Vascular kidney diseases

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Vascular kidney disorders

- Vascular nephropathy
  - Hypertensive nephropathy
  - Atherosclerotic renovascular disease
  - Atheroembolic kidney disease
- Ischemic kidney disease
  - Thrombosis or occlusion of renal blood vessels
Ischemic kidney disease

- Atherosclerotic renovascular disease
- Atheroembolic kidney disease
Atherosclerotic ischemic kidney disease

- Rising prevalence due to ageing population
- Frequent signs of AS in other arteries
- Hemodynamically significant AS of renal arteries leads via parenchymal ischemia to glomerulosclerosis and interstitial fibrosis
- **Cause of renal failure in 15-25% of patients starting RRT**
Ischemic nephropathy
Etiology and pathogenesis

- Decreased perfusion pressure if the vascular lumen is narrowed by > 70 %
- Activation of the renin-angiotensin-aldosterone system
- Endothelial dysfunction, decreased availability of NO
- Presence of common risk factors of atherosclerosis
- Release of cytokines, chemokines and growth factors from infiltrating monocytes/macrophages
Pathogenesis of RVH and ischemic nephropathy
Ischemic nephropathy
Clinical picture

- Age > 60 years
- Arterial hypertension
- Signs of atherosclerosis in other localisations:
  - IHD - 28%
  - AS of peripheral vessels - 72%
  - Suffered a stroke - 17%
  - Carotic stenosis - 20%
Ischemic nephropathy
Laboratory findings

- Hyperlipidemia
- Decreased renal functions
- Proteinuria 1-3 g/24 h
- Minor erythrocyturia
Ischemic nephropathy
Examination methods

- Systolic-diastolic murmur in the abdominal region laterally to the umbilicus
- Duplex kidney ultrasound
- Dynamic kidney scintigraphy
  (A decrease of the GF of the affected kidney below 40 % of total GF is significant)
- Spiral CT-angiography
- MR-angiography
- Renovasography
Diagnostic armamentarium in renovascular stenosis

- Scintigraphy with ACEi
- Duplex sonography
- MRI angiography
- Spiral CT angiography
Renal artery stenosis

Aortogram shows a focal stenosis of the left renal artery with poststenotic dilatation (arrow). The right renal artery has a normal caliber and is delivering contrast to the right kidney well before the left kidney receives contrast.

Courtesy of Jonathan Kruskal, MD.
Revascularization versus Medical Therapy for Renal-Artery Stenosis

The ASTRAL Investigators

ABSTRACT

BACKGROUND
Percutaneous revascularization of the renal arteries improves patency in atherosclerotic renovascular disease, yet evidence of a clinical benefit is limited.

METHODS
In a randomized, unblinded trial, we assigned 806 patients with atherosclerotic renovascular disease either to undergo revascularization in addition to receiving medical therapy or to receive medical therapy alone. The primary outcome was renal function, as measured by the reciprocal of the serum creatinine level (a measure that has a linear relationship with creatinine clearance). Secondary outcomes were blood pressure, the time to renal and major cardiovascular events, and mortality. The median follow-up was 34 months.

RESULTS
During a 5-year period, the rate of progression of renal impairment (as shown by the slope of the reciprocal of the serum creatinine level) was −0.07×10−3 liters per micromole per year in the revascularization group, as compared with −0.13×10−3 liters per micromole per year in the medical-therapy group, a difference favoring revascularization of 0.06×10−3 liters per micromole per year (95% confidence interval [CI], −0.002 to 0.13; P = 0.06). Over the same time, the mean serum creatinine level was 1.6 μmol per liter (95% CI, −8.4 to 5.2 [0.02 mg per deciliter; 95% CI, −0.10 to 0.06]) lower in the revascularization group than in the medical-therapy group. There was no significant between-group difference in systolic blood pressure; the decrease in diastolic blood pressure was smaller in the revascularization group than in the medical-therapy group. The two study groups had similar rates of renal events (hazard ratio in the revascularization group, 0.97; 95% CI, 0.67 to 1.40; P = 0.88), major cardiovascular events (hazard ratio, 0.94; 95% CI, 0.75 to 1.19; P = 0.61), and death (hazard ratio, 0.90; 95% CI, 0.69 to 1.18; P = 0.46). Serious complications associated with revascularization occurred in 23 patients, including 2 deaths and 3 amputations of toes or limbs.

