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Advances in Imaging of Rheumatoid Arthritis

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Several new imaging modalities have been found useful in clinical evaluation of patients with rheumatoid arthritis (RA). Magnetic resonance (MR) imaging has proven to be an excellent noninvasive method to evaluate the spine, shoulder, hip, and knees; its use for the evaluation of smaller joints is still being investigated. In patients with RA, MR imaging has been used to evaluate cervical spine instability, rotator cuff tear, osteonecrosis, and osteomyelitis. Patients with RA may have advanced osteoporosis, predisposing to insufficiency fractures. This includes fractures associated with increased activity after hip or knee arthroplasty. Newer methods for measuring the degree of osteoporosis include single photon absorptiometry, dual photon absorptiometry, quantitative computed tomography (CT), and dual-energy projection radiography. It has not yet been determined which of these methods will be most widely used in the future, but quantitative CT and dual-energy projection radiography currently show the most promise. Ultrasonography provides an excellent noninvasive method for the diagnosis of popliteal cysts, and color Doppler sonography can differentiate cyst and popliteal aneurysm. As compared to radiography or conventional CT, high-resolution CT provides an improved method to detect the early changes of RA in the lung parenchyma.

This article reviews recent advances in diagnostic imaging that have proven to be useful in the evaluation of patients with rheumatoid arthritis (RA). An emphasis has been placed on the appropriate application of the newer imaging modalities with respect to specific pathologic disorders associated with RA.

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MAGNETIC RESONANCE IMAGING

In the appropriate clinical setting, magnetic resonance (MR) imaging can be extremely useful in the evaluation of the patient with RA. This modality possesses several advantages over conventional radiography, including the following: (1) excellent depiction of bone marrow, which allows early detection of tumor, infection, or ischemic necrosis; (2) high soft-tissue contrast allowing differentiation of soft-tissue structures, such as muscles, cartilage, and ligaments; (3) the capability of imaging in any plane, including oblique; (4) freedom from beam-hardening encountered in computed tomography (CT), and reduction of streaking artifact resulting from some metallic implants. MR imaging is performed without ionizing radiation, and there are no known hazards. The main disadvantages of MR imaging are its high cost and lengthy examination time. MR imaging should therefore be used only when sufficient information cannot be obtained with less expensive noninvasive methods, and when the information will significantly affect the clinical management of the patient. MR examinations are most successful when they are tailored to the specific clinical problem.[17] Because many MR findings are nonspecific, imaging should be performed with full knowledge of relevant clinical data and results of other examinations, especially plain roentgenograms.[3]

THE SPINE

MR is a superb imaging modality for the spine, and can depict the spinal cord, brain

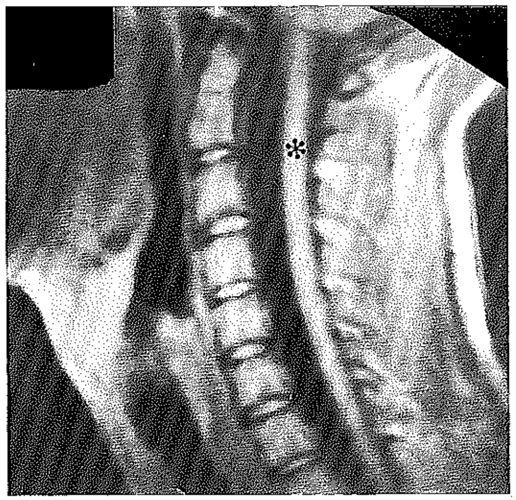


FIG. 1. T1-weighted sagittal image of a normal cervical spine. The spinal cord (*) is clearly visualized within the low-signal intensity spinal fluid.

