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Diagnostic Value of High-Resolution B-Mode and Doppler Sonography for Imaging of Hand and Finger Joints in Rheumatoid Arthritis

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Objective. **High-resolution sonography enables a detailed assessment of intraarticular and extraarticular soft tissue abnormalities of joints affected by rheumatoid arthritis (RA). This study was undertaken to evaluate the diagnostic value of B-mode sonography and power Doppler compared with that of clinical examinations and conventional radiography.**

Methods. **The study group comprised 47 patients (14 men, 33 women) with different grades of RA; 31 patients were rheumatoid factor (RF) positive, and 16 were RF negative. The wrists, first through fifth metacarpophalangeal joints, and second through fifth proximal interphalangeal joints of these patients were scored with ultrasound in B-mode and power Doppler application, using a standardized technique. Involvement and severity of inflammation, as well as vascularization, were scored according to a new 3-point scale. The results were correlated with benchmarks of the clinical and radiologic investigations. Clinical status and conventional radiologic status were determined according to the Disease Activity Score and the Larsen score.**

Results. **After preliminary studies in 15 patients, 39% of 704 joints were found to be abnormal by clinical investigation. Erosions were detected by radiography and sonography in 23% and 43% of joints, respectively. Hypervascularization was observed in 34% of 704 joints by power Doppler application. There was a significant correlation ($P < 0.001$) between the different methods for the detection of the severity of lesions. Use of a modern, state-of-the-art power Doppler program was necessary for semiquantification, and a standardized investigation technique and scoring system provided sufficient quality measures.**

Conclusion. **Sonography detects 20% more abnormalities than does radiography, and sonography has the potential to provide simple grading of disease activity. The rate of detection of abnormalities was slightly higher with clinical examination compared with sonography.**

The activity of joint inflammation in rheumatoid arthritis (RA) has been characterized according to clinical findings and laboratory tests, including tests for rheumatoid factor (RF), antinuclear antibody (ANA) titer, C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR) (1). Among all imaging modalities, conventional radiography has been recognized as an integral tool to detect and characterize the extent of destruction as manifested by joint space narrowing, juxtaarticular demineralization, erosions, and mutilation (2). Based on such findings, progressive damage in joints can be documented and assessed using a dedicated scoring system such as that introduced by Larsen (3–5). Magnetic resonance imaging (MRI), with high gradient-field strength and surface coils, has been reported to be more sensitive than radiography for the detection of erosions and for the detailed analysis of the various forms of soft tissue involvement (6–11). With MRI, quantification of the volume of synovial hyperplasia is possible (4,12–14).

Sonography has been reported to be useful for the detection of popliteal cysts and for the differentiation of soft tissue swelling in major and minor joints (14,15). The main limitation of sonography for rheumatologic applications has been the lack of standardization in performing and documenting the normal and abnormal anatomy of the joints. Reports of several investiga-

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tional techniques to visualize the superficial structures of the musculoskeletal system have been published, but very few contain relevant recommendations about the evaluation of arthritis and tenosynovitis (6,15–17).

There are conflicting reports about the correct interpretation of sonographic signs of inflammation and how to differentiate these signs from artifacts (17,18). Recently, technologic improvements in sonography have led to a significant increase in spatial and contrast resolution as well as in color Doppler sensitivity. Artifacts that appear as small phase shifts arising from strong stationary scatters that produce signals can be suppressed by using machines with better phase-locking circuitry or infinite impulse response filters. To address the problem of the high sensitivity of the technique to motion, we have applied lower pulse repetition frequency (PRF) on the Doppler system and greater color-gain settings that are used for locations with respiratory or pulsation artifacts. These settings result in greater compatibility with the instrumentation of sonography machines, with easier handling and shortening of investigation time.

With power Doppler sonography, B-mode image information is enhanced by the depiction of the vascularity of soft tissue, and ultrasound diagnosis as a whole appears to be even more sensitive for the differentiation of synovitis and joint effusion and for quantification of the degree of inflammation (15,16,18–21). This may allow earlier detection of RA and improve treatment options, as shown by Stone et al (17).

