Management of renal and ureteric stones

Renal calculi

Natural history of renal calculi

- Glowacki 1992 (n=107)
  - 32% episode of renal colic within 2 yrs
  - 50% symptomatic within 5yrs (10% per yr)
- Hubner 1993 (n=63) 7 year outcomes:
  - 45% increased in size
  - 70% symptomatic
  - 40% required surgery
- Burgher 2004 (n=300)
  - 77% increased in size
  - 26% required intervention

Renal calculi

In general

- Upper/mid poles
  - < 1cm **ESWL**
    FURS
  - 1-2cm **ESWL**
    FURS
  - > 2cm **PCNL**
    ESWL with stent
    ?FURS
- Lower pole
  - < 1cm **ESWL**
    FURS
  - 1-2cm **FURS or ESWL or PCNL**
  - > 2cm **PCNL**

Lower pole calculi (Raman and Pearle 2008)

Data from Glowacki and Burgher (above) demonstrate that 'asymptomatic' lower pole stones increase in size under observation and become symptomatic in 25-50% of cases

ESWL not without its complications however, and risks and benefits should be carefully weighed in each case

Management options comprise ESWL, FURS and PCNL

(i) ESWL

- Factors affecting efficacy of ESWL
  - Stone size clearance inversely prop. to stone size
  - Composition
  - Location
  - Anatomy*
  - ?Body habitus**

*Anatomical factors

- Infundibular length, width and infundibulopelvic angle
- If angle < 70 degrees, length > 3cm or width < 5mm clearance rates reportedly < 50% (Bumino 2002)

**Skin-to-stone distance >9-10cm a/w reduced efficacy of ESWL

Outcomes

Meta-analysis of 2927 patients at 13 centres (Lingeman 1994) showed ESWL to be less efficacious than PCNL (59% vs. 99% respectively). Results of ESWL:

90% clearance for upper and mid-pole stones

59% clearance for lower pole stones. Of these;

<= 10mm	74%
11-20mm	56%
> 20mm	33%

Lower Pole Study Group 1 (Albala 2001) prospectively randomised 128 patients with stones up to 3cm to either ESWL or PCNL. Overall stone clearance 37% for ESWL vs. 95% for PCNL. Results of ESWL:

<10mm	63%
11-20mm	23%*
21-30mm	14%*

* **Very poor results for stones >10mm**. Discrepancy with Lingeman et al may be explained by the observation that many studies in Lingeman's meta-analysis were sponsored by lithotriptor companies

Some recent evidence that stone-free rates improved with adjuvant PDI therapy (percussion, diuresis (500ml fluid) and inversion) Chiong 2005

(ii) FURS

Contemporary stone free rates 60-80% reported

Lower Pole Study Group randomised stones < 1cm between FURS and ESWL (50% clearance vs. 35% respectively but low power and non-significant)

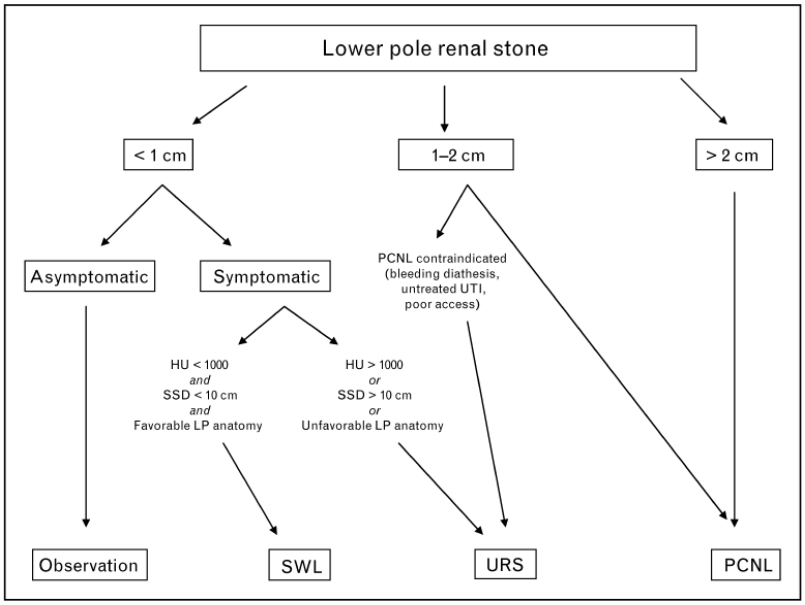
Lower Pole Study Group randomised stones 1-2.5cm between FURS and PCNL (37% clearance vs. 71%) – surprisingly no difference in convalescence but patients stented in FURS group