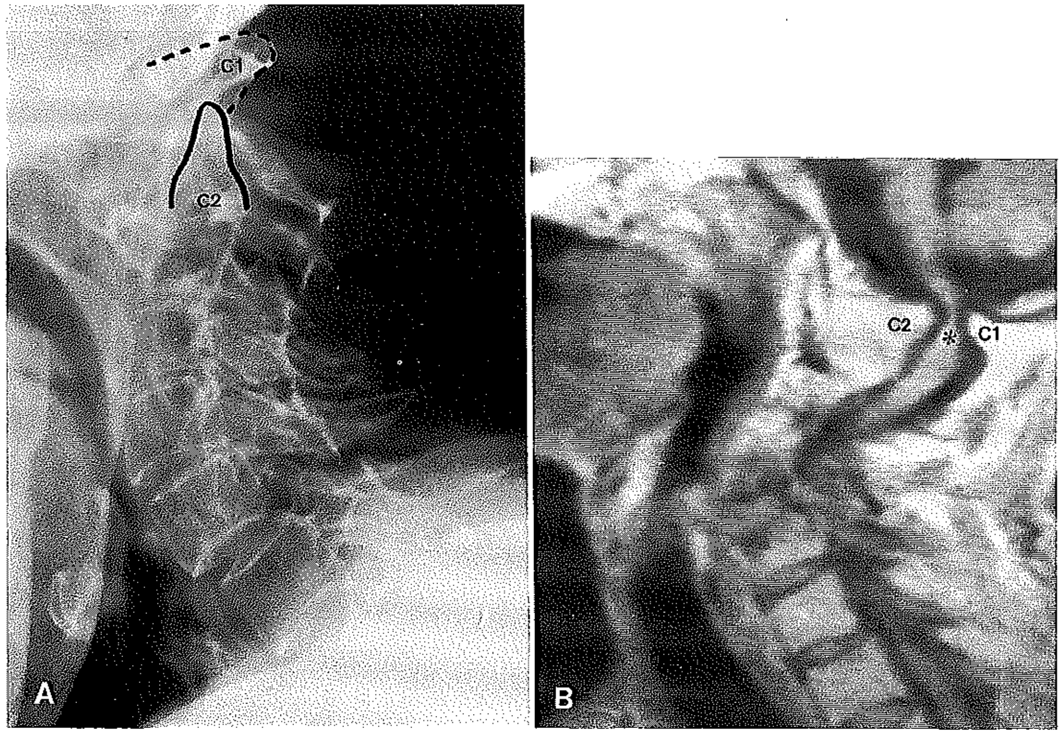
stem, cerebrospinal fluid, and extradural structures such as the vertebral bodies and disks with exquisite detail. The high soft-tissue contrast of MR imaging obviates the need for contrast agents (Fig. 1). In addition, the capability of showing pathology in multiple planes (especially the sagittal plane) is an advantage over CT.

Cervical spine involvement in RA patients may cause pain and severe neurologic symptoms, including paresis and paresthesias. In the past, plain roentgenograms, myelography, and CT myelography may have been required to obtain sufficient information for the management of patients. Myelography is often difficult to perform on patients with severe RA, and axial images are not optimal for demonstrating the relationship of the cord and spinal canal.[2] MR imaging can reliably demonstrate abnormalities of the craniocervical region (Fig. 2)[2,12,13,32,47,51] and it provides an easy method for detecting cord compression because of vertebral subluxation, disk extrusion, or pannus formation. Plain roentgenograms in flexion and extension will show atlantoaxial subluxation but cannot demonstrate pannus formation, which frequently compromises the canal.[47,51] The spine may be imaged during the MR examination in both flexion and extension to delineate the dynamic relationships of the cord to surrounding bony structures.[51] However, some investigators advocate imaging only in the neutral position because compression of the cord is usually obvious and further neurologic sequelae could result from these positioning maneuvers.[32,47] In patients with severe atlantoaxial subluxation, flexion and extension roentgenograms combined with MR imaging in the neutral position have been found to be adequate for preoperative evaluation. Postoperative evaluation is needed only if residual or new symptoms occur. Using short pulse sequences, the artifacts of stainless steel wires from a posterior fusion can be confined to the posterior neck region, allowing adequate examinations of the cervical spine. After surgical stabilization, periodontoid pannus has been shown to decrease in size in MR images, a change that is believed to be the result of reduced joint motion.[32]

The Shoulder

The shoulder is often affected by RA. Clinical symptoms include pain and restricted mobility. Inflamed synovial tissue leads to progressive erosion of the rotator cuff tendons adjacent to the greater tuberosity with subsequent narrowing of the space between the humerus and inferior surface of the acromion.[50] Inflammation of the acromioclavicular joint or subacromial bursa may result in shoulder impingement syndrome. Tendon erosion and chronic impingement may lead to rotator cuff tear.

MR imaging allows excellent delineation of the soft-tissue anatomy of the shoulder.[56] Individual muscles and cuff tendons may be evaluated without the injection of contrast material. MR imaging is well suited for evaluation of shoulder impingement, showing both bursitis and tendinitis as well as compression of the supraspinatous tendon or subacromial bursa by osteophytic spurs or cap-



FIGS. 2A AND 2B. A 70-year-old woman with RA had severe neck pain and paresthesias. (A) Lateral roentgenogram of the cervical spine. There is severe osteoporosis and extreme atlantoaxial subluxation. (B) Sagittal T1-weighted image at level of the foramen magnum. The spinal cord (*) is compressed between the ring of C1 and the odontoid process of C2.

sular hypertrophy of the acromioclavicular joint.[55] MR imaging is also useful for detecting rotator cuff tears. Partial tears may be difficult to depict, but large or full-thickness tears produce characteristic findings on MR images.[55]

Sonography has also been used in the diagnosis of rotator cuff tears. However, the accuracy of sonography in this endeavor is operator dependent. The future of rotator cuff sonography remains somewhat controversial, with recent articles offering conflicting results.[11,59] A recent questionnaire revealed that few radiologists have the expertise required to perform diagnostic rotator cuff sonography.[27] Compared to sonography, MR imaging has the advantages of depicting the entire rotator cuff, as well as the glenoid labrum. Even with its greater cost, it appears that MR imaging will be preferred over sonography for the evaluation of rotator cuff tears in most institutions.

