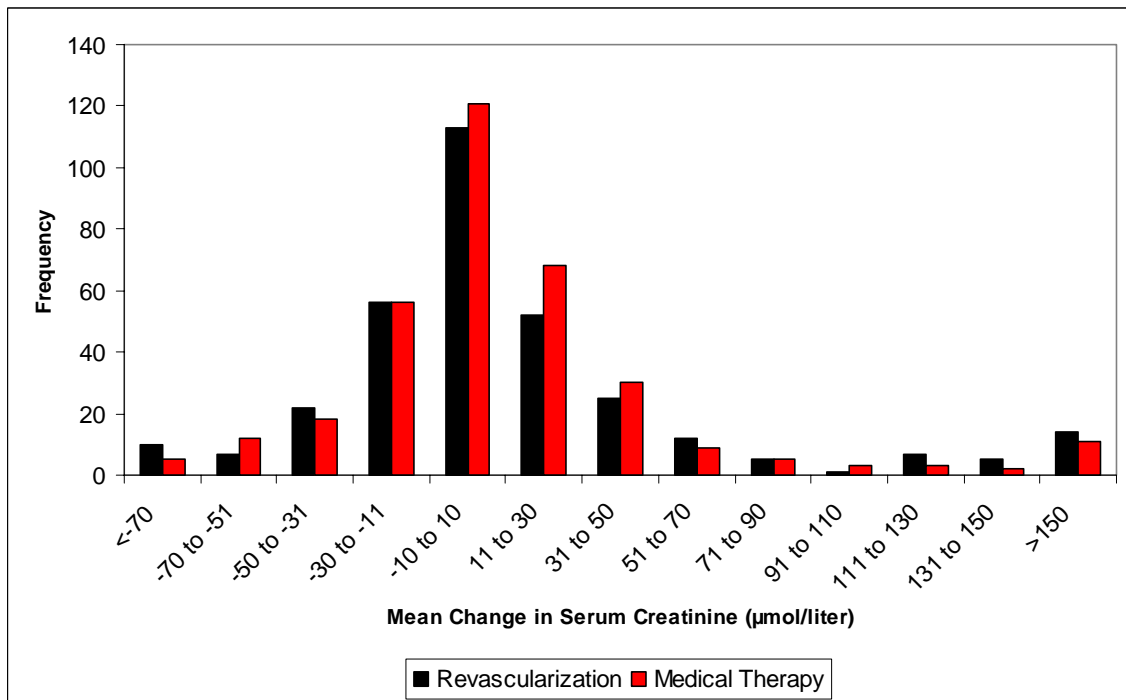
1 year	N=329 196.46 (123.69)	N=343 191.96 (111.71)	4.50 (-13.34 to 22.34)	0.62
2 year	N=263 188.48 (115.08)	N=272 199.47 (116.01)	-10.99 (-30.62 to 8.64)	0.27
3 year	N=191 195.96 (126.42)	N=183 214.81 (142.97)	-18.85 (-46.26 to 8.56)	0.18
4 year	N=127 198.76 (127.92)	N=119 203.16 (115.78)	-4.40 (-35.10 to 26.31)	0.78
5 year	N=72 209.47 (103.40)	N=61 184.41 (120.49)	25.06 (-13.34 to 63.46)	0.20
Mean systolic blood pressure (standard deviation) – mm Hg				
Baseline	N=385 148.79 (24.28)	N=388 152.05 (25.23)	-3.27 (-6.76 to 0.23)	0.07
1-3 month	N=346 147.77 (25.29)	N=361 151.60 (26.08)	-3.83 (-7.63 to -0.03)	0.05
6-8 month	N=332 146.58 (25.15)	N=350 149.09 (25.16)	-2.52 (-6.30 to 1.27)	0.19
1 year	N=321 145.66 (23.21)	N=336 148.20 (24.22)	-2.54 (-6.18 to 1.10)	0.17
2 year	N=257 142.05 (24.80)	N=264 145.80 (23.83)	-3.75 (-7.93 to 0.44)	0.08
3 year	N=197 143.02 (24.03)	N=178 144.01 (21.90)	-0.99 (-5.68 to 3.70)	0.68
4 year	N=125 144.18 (25.98)	N=124 143.56 (25.62)	0.61 (-5.83 to 7.05)	0.85
5 year	N=71 141.17 (25.66)	N=62 141.27 (25.49)	-0.11 (-8.90 to 8.69)	0.98
Mean diastolic blood pressure (standard deviation) – mm Hg				
Baseline	N=384 76.32 (12.24)	N=388 75.89 (12.58)	0.43 (-1.33 to 2.18)	0.63
1-3 month	N=344 74.70 (12.05)	N=361 75.07 (12.84)	-0.37 (-2.21 to 1.48)	0.70

