Acute Renal Failure

HISTORY OF PRESENTING ILLNESS

There are 3 distinctive forms of acute renal failure, with different histories. They all share some components.

- Thirsty
- Dizzy
- Oliguric
- Hypotensive
- In Heart Failure (low output)
- Recently has been
  - Vomiting
  - Diarrhoea-ing
  - Haemorrhaging
  - Coagulopathic eg. DVT
- May be dehydrated because
  - septic
  - Elderly
  - Comatose
  - Sedated
  - Idiot intern forgot to write anything up in the fluid chart

- Haematuric (frank red)
- Tea-coloured myoglobinuria (Especially with MYALGIA or some sort of severe TRAUMA)
- Frothy urine
- Oedematous
- Hypertensive
- Recent Infection (? THROAT ?)
- Recent IV contrast study
- Drugs used recently, eg.
  - NSAID + ACE-Inhibitor + Lasix
  - Gentamicin (or any aminoglycoside)
  - Aspirin + Caffeine (alcoholics)
  - Cyclosporin (immune suppression)
  - Amphotericin (anti-fungal, in HIV)

- Getting hard to pee of late
- Obstructive symptoms, dribbling and whatnot
- Urgency
- Frequency
- Hesitancy
- Hematuria
- Renal colic or Hx of stones
- Previous gynae surgery
- Only one kidney (other one donated, diseased or simply never existed)

DRUGS eg.
- Acyclovir
- Methotrexate
- Sulfonamides

All form tubular crystals

By the end of your history-taking its should be blindingly obvious where the problem is.

PRE-RENAL CAUSE | INTRA-RENAL CAUSE | POST-RENAL CAUSE

Physical Examination → FIRST THINGS FIRST: WHATS THE BLOOD PRESSURE??

LOOK FOR:
- JVP way low?
- Skin turgor all gone?
- Mucosa dry as a bone?
- Tachycardia?
- Postural hypotension?
- Pale as a sheet?

…could your patient be dehydrated, or bleeding internally somewhere? FIND OUT WHERE.

If that's not their problem;
- Are they vasculopathic? I.e…
- Have they got atheromae everywhere? Is there a RENAL ARTERY BRUITT? Could they have haemorrhaged into a renal artery atheroma?

Alternatively,
- Is the LVEF enough to perfuse the kidneys?
- Is there an AORTIC ANEURYSM diverting blood flow from their kidneys?

LOOK FOR:
- Purpura, rash, keratitis: Systemic vasculitis?
- Oedema
- Hypertension
- Sore red throat with the typical pus of strep pharyngitis
- Ischaemic limbs
- Signs of major trauma
- Stigma of diabetes

LOOK FOR:
- Distended bladder
- Renal angle tenderness (Murphy's kidney punch)
- Surgical scars (how many kidneys left?…)

MOST COMMON PRESENTATION IS DUE TO DEHYDRATION IN AN ELDERLY PERSON WHO HAS JUST HAD A CONTRAST STUDY

If none of those;
- Are they Atrially Fibrillating?
  - If yes, are they properly heparinised / warfarinised?
- Track Marks of the Junkie? (Endocarditis with septic emboli?)
- Have they recently fractured a big long bone? (marrow fat embolus) COULD THEY HAVE THROWN A CLOT into their last working kidney?

Or maybe…
- Are they mid-liver-failure? i.e is all the body fluid sequestered in their abdomen as ascites, and that's why they aren't perfusing their kidneys?
- ARE THEY SEPTIC and just too old to develop a raging temperature?

INVESTIGATIONS

URINE OUTPUT:

supra-pubic catheter

get a catheter in, the easy way or the hard way

ANURIA: **Not many things will make you completely ANURIC.**

- **complete obstruction of urethera by a huge angry prostate**
- **Rapidly Progressive Glomerulonephritis**
- **Total obstruction of the renal arteries** (or your last renal artery)
- **Bilateral Diffuse Renal Cortical Necrosis** (for whatever reason)

OLIGURIA: **Most ARF patients will be oliguric. This includes**

- **partial obstruction of last remaining ureter by a stone**
- **partial renal artery stenosis**
- **renal embolism** (for whatever reason)
- **HEPATORENAL SYNDROME** (in liver disease, where the sequestration of fluid in ascitic compartments leads to over-activity of the RAAS system and hence vasoconstriction of the renal vessels)

Oliguria is defined as a urine volume less than 500 ml of urine over 24 hours (or less than 20 mls/hr).