The aim of the present study was to detect and analyze synovial changes of the hands of patients with RA, based on a feasible and reproducible technique of sonographic investigation and interpretation. In addition, we evaluated the diagnostic value of B-mode and power Doppler sonography in conjunction with clinical examinations and conventional radiography.

PATIENTS AND METHODS

After giving informed consent, 47 patients (14 men, 33 women) with a mean (±SD) age of 58.7 ± 12.3 years (range 25–82 years) with different grades of RA, diagnosed according to the American College of Rheumatology (formerly, the American Rheumatism Association) 1987 revised criteria (22), were enrolled prospectively in the study. Standard clinical and laboratory evaluations were performed according to the recommendations by Villaverde et al (1). Laboratory studies included testing for RF, ANA, ESR, and CRP. Medication use was allowed. Exclusion criteria were age <21 years, pregnancy, a history of hand or wrist trauma, or other forms of diseases of the hand. Sonograms and radiographs were obtained within the first week after admission to the hospital.

Image investigation techniques. With sonography, patients were evaluated according to a 5–12-MHz gray scale (HDI 5000; ATL Ultrasound, Bothell, WA) with B-mode and power Doppler application, using a standardized technique. The patient was seated at the scanning table opposite the investigating physician, with his or her hands placed flat on the table surface. Two radiologists and 2 radiology residents performed the evaluation (after thorough instruction), and the results were compared to determine precision and feasibility. Findings were interpreted in consensus, and if there was any disagreement among the investigators, the examination was repeated. Synthetic plastic blocks were used to improve contact between the surface of the transducer and the hands and fingers and to reduce near-field artifacts (14).

The maximum axial resolution of 0.5–0.1 mm can be achieved with a transducer frequency of 5–12 MHz (23). Documentation of normal and abnormal structures of the joints of the hands for rheumatologic purposes was obtained according to recommendations in the literature (9,24). Standard cuts for documentation were performed by B-mode and power Doppler sonography application.

We applied lower PRF and greater color gain settings, based on the settings published in the literature. Gain settings were corrected by placing the signal within a large vessel such that the signal was entirely derived from blood (18). The mean transit time for flow in the tissue could not be measured with our software, and an appropriate quantification was not possible; however, we measured an increase in the amount of moving blood in which there was a measurable Doppler shift. To avoid artifacts, we selected the color gain setting on a level slightly higher than noise and used synthetic plastic blocks.

Radiographs of the hands were obtained at the time of the ultrasound examination. Radiography was performed according to the following parameters: posteroanterior projection, 41 kVp, 24 × 30 cm film size, 8 mA using Kodak (Stuttgart, Germany) Ortho Fine screen, and a speed class of 200. Each hand was exposed separately, with 70–90° abduction of the upper arm and elbow flexion of 90°; hands were placed flat on the surface of the film cassette, with the central beam oriented perpendicular and focused on the head of the third metacarpal bone.

Criteria of image analysis and quantification in high-resolution B-mode. Joints were assessed as normal if there was no pain or swelling, no radiographic abnormality, and no sonographic abnormality. Erosions were defined by an abrupt discontinuity of the cortex, with acoustic enhancement within the subjacent marrow (9,25). For quantification of the severity of joint involvement, we used a 4-point scale as follows: 0 = no changes, 1 = slight changes, 2 = moderate changes, and 3 = strong changes of the soft tissue and erosions of the joint. The parameters for this score included erosions, effusion, synovial thickening, expanded tendons, joint space narrowing, and "rheumatic nodules" (26,27). Power Doppler standardization was based on 2 criteria. First, the small vessels of the hands (dorsal metacarpophalangeal [MCP] arteries) had to be visible, and second, the color gain setting had to be selected on a level slightly higher than noise. The parameters for the power Doppler image were no, small, moderate, and strong vascularization scored 0, 1, 2, and 3, respectively (Figures 1A–D). The maximum potential score for B-mode and power Doppler evaluation measured for one hand was 33.

