Renovascular hypertension Update

Seminars in Hypertension Management

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Important correctable cause of secondary HT

- <1% in mild elevations of BP

- 10-45% acute, severe, refractory HT
Clinical:

- Early Age of Onset <30 years of age
- Late Onset >55yrs with severe HT
- Refractory/ Resistant HT despite medication > 3 anti HT medications
- Acute rise BP in previously stable hypertensives
- Malignant HT
- Acute elevation in Cr after ACEI/ARB
- Severe HT with recurrent Flash pulmonary oedema
- Abdominal bruit localised to one side

Causes

- Fibromuscular dysplasia (FMD)
- Atherosclerosis
Fibromuscular dysplasia (FMD)

- noninflammatory, nonatherosclerotic disorder leading to arterial stenosis
- occurs in every arterial bed
  - Renal 60-75%
  - Internal Carotids

Clinical: (FMD)

- $F>M= 10:1$
- Age <50yr
- accounts for 105% of renovascular HT
- Bilateral disease in 50%
- HT
- progressive worsening of renal function is relatively rare.
  - usually occurs in intimal / perimedial FMD
Atherosclerosis

- accounts for 5-22% of CRF in age > 50yrs
- associated with systemic atherosclerosis
  - 4-5x higher rates of coronary, cerebrovascular, peripheral arterial and heart failure rates

How common is the problem?

- 4000 patients
- abdominal aortography immediately after coronary angiography

*Conlon PJ et al. Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography. KI 2001 Oct; 60(4):1490-7*
Incidental RAS:

- >=50% lesion
  - 9.1%
- >=75% lesion
  - 4.8%
  - significantly associated with reduction in survival (57% vs 89%)
- Bilateral
  - 0.8%

Progression of Atherosclerosis

How fast?
Prospective study of atherosclerotic disease progression in the renal artery


Follow up duplex US of 295 kidneys over 33 months
cumulative incidence of progression at 3 yrs:

- < 60% stenosis
  - 28%
- > 60% stenosis
  - 49%

- complete occlusion occurred only in 3% cases

Tests

- Renal arteriography
- Magnetic Resonance Angiography
- Computer Tomographic Angiography
- Duplex Doppler Ultrasonography
- Others
Renal arteriography

Gold Standard

Magnetic Resonance Angiography
MRA: Newer studies:

- Sensitivity 100%
- Specificity 71-96%
- Technical improvements continue:
  - the use of breath-hold MR angiography with paramagnetic contrast material, gadopentate dimeglumine, substantially improves the ability to visualize some (but not all) accessory arteries

Computer Tomographic Angiography

- combines diagnostic accuracy of arteriography with low risk of IV DSA
- Accuracy lowers when serum Cr > 150umol/L
  - due to reduced renal blood flow
Duplex Doppler Ultrasonography

- Provides Both anatomical and functional assessment of renal arteries
- possible to detect bilateral disease or recurrent disease
- Problems:
  - time consuming
  - very operator dependent

Other tests:

- Plasma Renin
  - elevated in 50-80% cases
- Captopril Renogram
  - ACEI induced decline in GFR in stenotic kidney
  - 2005 ACC/AHA guidelines: no longer used as screening test
- IVP
  - decrease in renal size
  - delayed caliceal appearance time
Treatment

- Unilateral vs Bilateral RAS
- Atherosclerosis vs FMD

Bilateral RAS
Indication:

- hemodynamically significant stenosis
- Both vessels showing >75% stenosis

3 Modalities:

- Anti-HT medications
- Percutaneous angioplasty
- Surgery
Anti HT medications

ACEI/ARB +/- HCTZ

- bilateral renal ischaemia induces activation of RAS
  - Na+ expansion
  - Volume expansion

- But: hemodynamically mediated decline in GFR
  - Rise in Cr
  - Can you have both BP control and stable renal function?
  - Would normalisation of BP lead to long term ischaemic atrophy?
  - Atherosclerotic lesions do progress
Ca channel Blockers

- dilates preafferent arteriole
- easier to maintain serum Cr
- ?

  - some animal studies suggest that calcium channel blockade may not protect the stenotic kidney and may worsen the hypertensive injury in the nonstenotic kidney when compared to ACE inhibition

Beta Blockers
Risk factor reduction

Percutaneous angioplasty + stent placement

- Predictive factors for benefit:
  - High systolic BP
  - Renal insufficiency

Renal artery angioplasty and stent placement: predictors of a favorable outcome. Burket MW; Cooper CJ; Kennedy DJ; Brewster PS; Ansel GM; Moore JA; Venkatesan J; Henrich WL. Am Heart J 2000 Jan;139(1 Pt 1):64-71.
Surgery

- Revascularisation

- Nephrectomy for nonfunctioning, atrophic kidney

2005 ACC/AHA guidelines:

- surgery in patients with atherosclerotic renal artery stenosis who have indications for revascularization and have multiple small renal arteries or require aortic reconstruction near the renal arteries for other indications (e.g., aneurysm repair or severe aortoiliac occlusive disease)
Unilateral RAS