6-8 month	N=330 74.12 (12.41)	N=349 73.92 (11.75)	0.20 (-1.62 to 2.02)	0.83
1 year	N=320 73.39 (11.92)	N=335 74.67 (12.41)	-1.28 (-3.15 to 0.59)	0.18
2 year	N=256 72.25 (12.00)	N=262 72.54 (11.86)	-0.30 (-2.36 to 1.76)	0.78
3 year	N=197 72.85 (11.08)	N=178 72.31 (11.76)	0.53 (-1.79 to 2.85)	0.65
4 year	N=125 75.05 (11.79)	N=123 71.57 (11.93)	3.48 (0.51 to 6.45)	0.02
5 year	N=70 72.96 (12.02)	N=63 70.37 (13.27)	2.59 (-1.75 to 6.93)	0.24

For reciprocal serum creatinine, a positive difference is in favor of revascularization.

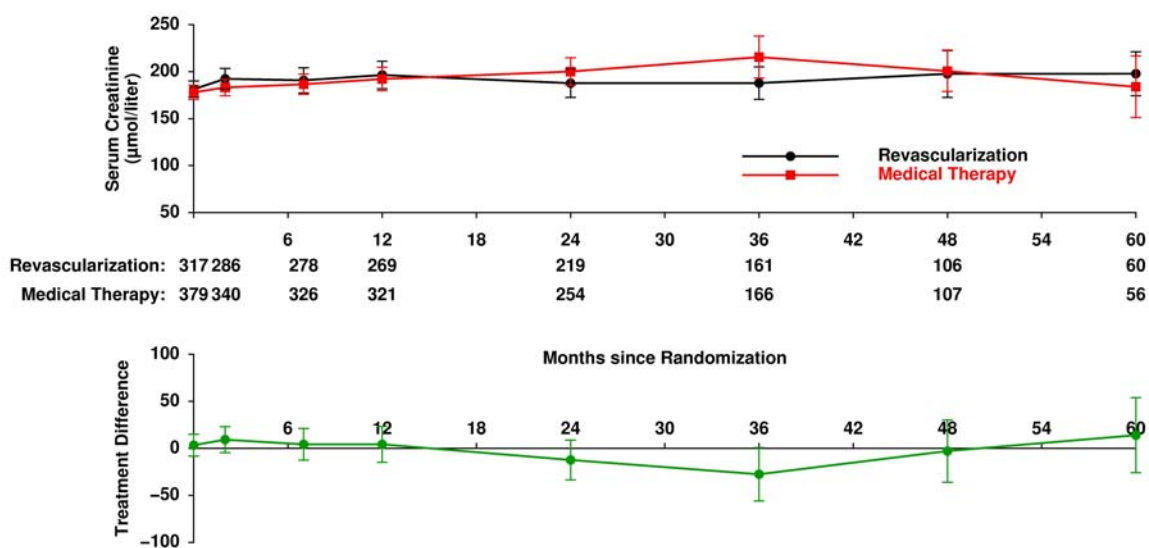
For serum creatinine and blood pressure, a negative difference is in favor of revascularization.

Supplementary Appendix Figure 2: Mean Change in Serum Creatinine ($\mu\text{mol/liter}$) between Randomization and 1 Year



Negative change indicates an improvement in renal function over time.
Positive change indicates a worsening renal function over time.

Supplementary Appendix Figure 3: Per-Protocol Analysis of Serum Creatinine ($\mu\text{mol/liter}$)