(iii) PCNL

Stone-free rates 95% (100%, 93% and 86% for stones <1cm, 1-2 cm and > 2cm respectively from LPS1 from Albala 2001)

Generally stones > 2cm in size

Ramon and Pearle treatment algorithm



Staghorn calculi

Magnesium ammonium phosphate (coffin lids) and carbonate apatite
May be partial or complete
Natural history of staghorn calculi defined by Blandy and Singh (Published 1976, n=185; 60 patients observed; 125 patients operated) 10 yr mortality was 28% in observation group (cancer in 4, pyonephrosis in 16) vs. 7% in operated group. Retrospective study – problem with selection bias.
Recently updated by Teichmann et al 1995; n=177, 30% renal deterioration, 3% mortality in partially cleared group vs. 67% in refused treatment group.
Overall unRx leads to ~50% delayed nephrectomy rate for sepsis
Complications of PCNL

- Infection*
- Haemorrhage
- Pelvic perforation
- Renal colic
- AV Fistulae
- Pneumothorax**
- Hydrothorax**
- Injury to adjacent viscera***
- Residual stones****

* Best predictor of organism causing post-PCNL sepsis is stone culture or intra-operative renal pelvic urine, NOT pre-op MSU.
** A/w upper pole puncture; always perform in full expiration
*** Most commonly in thin female patients with retro-renal colon.
**** Recurrence rates after PCNL related to adequacy of clearance
Total clearance 10% recurrence
Partial clearance 23% recurrence

What's new in PCNL?

- Supra 12th rib access
- Tubeless (stent or truly tubeless)
- CT info and skin-stone depth
- 3D CT reconstruction
- Mini percs
- Flexible instrumentation

Are residual fragments(<4mm) important?

Yes

- On follow-up 40-60% patients demonstrate stone growth or symptoms*
- ~25% become stone-free and 25% stay the same
- * lower for children ~33%

Open surgery

Still has limited role; large centres report 1-5% open surgery rate

Indications for open surgery:

- Complex stones
- Treatment failure with PCNL
- Morbid obesity
- Concomitant open surgery
- Partial or complete non-functioning kidney
- Stone in inaccessible transplanted/ectopic kidney

Options for open surgery

- Pyelolithotomy
- Pyelonephrolihotomy
- Anatrophic nephrolithotomy
- Partial nephrectomy
- Pyeloplasty and pyelolithotomy
- Ureterolithotomy
- Ureterolithotomy and ureteroneocystotomy

Ureteric stones

Acute ureteric colic

Aetiology
- Passage of renal calculi
- Blood clot
- Tumour
- Sloughed renal papilla

Diagnosis

Flank pain	40-70% PPV
Haematuria	60% PPV; 85% sensitivity
Plain film	50% sensitivity all-comers; 70% radiologists
USS	50% sensitivity
IVU	80% sensitivity; 90% specificity
CT	**95% sensitivity; 95% specificity**

CT features of obstruction

Hydronephrosis	80% sens.
Hydroureter	80%
PN stranding	50%
Renal swelling	60%
Periureteric rim	60%

HU can indicate hardness of stone
- Range 250 – 1000 HU generally
- Uric acid stones ~350
- Calcium oxalate ~ 650
- Cystine ~ 900 +
- However high degree of overlap and HU alone have not been shown to predict response to ESWL
- Recent evidence suggests that HU<900 and skin-to-stone distance of <9cm predicts successful ESWL in >90% (Perks 2008)

Management

Conservative vs. intervention (ESWL vs. rigid URS)

Likelihood of passage related to location and size (EAU)
- < 4mm diameter - more than 80% chance of passage
- < 7mm
  - Proximal ureter - 25%
  - Mid ureter - 45%
  - Distal ureter - 70%
- Two thirds pass within 4 weeks (Hubner 1993)