Medical therapy

- indicated in all patients
- ACEI/ARB +/- HCTZ
- Ca channel Blockers
- Beta Blockers
Problems with Medical therapy:

- progressive Stenosis
  - 30-60% increase in stenosis within 4-7 years
  - Atherosclerosis > fibromuscular dysplasia

- Long term ischaemic loss of renal mass

Percutaneous Angioplasty

- success rate dependent on:
  - site of lesion
  - pathology
Site of lesion:

- Best: incomplete occlusion in the main renal artery
- Poor: total occlusions / ostial lesions

pathology:

- Atherosclerosis
  - Cure rates: 8-20%
  - 2 year restenosis: 8-30%
- Fibromuscular dysplasia
  - Cure rates: 50-85%
  - 2 year restenosis: <10%
Percutaneous Angioplasty + Stenting

- recommended in ostial atherosclerotic lesions
- long term benefits await further trials

Surgery

- Bypassing stenotic segment
- Nephrectomy of small atrophic kidney
- Predictor of clinical response
  (normalisation of BP):
  - <5 yr history of HT
Mr. Cheung
51/M
HT
ESRF of unknown cause.
USG: bilateral small kidney.
CAPD started on 11/2002.

Cadaveric renal transplant on 26/12/2002.
Urine output right away according patient
no HD/CAPD done after OT
Best Cr 118 umol/L
other details unknown
discharge from hospital D20
seen in transplant clinic on 29/1/2003

- no particular c/o
- good urine output
- BP150/95 mmHg
  - wound healing well
  - graft : nontender.
  - urine dipstix: Alb 1+/RBC -ve

Medications:

- Cyclosporine A 200mg BD
- Prednisolone 20mg daily
- MMF 500mg bd
- Acyclovir 200mg tds
- Betaloc 25mg bd
05/02/2003

- Septrin 480mg daily was added
- Betaloc was changed to Diltiazem


- Cr 135→ 133→122→ 132 umoL
- BP 16/4/2003: 151/91 mmHg
- 21/5/2003: 174/110 mmHg
- 26/5/2003: 178/86 mmHg
- ↑ dosage of aldomet, diltiazem and betaloc
Doppler USG of graft Kidney (17/6): normal echogenicity with preserved cortico-medullary differentiation. Doppler findings are unremarkable with RI of interlobar arteries ranges from 0.58 to 0.61. Graft kidney was 10.5 cm in length.

- Cr ~153 on 23/6/2005 (~120-150)
- C/O ankle edema
- stopped septrin /acyclovir/diltiazem
- **Ramipril + Betaloc+ Aldomet** on 25/6/2003

Clinical admission on 1/7/2003 for abnormal RFT

- post-renal transplant 6mth
- C/O Generalised oedema,
- decrease urine output.
- no other urinary symptoms
- not on herbs/NSAID
- BP 154/80mmHg
- euvolumic
- afebrile
- Urine multistix: RBC 1+, albumin 1+
- no graft tenderness

- **Cr: 1031**
- WCC 5.1, Hb 11.6, platelet 133.
- MUS: no growth
- CMV pp65 antigenaemia: -ve

**USG Abdomen**

- USG of abd: transplant kidney over right iliac fossa with normal size and outline, 10.3 cm in length. No definite perinephric fluid collection is seen. Pelvicalyceal system is not dilated. No renal stone of renal mass is noted. Main renal vein is patent. Sampling of intra-renal vascular resistance within normal limit (RI 0.6-0.7)
Renal Bx

- 1) consistent with borderline acute cellular rejection.
- 2) Features suggestive of mild ATN
- 3) Presence of CMV virus inclusions within renal tubules.

- 3x pulse methyprednisolone was given
- Increase prednisolone to 40mg daily.
- 2/52 Iv ganciclovir was started
- Put on IPD
- Cr level: 1031>669->400
- Increase of urine output 1-1.5 L per day

Plan:
- 1) outpatient IV ganciclovir
- 2) Captopril DTPA scan to R/O RAS after RFT
  stabilized
7-8/2003:

- Urine output increased to 1-1.5 L daily
- Cr further improve 400->277->185

- **Captopril Renogram**: DTPA prompt perfusion of the graft kidney, renogram reach its peak within 3.5 minutes, tracer washout is satisfactory
  Conclusion: **no evidence of RAS**

22/8/2003

- C/O Decreased of urine output again.
- Cr 169(14/8)->465(21/8)->648(22/8)

- Doppler US 23/8/03: In anastomotic site, arterial flow shows high resistance flow (RI 1.2) with increase peak systolic velocity (~330m/s). However, main renal art and intralober renal art show low-resistant flow with RI<0.7
29/8: renal bx: Some tubules suggestive degenerative and regenerative change. The glomeruli, capillaries, mesangium and capsules are unremarkable. IF microscopy show no deposits. Features are suspicious of ATN.

- Cr 1065
- Put on APD

**MRI Angiography**

- MRI angiogram on 8/9/03: highly suggestive of underlying renal artery stenosis at the site of renal artery anastomosis.

