Rheumatoid Arthritis: A Practical Guide to State-of-the-Art Imaging, Image Interpretation, and Clinical Implications

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Rheumatoid arthritis (RA) is a chronic systemic disease of unknown origin that predominantly involves synovial tissue. RA affects 0.5%–1.0% of the global population, with females affected more frequently than males. Early diagnosis and initiation of proper therapy help modify the course of the disease and reduce the degree of severe late sequelae. Radiology plays a key role in diagnosis and management of RA. Currently, magnetic resonance imaging is the best imaging modality because it depicts soft-tissue changes and damage to cartilage and bone even better and at an earlier stage than does computed tomography. Ultrasound and conventional radiography are more readily available but cannot show the entire spectrum of the disease. Diagnosis and differential diagnosis are achieved by identifying certain radiologic parameters, which are also used for grading purposes. The disease does not follow a linear course, especially with the early initiation of potent therapy. Knowledge of the imaging findings enables the radiologist to accurately select the most helpful imaging technique. Familiarity with the pathophysiologic mechanisms of RA, the imaging findings, and the grading systems and a basic knowledge of therapeutic regimens are prerequisites for a tailored diagnostic approach by the radiologist.

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Abbreviation: RA = rheumatoid arthritis

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Introduction

Rheumatoid arthritis (RA) is a chronic systemic disease affecting approximately 0.5%–1% of the global adult population with an estimated annual incidence of 12.0–24.5 males and 23.9–54.0 females per 100,000. RA occurs two to three times more often in women than in men. The incidence is largely consistent racially and geographically, and the peak age of onset lies between the ages of 45 and 65 years (1,2).

The etiology of RA is unknown but seems to be multifactorial. There is a certain genetic susceptibility, and studies in twins indicate a concordance of about 15%–20%. As many as 70% of patients with RA express HLA-DR4. Environmental factors (smoking) or infectious agents are suggested to play a role in the etiology, but their contribution has yet to be defined (1,3–5).

RA is regarded as an autoimmune disease in that in genetically susceptible patients, certain putative antigens that are presented by macrophages produce T-cell–mediated autoreactivity against a joint component (6–12).

The diagnosis of RA requires a spectrum of disease manifestations. The 1987 traditional diagnostic criteria of the American College of Rheumatology (ACR) (Table 1) and the classification tree format of those criteria (Fig 1) are widely recognized (13). The classification tree is slightly superior in terms of sensitivity, specificity, predictive value, and accuracy. Sugimoto et al (14,15) have shown that including magnetic resonance (MR) imaging in the traditional diagnostic criteria and the classification tree contributes to a more accurate diagnosis of RA, especially in its early stages (Fig 2). Bilateral soft-tissue enhancement in the wrist and/or the metacarpophalangeal and/or proximal interphalangeal joints was used as the defining MR imaging criterion. An accuracy of 94% was reported in a small patient group compared to 81% and 83% with the traditional method and the classification tree, respectively (13–15).

Table 1

| The 1987 Traditional Diagnostic Criteria of the American College of Rheumatology for the Diagnosis of RA |
| Morning stiffness in and around joints that lasts at least 1 hour before maximal improvement |
| Soft-tissue swelling of at least three joints that is observed by a physician |
| Swelling (arthritis) of the metacarpophalangeal, proximal interphalangeal, or wrist joints |
| Symmetric swelling (arthritis) |
| Subcutaneous rheumatoid nodules |
| A positive test for rheumatoid factor |
| Radiographic signs: erosions or periarticular osteopenia in hand or wrist joints |

Note.—Criteria 1–4 must have been present for at least 6 weeks. Four or more criteria have to be met.

Figure 1. Classification tree of the American Rheumatism Association for the diagnosis of RA. MCP = metacarpophalangeal joint.

Figure 2. Proposed new classification tree for the diagnosis of RA. This classification tree includes the MR imaging criterion of bilateral enhancement in the wrists, metacarpophalangeal joints (MCP), or proximal interphalangeal joints.
In this article, we describe the spectrum of radiologic findings in RA with respect to the underlying pathophysiologic process, present the preferred sites and the characteristic pattern of joint involvement, comment on different grading systems, and give an overview of the therapeutic options and prognosis. References to differential diagnoses are given where necessary. Subforms such as the juvenile, systemic, or cystic type have different disease courses than the common adult form and will not be described in this article.