(i) Conservative management
- Analgaesia
  - Diclofenac more effective vs. opiates in acute phase
  - Diclofenac 50mg tds prevents recurrent pain in patients managed consevatively
  - No evidence that NSAIDs impair renal function in patients with normal renal function

Medical expulsive therapy

Remains controversial
Detrusor and distal ureter = alpha-1d receptors
Tamsulosin most selective for alpha 1a and 1d receptors.
No evidence of benefit for tamsulosin vs. other alpha-blocker
Hollingsworth metaanalysis (Lancet 2006) **65% greater chance of stone passage** with alpha blocker* than controls. Potential small benefit for additional steroid therapy. NNT = 4. Duration of therapy = tamsulosin 0.4mg for 28 days. However, tamsulosin not licensed in UK for MET
Recent randomised controlled trial by Hermanns 2009 (n=100) showed no difference in passage (87% for tamsulosin, 89% for placebo) although reduced analgaesia and earlier stone passage in tamsulosin group.
SUSPEND (spontaneous urinary stone passage enabled by drugs – Sam McClinton from Aberdeen) is a UK PC-RCT currently recruiting patients to either placebo, calcium channel blockers or alpha-blockers

Contraindications to conservative therapy

Stone > 7mm diameter
Uncontrolled pain
Infection
Obstructed solitary kidney
Bilateral obstruction

(ii) Intervention for proximal ureteric stones

a) ESWL

Level of stone in the ureter	No. of patients	Stone free % (range)	Auxiliary procedures %	Anaesthesia %	Re-ESWL %
Proximal (30 reports)	8,825	77.4 (63-100)	13.0	11.3	10.0
Mid (24 reports)	429	80.3 (60-98)	4.3	4.3	8.2
Distal (38 reports)	6,896	77.9 (59-100)	12.9	11.1	9.4

Overall EAU found 81% stone-free rate with 12% re-treatment rate. Very similar to large US study using Siemens lithostar (Mobley 1994; stone-free rate 84%, retreatment rate 11%

b) URS (% stone-free rates)

	<1990	1990-1995	1996	1999
Renal	ND	96	ND	76-91
Ureteral				
UU	50	95	96	98
MU	62	69	91	99
LU	95	61	93	98

Results for ureteroscopy have shown a dramatic improvement over the last 10 years, such that > 97% patients rendered stone-free with URS.
Moreover ~ 95% require only one treatment
Results compare favourably with ESWL, but requires GA and more morbidity than with ESWL

Steinstrasse
Defined as stone burden >5cm in length
Typically after ESWL
1% overall
5% stones > 2cm
40% following ESWL for staghorns
URS preferred modality; exception is for large leading stone which may be amenable to ESWL
Stenting does not reduce the likelihood of steinstrasse

PCN vs. nephrostomy for acute decompression?
No clear consensus
Postal survey of UK Radiologists and Urologists (BJMSU) organised by Section of Endourology
Ureteric obstruction with sepsis
Urgent nephrostomy preferred. Stent preferred for uncorrectable coagulopathy
Ureteric obstruction for acute renal failure
Semi-urgent de-obstruction. 50:50 nephrostomy vs. JJ stent
Nx has advantages – allows antegrade study, obviates need for anaesthetic in patients with new biochemical/cardiovascular abnormalities
2 x randomised trials of PCN vs. JJ stent; Pearle 1998 and Mokmalji 2001. No difference in recovery between two, although reduced duration of Abx Rx in nephrostomy group and Mokmalji reported a 20% failure rate for stenting

Stenting for malignant ureteric obstruction?
Must determine whether will lead to reasonable duration of good quality life
4 categories (Watkinson criteria)
1. non-malignant complication
2. unRx malignancy
3. relapsed disease with treatment options
4. relapsed disease with no treatment options
Stenting advocated in 1, 2 and 3. Give patient options in category 4 (However overall survival 38 days after nephrostomy with many not leaving hospital)
Extrinsic ureteric obstruction due to malignancy a/w only 50% patency rate at 3 months
Options:
Large bore stents (8F)
2 stents
Memocath short stenting
Metallic full length stenting
Extra-anatomical stenting