CONCLUSIONS
We found substantial risks but no evidence of a worthwhile clinical benefit from revascularization in patients with atherosclerotic renovascular disease. (Current Controlled Trials number, ISRCTN59586944.)

Revascularization versus Medical Therapy for Renal-Artery Stenosis

A  Reciprocal of Serum Creatinine

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>Revascularization</th>
<th>Medical therapy</th>
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<tr>
<td>0</td>
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<tr>
<td>24</td>
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<td>36</td>
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<td>48</td>
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<tr>
<td>60</td>
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No. of Patients

Revascularization: 403 349 336 329 263 191 127 72
Medical therapy: 403 363 347 343 272 183 119 61

B  Serum Creatinine

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>Revascularization</th>
<th>Medical therapy</th>
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</table>

No. of Patients

Revascularization: 403 349 336 329 263 191 127 72
Medical therapy: 403 363 347 343 272 183 119 61
Revascularization versus Medical Therapy for Renal-Artery Stenosis

A Systolic Blood Pressure

B Diastolic Blood Pressure

Revascularization versus Medical Therapy for Renal-Artery Stenosis

A First Renal Event

\[ p = 0.88 \]

B First Cardiovascular Event

\[ p = 0.61 \]
BACKGROUND
Atherosclerotic renal-artery stenosis is a common problem in the elderly. Despite two randomized trials that did not show a benefit of renal-artery stenting with respect to kidney function, the usefulness of stenting for the prevention of major adverse renal and cardiovascular events is uncertain.

METHODS
We randomly assigned 947 participants who had atherosclerotic renal-artery stenosis and either systolic hypertension while taking two or more antihypertensive drugs or chronic kidney disease to medical therapy plus renal-artery stenting or medical therapy alone. Participants were followed for the occurrence of adverse cardiovascular and renal events (a composite end point of death from cardiovascular or renal causes, myocardial infarction, stroke, hospitalization for congestive heart failure, progressive renal insufficiency, or the need for renal-replacement therapy).

RESULTS
Over a median follow-up period of 43 months (interquartile range, 31 to 55), the rate of the primary composite end point did not differ significantly between participants who underwent stenting in addition to receiving medical therapy and those who received medical therapy alone (35.1% and 35.8%, respectively; hazard ratio with stenting, 0.94; 95% confidence interval [CI], 0.76 to 1.17; P = 0.58). There were also no significant differences between the treatment groups in the rates of the individual components of the primary end point or in all-cause mortality. During follow-up, there was a consistent modest difference in systolic blood pressure favoring the stent group (−2.3 mm Hg; 95% CI, −4.4 to −0.2; P = 0.03).

CONCLUSIONS
Renal-artery stenting did not confer a significant benefit with respect to the prevention of clinical events when added to comprehensive, multifactorial medical therapy in people with atherosclerotic renal-artery stenosis and hypertension or chronic kidney disease. (Funded by the National Heart, Lung and Blood Institute and others; ClinicalTrials.gov number, NCT00081731.)
### Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