- Renal angiogram +angioplasty performed on 15/9/03
Progress

- Cr 896(12/9)->336(15/9)->199(25/9)->134(9/10)

- Anti HT medication reduced to Diltiazem SR 90mg daily

- BP 135/85mmHg

Thank You

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Transplant Renal artery stenosis (TRAS)

- Relatively frequent cause of refractory HT and allograft dysfunction in renal transplant patients
- It is important because it is potentially curable
- Incidence rates vary from 1% to 23%.
  - Different techniques used in diagnosis

Most frequent presentation:

- Increasingly severe HT with/without allograft dysfunction, between 3 months to 2 yrs after Tx, (but can present at any time after transplantation)
- Use of ACEI may produce dramatic presentation
  - Rapid deterioration of RFT, or event acute renal failure, severe hypotension
Causes

- Technical cause
  - trauma (e.g. clamping, cannulation, traction) to donor or recipient art during procurement or transplantation
  - suture technique
    - TRAS has been more commonly observed after end-to-end arterial anastomosis esp. when endarterectomy is required to render the hypogastric art suitable for use.
    - TRAS is rare when a Carrel patch of the donor aorta is used for end-to-side anastomosis to the external iliac art.

- Immunologic cause
  - rabbit arterial endothelium exposed to xeno and alloantibodies developed intimal proliferation
  - in humans, histological changes (extensive fibrous endarteritis and intimal proliferation) in the stenosed arteries strikingly similar to vascular lesions of renal allograft rejection.
  - However, a similar incidence of TRAS in HLA-identical living-related donor grafts has also been found.
  - Immunologic factors may not be the major etiologic determinant.
Cyclosporin A

- cases report that TRAS completely resolved after the withdrawal of cyclosporin

Diagnosis

- Presence of renal bruit
  - indicate increased vascular turbulence, lack both sensitivity and specificity for TRAS
  - TRAS can be presence with no audible bruit
Plasma renin activity
- renal hypoperfusion induced renin production from juxtaglomerular cells
- result is hard to analysis due to influences from antihypertensive used and patients native kidneys

- selective venous sampling (from the vena cava, the infra- and supra renal iliac and renal veins) with with without captopril augmentaiton increases the specificity

- Disadvantages: expensive, invasive, requires meticulous technique (esp in handling and labeling of samples), results are not readily available

Radiological imaging
- Duplex and color-flow Doppler USG
  - highly sensitive
  - noninvasive
  - useful for screening
  - intrarenal resistant index (RI): calculated from the signals of the segmental renal arteries, can detect RAS with a sensitivity of 70% to 93% and a specificity of 90% to 96%
  - 10-20% rate of failure
• Spiral CT angiogram
  • provide satisfactory 3-dimensional reconstruction of vessels and requires less IV contrast then conventional angiography

• MRI angiogram
  • mainly the 1st 3cm of the renal art can be visualized with accuracy and excessive motion artifact may encounter

➢ Isotopic renography performed before and after a dose of captopril
  • reported sensitivity of 75% and specificity of 67%
  • however, it is highly predictive of physiologically significant renal art stenosis
Digital subtraction angiography

- Gold standard for diagnosis of TRAS
- To evaluate the extent of intrarenal vascular disease and the dimensions of the kidneys.
- Diagnostic in 93% of cases
- Invasive, contrast nephropathy.
  - Low or iso-osmolar contrast for normal renal function
  - CO2 angiography for renal insufficiency
- Reserved for patients with features that are compatible with TRAS

Treatment

1) Conservative treatment
2) Percutaneous transluminal renal angioplasty
3) Surgical correction
Conservative treatment

- spont regression of TRAS has been described
- most patients experience poorly controlled hypertension and worsening allograft function
- Hemodynamically significant stenosis (>70% stenosis, pressure gradient >15mmHg) are likely to produce impaired function and have a tendency to progress with a substantial risk of graft loss

PTRA

- Technical success rate is over 80%.
  - BP control improved over 75% and renal function stabilized or improved in over 80%.
  - A 60% failure rate reported in those patients with arterial kinking
- Complication such as arterial rupture, dissection and thrombosis occurs at rate of 10%
Restenosis rate range of 10% to 33%.
PTRA is repeatable and a repeat procedure can maintain long-term improvement.
Metallic stents have been used recently to treat recurrent TRAS.

In general, PTRA is recommend as the intervention of 1st choice for TRAS that are short and linear.
Surgical correction

- Resection and revision of anastomosis, saphenous vein bypass graft of the stenotic segment, patch graft, localized endarterectomy
- Difficult operation and technically demanding

- High success rate 65-95%,
- Recurrent rate of approximately 12%.
- A significant risk of graft loss (15-20%), ureteral injury (14%), reoperation (13%) and mortality (5%).
Summary

1) TRAS should be considered in any patients who has severe hypertension or unexplained deterioration in renal function at any time after transplantation.

2) Several imaging techniques are available to confirm the diagnosis and their use will depend, in part, on the center experience.

3) PTRA is the 1st choice of intervention if needed.