MR imaging has also been successfully used for evaluating glenohumeral instability[31,54] and ischemic necrosis of the humeral head.

THE KNEE

The knee is frequently affected in RA (Fig. 3). Symmetric bilateral narrowing of the joint space with or without erosions typically occurs.

High resolution, thin-section MR images are capable of demonstrating the important soft-tissue structures of the knee, including the cruciate ligaments, collateral ligaments, and menisci.[48] MR images are more sensitive

FIG. 3. An 18-year-old man had knee pain and swelling. A sagittal T1-weighted MR image at the level of the posterior cruciate ligament. The joint was filled with an intermediate signal intensity tissue. Biopsy revealed pannus, which led to the diagnosis of RA.

than plain roentgenograms or scintigraphy in the detection of osteonecrosis of the knee. MR imaging can also be used to evaluate effusions and popliteal cysts.[28]

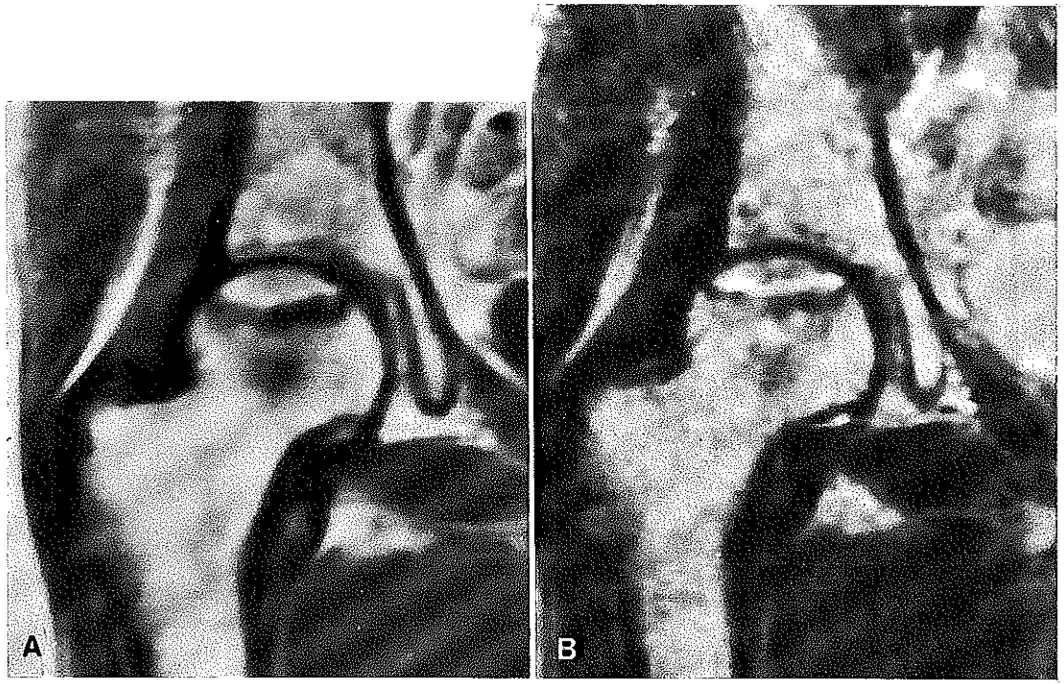
THE HIPS

The hips are affected less often than the knees in RA. Typical roentgenographic findings of RA are bilateral symmetric joint space narrowing with central femoral head migration, which eventually results in protrusio acetabula.[50]

A potential complication of corticosteroid therapy is steroid-induced ischemic necrosis of the hips. Ischemic necrosis of the hips may cause serious morbidity including pain, collapse of the femoral head, and secondary osteoarthrosis of the hip joint. To halt or possibly reverse the disease, early diagnosis is essential. Early diagnosis may lead to treatment with core decompression, rotational osteotomy, or decreased weight bearing. If the femoral head has collapsed, arthroplasty may be indicated.

MR imaging is more sensitive for the early detection of ischemic necrosis than radiography, CT, or radionuclide scanning.[4,15,30,36,42] In MR images, ischemic necrosis is evident as a decrease in the normal high MR signal intensity of bone marrow in T1-weighted images, which remains, at least in part, low signal in T2-weighed images. In the femoral head, ischemic necrosis is manifested by a band or ring, or a focal region of low-signal intensity in the subchondral marrow (Fig. 4).