<table>
<thead>
<tr>
<th>End Point</th>
<th>Stenting plus Medical Therapy (N=459)</th>
<th>Medical Therapy Only (N=472)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>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†</td>
<td>161 (35.1)</td>
<td>169 (35.8)</td>
<td>0.94 (0.76–1.17)</td>
<td>0.58</td>
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<td>Components of primary end point‡</td>
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<td>Death from cardiovascular or renal causes</td>
<td>20 (4.4)</td>
<td>20 (4.2)</td>
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<td>Stroke</td>
<td>12 (2.6)</td>
<td>16 (3.4)</td>
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<td>Myocardial infarction</td>
<td>30 (6.5)</td>
<td>27 (5.7)</td>
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<tr>
<td>Hospitalization for congestive heart failure</td>
<td>27 (5.9)</td>
<td>26 (5.5)</td>
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<tr>
<td>Progressive renal insufficiency</td>
<td>68 (14.8)</td>
<td>77 (16.3)</td>
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<td>Permanent renal-replacement therapy</td>
<td>4 (0.9)</td>
<td>3 (0.6)</td>
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<td>Secondary clinical end points‡</td>
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<tr>
<td>Death from any cause</td>
<td>63 (13.7)</td>
<td>76 (16.1)</td>
<td>0.80 (0.58–1.12)</td>
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<td>Death from cardiovascular causes</td>
<td>41 (8.9)</td>
<td>45 (9.5)</td>
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<td>Death from renal causes</td>
<td>2 (0.4)</td>
<td>1 (0.2)</td>
<td>1.89 (0.17–20.85)</td>
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<td>Stroke</td>
<td>16 (3.5)</td>
<td>23 (4.9)</td>
<td>0.68 (0.36–1.28)</td>
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<td>Myocardial infarction</td>
<td>40 (8.7)</td>
<td>37 (7.8)</td>
<td>1.09 (0.70–1.71)</td>
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<tr>
<td>Hospitalization for congestive heart failure</td>
<td>39 (8.5)</td>
<td>39 (8.3)</td>
<td>1.00 (0.64–1.56)</td>
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<td>Progressive renal insufficiency</td>
<td>77 (16.8)</td>
<td>89 (18.9)</td>
<td>0.86 (0.64–1.17)</td>
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<tr>
<td>Permanent renal-replacement therapy</td>
<td>16 (3.5)</td>
<td>8 (1.7)</td>
<td>1.98 (0.85–4.62)</td>
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Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

Hazard ratio with stenting, 0.94 (95% CI, 0.76–1.17)  
P=0.58 by log-rank test

<table>
<thead>
<tr>
<th>Years from Enrollment</th>
<th>Event-free Survival (%)</th>
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<tr>
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<tr>
<th>No. at Risk</th>
<th>Medical therapy alone</th>
<th>Stent plus medical therapy</th>
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<td>472</td>
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Recent indication for endovascular revascularisation

- Recent indications for endovascular revascularisation are limited
- Farmacotherapy is the main approach of treatment
- Recommendation for revascularisation:
  - Significant stenosis (>70%) in case of solitary kidney
  - Significant stenosis (>70%) of one of both renal arteries with difficult control of BP (3 or more antihypertensive drugs) and simultaneously:
    - progressive worsening of kidney function (serum creatinine levels > 150 μmol/l)
    - recurrent lung oedema
    - chronic congestive heart failure with recurrent episodes of decompensation
Ischemic nephropathy
Criteria for an intervention

- Kidney > 8 cm along the longitudinal axis
- Renal artery peripheral to the stenosis is open (RI < 0.80)
- Renal periphery is supplied from a collateral vascular network (angiographic or scintigraphic confirmation)
- Biopsy shows minimal glomerular sclerosis and minimal tubular atrophy
Conservative therapy of RVH

- **Antihypertensive therapy**
  - ACE inhibitors/AT$_1$ blockers
  - Ca blockers
  - Diuretics
  - Other antihypertensive drugs

- **Antiaggregation therapy**
  - after revascularization

- **Other therapy**
  - Weight loss, stop smoking, statins, antioxidants, folic acid, xanthine oxidase inhibitors
Atheroembolic kidney disease
Etiology and pathogenesis

- Embolisation of cholesterol particles sized 150-250 μm into peripheral branches of the renal vascular tree
- Associated with diagnostic or therapeutic interventions, less frequently develops spontaneously
- Elderly patients, hypertensive patients and smokers with symptoms of generalised AS, aneurysm of the abdominal aorta and hypercholesterolemia
- The cause of about 10 % of unexplained renal failures in patients older than 70 years
Atheroembolic kidney disease
Clinical picture

- Pain in the lumbar region
- Increased blood pressure
- Oliguria
- Rapidly progressing renal insufficiency
- As a result of microembolism other organs may be affected, in particular the brain, lungs, skin and the gastrointestinal tract
Atheroembolic kidney disease
Laboratory findings

- High leukocyte counts, high eosinophils
- Proteinuria
- Erythrocyturia, leukocyturia
- Decrease complement levels
- Serum levels of amylase, liver and muscle enzymes may be increased
- Increased plasma renin activity
- Increased fractional sodium extraction
Atheroembolic kidney disease