NORMAL OUTPUT: **A lot of ARF patients will be making urine as usual.**

- **Acute Glomerulonephritis** (there's still enough urine, its just turned red)
- **Nephrotoxic Acute Tubular Necrosis** eg. after contrast study
- **Ischaemic Acute Tubular Necrosis** eg. after volume depletion / heart failure
- **Rhabdomyolysis ATN – normal urine volume at first, but it is tea-coloured.**

So, your patient is peeing tea.
This could be due to rhabdomyolysis. CK enzyme elevation will support this diagnosis (it's the creatine kinase which leaks from damaged muscles).

BEWARE: myoglobin, being full of heme, will cross-react with the heme-sensing "blood" part of the dipstic urinalysis, and give a false positive for blood.

URINALYSIS :

SEDIMENT WILL BE NORMAL IN MOST CASES OF PRE and POST RENAL FAILURE.
There is no reason for anything to be happening in the urine if somebody has blocked the blood supply to the kidney, or blocked off the outflow of urine through the urethra (eg. the prostate).

HOWEVER: Multiple red cells of a normal shape suggest post-renal calculi.
(bled from the shredded walls of the ureter as the calculus scrapes along them)

In INTRA-RENAL FAILURE, the SEDIMENT HAS MEANING:

- **Granular casts** - ATN, glomerulonephritis, interstitial nephritis.→→
- **RBC casts** - Glomerulonephritis, malignant HTN
- **Rouleaux RBC casts** = multiple myeloma
- **WBC casts** - Acute interstitial nephritis, pyelonephritis
- **Eosinophiluria** - Acute allergic interstitial nephritis, atheroembolism
- **Crystalluria** - Acyclovir, sulfonamides, methotrexate, ethylene glycol toxicity, IV contrast

Got brown casts made of tubule cells?
ITS ACUTE TUBULAR NECROSIS

FBC

MAINLY FOR COMPLETENESS. Most changes with acute renal failure will not change the blood count, with the following exceptions:

Hb **will be reduced in chronic renal failure that has turned acute.**
- Also look at the RBC indices; you expect normochromic normocytic anaemia

WCCs **will be meaninglessly elevated in SEPSIS** (you knew it was sepsis before you saw the FBC)

EUC is WHERE THE MONEY IS:

Creatinine and Urea will be HIGH

Creatinine elevation pretty much defines ARF. You can pretty well guess that they also will be

- **HYPERKALEMIC and**
- **HYPOCALCEMIC and**
- **HYPERPHOSPHATAEMIC**

ECG: **tall peaked T waves reaching as high as the QRS**
Look like knives- no rounded tip, very sharp
Extremely high K+ = the whole ECG becomes sinusoidal

IMAGING: Renal Ultrasound

This consumes time, and may not teach you very much.
MASSIVE HYDRONEPHROSIS will show up with ultrasound (eg. in long standing urinary retention)
TINY DEAD KIDNEYS will be expected if the patient has had chronic renal failure for years and has recently suffered an exacerbation (eg. chronic glomerulonphritis)

Renal Vein + Artery Doppler

You may discover to your delight that there is indeed **a huge thrombus occluding the renal artery**.
OR you may find that there is **significant stenosis**

Renal Artery Angiogram (percutaneous or MRI)

Indications are very much the same as above. A Percutaneous angiogram also offers some help in clearing the blockage (eg. angioplasty or stenting). However harsh iodinated angiography dye may kill off the last of your kidney, whereas gentle Gadolinium MRI contrast will not do any harm. Mmmm, Gadolinium.

CT scan may show hydronephrosis and maybe even the site of the blockage, as you follow the distended ureter down the slices.

Chest X-ray will tell you if you need to be worried about pulmonary oedema; it will also point the way towards some weird diagnoses (eg. Wegener's Granulomatosis or Goodpasture Syndrome which can cause an acute glomerulonephritis)

So, you still have NO IDEA why your patient is deteriorating.

It may be necessary to resort to RENAL BIOPSY. Especially if glomerulonephritis is suspected

This procedure carries all the risks implied in puncturing a deep organ with a big needle.
A questionnaire among Antipodean nephrologists revealed that abour 30% of them would prefer to wait until 4 weeks into the ARF before they would biopsy.