Stones in pregnancy

90% women develop hydronephrosis in pregnancy
Due to compression by fetus and effects of progesterone on ureter
Right > left (sigmoid thought to be protective)
Renal colic no more common in pregnancy than in non-pregnant women
Although pregnant women hypercalciuric and hyperuricosuric with increased urinary stasis, urinary inhibitors and GFR increased, offsetting risk
Management considerations

- 75% stones will pass spontaneously; 25% will require intervention
- Calculus associated sepsis a/w pre-term labour
- Persistent obstruction a/w risk of permanent renal impairment
- Fetal radiation dose < 1 milligray (AXR/MAG3) a/w tiny increased risk of childhood cancer
- Fetal radiation dose > 1 milligray (IVU/CT) a/w 2-fold increased risk of childhood cancer
- Effects of unenhanced MRI in pregnancy unknown
- No evidence of pre-term labour for general anaesthetic alone
- Ureteroscopic stone extraction may be performed safely in first and second trimesters
- Stents and nephrostomies encrust rapidly in pregnancy

Management recommendations

- Trial of conservative therapy advocated in most patients
- If fails to settle, unenhanced MRI preferred imaging modality
- First and second trimesters
  - Stone < 1cm — stent/PCN or primary URS
  - Stone > 1cm — stent/PCN
- Third trimester
  - Any stone size — stent/PCN & Rx post-partum induce

Appendix

Assessment of stone size

Diameter

Surface area

SA = l x w x π x 0.25

Volume

Vol = SA x 0.6

Radiation exposure

Gray	absorbed dose measured in joules/kg
Sievert	attempt to quantify the biological effects of radiation [1Gy to bone is not same as 1Gy to small bowel]. Also known as dose equivalent measured in J/kg Gray x Q x N where Q = type of radiation, and N = type of tissue, volume of radiation and time of exposure

CXR	0.02 mSv
MAG3	0.4 mSv
KUB	0.5 mSv
DMSA	1.0 mSv
3-film IVU	1.5 mSv
6-film IVU	2.5 mSv
CTKUB	4.7 mSv
CTU	10 mSv

Annual background radiation 2-3 mSv
Annual occupational limit for effective dose = 50 mSv
Lifetime risk of fatal cancer 1 in 5 (20%)
X-ray dosage of 10 mSv increases risk by 1 in 2000 (0.05%)

Contrast administration

All contrast agents have a 2,4,6-tri-iodinated benzene ring.
Type of molecule at position 1 important: carboxyl group = ionic dissociation (high osmolar contrast media); hydroxyl group = water soluble (low osmolar contast media)
Allergy, anaphylaxis, renal failure and lactic acidosis important side effects of contrast administration
Side effects 5-10 x higher with high osmolar (ionic) contrast media
Increased risk of severe reaction in patients with history od severe allergy, asthma (6x),

(i) Allergy

Flushing, rash, oedema
2-4% of patients
Treat with antihistamine (chlorpheniramine 10mg PO/IV) +/- IVI and steroids (100mg hydrocortisone IV)

History of allergy not a contraindication to further contrast. However, ensure only LMW non-ionic contrast and pre-treat with steroid (6 hrs prior) and antihistamine (1hr prior) [NB. no evidence of benefit of steroids however]
No increased risk of allergy in patients with shellfish allergy

(ii) Anaphylaxis

Laryngospasm, hypotension, tachycardia, cardiac arrest
Fatal reaction 1:100,000
Immediate management

- Sit up
- Oxygen
- IV fluid bolus
- 0.5 mg adrenaline IM (RCR guidance)
- 10mg chlorpheniramine IV
- 100mg hydrocortisone IV
- Call anaesthetist

Reaction	Ionic contrast media 1200 mosm/l	Non-ionic contrast media 600 mosm/l
	e.g urograffin	e.g niopam/omnipaque
Non-fatal allergic	1:50	1:250
Life-threatening	1:500	1:2500
Fatal anaphylactoid*	1:100,000	1:100,000

* Thought to be an overestimate: US FDA reports 1:1,000,000 administrations.
NB. anaphylactoid is correct term, not anaphylactic because not IgE mediated
Number after contrast media (e.g. Niopam 200) indicates amount of iodine (mg/ml)