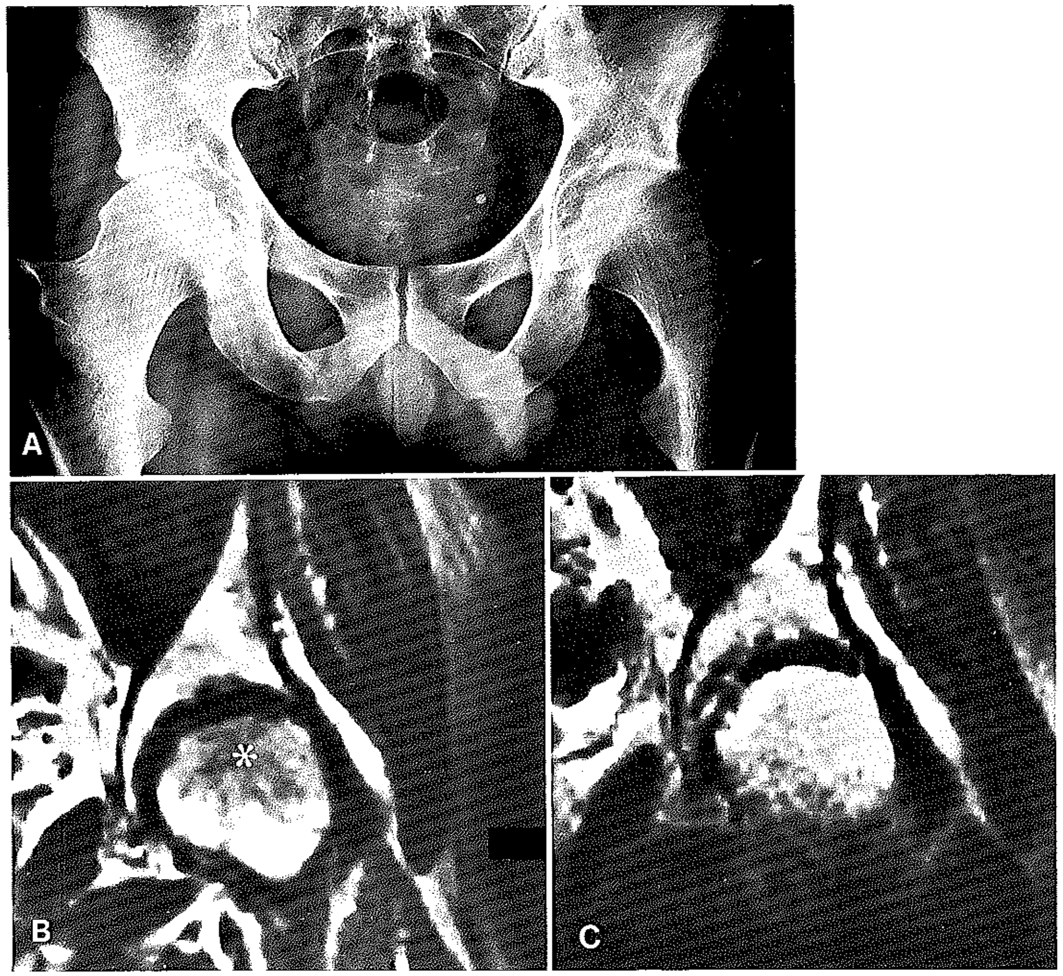
Whereas MR imaging is the most sensitive test for the detection of ischemic necrosis, a recent study of patients at high risk for ischemic necrosis with hip pain suggested that a normal MR image does not rule out the pres-



FIGS. 4A AND 4B. A 34-year-old woman had been treated with corticosteroids for several years. (A) Coronal T1-weighted MR image of the femoral head. There is a ringlike band of decreased signal, typical for ischemic necrosis. (B) Coronal T2-weighted MR image. Much of the ring maintains a low-signal intensity. The inner ring of high-signal intensity is believed to represent capillary-rich fibrovascular tissue.

ence of ischemic necrosis. It was believed that MR imaging, like radiography, demonstrates a macroscopic anatomic response to cell death that could lag behind the initial microscopic insult.[21] In a second study, it was recommended that negative MR imaging studies be followed with technetium 99m radionuclide bone scan to increase sensitivity in high-risk populations.[6] In a third study, MR imaging was used to evaluate the extent of ischemic necrosis in the femoral head before core decompression.[7] Femoral head collapse after decompression only occurred in those hips with more than 25% involvement of the weight-bearing portion of the head. It was recommended that MR imaging be used as the selection criteria for those patients who would be helped by core decompression. However, it is unclear whether core decompression in early ischemic necrosis is beneficial, and because of its high cost, MR imaging should be limited to those cases in which the findings may alter clinical management.