Barrier Keywords:
Immunofluoresecence
Electron Microscopy

Contraindicated if:
- **Only one functional kidney**
- **Hideous coagulopathy (just wont clot)**
- **Small kidneys on ultrasound (fibrotic)**

With a renal biopsy, a skilled pathologist will be able to return to you with a diagnosis from one among a massive number of acute glomerular and tubulointerstitial problems, the list of which would take a semester to describe.

EMERGENCY MANAGEMENT OF ACUTE RENAL FAILURE

… should begin before a definitive diagnosis is made.

1. **URINARY CATHETER: if the problem was an obstructive prostate, you just solved it.**
   Now just a matter of sitting out the diuresis phase and waiting for your elective TURP.
2. **HYPOVOLEMIA is your enemy. FLUID OVERLOAD is also your enemy.**
   It is necessary to take great care with the fluid management of someone in ARF of any aetiology.
   HYPOVOLEMIA should be reversed until the JVP is seen. USE NORMAL SALINE.
   Having given a bag of saline stat, see if the patient has responded (i.e, is there now more urine being produced?)
   NO RESPONSE TO FLUID CHALLENGE: try a loop diuretic.
   Still nothing?
   TIME TO CONSIDER DIALYSIS.

   If you did manage to coax your anuric dehydrated patient back into oliguria,
   Continue the fluid replacement according to output: 100ml out = 100ml in
   THIS SHOULD MAINTAIN PEFUSION OF THE KIDNEYS AND IMPROVE WASH-OUT
   (which is the beneficial movement of weird debris out of the tubules and into the toilet)

3. **WHATS THE pH? Diseased kidneys cannot regulate acid-base balance.**
   You must act as your patients kidneys, topping up the bicarbonate as needed.
   ACIDOSIS may be aggravated by the pulmonary oedema due to your overzealous fluid management, as well as the renal pathology. Make certain the patient is able to regulate at least the respiratory component of the pH equation.

4. **WATCH THE ELECTROLYTES. ARF patients die from cardiac causes.**
   HYPERKALEMIA: stack all the methods of lowering potassium known to you one on top of another, especially if the patient has K+ approaching 7.0
   This means:

Everything goes with **CALCIUM GLUCONATE** which is cardioprotective by increasing threshold potential and thus averting a fatal episode of VT

Give 10% dextrose (healthy young person should be able to generate their own insulin)
Or… Give 10% dextrose AND rapid-acting insulin
Resonium resin orally. (scavenges K+ from gut wall)
Salbutamol (ventolin) – beta agonists in general will increase K+ uptake
Loop Diuretic (will cause K+ wasting from tubules)
Last ditch effort is DIALYSIS.

CONTROVERSIAL MEASURE:

DOPAMINE goes in and out of favour: rumoured to dilate renal arteries. Lower doses stimulate mainly dopaminergic receptors that produce renal and mesenteric vasodilation; cardiac stimulation and renal vasodilation produced by higher doses. **Pure anecdote, most recent study failed it in terms of urine output benefit, and showed that it had pro-arrhythmic effects. Best renal vasodilator is still fluid replacement until euvolemia.**

It is meaningless to speak of prognosis and epidemiology of this problem, as it is too wide a spectrum of disorders to be considered beneath the same umbrella term “acute renal failure”. Rhabdomyolysis as the cause of acute renal failure is almost unheard of in the Australian community, where renal vein thrombosis and acute glomerulonephritis are the norm. ATN, however, is the complication of almost every acute renal impairment.

Mechanism of Acute Renal Failure secondary to Rhabdomyolysis

HIDEOUS INJURIES

Crush injury, pressure sores, freezing injuries, extensive burns, psychopathically excessive exercise, vascular disease causing whole-limb ischaemia, widespread sepsis, inflammatory myopathy, blast injury eg. bomb explosion, alcoholism, and over-use of MDMA in a rave dance-club setting

Widespread cell destruction, on a massive scale, and thus **TORRENTIAL LEAKAGE OF CELLULAR CONTENTS**

URIC ACID , Lactic acid,

MYOGLOBIN

PHOSPHATE

POTASSIUM

Metabolic Acidosis

Excess phosphate combines with serum calcium and leads to **HYPOCALCEMIA**

In combination hyperkalemia and hypocalcemia lead to increased **CARDIAC TOXICITY eg. ARRHYTHMIA**