Pathophysiology

In RA, the synovium is the site of the pathologic process and synovial joints as well as tendon sheaths are involved. In the course of the disease, adjacent structures such as the bone, tendons, capsule, and ligaments typically are involved.

In a synovial joint (Fig 3), the surface of the articulating bones is covered with cartilage except for a small region at the insertion of the joint capsule where—between the insertion of the fibrous capsule and the cartilage—the bone is covered by synovium only, the so-called “bare area.” Owing to the direct contact with the synovial tissue—without any protecting layer of cartilage—the bone surface in this location is very susceptible to synovitis-induced bone destruction.

The periosteum is continuous with the fibrous outer layer of the capsule. The internal synovial layer is arranged in folds and is covered by A cells derived from bone marrow and B cells of mesenchymal origin—the latter capable of phagocytosis. The two layers frequently are separated by fat.

The subsynovial tissue is rich in vessels. The interchange of fluid between vessels and the intraarticular space is facilitated due to lack of a basal layer under the synovialocytes. Synovial fluid is a dialysate of plasma, containing cells such as neutrophils and phagocytes. The content of fibrinogen and protein is lower compared with that in plasma. It acts both as a lubricant and as a nutrient. The nutrition of cartilage is provided through diffusion from the synovial fluid, by blood vessels that pass from the subchondral bone plate into the deep layers of the cartilage, and via blood vessels at the synovium-cartilage interface (16–18).

Synovial hyperplasia and formation into pan-nus is the fundamental pathogenesis of RA. This process is mediated by production of various cytokines, for example, tumor necrosis factor α (TNF-α) and interleukin 1 (IL-1) by antigen-presenting cells and T cells. Hyperemia and pain-induced inactivity lead to collateral changes involving the osseous compartment early on. Synovial tissue is invaded by local macrophages, fibroblasts, and activated lymphocytes. The next step in the pathophysiologic cascade is the invasion of the articular cartilage and bone by secretion of degrading enzymes, mainly metalloproteinases. TNF-α and IL-1 also play a prominent role in bone destruction (6–12). Intraarticular loose bodies may develop as a consequence of the inflammatory process, thus perpetuating the inflammation themselves. If ineffectively treated, the disease may be disabling and mutilating, producing ankylosis, deformity, and severe secondary degenerative osteoarthritis.

Imaging

Since early changes are nonosseous in nature, ultrasound (US) and MR imaging are superior to conventional radiography and computed tomography (CT) in terms of disease detection. In the developed world, arthritis is treated with a combination of potent disease-modifying drugs early on and therefore osseous changes are delayed. Therefore, sonography and MR are the imaging methods of choice. Naturally, reactive changes and bone destruction can be well appreciated with MR imaging. In summary, the diagnostic value of conventional radiography and CT in RA seems to be inferior to that of sonography and MR imaging, a view that should be translated into the clinical routine.

When imaging RA, it has to be taken into consideration that the time course of disease progression is not linear and that joint involvement is not uniform. In a single individual, various imaging findings may be present in different joints at any
time, especially at an early stage. Therefore, each joint has to be evaluated exactly and independently.

There is no general consensus on which joints to image. For diagnostic purposes, symptomatic joints and joints typically involved in RA (wrist and hand joints) should be imaged. In the follow-up, wrist and hand joints are preferred sites to assess the treatment efficacy. Other sites—for example, the foot joints—could also be used to evaluate disease activity, when initially affected.

US with high-resolution probes (7.5 MHz and higher) is limited to superficial joints and superficial sites of inflammatory involvement. Many investigators tend to examine symptomatic sites only and fail to depict less symptomatic or non-symptomatic joints. Power Doppler US with and without an echo-enhancing contrast agent may be helpful for the evaluation and quantification of disease activity (19–21). However, there is controversy about this issue in the literature (22,23), and the amount of available data is rather small. Therefore, this technique cannot be generally recommended for the time being.

When conventional radiography is used, optimal resolution has to be ensured. In most centers, a certain number of joints are imaged at certain time intervals according to local protocols in order to evaluate osseous changes. The most frequently affected joints (at least the hands, feet, and cervical spine) and the symptomatic joints should be included.

CT is infrequently used in the clinical routine as it is inferior to MR imaging and has the disadvantage of radiation. Practically speaking, it may be limited to indications where a precise assessment of bone destruction and stability is paramount, such as in a preoperative setting or in the spine.