Transient regional osteoporosis, a condition of unknown etiology, may be confused with ischemic necrosis both clinically and by MR imaging (Fig. 5).[10] In transient regional osteoporosis of the hip, severe pain is associated with marked osteoporosis that is evident roentgenographically. ^{99m}Tc radionuclide bone scans show marked diffuse tracer uptake in the femoral head. Typical MR findings are decreased marrow signal intensity in T1-weighted images, but normal to increased signal intensity in T2-weighted images. Thus, the high signal in T2-weighted images distinguishes this entity from ischemic necrosis. These MR signal changes are believed to reflect edema in the bone marrow. Patients with transient osteoporosis recover spontaneously after six to ten months,[10,66] at which time the roentgenogram returns to normal.



FIGS. 5A–5C. A 45-year-old man had severe pain in the left hip. (A) Roentgenogram shows marked decreased bone density in the left hip. (B) T1-weighted coronal MR image. There is a region of abnormally low-signal intensity (*) in the femoral head. (C) T2-weighted coronal MR image. The low-signal intensity region has converted to high-signal intensity. This is believed to represent marrow edema, and it is characteristic for transient regional osteoporosis.

THE HAND AND WRIST

RA commonly affects the hands, causing osteoporosis, soft-tissue swelling, marginal bone erosions, and joint-space narrowing. MR provides excellent depiction of the hand and wrist,[65] and it allows early detection of several of the changes associated with RA. When MR imaging was compared to plain roentgenograms, bony erosions were detected more frequently with MR imaging.[5] Subluxations were well depicted by both modalities, but MR imaging was superior in demonstrating soft-tissue derangement. Distension of tendon sheaths by synovial fluid[5] and pannus formation around interphalangeal joints[64] were only depicted in MR images. It was concluded that because of superior soft-tissue contrast and tomographic capabilities, MR is more sensitive than plain roentgenograms in demonstrating articular changes of RA. This is, however, at a far greater cost, and the clinical significance of the increased sensitivity of MR imaging remains to be proven.

Osteomyelitis

Medications such as steroids interfere with normal host-defense mechanisms, and joints damaged by RA are more susceptible to infection. Septic arthritis and osteomyelitis may therefore occur as a complication of RA and its therapy.[49] In the past, radionuclide scanning was the most sensitive test for the detection of osteomyelitis. However, soft-tissue inflammation interferes with the detection of osteomyelitis by radionuclide scans. Numerous studies have demonstrated that MR imaging is equal to or more sensitive than radionuclide scan for the detection of osteomyelitis.[8,38,60,61] Acute osteomyelitis causes an increase in intramedullary water from edema, hypermia, and exudate, and causes a low to intermediate signal in T1-weighted images and a high signal in T2-weighted images. T2-weighted images are needed to identify active infection.[60] Normal signal intensity in bone marrow excludes the diagnosis of osteomyelitis. The extent of soft-tissue abscess or cellulitis can also be demonstrated with MR imaging. Localization of infection and inflammation in soft tissues, tendon sheaths, and joints allows accurate preoperative evaluation.[8] The presence of orthopedic devices often does not interfere with diagnostic MR imaging.[8,38]

BONE DENSITOMETRY

RA is often accompanied by two forms of osteoporosis. The first, periarticular bone loss, is well recognized and is mediated by local mechanisms.[52] The second, a generalized osteoporosis with loss of bone from the axial and appendicular skeleton, is thought to be related to many factors including disuse, steroid therapy, or a process inherent to the disease itself.[45]