Sodium and water move into the damaged muscle: **MANY LITRES MAY BECOME SEQUESTERED!**

Injury-related haemorrhage **(or, drugged +/- drunken dehydration)**

Low molecular weight → means it easily excreted, thus **tea coloured urine** and **blood +++ on urinalysis** because the dipstick only tests for heme

ACIDURIA

MYOGLOBINURIA

HYPOVOLEMIA

HYPOTENSION

Myoglobin in the bloostream scavenges NO, and this causes **reduced vasodilation**

Low urine pH means lower solubility of the heme units

RENAL HYPOPERFUSION
Due to vasoconstriction secondary to RAAS activation

Reduced GFR,
thus reduced rate of wash-out

MYOGLOBIN PRECIPITATES INTO TUBULAR CASTS

MAJOR PATHOLOGY HAPPENS HERE:
Now you got iron-rich protein congealing up your tubule. This has numerous unsavoury CONSEQUENCES:

MECHANICAL:

Tubules crammed full of myoglobin casts become dilated with backpressure, and the fragile tubular **brush border is destroyed** by the crude effect of having proteinaceous waste forced through it.

Loss of brush border: Its full of enzymes, eg. carbonic anhydrase, which produces your renal bicarbonate- and so **THE ABILITY TO REGULATE ACID- BASE BALANCE IS LOST** which contributes to the heme-depositing tubule-clogging aciduria

Eventually the macrophages will come and bulldoze down the dead tubules and clean out all the myoglobin.

BIOCHEMICAL

Myoglobin is a protein, and the tubule attempts to transport it back into the bloodstream using its normal mechanism of ATP-dependant transport There being so much of it, the ATP reserves of the blood-starved tubule are depleted rather quickly.
ATP depletion means you cant power all those ion pumps, and thus control of electrolyte concentration is lost.

PROLONGED ATP DEPLETION
(i.e. you DONT get the kidneys re-perfused)
= CORTICAL NECROSIS
= no recovery

CELLULAR + GENETIC:

Iron, of which myoglobin is full, seems to be toxic to the tubule epithelium. By itself its a free radical, and it will generate new free radicals when you reperfuse the kidneys with your well-intentioned litre of IV saline- because oxygen will actually be able to get down there.
Superoxide Dismutase will cope with this ...for a while. Then, the oxidative stress will burn the DNA and the lipid bi-layers.
This is irreversible.

OTHERWISE...

Lots of mitosis and a little fibrosis: the kidneys restore their architecture; tubule cells recover their ion pump functins AFTER the tubules are cleared up, and thus there is a period of **massive polyuria** , while the urine concentrating mechansms still havent come back online . this is the so-called **DIURESIS PHASE.**

Acute Glomerulonephritis

- **Abrupt onset of obvious macroscopic hematuria**
- **Oliguria**
- **Sudden decrease in glomerular filtration rate →**
- **Proteinuria below nephrotic range (<3g/day)**
- **OEDEMA** occuring as a result of sodium retention and not hypoalbuminaemia

ITS ALMOST ALWAYS A POST-INFECTIOUS SITUATION!

Triggering Events:

- **POST-INFECTIOUS eg. post-streptococcal**
  - **Mainly in young children with a runny nose**
  - **Occurs ~2weeks after the initial infection**
  - **Mediated by immune-complex deposition AND by the accumulation of streptococcal antigens in the glomerular filtration membrane... which then attract all kinds of immune retribution, mainly in the shape of angry complement and macrophages.**

Creatinine: measure of GFR

released from skeletal muscle at a steady rate; high level is associated with large muscle mass and exercise

high creatinine better be found in a large well-muscled patient, not a frail 90 yr old woman.

THUS in a hypovolemic patient the GFR will drop and thus the serum creatinine will RISE

Normal creatinine = GFR must be OK

FILTRATION RATE: ~100 ml per minute; = Carefully controlled!

Very steady between 90 and 200 systolic

only extremes of blood pressure influence the GFR.