(iii) Renal failure

Defined for radiological purposes as serum creatinine >= 130umol/l
Contrast induces afferent arteriolar vasoconstriction leading to tubular ischaemia
Contrast induced nephropathy defined as creatinine rise of 25% or 44umol in the 3 days following contrast without other cause
Risk groups

- Elderly >70
- Renal impairment (>140-150umol/l)
- Dehydration
- Diabetes
- CCF
- Concurrent nephrotoxics

Maximum dose of iodine in grams should not exceed the patients estimated GFR
Strategies for preventing contast-induced nephropathy

- Avoid in renal impairment unless absolutely necessary
- Stop concurrent nephrotoxics
- Pre-hydrate
- ?N-acetylcystine 600mg bd 24 hours pre-contrast*
- Avoid toxic doses of iodine

Avoid repeat administration within 48 hours

* Evidence for NAC controversial. Not currently recommended by Royal College of Radiologists

Long-term outcome of contrast-induced nephropathy

(iv) Lactic acidosis

Contrast administration in patients taking metformin believed to increase the risk of lactic acidosis, especially in those with renal impairment

Mechanism = worsening renal function through mechanisms above lead to accumulation of metformin, which itself a/w lactic acidosis

Current guidelines (RCR 2009):

Metformin is not recommended for use in diabetics with renal impairment, because it is exclusively excreted via the kidneys. Accumulation of metformin may result in the development of the serious complication lactic acidosis. Although the incidence of lactic acidosis following contrast administration in diabetic patients receiving metformin appears to be extremely low, extra care should be exercised in these patients [9].

Advice

- *If the serum creatinine is normal, and a low volume of contrast agent (up to 100 ml) is to be administered intravenously, no special precaution is required.*
- *If the serum creatinine is normal, but more than 100 ml of contrast agent or the intra-arterial route is to be used, metformin should be withheld for 48 hours after the procedure.*
- *If the serum creatinine is raised, the need for the contrast agent should be re-assessed. If contrast injection is deemed necessary, metformin should be withheld for 48 hours before and 48 hours after the contrast is given and the renal function re-assessed before restarting the metformin treatment.*

(v) Untreated hyperthyroidism

Contrast administration not recommended until disease treated

Ionising radiation and pregnancy (RCR guidelines 2009)

Fetal death, malformation, growth retardation and severe mental retardation require doses over 100mGy; normal radiological procedures never exceed such a dose

Advice

The radiation dose to the embryo or fetus that is likely to result from any diagnostic procedure in current use should present no risk of causing fetal death, malformation, growth retardation or impairment of mental development.

Risk of childhood malignancy with fetal radiation exposure. Risk increases proportional to fetal radiation dose. No safe time after first 3-4 wks of pregnancy

Childhood cancer risk

Normal baseline risk	0.2%	(1:500)
Fetal radiation exposure <= 1mGy	0.21%	(1:475)
Fetal radiation exposure > 5 mGy	up to 0.4%*	(1:250)

*Oxford survey of childhood cancers found that a fetal radiation exposure of 25 mGy a/w doubling of childhood cancer risk

Advice

For the majority of diagnostic medical procedures, giving fetal doses up to about a milligray (the first three groups in the table), the associated risks of childhood cancer are very low (less than 1 in 10,000) and judged to be acceptable when compared with the natural risk (of around 1 in 500). Consequently, all such examinations can be carried out on pregnant women, as long as they have been clinically justified and the dose is kept to a minimum consistent with the diagnostic requirements. The very low risks of childhood cancer from these examinations are certainly not sufficient to justify termination of the pregnancy (particularly in view of the associated risks to the health of the mother).

Exposure of pregnant women to the higher dose procedures (the last two groups in the table) lead to fetal doses in excess of a few milligray, and – at the highest doses – may result in a doubling of the childhood cancer risk compared to the natural rate. Consequently, such examinations should be avoided on pregnant women, if this can be achieved without serious detrimental effects to their health. However, if such examinations are considered to be clinically justified or are carried out inadvertently, the childhood cancer risk associated with them is still low in absolute terms (below 1 in 200 and mostly below 1 in 1000) and termination of the pregnancy would not be justified solely on the basis of the radiation risk to the unborn child.