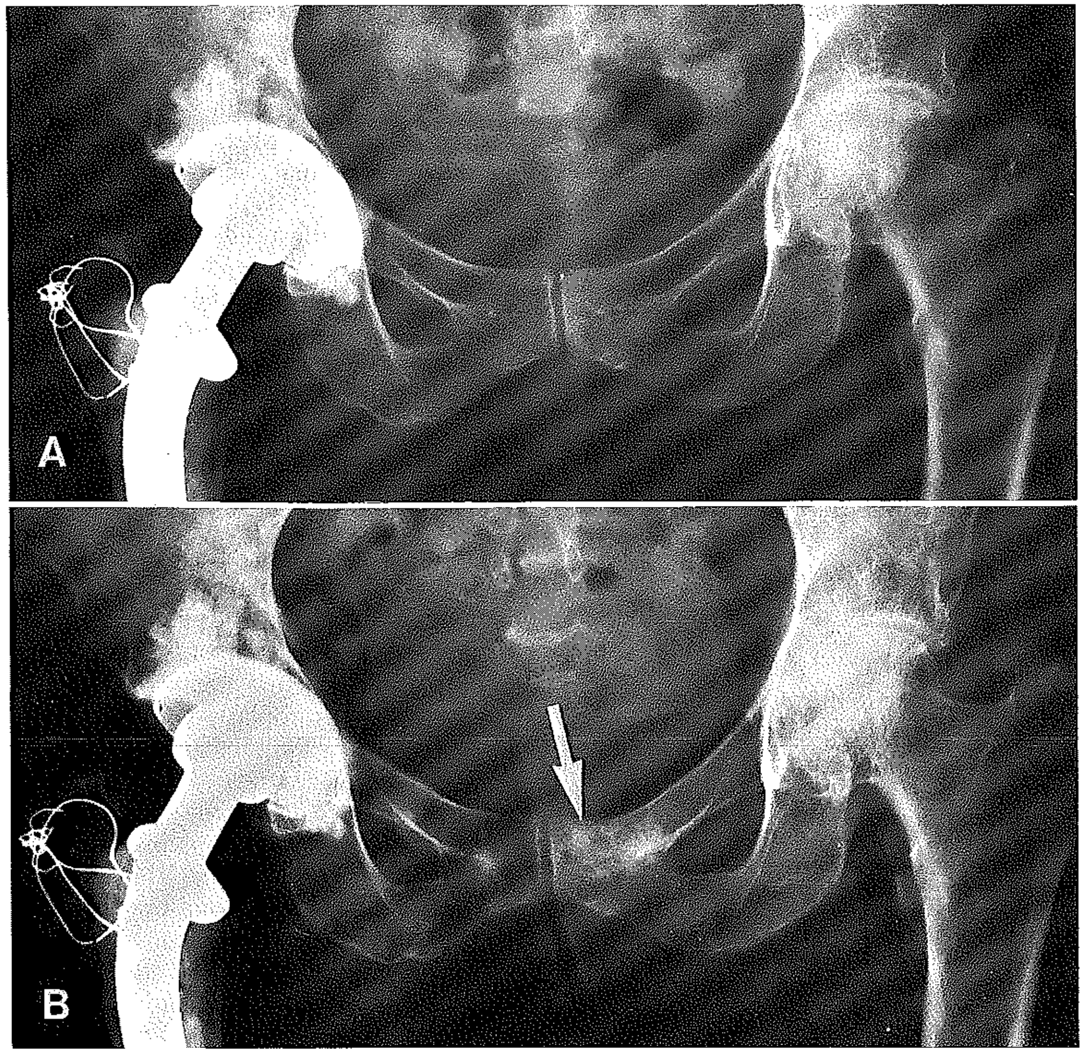
Bone loss from the axial skeleton renders patients with RA more susceptible to vertebral body fractures. The principal determinant of vertebral strength and resistance to crush fractures is trabecular bone density, and to a lesser extent, the strength of cortical bone.

Joint destruction resulting from RA may require arthroplasty to relieve pain and restore function. The major causes of pain after arthroplasty are loosening or infection of the components.[37] Insufficiency fractures are a less frequent complication of arthroplasty in patients with RA, and may become manifest in a similar fashion.

In patients with RA, insufficiency fractures may occur *de novo* in the long bones, and result in insidious pain and local tenderness over the bone rather than the joint. If the fracture is near a joint, the pain may be mistaken for an exacerbation of synovitis.[18]

Insufficiency fractures are increasingly recognized after arthroplasty (Fig. 6).[29,33,40,58] Stress fractures of the pubic rami or the femoral neck have been seen after total hip or knee arthoplasty. Because arthroplasty significantly reduces pain, patients may suddenly increase their activity levels. This increased activity without protection of osteoporotic bone may be the cause of insufficiency fractures.[40] It has been recommended that patients with significant osteoporosis return to weight bearing and ambulation gradually after hip or knee arthroplasty to minimize this risk.

In the setting of insufficiency fracture, early roentgenograms are often normal or findings may be subtle. ^{99m}Tc radionuclide bone scanning offers a highly sensitive method to identify stress fractures up to one to four weeks before roentgenograms are abnormal.[18] The fractures are visualized as a focal increase of radioisotope tracer in the region of the abnormality. MR imaging has also been used to image stress fractures. An area of bandlike low-signal intensity in T1-weighted images within the intramedullary space, which is contiguous with the cortex, is



FIGS. 6A AND 6B. One month after a right total hip arthroplasty, a 66-year-old woman with RA came to the emergency room experiencing left groin pain. (A) Anteroposterior roentgenogram of the pelvis. The right total hip arthroplasty is unremarkable, and there is severe RA of the left hip. (B) Anteroposterior roentgenogram of the pelvis one month later. There are areas of increased density in the left pubic bone (arrow), and right pubic rami, evidence of healing stress fractures that were not yet visible in the earlier roentgenograms.

presumed to represent microfracture or bone sclerosis. High-signal intensity on T2-weighted images presumably represents hemorrhage or edema. Whereas the bone scan is more widely used because of its lower cost, MR imaging may be useful in equivocal cases.[35]

There has been a recent proliferation of noninvasive modalities to evaluate bone density. A great deal of controversy, however, surrounds the clinical utility of these measurements. Most studies document a significant decrease in bone density in the spine and hips of RA patients. One study performed in RA patients concluded that decreased physical activity and steroid therapy (in men) were the most important determinants of axial bone loss.[52] Another recent study of women, however, found a correlation between osteoporosis, body weight, and duration of menopause, whereas the duration of disease, functional status, and cumulative steroid dosage were not predictive.[45]

Four basic techniques are available to measure bone mineral content: single photon absorptiometry (SPA), dual photon absorptiometry (DPA), quantitative CT (QCT), and dual-energy projection radiography (DEPR).