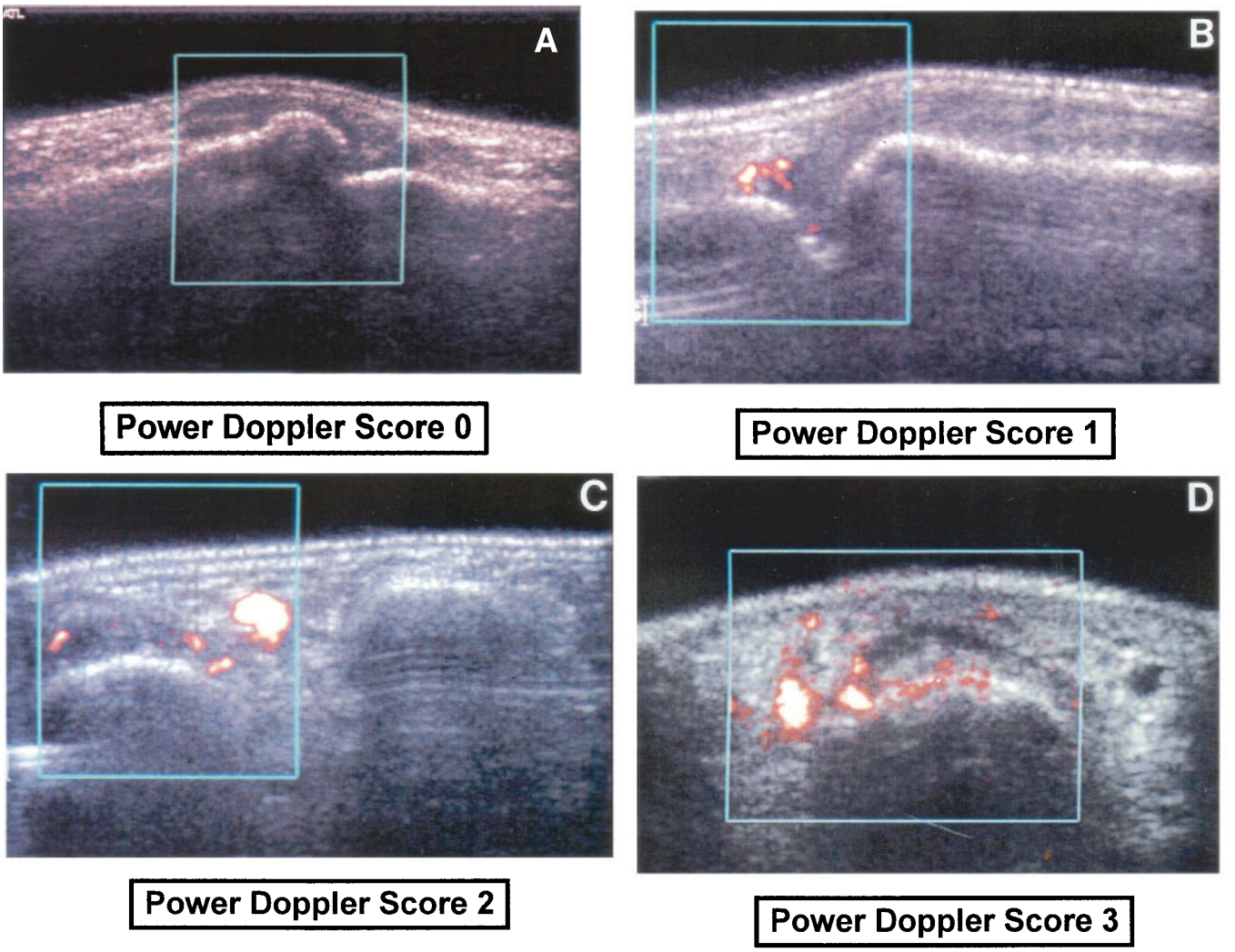

Figure 1. Images of metacarpophalangeal (MCP) joints showing different degrees of vascularity, expressed as a colored power Doppler signal. **A,** Standard sagittal cut through the first MCP joint, showing no vascularity. The hypoechoic joint effusion appears dark, and the bone margin of the phalanx appears as a white line. **B,** Standard sagittal cut through the third MCP joint, showing a small amount of vascularity. **C,** Standard transverse cut through the fourth MCP joint, showing moderate vascularity. **D,** Standard transverse cut through the third MCP joint, showing strong vascularity.