MR is the best imaging modality for RA, although it is time-consuming and expensive. In the clinical routine, usually one or both hands, typical and early sites of RA manifestation, are examined to help establish the diagnosis or in the follow-up for assessment of the treatment efficacy. This approach is reflected in the literature, where most MR imaging disease activity scores are based on findings in the hand and wrist joints. Axial and sagittal imaging should be performed on the basis of coronal images to correctly define pathologic changes. A multiplanar approach is especially useful for the distinction between erosions and pre-erosive changes and for the assessment of pannus. The protocol should include T1-weighted sequences without and with contrast material, a T2-weighted sequence, and a sequence suited for cartilage evaluation. Fat saturation techniques are useful in combination with T1-weighted contrast-enhanced and T2-weighted sequences.

### Table 2: Important Para- and Extraarticular Findings in RA

<table>
<thead>
<tr>
<th>Location</th>
<th>Findings</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tendons</td>
<td>Synovitis of tendon sheaths, tenosynovitis, tendon rupture</td>
<td>The extensor carpi ulnaris, flexor carpi ulnaris, flexor carpi radialis, and extensor carpi radialis are frequently involved</td>
</tr>
<tr>
<td>Bursae</td>
<td>Synovitis, erosions of abutting bone</td>
<td>The retrocalcaneal, olecranon, and subacromial bursae are frequent sites of involvement</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>Rheumatoid nodules*</td>
<td>Calcification is an unusual feature; rheumatoid nodules may ulcerate, drain, and give rise to an infection</td>
</tr>
<tr>
<td>Bones</td>
<td>Osteopenia, bone fracture, avascular osteonecrosis</td>
<td></td>
</tr>
<tr>
<td>Systemic†</td>
<td>Vasculitis, myopathy, cardiovascular disease†</td>
<td>RA may manifest as a systemic disease with anemia, lymphadenopathy, hepatosplenomegaly, iridocyclitis, leg ulcers, myopericarditis, serositis, leukocytosis, rheumatic rash, and fever</td>
</tr>
</tbody>
</table>

*Granulomas (type IV allergic reaction) associated with seropositivity and typically situated between osseous prominences and the skin at pressure points.
†These findings often affect juvenile and young patients.
‡Due to high levels of C-reactive protein.
Imaging Findings

In the following section, different imaging findings are presented, the underlying pathophysiologic changes are described, and characteristic images obtained with the favored imaging technique are shown.

Although the disease process is not linear, a kind of inflammatory cascade seems rational, and the description of the various imaging findings follows this assumption as tightly as possible. There will be an overlap of findings, as some of the symptoms may well occur simultaneously.

The description focuses on the pathologic findings in the joints. A summary of important extraarticular changes is given in Table 2.

Hyperemia

Hyperemia is the first step in the inflammatory cascade that can be identified with imaging. Power Doppler contrast-enhanced sonography and MR imaging (especially T1-weighted contrast-enhanced sequences with spectral fat saturation and water-weighted inversion-recovery images) are very helpful in identifying the pathologic condition (Fig 4). Hyperemia may regress totally. It is a hallmark of acute inflammation and is also seen in exacerbation of chronic disease. No radiographic changes are seen in this condition as long as there is no profound soft-tissue edema or joint effusion (19,24–31).

The association of synovial hyperemia and enhancement of the synovium has been documented in the literature (32,33). It is postulated that the degree of enhancement depends on tissue perfusion and tissue permeability (34).

The degree of enhancement has been assessed qualitatively (34,35) and quantitatively (36). Huang et al (36) documented an association of enhancement rates with the degree of joint inflammation, the pain score at baseline, and the probability of developing erosions after 1 year. The static synovitis score was found to be the strongest predictor of erosions (36). However, these results are not uniformly accepted.

Synovitis

Cytokines mediate capillary leakage and edema in the acute phase. This facilitates synovial swelling and leads to widening of the joint space, which may well be exaggerated by effusion. This process is reversible. As the inflammation goes on, an infiltration by inflammatory cells is noted. As long as there is no fibrosis and no cartilage or bone destruction, it is to be assumed that the process might be fully reversible. Lymphatic tissue organizes. A spectrum of cytokines and proteases is excreted, causing destruction of cartilage and bone.