INCREASED BP = reflex contraction of smooth muscle in afferent arteriole, thus reduced flow still means GFR maintained at the same level

Natural History

RESOLVES SPONTANEOUSLY! No cause for dismay

Strep infection;

1-2 weeks later: onset of oedema + hemoproteinuria
1-2 weeks of oedeme and hemoproteunuria with massively elevated creatinine and Na+
1-2 weeks of wild diuresis
1-2 weeks of continuing creatinine abnormalities, tapering off;
6 months of hematuria
X years of proteinuria (variable; persists for 10 years in 2% of patients)

Only 1 or 2% of post-strep GN patients progress to ESRF

Diagnostic Side-Dishes

BIOPSY with immunofluorescence and electron microscopy is the *ONLY MEANS OF DIAGNOSIS...*

Certain immunological chan
take place in post-infectious GN, and these can be employed to point the way towards a diagnosis.

COMPLEMENT components, esp. C3 are depressed during the early course.
THESE SHOULD RETURN TO NORMAL 6-8 weeks after onset
IF THEY HAVE NOT: !! RED FLAG !! it may be lupus nephritis

STREP ANTIBODIES wont diagnose post-strep GN for you, but they will tell you if a strep infection has taken place recently.
...Look for antibodies to...

- **Streptolysin O** (be warned- only 66%of streptococci wield this weapon)
- **Streptokinase**
- **Hyalouronidase**
- **Nicotinamide Dinucleotidase**

MANAGEMENT IS SUPPORTIVE and consists of....

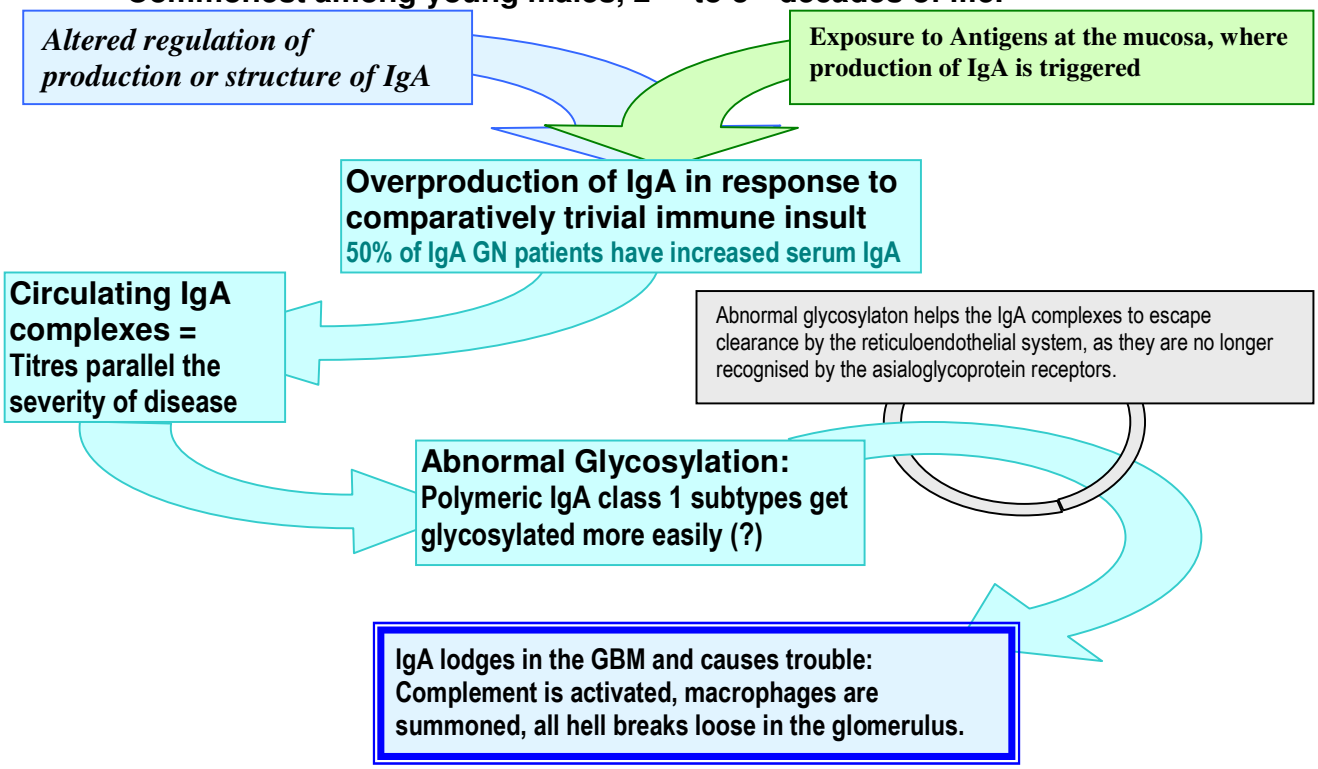
MANAGING FLUID OVERLOAD with diuretics
MANAGING HYPERTENSION which results from fluid overload with conventional agents