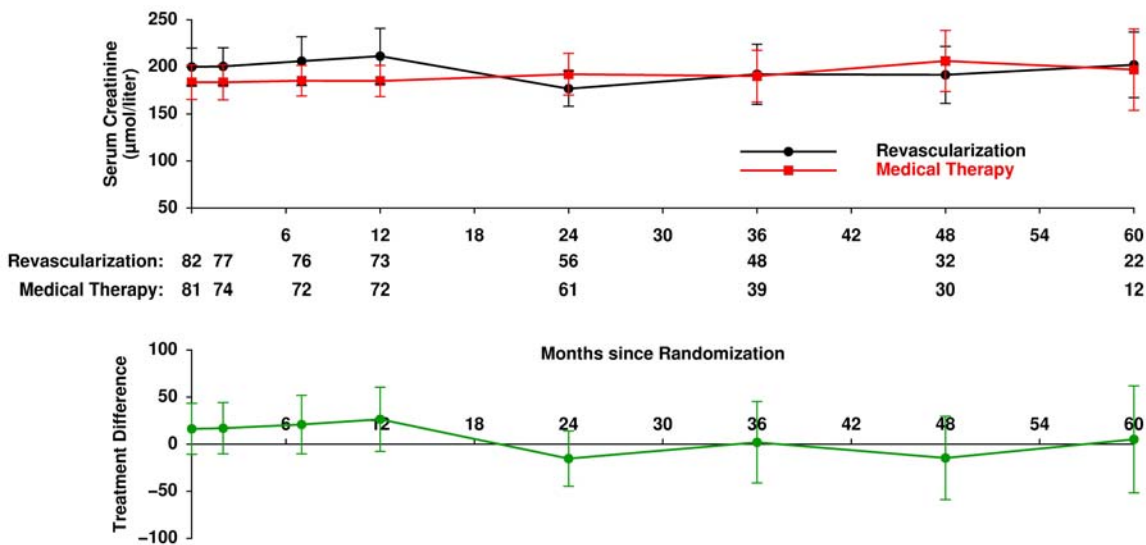
Footnote:

Per-protocol analysis based on the 317 patients' allocated revascularization which was successfully completed versus the 379 patients who remained on medical management.

A negative treatment difference is in favor of revascularization.

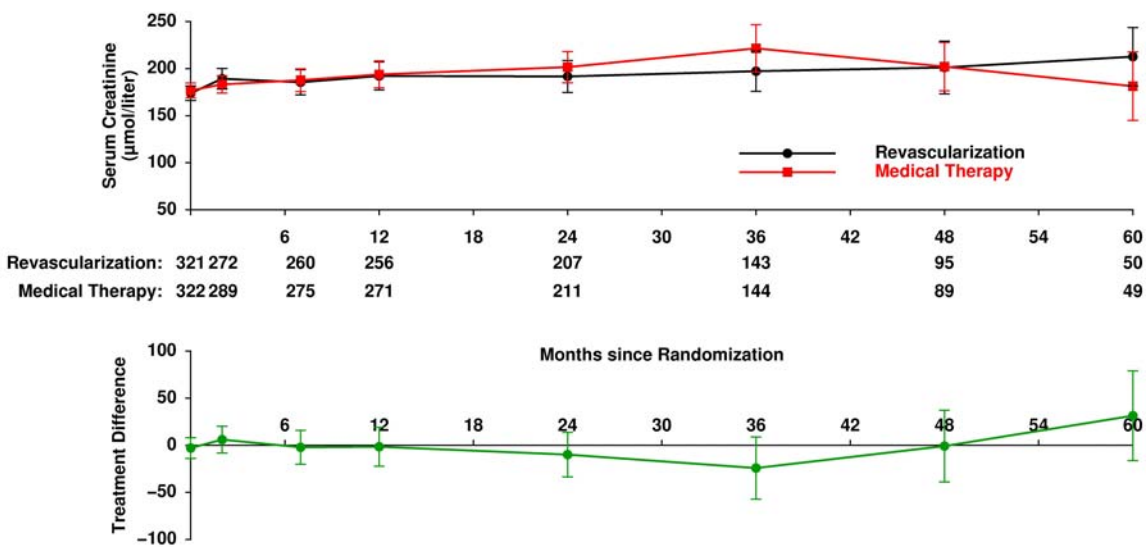
Supplementary Appendix Figure 4a: Serum Creatinine ($\mu\text{mol/liter}$) in the 163 Patients with

Very Severe Anatomical Disease



Supplementary Appendix Figure 4b: Serum Creatinine ($\mu\text{mol/liter}$) in Patients with less

Severe Anatomical Disease



Footnote:

Severe anatomical disease defined as those patients with bilateral renal-artery stenosis $>70\%$ ($n=103$) or renal-artery stenosis $>70\%$ in a solitary functioning kidney ($n=60$).

A negative treatment difference is in favor of revascularization.