Initially, the inflammatory tissue thickens at the bare areas (Fig 5), gradually extending into the joint space across the cartilaginous surfaces.
The advanced stages of synovitis are almost always accompanied by other radiologic symptoms, such as subcortical cysts (Fig 6)—which are considered pre-erosions by some authors—and clear erosions. They typically first evolve at the bare areas due to the direct contact of synovium and cortical bone. Later in the course of the disease, destruction of cartilage and cortical layers also involves the central portions of the articulating bone surfaces.

Synovial tissue of tendon sheaths is naturally involved in RA (Figs 7, 8). It should be stressed that the extensor carpi ulnaris is a typical and early site of RA manifestations at the wrist. The inflammatory process may well lead to erosions of the styloid process of the ulna in the course of the disease.

The definition of pannus is inconsistent in the literature. Some use the term when associated destruction of bone or cartilage is noted (37); others use it to describe a tumorlike focal proliferation of inflammatory tissue. Hypervascular and hypovascular (Fig 9) pannus may be differentiated; the former term is used to describe a more active form (37).

MR imaging is an excellent tool for assessing synovial swelling and volume. The use of a T1-weighted spin-echo sequence early after intravenous contrast material administration is highly recommended, as it helps differentiate effusion...
Gadolinium contrast material may diffuse into the synovial fluid, causing equilibration of signal intensity between synovium and effusion in less than 5 minutes (39). MR imaging is clearly superior to conventional radiography in the assessment of synovial disease (40,41). The latter relies on indirect and nonspecific signs such as joint space widening, soft-tissue swelling, and dislocation and effacement of fat pads (24). Contrast-enhanced color Doppler US helps detect and define synovial changes. Evaluation of pannus, pannus differentiation (hypervascular, hypovascular, and avascular), and assessment of intraarticular vascularization can be performed (42,43).

Several authors have made use of quantitative and semiquantitative analysis of synovial volume, more or less effectively linking it to disease activity (33,44,45). However, the measurement process is very time-consuming and therefore not appropriate for routine use for the time being. Other groups have measured the rate and magnitude of synovial enhancement quantitatively (46–48) with good correlation to histologic findings and clinical markers of disease activity (36).

**Effusion**

Effusion occurs early in the disease and is commonly associated with acute inflammation or exacerbation. In order to identify even small effusions in small joints, comparison to other joints is very helpful. Sonography and MR are the imaging methods of choice as they are much more specific than conventional radiography, which demonstrates only indirect signs such as joint space widening and soft-tissue swelling as well as shifting of fat pads. At MR imaging, it is essential to use pulse sequences that reliably help distinguish synovial tissue from effusion (Fig 11). We suggest a combination of T1-weighted contrast-enhanced spin-echo with fat saturation and T2-weighted spin-echo or gradient-echo sequences (24–28, 38,40,49).
Paraarticular Osteoporosis

Trophic changes and alterations in the microcirculation cause paraarticular osteoporosis based on the activation of osteoclasts near the joints as a collateral effect. This process may well be exaggerated by inactivity due to pain. It may take up to weeks to identify this change on conventional radiographs, as the findings may be very subtle in the beginning (Fig 12) (25,50). A comparison with standard reference film radiographs suggested for staging purposes by Larsen et al (51) may be helpful to the inexperienced reader.

Paraarticular osteoporosis is cited as an early sign of joint involvement in RA and is called a collateral phenomenon by some authors (25). Resnick (27) attributes it to the early synovial stage.

In the state-of-the-art literature, paraarticular osteoporosis is not much of an issue today, as it represents a secondary indirect sign of synovitis that is demonstrated by MR imaging or sonography directly (52). However, this symptom is still important in the daily routine, as the first-line imaging tool in many centers is conventional radiography.

Owing to osteoclast activation and to direct inflammatory action, effusion content, and pannus (transchondral or direct extension), the subchondral end plate is degraded and becomes translucent (25,27).

Together with the paraarticular osteoporosis, unsharp cortical end plates are considered to be early radiographic changes.

Changes in the Bone Marrow

Marrow edema and enhancement of subcortical bone is a frequent collateral finding with joint involvement. It may precede subcortical cysts and erosions (Fig 13) but may also regress without any subsequent damage to the bone. There is no necessary relation to osteoporosis on conventional film radiographs. This symptom can be identified only with MR imaging, and water-sensitive sequences are very useful in this respect. Affected marrow will readily show significant uptake of contrast material.