Asymptomatic Hematuria in Glomerulonephritis

BEWARE! Asymptomatic hematuria can mean ANY DAMN THING.
Glomerulonephritis is JUST ONE POSSIBILITY.
BUT!... if there is also PROTEINURIA, you must keep GN in the back of your mind.

IgA Nephropathy is the commonest GN cause of asymptomatic hematuria

Commonest among young males, 2nd to 3rd decades of life.



PRESENTATION and NATURAL HISTORY

- In 50-60% of cases **ASYMPTOMATIC GROSS HEMATURIA**
- In 30% of cases, **ASYMPTOMATIC MICROSCOPIC HEMATURIA**
- In 10% of cases, NEPHROTIC SYNDROME or ACUTE GLOMERULONEPHRITIS
- **Simultaneous Respiratory or GIT infection**
- 10-20 years later, END STAGE RENAL FAILURE . Especially if:
  - elderly
  - male
  - hypertensive
  - proteinuric
  - already crappy kidneys

AT-RISK GROUP!! Should at least ATTEMPT TO RETARD PROGRESSION TO END STAGE RENAL FAILURE

SO WHAT DO I DO?

Supportive management.

- Keep fluid balance in the realms of normality
- Diuretics for overload, saline for dehydration.
- If your patient runs the risk of progressing to ESRF, try corticosteroids or fish oil.
- **ACE inhibitors for all!**
- **Ang II receptor blockers for some.**

So many trials, so many mixed results:

- **Corticosteroids:** decrease proteinuria, but no change in disease progression. Pfft.
- **Fish Oil**: n-3 fatty acids should limit the production and/or action of cytokines at the glomerulus. Some success. One very wonky trial showed extreme benefit. 6% fish-oilers doubled their serum creatinine over 4 yrs , versus 33% of placebo group.
- **ACE inhibitors**: there is OBVIOUS BENEFIT; **All experts agree**.

Rapidly Progresive Glomerulonephritis

Just like acute glomerulonephritis, but in fast forward: rapid decline in renal function , and subsequent end-stage renal failure within days or weeks.
LUCKILY ITS RARE. 2 to 4% of GN are rapidly progressive.

PATHOLOGICAL HALLMARKS:
Cellular crescents
surounding the glomeruli.
- these are made of endothelial cells, mononuclear infiltrate and recruited fibroblasts.

ALSO:
- linear deposition of immunoglobulins all along the GBM in 20%
- granular (blobby) deposition of these Ig's in the GBM in 30%.
- In the remainder of pts, no immune deposits of any sort are detectable.

Natural History

- **INSIDIOUS ONSET:**
  - **Malaise, lethargy, microscopic hematuria**
  - **Proteinuria in ~30% of patients**
- **KNOW TO LOOK FOR RARE DISEASES KNOWN TO BE ASSOCIATED WITH RAPIDLY PROGRESIVE GN:**
  - **a VASCULITIS of some sort, be it**
    - **WEGENER'S GRANULOMATOSIS,**
    - **MICROSCOPIC POLYANGIITIS, or**
    - **CHURG-STRAUSS SYNDROME**
  - **CRYOGLOBULINAEMIA**
  - **SYSTEMIC LUPUS ERYTHEMATOSUS**
  - **GLOMERULAR BASEMENT MEMBRANE ANTIBODIES**
  - **GOODPASTURE'S SYNDROME (also haemoptysis)**

MANAGEMENT is AGGRESSIVE and DETERMINED.

Kick-start with **IV corticosteroids and cyclophosphamide**
Monitor progress: if response is limited move on to **PLASMA EXCHANGE**
(thats if you can identify an antibody as the culprit)

Renal survival is most closely related to serum creatinine titres at presentation.
Only 40% of patients escape dialysis at 1 year of follow-up.