

1. Introduction

In renal transplant patients there are numerous causes of bone disease including hyperparathyroidism, adynamic bone disease, osteomalacia and osteoporosis. It is possible for these conditions to co-exist.

Bone mineral density decreases by 4-10% in first six months post-transplant although this may be improved on newer immunosuppressant regimes. In first 5 years post-transplant 22.5% patients suffer a fracture – 4x higher than the general population.

POST TRANSPLANT HYPERPARATHYROIDISM

Many patients who receive a renal transplant have hyperparathyroidism at the time of transplant, which usually recovers with replacement of adequate renal function. However, PTH remains high in nearly 45% patients 2 years post-transplant

In the early post-transplant period phosphate supplements are indicated if serum phosphate is persistently < 0.6mmol/L

Renal transplant patients may continue to have a degree of chronic renal impairment and need ongoing therapy with phosphate binders, and Vitamin D analogues to suppress secondary hyperparathyroidism

In the in the longer term:

- parathyroidectomy may be needed if hypercalcaemia (serum calcium persistently > 3 mmol/L) (**consultant decision**)
- cinacalcet (30-90mg daily) may be used to suppress post-transplant hyperparathyroidism in a patient who is not fit for parathyroidectomy (**consultant decision**)

Fracture risk

Renal transplant recipients may have many risk factors for fracture as below

Age >50 years
Hypogonadal male or female
Prior fragility fracture including vertebral fracture
Prolonged oral glucocorticoid use before transplant
Low body mass index
First degree relative with osteoporosis
Postural instability, peripheral neuropathy, reduced visual acuity, falls in past 6 months
Pre-transplant iPTH >50 pmol/L
Type 1 diabetes

Laboratory Investigations

- U&E, Calcium, Phosphate, Alkaline phosphatase – measure routinely at each visit

Magnesium – some patients maybe hypomagnesaemic (especially on PPI)
Thyroid function tests
- PTH - measure no more than 3 monthly in first 12 months. After one year measure PTH only at annual review unless active bone problems suggestive of hyperparathyroidism
- 25-OH vitamin D – measure once at first annual review. Only measure again to assess response to repletion therapy if there was vitamin D deficiency
- Testosterone/SHBG; LH, FSH, Oestradiol, – only measure if significant osteopenia/osteoporosis and clinical suspicion of gonadal failure.
- In some patients consider assessment of bone turnover markers (Bone Alkaline phosphatase, PINP and CTX)

Imaging

1. Policy for Use of DEXA Scanning

DEXA scanning is not offered to transplant patient's aged > 65 years

Use FRAX score with NOGG guidance to decide if DEXA scan also indicated¹.

In patients age < 65 years, DEXA is only done if FRAX/NOGG risk assessment suggests a DEXA scan is indicated

2. Other techniques

A plain thoraco-lumbar Xray may show signs of vertebral fracture

A quantitative CT may be useful in some patients following discussion with the Metabolic Bone clinic

MANAGEMENT OF VITAMIN D DEFICIENCY

25-OH vitamin D level is measured once only at first annual review.

Vitamin D insufficiency: 25-OH vitamin D level 25-50 nmol/L (10-20 ng/ml).

Treat with Fultium-D3 (colecalciferol) **1600 units daily** as long term therapy (It is not necessary to measure the 25-OH vitamin D level again).

Vitamin D deficiency: 25-OH vitamin D level < 25 nmol/L (<10ng/ml).

Treat with **Fultium-D3 3200 units daily for 12 weeks** .

If a repeat 25-OH vitamin D level is still < 25 nmol/L (<10ng/ml), continue **Fultium-D3 3200 units daily for a further 12 weeks**, and check level again.

¹ www.shef.ac.uk/FRAX/tool.jsp. Input patient data. Unless BMD already done, leave 'Select BMD' blank. Press **Calculate**. Press **View NOGG Guidance** for recommendation.

Once the vitamin D level is > 25 nmol/L (>10ng/ml), reduce dose to **Fultium-D3 1600 units daily** as long term therapy (It is not then necessary to measure the 25-OH vitamin D level again). ,

MANAGEMENT OF OSTEOPENIA AND OSTEOPOROSIS

Prevention

1. Calcichew D3 Forte or Adcal-D3 2 tablets daily – given as long term treatment in all patients not at risk of hypercalcaemia from time of transplant.
2. Each new transplant patient will receive 2 doses of pamidronate for bone protection providing their calcium level is >2.3 mmol/L.