The prognostic role of bone marrow edema is expressed in its high negative predictive value for the emergence of erosions (53).

Narrowing of the Joint Space

Progression of the destructive process and the formation of scar tissue and fibrosis lead to concentric joint space narrowing (Fig 14), a finding formerly ascribed to early stages of RA when conventional radiography was the only imaging method available. From the current point of view, this symptom indicates an advanced stage of RA, as was explicitly proved by Lehtinen et al (54) in the glenohumeral joint. They did not find joint space narrowing early in the disease process.

Joint space narrowing is an important sign of RA that sometimes may be subtle and difficult to identify. It is caused by destruction of cartilage, which is the twofold effect of deprivation of nutrition and destruction.

In contrast to the eccentric joint space narrowing in osteoarthritis, the narrowing is predominantly concentric in RA.

Subcortical Cysts

Cystic changes in the subcortical bone are easily identified on plain radiographs as translucent lesions (Fig 15) and are frequently associated with unsharp cortical end plates. Owing to reparative processes, they will be surrounded by a sclerotic
Figure 12. Paraarticular osteoporosis in a patient with RA. Radiograph shows increased bone lucency at the radiocarpal, carpometacarpal, metacarpophalangeal, and proximal interphalangeal joints and in the carpus.

Figure 13. Acute painful arthritis of the third metacarpophalangeal joint. Coronal contrast-enhanced fat-saturated T1-weighted MR image shows extensive thickening and hyperenhancement, findings consistent with synovitis. The enhancement of the bone marrow (*) is indicative of inflammatory involvement or a reactive response. The cortical layer of the metacarpal head is thinned.

Figure 14. Narrowing of joint spaces in long-standing RA. Radiograph (detail view) shows narrowing of the joint spaces of the second and fourth metacarpophalangeal joints (*). The concentricity of the narrowing is a hallmark of arthritis, whereas joint space narrowing due to degenerative changes is eccentric.

Figure 15. RA of the wrist. Radiograph (detail view) shows a ballooned ulnar styloid process. There are small cysts (**) in the styloid process and scaphoid bone. The radiocarpal joint space is narrowed.
rim (Fig 16). They evolve months after the onset of symptoms, and Freyschmidt (25) describes them as direct signs of arthritis. However, the underlying pathogenetic process has not been elucidated in detail, as pathologic-radiologic correlation is difficult to achieve due to the lack of biopsy specimens. These cysts may contain fluid, synovium, or both with or without communication with the joint.

Resnick (24) indicates that there is an association with transchondral expansion of superficial pannus or direct extension of subchondral pannus into bone (Fig 17). Joint decompression might be another contributing factor, and physical activity could subsequently be linked. Some patients with a high level of activity tend to develop large cysts: the robust reaction type of Resnick (24). It may be most reasonable to consider subcortical cysts arising in the context of arthritic joint involvement as a type of early erosion with direct expansion of inflammatory tissue from the joint into the bone, where the disruption of the cartilage and/or cortical bone is too small to be visualized with imaging.

Distinction between the pathogenesis of subcortical cysts, whether linked to the inflammatory and—as postulated—microerosive process or not (simple bone cysts, intraosseous ganglia, and osteoarthritic cysts), may be impossible morphologically. However, there are some helpful parameters.

Some authors state that enhancement on MR images is more typical for the “arthritic” cysts of RA and less frequently seen in simple bone cysts and intraosseous ganglia (55), a criterion we do not find very reliable. A number of more than three, an eccentric location, and unsharp margins increase the likelihood that the subcortical cyst is the result of an inflammatory joint process. At MR imaging, arthritic cysts usually do not contain fat or trabecular bone (56).
Erosions
Up to 47% of patients may develop erosions within 1 year after onset of RA (57).
Cartilage destruction and erosions are due to cytokines and proteases secreted by the inflamed synovium and pannus. Naturally, erosions arise at the bare areas first due to the lack of the protecting cartilage layer there. The diagnosis of erosions is very important as it may well influence therapy.

MR imaging demonstrates erosions first (Fig 18): McQueen et al (55) reported carpal erosions in 45% of patients on MR images 4 months after the onset of symptoms, while only 15% of patients had erosions on plain radiographs. Other studies confirm the superiority of MR imaging and CT to conventional radiography (35,58,59). This may well be due to the fact that plain radiography is limited in terms of projection and to the sensitivity of MR imaging for detecting early bone marrow edema and subcortical cysts, which frequently resemble pre-erosions (29,40,41,59). Sometimes, contrast enhancement helps distinguish erosions and pre-erosions from simple and degenerative bone cysts, which are less likely to enhance (55).