Diagnosis

- Only based on renal biopsy
  - Direct signs:
    Findings of cholesterol crystals in the lumen of arteriols under a polarising microscope
  - Indirect signs:
    Re-canalisation of arterioles, endothelium proliferation, giant-cell reaction in the vicinity of capillaries, tubulointerstitial fibrosis with eosinophilic and mononuclear infiltration, tubular necrosis
Atheroembolic kidney disease
Histology
Atheroembolic kidney disease

Therapy

- Symptomatic
  - Adequate hydration
  - Blood pressure control
  - Discontinuation of interventions
  - Discontinuation of anticoagulation therapy
- Dialysis in case of renal failure
Renal infarction
Renal infarction
Etiology and pathogenesis

- Embolism from the left atrium during atrial fibrillation
- Embolism from adherent thrombosis in the left ventricle after myocardial infarction
- Embolism from vegetations in infectious endocarditis
- Renal artery thrombosis adhering to pre-existing atherosclerotic lesions or traumatic intimal injury
- Occlusion due to dissecting aneurysm of the aorta or the renal artery
- Complication of endovascular interventions
- In association with the anti-phospholipid syndrome
Renal infarction
Clinical picture

- Sudden nausea, vomiting
- Pain in the lumbar regions or diffuse abdominal pain
- Elevated temperature
- Acute blood pressure elevation
Renal infarction
Laboratory findings

- High leukocyte count in peripheral blood
- Increased creatinine concentration (larger or bilateral infarction)
- Microscopic or macroscopic hematuria (30-50% of patients)
- Striking is the significant elevation of LDH activity (often more than 4x the normal value), aminotransferase activity is usually not increased
- ECG recording (atrial fibrillation)
- Imaging methods (colour Doppler ultrasound, MR-angiography or CT-angiography)
Renal infarction
Differential diagnosis

- Kidney stones
  (pain in the lumbar region and hematuria)
- Acute pyelonephritis
  (pain in the lumbar region and elevated temperature)
- Acute occlusion of mesenteric vessels with small intestine infarction
- Acute cholecystitis
- Acute pancreatitis
Renal infarction
Therapy

- Anticoagulation therapy, i.e. heparin followed by warfarin (target INR 2-3; in patients with atrial fibrillation 2.5-3.5)
- Intraarterial thrombolysis
- Angioplasty (the main factor for the success of endovascular therapy is a timely intervention)
- Surgical therapy is nowadays only reserved for cases of post-traumatic occlusion of the renal artery, where surgery is indicated for other injuries
Acute renal vein thrombosis

- Nephrotic syndrome
- Trauma
- Complication of interventions in the renal vein (phlebography, surgery)
- Hypercoagulation (thrombophilic) states
- Spontaneous
Chronic renal vein thrombosis

- Nephrotic syndrome
- Tumours
- Retroperitoneal fibrosis
- Veno-occlusive disease
Renal vein thrombosis
Clinical picture

- Acute thrombosis
  - Pain in the lumbar region
  - Elevated temperature
  - Decreased glomerular filtration
  - Hematuria
  - Nephrotic proteinuria

- Chronic thrombosis
  - Development of severe nephrotic sy
Hypertensive nephrosclerosis
Pathologic-anatomic correlate

- Hypertrophy of lamina media of renal arterioles due to increased deposition of collagen
- Arteriolar lumen becomes narrowed, peripheral vascular resistance increases
- Secondary FSGS develops in some patients
Hypertensive nephrosclerosis

Diagnosis

- Long history of arterial hypertension
- Decreased glomerular filtration
- Proteinuria < 1 g/24 h (with the exception of patients with FSGS)
- Urinary sediment is usually normal
- Ultrasound examination may find slightly smaller kidneys (< 10 cm), with uneven surface and reduction of cortical layer (< 10 mm)
Hypertensive nephrosclerosis Therapy

- Increased physical activity
- Protein intake restriction to 0.8 g/kg
- Salt intake restriction to 5-6 g/day
- Correction of arterial hypertension (ACEI)
- Hypolipidemic drugs (statins)
- Treatment of hyperuricemia (xanthine oxidase inhibitors)
- Treatment of hyperhomocysteinemia (folic acid)
- Treatment of nephrotic proteinuria (ACEI + sartans)