If calcium level is <2.3 mmol/L, reschedule the pamidronate infusion after calcium correction. The dose is based on patients' weight (0.5mg/kg) and is rounded to the nearest vial (either 30mg or the maximum, 45mg).

- Dose 1 – while an in-patient during the first post-operative week.
- Dose 2 – 4 weeks post transplant in the Day Case Unit

POST TRANSPLANT OSTEOPOROSIS.

Risk assessment

Assess risk at first annual review visit after transplant.

Management of known reduction in bone density

1. Lifestyle measures
2. Stop smoking, moderate alcohol intake, regular weight bearing exercise, avoid falls, adequate dietary calcium
3. Continue Calcichew D3 Forte or Adcal-D3 2 tablets daily
4. Consider HRT in peri- or post-menopausal women for 3 years
5. Testosterone in hypogonadal men
6. Treat renal osteodystrophy
7. Reduce corticosteroid dosage.
 - Consider prednisolone reduction or withdrawal (**consultant decision**)
 - Consider steroid free immunosuppression *ab initio* in patients with pre-transplant osteoporosis (**consultant decision**).
8. Oral bisphosphonate treatment may be indicated for patients:
 - Age > 65 years or with a history of low trauma fracture who must continue corticosteroid therapy
 - Under age 65 years when:
FRAX/NOGG ± DEXA scan evaluation indicates high fracture risk in or

DEXA scan evidence of osteopenia (T score between 0 and - 1.5) may be an indication if there

Post Renal Transplant Bone Disease UHL Renal Transplant Guideline v2

Lead author: Peter Topham. Last review May 2019; Guideline approved by Renal Guidelines Group 14/06/2022
Next Review: June 2025 Trust Ref C13/2003

is deterioration on sequential scans

Usually give Alendronate 70mg once weekly – avoid when eGFR < 35 ml/min

Recent advice suggests patients who are not at “high risk” of fracture and who have received a bisphosphonate for 5 years should have a “Drug Holiday” and be re-assessed after 2 years.

Use bisphosphonates cautiously in patients with low serum PTH levels who may have adynamic bone disease.

AVOID bisphosphonates if serum PTH level < 1 after total parathyroidectomy (risk of adynamic bone disease and fractures).

*Bisphosphonates bind potently to mineralized bone with a half-life of almost 10 years and should be reserved for patients with osteoporosis at high risk of fracture
Avoid bisphosphonate in women who may plan pregnancy*

Denosumab (a humanized monoclonal antibody against the receptor activator NF-κB ligand) is an alternative to bisphosphonates in some patients but requires referral to Metabolic Bone clinic.

Specialist referral

A minority of patients may need referral to the Osteoporosis Clinic. For example young patients with osteoporosis who need corticosteroids but cannot have a bisphosphonate (**Consultant decision**).

2. Scope

Doctors, nurses and pharmacists working in renal transplant unit

3. Education and Training

No specific training required

4. Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

5. Supporting Documents and Key References

1. Bouquegneau A, et al Bone disease after kidney transplantation. Clin JASN 2016; Feb 15 1-15.
2. Alder RA et al. Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. Bone Miner Res_ 2016 Jan;31(1):16-35.
3. Lim SYL & Bolster MB. Current approaches to osteoporosis treatment. Current Opinion in Rheumatology. 2015; 27 (3): 216-224

6. Key Words

Renal transplant, bone disease, hyperparathyroidism, osteoporosis, corticosteroids, bisphosphonates

This line signifies the end of the document

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT			
Author / Lead Officer:	M Nicholson S Carr	Job Title: Professor of Transplant Surgery Consultants	
Reviewed by:	P Topham, S Malik		
Approved by:	Transplant MDT Meeting	Date Approved: May 19	
REVIEW RECORD			
Date	Issue Number	Reviewed By	Description Of Changes (If Any)
May 2016	1	S CARR	Change to Vit D section, addition of information on bisphosphonate holiday, update references and other minor alterations
May 2019	2	S CARR Transplant MDT Meeting	No changes.
DISTRIBUTION RECORD:			
Date	Name	Dept	Received