Sonography can be used to detect erosions too (Fig 19) (60,61). However, it is operator dependent, lacks sensitivity and specificity, and does not demonstrate pre-erosions and is therefore not widely applied for this purpose. Furthermore, it is limited to certain target areas.

In some patients, the inflammatory process ceases to be active with and even without therapy and the borders of the erosions become sclerotic and might even heal (Fig 20). In others, erosions progress even with therapy and clinical improvement (59). These data indicate different possible pathologic mechanisms in RA.

Late Findings
In advanced stages, the inflammatory process may lead to massive erosions and bone mutilation as well as destruction of the soft-tissue structures of and around the joint (Fig 21). Scar formation, fibrosis, subluxation or luxation, and finally fibrous and bony ankylosis are late sequelae of the disease (Fig 22).

The amount of cartilage destruction may be assessed with MR imaging—the fat-suppressed three-dimensional spoiled gradient-echo sequence is among the most helpful sequences (45,62)—and with sonography (61,63). Cartilage
thickness, a helpful qualitative marker for advanced conditions, has not been included in major MR imaging scaling scores due to the difficulty of obtaining exact measurements.

Subluxation may be caused by laxity of the capsule and ligaments due to inflammatory destruction or by capsular shrinkage due to fibrosis and scar formation—two different pathomechanisms causing the same imaging finding. Changes at the site of tendons and tendon sheaths act as contributing factors. Ulnar deviation of the second to fifth metacarpophalangeal joints is the most frequent type of subluxation in RA and may manifest fairly early, whereas other characteristic deformities are more likely to be found in advanced stages (Table 3).

Ankylosis represents a very late stage of RA. It is a much less frequent finding now due to improved medical therapy. Direct contact of the bony surfaces is a prerequisite for its development. Ankylosis may be both fibrous as well as bony.

**Table 3**

<table>
<thead>
<tr>
<th>Name of Deformity</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Mallet finger*</td>
<td>Laxity or disruption at the insertion of the extensor tendon on the distal phalanx, thus causing the distal phalanx to drop</td>
</tr>
<tr>
<td>Swan-neck deformity</td>
<td>Hyperextension at the proximal interphalangeal joint and flexion at the distal interphalangeal joint</td>
</tr>
<tr>
<td>Boutonnière deformity</td>
<td>Flexion at the proximal interphalangeal joint and hyperextension at the distal interphalangeal joint</td>
</tr>
<tr>
<td>Hitchhiker deformity</td>
<td>Flexion at the proximal metacarpophalangeal joint and hyperextension at the distal interphalangeal joint</td>
</tr>
</tbody>
</table>

*Rare finding involving the four ulnar fingers.

**Intraarticular Loose Bodies**

Intraarticular small loose bodies are a frequent by-product of the destructive inflammatory process, often including osseous and cartilaginous fragments. Some of the fragments are embedded in the inflamed synovial tissue.

A subset of loose bodies resembling polished rice are called rice bodies. They are grossly visible. First described in tuberculous arthritis, they are now most commonly associated with RA and are recognized as a very characteristic feature of RA, distinguishing it from other forms of arthritis (64,65). Their nature is multifactorial. They may be end products of inflammation or sloughed fibrinogen-coated infarcted synovial tissue (66,67). Alternatively, a precipitate of fibrin and fibronectin may be the initiating factor (68), or it may be a core of mononuclear cells (leukocytes or synovial cells) according to Popert et al (64). In summary, they represent a heterogeneous group of particles that may contain collagen, fibrinogen, fibrin, fibronectin, mononuclear cells, blood cells, and amorphous materials (69). Apatite crystals have been identified (67).
Apart from their high diagnostic specificity, their clinical significance is unclear. Some evidence suggests that rice bodies might be associated with frequent recurrence of synovitis (68) and removal may provide symptomatic relief in affected joints (64).

Rice bodies can best be identified sonographically and with MR imaging by using a spin-echo sequence with long echo time or T1-weighted spin-echo imaging after intravenous contrast material administration (Fig 23) (70–72).