SPA utilizes a radionuclide isotope source. This modality can be used to assess the appendicular skeleton at sites where cortical bone predominates, such as the midshaft radius. Rectilinear SPA has the ability to assess sites of greater trabecular bone content, such as the calcaneus and distal radius. The primary advantages of SPA are its low cost, high precision, and short examination time. SPA cannot, however, provide bone-density measurements for the hip or the spine, areas that are clinically far more important.

DPA has evolved from SPA. This method has the advantage of being able to measure bone density in the spine and the hip. Because DPA is relatively insensitive to the marrow fat content of the spine, the proportion of fatty versus hematopoietic marrow within the vertebral body does not significantly affect readings. Other advantages include low cost, precision, and low radiation exposure. The examination time for DPA is, however, significantly longer than for other techniques.[20]

DEPR is a relatively new technique that is similar to DPA, but it uses an X-ray tube as the energy source instead of a radioisotope. Numerous acronyms have been used for this method, including DER (dual-energy radiography), DRA (dual-energy radiographic absorptiometry), and QDR (quantitative digital radiography). DEPR is used to measure mineral content in clinically important sites such as the spine and the hips. Because of the enhanced flux from the X-ray tube in DEPR, the scan speed and collimation are enhanced, resulting in reduced scanning time and improved resolution.[22] DEPR also offers a low radiation dose, short examination time, and higher precision than DPA. In a recent report, the *in vitro* longitudinal precision error was reduced from 1.3% with DPA to 0.44% with DEPR.[22] This increase in precision may enable detection of bone mineral changes in individuals over shorter periods of time.

QCT has the ability to measure the trabecular bone content of the spine; this is the only technique that does not combine cortical and trabecular bone as an integral value. The merits of QCT are offset by a higher radiation dose to the patient and slightly higher cost. In addition, QCT is sensitive to the amount of fatty marrow present.

All of the techniques listed above can demonstrate the progressive loss of bone density with RA or advanced age. Osteoporosis appears to be a continuum, and individuals with the lowest bone density are at the greatest risk of fracture.[20] In a recent prospective study, women with decreased bone density had an increased risk of hip fracture.[16] Genant *et al.*[20] recently recommended four applications for appropriate use of bone densitometry: (1) to establish the diagnosis of osteoporosis or to assess its severity, (2) to assess patients with metabolic diseases known to affect the skeleton (including RA patients on chronic steroid therapy), (3) to assess perimenopausal women before initiation of estrogen therapy, and (4) to monitor efficacy of treatment, and define those patients in whom conservative therapy such as calcium and exercise should be used versus more aggressive treatment such as estrogen or calcitonin therapy for those found to be at higher risk.

ULTRASONOGRAPHY

Popliteal cysts occur in conjunction with several forms of pathology, including RA, osteoarthrosis, and meniscal injuries.[19] These cysts arise from abnormal distension of the gastrocnemio-semimembranosus bursa behind the knee, and may communicate with the joint.

Popliteal cysts may be asymptomatic and clinically undetectable.[23] They can, however, cause pain and impair function. When large, they may rupture and dissect into the calf. Popliteal cysts are found in up to 31% of RA patients with painful calves.

In the past, arthrography has been used to detect popliteal cysts. This modality is invasive, and a communication between the cyst and the joint must be present for arthrographic diagnosis. Persistent communication with the knee joint is reported in only 50% of popliteal cysts. In addition, arthrography may fail to show portions of the cyst containing thick gelatinous fluid.[34]

More recently, ultrasound has been widely used for cyst evaluation. This noninvasive technique, unlike arthrography, does not depend on persistent communication between the joint space and the cyst. Ultrasound demonstrates normal muscle fibers and connective tissue as mixed echogenic structures, whereas the cyst itself is usually a sonolucent mass with good transmission of sound. Occasionally, cysts with debris may show internal echoes. Serial examinations with ultrasound allow accurate measurement of cyst size in response to therapy.