Supplementary Appendix Table 3: Overall Incidence of Renal and Cardiovascular Events and Mortality

	Revascularization	Medical Therapy	P value
Renal Events	(N=383)	(N=392)	
Acute kidney injury	25 (7%)	23 (6%)	0.70
Dialysis	36 (9%)	40 (10%)	0.71
<i>For end-stage renal disease</i>	30	31	
<i>For acute kidney injury</i>	6	9	
Transplantation	0 (-)	0 (-)	-
Nephrectomy	2 (0.5%)	1* (0.3%)	0.62
Renal arterial occlusion	5 ^Ω (1%)	4 ^Ω (1%)	0.75
Death due to renal failure	10 (3%)	17 (4%)	0.19
Number of renal events / Number of patients†	73 / 57 (15%)	80 / 58 (15%)	0.97
Cardiovascular Events	(N=386)	(N=395)	
Myocardial infarction	36 (9%)	37 (9%)	0.98
Hospitalization for angina	29 (8%)	34 (9%)	0.57
Hospitalization for fluid overload/cardiac failure	47 (12%)	60 (15%)	0.22
Coronary artery procedure (e.g. CABG or PCTA)	15 (4%)	16 (4%)	0.91
Other arterial procedure (e.g. amputation)	45 (12%)	29 (7%)	0.04
Stroke	24 (6%)	23 (6%)	0.82
Cardiovascular death	42 (11%)	45 (11%)	0.82
Number of cardiovascular events / Number of patients	238 / 141 (37%)	244 / 145 (37%)	0.96
Deaths[£]	(N=403)	(N=403)	
Cardiovascular	42 (10%)	45 (11%)	0.73
Renal	10 (2%)	17 (4%)	0.17

Infection	17 (4%)	14 (3%)	0.58
Cancer	15 (4%)	13 (3%)	0.70
Other/Unknown	30 (7%)	31 (8%)	0.89
Total Number of Deaths	103 (26%)	106 (26%)	0.81

* One medical therapy patient had a partial nephrectomy due to renal carcinoma.

Ω All renal arterial occlusions in the revascularization arm and one renal arterial occlusion in the medical therapy arm occurred intra-procedurally.

† Not including renal arterial occlusions or partial nephrectomy due to renal carcinoma.

£ Specific causes of death listed are not exclusive, as some patients had multiple causes of death.

Supplementary Appendix Table 4: Complications of Revascularization Procedure

	Revascularization	Medical Therapy
Peri-procedural complications (within 24 hours)	(N=335)	(N=24)
Renal or stent embolization	5 (1.5%)	0 (-)
Renal arterial thrombosis or occlusion	4 (1%) [†]	0 (-)
Renal arterial perforation or dissection	3 (1%)	1 (4%)
Non-renal embolization	3 (1%) ^Ω	0 (-)
Stent misplacement requiring additional stent	10 (3%)	0 (-)
Distal stent retrieval or deployment	1 (0.3%)	0 (-)
Balloon rupture	1 (0.3%)	0 (-)
Need for surgical rescue	0 (-)	0 (-)
Access vessel damage	7 (2%)	0 (-)
Pulmonary edema ^σ	1 (0.3%)	0 (-)
Femoral artery aneurysm at puncture site ^σ	1 (0.3%)	0 (-)
Myocardial infarction ^σ	1 (0.3%)	0 (-)
Number of events / Number of patients	37 / 30	1 / 1
Post-operative complications (between 24 hours and 1 month post procedure)^x	(N=280)	
Groin hemorrhage/hematoma	32 (11%) [^]	-
Deterioration in renal function	30 (11%) ^ε	-
Pseudoaneurysm	3 (1%)	-
Renal artery occlusion	1 (0.4%)	-
Local infection at puncture site	1 (0.4%)	-
Death within 30 days	2 (0.7%)	
Number of events / Number patients	69 / 55	-

† Two renal arterial thrombosis/occlusion events were also reported as serious adverse events.

Ω All three non-renal embolization events were also reported as serious adverse events, with patients having cholesterol embolism leading to peripheral gangrene and amputation of toes or limbs.

σ Events reported as serious adverse events.

χ Data only collected in patients randomized to revascularization, and data were only available in 280 of the 335 patients where revascularization was attempted.

λ Four groin hemorrhages resulted in hospitalization that were also reported as serious adverse events.

ε Two cases of deterioration in renal function were also reported as serious adverse events (arterial occlusions).

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In addition to the Writing Committee, the following investigators participated in the ASTRAL trial:

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Serious Adverse Event Safety Committee:

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