**Pattern of Disease**

Unless highlighted, the described imaging findings are nonspecific for RA but may also be observed in other forms of arthritis. Therefore, additional criteria have to be derived to improve the accuracy of the radiologic diagnosis. The most reliable parameter is the pattern of joint involvement, which is very characteristic and typical of RA. The absence of proliferative changes (unless in secondary osteoarthritis) helps in the distinction from seronegative spondylarthropathies such as psoriatic arthritis or Reiter syndrome.

The hallmark of RA is bilateral symmetric arthritis of more than three joints (polyarthritis). Over 60% of patients initially present with symmetric arthritis of multiple small hand joints. Typically, the second and third metacarpophalangeal and the third proximal interphalangeal joints are involved early in the course of the disease; the ulnar (Fig 24) and radial aspects of the radiocarpal joint and the intercarpal, carpometacarpal, metacarpophalangeal, and proximal interphalangeal joints are other common sites. Simultaneous synovitis of tendon sheaths of the wrists and hands is another distinct finding.

Bilateral and symmetric involvement of foot joints is another typical manifestation of RA. The metatarsophalangeal (Fig 25) and the interphalangeal (great toe) joints are favored sites. All midfoot joints may be involved. The talonavicular, subtalar, and tarsometatarsal joints are specific target areas. The possibility of retrocalcaneal bursitis should be kept in mind. Changes may occur at the insertion of the plantar aponeurosis and the Achilles tendon.

Involvement of the talocrural joint may be associated with a sinus tarsi and tarsal channel (compression of the tibial nerve) syndrome. Tendovaginitis, tendinitis, and rupture of the tibialis anterior tendon may complicate the process, further destabilizing the joint (73).
Later in the course of the disease, large extremity joints (Fig 26), joints of the vertebral spine—especially the cervical spine and the atlantoaxial joint (Fig 27)—and other joints may be affected. The superolateral aspect of the humeral head is a typical location (Fig 28); atrophy and rotator cuff tear are frequent local complications. Involvement of the cervical spine represents a common manifestation of RA. The thoracic and lumbar spine is infrequently affected. Spinal joints, intervertebral spaces, and tendinous and ligamentous insertions can be inflamed. The occipito-atlantoaxial joints are involved frequently and early. Careful analysis of this area is indicated. Instability and subluxation are dreaded complications of RA in the spine. Spinal cord compression may be the result of subluxation and inflammatory tissue. Vertical and anterior atlantoaxial subluxations can be assessed with the use of commonplace measurement methods. However, note that subluxations may become visible only during flexion and extension when plain radiography is employed. Therefore, MR imaging is indicated in all cases of suspected involvement of the spine.

The hips and sacroiliac joints normally are not affected. If the sacroiliac joints are involved in RA, an asymmetric and unilateral distribution is most likely, in contrast to the bilateral and symmetric arthritis in most seronegative spondylarthropathies. Furthermore, erosions are shallower, sclerosis is milder, and ankylosis is rarer in RA.

Seronegative spondylarthropathies (morbus Bechterew, morbus Reiter, psoriasis) and gout typically involve different joints (lower extremity, sacroiliac joints, whole spine, or lower spine) than RA. Bony ankylosis, bony proliferation, and marked involvement of tendinous and ligamentous insertions are features of seronegative spondylarthropathies important for differential diagnosis from RA.

In a minority of patients, the onset of disease is atypical. Asymmetric, mono- and oligoarticular disease may be present and larger joints may be involved first. In these cases, differential diagnosis from other joint diseases (eg, ankylosing spondylitis, psoriatic arthritis, Reiter syndrome, gouty arthritis) is difficult when a target approach is used and typical discriminative changes have not evolved at the time of presentation.
Grading of RA

The first accepted and still best established grading systems are based on characteristic radiographic findings. These schemes—Larsen’s system (Table 4) (51), Scott’s modified version (74), and Steinbrocker’s grading (Table 5) (75)—are still used widely for clinical as well as research purposes. Their use is problematic for three reasons. First, there is the inherent difficulty of grading a disease that has a nonuniform course of progression and that also is influenced by the general early administration of disease-modifying drugs. Second, soft-tissue changes cannot be classified adequately since they are not depicted on conventional radiographs sufficiently. Therefore, advanced stages of RA are overrepresented when graded with conventional radiography. Third, there is no possibility for a refined classification of soft-tissue changes in a disease where all pathologic changes are associated with a synovialopathy.