The clinical presentation of a large unruptured cyst, ruptured popliteal cyst, and deep venous thrombosis may be similar.[53] Typically well-circumscribed cyst margins may be lost when the cyst ruptures. Ultrasound can also detect deep venous thrombosis in the lower extremity.[62]

Popliteal artery aneurysms usually result from atherosclerosis but are also found in association with trauma, surgery, and infection.[34] The differential of popliteal cyst versus popliteal artery aneurysm may apply to patients who develop a posterior knee mass, including those who have had knee arthroplasty. In patients in whom arteriography cannot be performed, ultrasonography is useful in determining aneurysm size, delineating thrombus, and defining aneurysms that are thrombosed and do not opacifiy with contrast.[57]

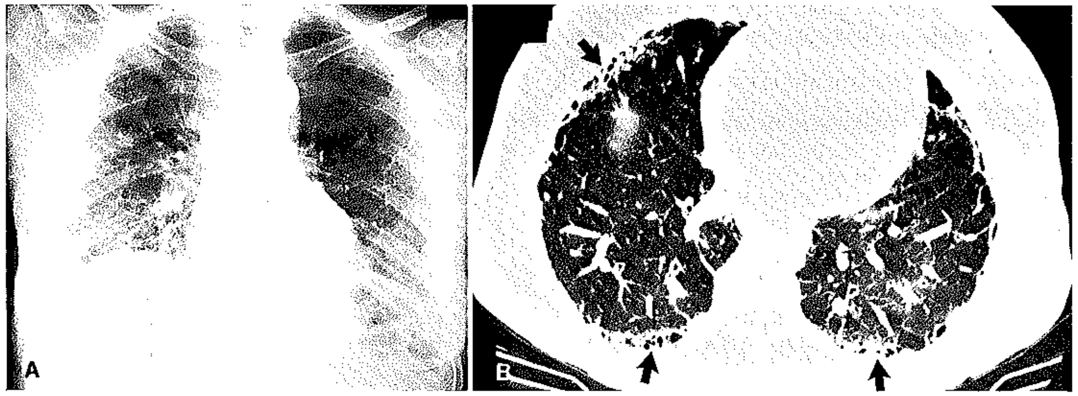
Color Doppler (color-flow ultrasound) imaging produces color-coded images of moving blood superimposed on a gray-scale background of anatomic information.[24] This can be useful in evaluating patients with vascular disease,[25] and may obviate arteriography.[46] Color Doppler imaging may be used to distinguish between simple popliteal cyst and popliteal artery aneurysm.[46] The diagnosis of aneurysm is made by establishing continuity of the mass with the popliteal artery, and the presence of pulsations within the aneurysm.

HIGH-RESOLUTION CT OF THE LUNG

As a systemic disease, RA may manifest itself in the thorax. Interstitial pulmonary disease is the most common form of rheumatoid lung disease.[14] Other pulmonary findings of RA include fibrosis, pleuritis, and rheumatoid nodules.

High-resolution CT (HRCT) is a recent development that has greatly affected thoracic imaging.[1] HRCT uses thin sections (1–3 mm) with reconstruction algorithms that greatly improve spatial resolution.[39] This provides information regarding lung architecture comparable to an anatomic examination.[41] HRCT can demonstrate normal and altered features of the secondary pulmonary lobule,[63] the basic unit of lung architecture that is comprised of three to five variable terminal bronchioles and acini.

Because of its increased spatial resolution, HRCT has been successfully applied to the detection and understanding of diffuse lung diseases such as that found with RA. Disease characterization has been based on distribution in central versus peripheral lung zones, localization relative to lobular anatomy, and characteristics of interstitial abnormalities (Fig. 7).[1] RA, other collagen vascular diseases, asbestosis, and usual interstitial pneumonitis have a characteristic appearance on HRCT: a peripheral rim of reticular densities



FIGS. 7A AND 7B. A 70-year-old woman with RA complained of mild shortness of breath thought to be due to congestive heart failure. (A) Chest roentgenogram revealed diminished lung volumes and increased interstitial markings at the lung bases. (B) High-resolution (CT) revealed fibrosis with honeycombing (arrows) in the periphery of the lower lobes, consistent with changes due to rheumatoid involvement of the lungs.

and honeycomb cysts with peripheral linear densities suggestive of thickened interlobular septa. Fine irregularity of the pleural surface and mediastinal interfaces cause the "shaggy heart" appearance.[9] Interstitial fibrosis is "patchy" in appearance; it affects the subpleural parenchyma first, and the more central lung zones later.[43,44] Because volume averaging obscures detail in thicker CT sections, the small honeycomb cysts of fibrosis are best seen with HRCT. The heterogenous mixture of normal lung with other areas of fine or coarse fibrosis characteristic of pulmonary fibrosis may only be visualized with HRCT.[43] HRCT findings may lead to earlier detection of lung disease in patients with RA. Because the distribution and severity of disease is best depicted with HRCT, this modality may be useful in selecting the optimal site and route for diagnostic biopsy in cases where indicated.[9]

HRCT has also been used to evaluate focal lung disease.[67] Because of its high spatial resolution, it is useful in the evaluation of lung nodules. Nodules indeterminate for calcification by other imaging modalities demonstrated calcification by HRCT in over 50% of patients, thus avoiding surgery. HRCT has also been used to evaluate the airways,[26] and has been shown to be comparable to bronchography for detection of bronchiectasis (cystic, varicose, and cylindrical).

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