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The classification of osteonecrosis in patients with cancer: validation of a new radiological classification system

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AIM: To validate a new, non-joint-specific radiological classification system that is suitable regardless of the site of the osteonecrosis (ON) in patients with cancer.

MATERIAL AND METHODS: Critical deficiencies in the existing ON classification systems were identified and a new, non-joint-specific radiological classification system was developed. Seventy-two magnetic resonance imaging (MRI) images of patients with cancer and ON lesions were graded, and the validation of the new system was performed by assessing inter- and intra-observer reliability.

RESULTS: Intra-observer reliability of ON grading was good or very good, with kappa values of 0.79–0.86. Interobserver agreement was lower but still good, with kappa values of 0.62–0.77. Ninety-eight percent of all intra- or interobserver differences were within one grade. Interobserver reliability of assessing the location of ON was very good, with kappa values of 0.93–0.98.

CONCLUSION: All the available radiological ON classification systems are joint specific. This limitation has spurred the development of multiple systems, which has led to the insufficient use of classifications in ON studies among patients with cancer. The introduced radiological classification system overcomes the problem of joint-specificity, was found to be reliable, and can be used to classify all ON lesions regardless of the affected site.

Introduction

Osteonecrosis (ON) is a potential complication in patients with malignancy, especially after leukaemia and lymphoma. The recognised risk factors for ON include corticosteroid therapy, high body mass index, and haematopoietic stem cell transplantation.[1] The reported incidence of ON varies tremendously from study to study. The incidence of asymptomatic ON in patients with childhood leukaemia is reported to be as high as 71.8% in screening studies utilising magnetic resonance imaging (MRI), whereas the incidence of symptomatic ON has been reported to be as low as 1.1%.[2,3]

The location and extent of ON has crucial bearing on the clinical significance of the disease. Small lesions located at a

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distance from the joints are usually asymptomatic, whereas larger lesions located close to the weight-bearing joints may lead to collapse of the articular surface, cause severe morbidity, and require joint arthroplasty procedures.[4–6] The use of a comprehensive ON classification system, including extent of involvement, is essential to improve the treatment of patients with ON.[7]

The major weakness of all existing radiological ON classification systems is joint specificity, as the patients with cancer may have ON lesions at multiple sites in various bones throughout the skeleton.[8] The multiplicity of lesions makes it impossible to use any of the existing single joint-specific classification systems to discuss or compare lesions within a patient, or among patients in whom different sites are affected.[8,11] A systematic review of the diagnosis and classification of ON in childhood leukaemia patients revealed that the majority of the studies did not use validated classifications or, indeed, any classification system at all.[9] This is an issue in adult ON studies as well.[10]

The aim of the current study was to assess the limitations of the existing ON classification systems with respect to the site and staging of ON in patients with cancer, and to address these shortcomings through the development, introduction, and validation of a new radiological classification system. This new system was designed to be suitable in all cases, regardless of the location of the ON lesion.

Material and methods

Specific issues addressed during the development process of the new classification system.

Defining and naming the site of ON

The definition of the ON site should be clearly described. In the new classification, bones are separated into two different categories according to their mechanical properties: weight bearing or non-weight bearing. In addition, bones are divided into two subgroups according to their anatomical properties: long or short. The specific location of the ON within the bone is separated into three categories in long bones: diaphysis, metaphysis, or epiphysis. In short bones, the categories used are body or surface.

Epiphyseal lesions are named according to the closest joint (e.g., the location of ON in the proximal epiphysis of the femur is “hip” and in the distal epiphysis is “knee” respectively). The ON lesions located within the diaphysis or metaphysis of a long bone are named according to the affected bone, except all ON lesions of the foot and hand, which are named by the affected extremity regardless of the specific site (e.g., ON in the diaphysis of the femur is located in “femur”, but ON in a metacarpal is “hand” and in a navicular bone is “foot”). ON of the talus is an exception and is included in the “ankle” rather than the “foot”. The location of ON in the vertebrae is “spine”.

Size and extent of ON lesions

ON lesions in patients with cancer may exhibit complex shapes with the typical serpentine rim, or they may present as several small lesions concentrated within a region of the bone. Defining the extent of such lesions is extremely difficult; however, determining the extent of ON is very significant, especially around the weight-bearing joints. The outcomes of cases with hip joint involvement seem to depend solely on the size of the ON lesion. Ito *et al.*[4] reported that the mean percentage area of ON in symptomatic hips was 39% and in asymptomatic hips was 27%. In addition, ON lesions that occupy >30% of the femoral head volume are associated with the worst prognoses.[5] ON around the knee joint seems to exhibit similar properties. In a study by Karimova *et al.*,[12] the lesions with <25% of articular surface involvement in the knee joint were more likely to be asymptomatic. In general, ON involvement of 30% or more of the epiphyseal articular surface was associated with an adverse prognosis and outcome.[12–14] Based on the literature, a single 30% involvement cut-off limit was used to define the boundary between less and more severe ON. Evaluation of the percentage of the involvement may be measured by any appropriate method, including a visual estimate. In the knee joint, each of the knee compartments represents half of the knee joint (the area of the whole knee joint is medial 50%+lateral 50%=100%). The patella is regarded as a separate ‘short bone’ and is not part of the articular surface of the knee joint.

Clinical significance of ON classification

The classification system should confer clinical value. ON lesions that are located in the lower extremities cause greater morbidity and are more often symptomatic.[11,14–17] Therefore, in the new classification system, ON lesions located within weight-bearing joints or bones are classified as more severe than those located within non-weight-bearing joints or bones. In addition, ON lesions located near the articular surface of the joint (epiphysis) are classified as more severe than those more distant.

The new classification system

Patients with ON are treated by different medical specialists. To achieve broad agreement among healthcare professionals working with ON patients, a collaboration between an orthopaedic surgeon, musculoskeletal radiologist, and paediatric haematologists and oncologists was obtained during the development process of the new classification system.

The flowchart of the new classification system is shown in Fig 1 In the new classification system, ON lesions are classified between grades 0 and V depending on the location and the extent of the lesions (Figs 2–5). In addition to the grading of ON, the classification system defines the location of ON in the skeleton.

Validation of the classification system

From the database of a tertiary level hospital, patients with ON were identified by using the International Classification of Diseases code for aseptic necrosis for any reason (M87.*). An initial search resulted in 279 patients with ON.