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The British OsteoNEcrosis Study: A Multi-Centre Prospective Study

Background

Osteonecrosis can be a debilitating consequence of treatment for acute lymphoblastic leukaemia (ALL). Some patients have asymptomatic lesions that spontaneously regress whilst others will need multiple joint replacements.

Little is known about the natural history of lesions, with limited understanding of the relationship between osteonecrosis and other markers of bone health. Bone mineral density of patients with ALL also appears to be lower at diagnosis than that of healthy peers, with a high incidence of vertebral fractures.

What we already know:

- Osteonecrosis most commonly affects patients who are diagnosed with ALL between 10 and 20 years of age
- The UK prevalence of symptomatic osteonecrosis is 5.5%
- Symptoms are typically reported around 14 months after diagnosis of ALL
- Asymptomatic osteonecrosis may affect up to 60% of patients
- Bone injuries are likely to develop within the first year of treatment

Study Design

BONES is a multi-centre prospective, longitudinal cohort study based at tertiary children's hospitals around the UK.

Research Population

Patients aged 10 to 25 years with a first diagnosis of acute lymphoblastic leukaemia (ALL) or lymphoblastic lymphoma



<http://childhealth.leeds.ac.uk/bones.html>



Osteonecrosis of left hip

Aims

The aims of the British OsteoNEcrosis Study (BONES) are to determine:

- The incidence of symptomatic and asymptomatic osteonecrosis in patients aged between 10-25 years undergoing treatment for acute lymphoblastic leukaemia (ALL) or lymphoblastic lymphoma, and variation in incidence at different time points in their treatment
- Risk factors for progression and development of symptomatic osteonecrosis in this population
- Specific radiological features predicting for progression or regression of osteonecrosis, with validation of a classification system for osteonecrosis
- Vertebral fracture incidence and bone mineral density in these patients

Methodology

Magnetic resonance imaging of lower limbs for assessment of osteonecrosis within 4 weeks of diagnosis, at the end of delayed intensification, and 1, 2 and 3 years after the start of maintenance therapy. Physiotherapy assessment will occur at the same time-points, with completion of the child health assessment questionnaire. Additional collection of clinical and biochemical data will include demographic information, prognostic and diagnostic data, BMI and phase of puberty, bone and lipid profile, PTH and vitamin D status. Bone mineral density and lateral vertebral assessment will be assessed at diagnosis and annually thereafter to a total of 4 assessments.

Data Analysis

A central review panel will assess MRI and DXA assessments. Vertebral fracture prevalence will be assessed using the Genant semi-quantitative method.

Chi squared tests will be used for categorical variables to compare baseline characteristics between patients with and without osteonecrosis. The two sample t-test will be used for continuous variables with a normal distribution and the Mann-Whitney U test will be used for continuous variables with a skewed distribution. We will examine effect modification by risk factors such as age, sex, ethnicity and risk group by performing stratified analyses

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