These shortcomings play an even more important role as advanced arthritic changes tend to appear less frequently with the use of improved therapeutic regimens.

Alternate classification schemes based on MR imaging findings have been suggested and virtually all radiologic symptoms have been employed in the evaluation, but no system has gained general acceptance up to now. Merging all data acquired with MR imaging into an acceptable and usable staging system for the daily routine seems to be virtually impossible. The variability of joint involvement and disease activity in examined areas, the sometimes low correlation of clinical and radiologic symptoms, and the fact that different sites may respond differently to RA therapy make the issue even more complicated. This may well explain the fact that no improved grading system is available, and due to the lack of alternatives many institutions still adhere to grading based on conventional radiography.

Treatment and Prognosis

Early initiation of combination therapy is the general consensus. Disease-modifying antirheumatic drugs (DMARDs) are the only class of drugs that have an influence on the course of the disease.

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<table>
<thead>
<tr>
<th>Table 4</th>
<th>Larsen System for Grading RA and Related Conditions by Using Standard Reference Film Radiographs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>Definition</td>
</tr>
<tr>
<td>0</td>
<td>No radiographic changes</td>
</tr>
<tr>
<td>1</td>
<td>Slight abnormality</td>
</tr>
<tr>
<td>2</td>
<td>Definite early abnormality</td>
</tr>
<tr>
<td>3</td>
<td>Medium destructive abnormality</td>
</tr>
<tr>
<td>4</td>
<td>Severe destructive abnormality</td>
</tr>
<tr>
<td>5</td>
<td>Mutilating abnormality</td>
</tr>
</tbody>
</table>

Source.—Reference 51.
Note.—A set of standard reference film radiographs has to be available for comparative purposes. Dislocation and bony ankylosis should not be considered in the grading.

<table>
<thead>
<tr>
<th>Table 5</th>
<th>Steinbrocker System for Grading RA on Plain Radiographs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Findings</td>
</tr>
<tr>
<td>I</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>II</td>
<td>Osteoporosis, muscle atrophy surrounding the joint*</td>
</tr>
<tr>
<td>III</td>
<td>Osteoporosis, destruction of bone and cartilage, exaggerated muscle atrophy,† joint deformities‡</td>
</tr>
<tr>
<td>IV</td>
<td>Osteoporosis, destruction of bone and cartilage, fibrous or bony ankylosis, exaggerated muscle atrophy,§ joint deformities¶</td>
</tr>
</tbody>
</table>

Source.—Reference 75.
*With or without extraarticular changes.
†Subluxation, ulnar deviation, hyperextension.
They represent the core of current treatment regimens and are given in combination. Their mechanism of action is immunosuppression and inhibition of certain cytokines, thus reducing the inflammatory activity. Nonsteroidal anti-inflammatory drugs (NSAIDs) are used in virtually every patient. Their analgesic, anti-inflammatory, and antiphlogistic effect is based on the inhibition of prostaglandin synthesis. Corticosteroids are indicated in active inflammatory disease. Physical therapy is the other pillar of treatment, aiming to preserve or re-establish joint function and motility.

It has been estimated that the life expectancy of persons with RA may be reduced by 3 years for women and 7 years for men. Before initiation of new treatment strategies, a rate of disability of 44% after 10 years of follow-up was reported by Sokka et al (76). The effect on the long-term survival and disability rates still remains to be seen. Owing to the ongoing activation of the inflammatory cascade on the one hand and side effects of the therapeutic regimen on the other, patients develop comorbid conditions. There is an increased rate of cardiovascular events, malignancy, infection, osteoporosis, and gastrointestinal disease (77–80).

Conclusions

Both the imaging findings and the typical pattern of involvement enable the radiologist to diagnose RA with a high degree of accuracy. The value of soft-tissue imaging modalities, especially MR, in evaluating symptomatic body regions cannot be overstressed in respect to the utmost need for very early detection of abnormalities, since the prognosis depends heavily on the immediate administration of a proper therapeutic regimen. The key issue in state-of-the-art management of RA on the radiologist’s side is to image the early manifestations before any destructive changes occur. Thus, the frequent initial radiologic approach in a suspected case of arthritis, the use of conventional radiography, must be replaced by MR imaging as the first-line modality. In addition, a grading system has to be derived that enables the reader to properly assess the soft-tissue component of the inflammatory process at the initial and control examination in order to provide reliable guidance to the treating clinician.

References


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