Finally, in addition to scores, the number of detected lesions (hypervascularization, swelling, or erosions) with the different diagnostic methods was calculated. A joint was regarded as being definitely involved if the score for B-mode or power Doppler sonography was >1. Differences between the distribution, number, and severity of the lesions for each joint were analyzed. The amount of time involved in the sonographic investigation was measured by the investigator to calculate the costs of the different methods for diagnosis.

All radiographs were scored according to the Larsen method (4), using newly created software (Rheuma Coach) developed in our radiology department for specifically located lesions. Damage to the joint not caused by RA was excluded. According to this method, lesions were counted bilaterally in the 8 proximal interphalangeal (PIP) joints, the 10 MCP joints, and the carpoulnar and radiocarpal joints. The maximum potential erosion score for each joint was 5, and the maximum for a single hand was 55. Disease activity within the hand and wrist was determined by reviewing the referring rheumatologist's clinical assessment on the day of admission to the hospital, according to the Disease Activity Score (28).

Clinical data included a detailed description of joint status, including swelling and tenderness on pressure, and of morning stiffness and use of medication at the time of admission. Relevant laboratory data included RF titer by latex fixation, fluorescent ANA, CRP, and ESR. CRP values were divided into 3 levels: low (<2.5 mg/dl), moderate (2.5–7.5 mg/dl), and high (>7.5 mg/dl). RF values were classified as low (titer 0–200), moderate (titer 200–1,000), or high (titer >1,000). ESR levels were classified as low (<30 mm/hour),

Table 1. Clinical characteristics of 47 study patients with rheumatoid arthritis*

Age, mean ± SD years	58.7 ± 12
Sex, % women	70
No. of swollen joints, mean ± SD	9 ± 6
No. of tender joints, mean ± SD	7 ± 6
Duration of morning stiffness, mean minutes	73
RF, mean ± SD titer	594.1 ± 661.6
RF positivity, no. of patients	31
ANA positivity, no. of patients	13
ESR, mean ± SD mm/hour	53 ± 32
CRP, mean ± SD mg/dl	4 ± 3
DMARD use, no. of patients	15
NSAID use, no. of patients	22
Steroid use, no. of patients	14

* RF = rheumatoid factor; ANA = antinuclear antibody; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; DMARD = disease-modifying antirheumatic drug; NSAID = nonsteroidal antiinflammatory drug.

moderate (30–80 mm/hour), or high (>80 mm/hour). Experienced rheumatologists evaluated the joints at the time of admission. The clinical joint status, including swelling and tenderness on pressure, was scored as 0 (normal) or 1 (pathologic). The relationship between RF seropositivity and the extent of disease, as measured by radiography and sonography, was evaluated. Investigators were blinded to other modalities and clinical data.

Statistical analysis. Statistical analysis was performed using SSPS 11.01 (SSPS, Chicago, IL). Collected data about the degree of vascularization obtained in specific finger joints were correlated with the data from lesions of the same finger joints measured by radiography and B-mode sonography, using Spearman's rank correlation and Pearson's correlation tests. For correlation of the evaluation of lesions detected by the different diagnostic methods, P values less than 0.01 were considered significant. For sensitivity of the detection of abnormalities, we used the Friedman test.

RESULTS

In patients with RA, standard documentation using high-resolution imaging techniques should be performed in 11 regions in each hand, with 2 images (in the axial and sagittal directions) in each region (Figures 1A–D). The mean investigation time was 14 minutes (range 10–23) for each hand; this was reduced during the course of the study.

After refinement of instrumentation and optimization of image documentation, the following standard cuts were shown to be useful: longitudinal and transversal cuts dorsally and ventrally for the carpoulnar and radiocarpal side, dorsal longitudinal and transversal cuts from the first through fifth MCP joints, and dorsal longitudinal and transversal cuts from the second through fifth PIP joints. The metacarpal articulations were imaged with 10–15° of palmar flexion, and the wrist was imaged dorsally in a neutral position.

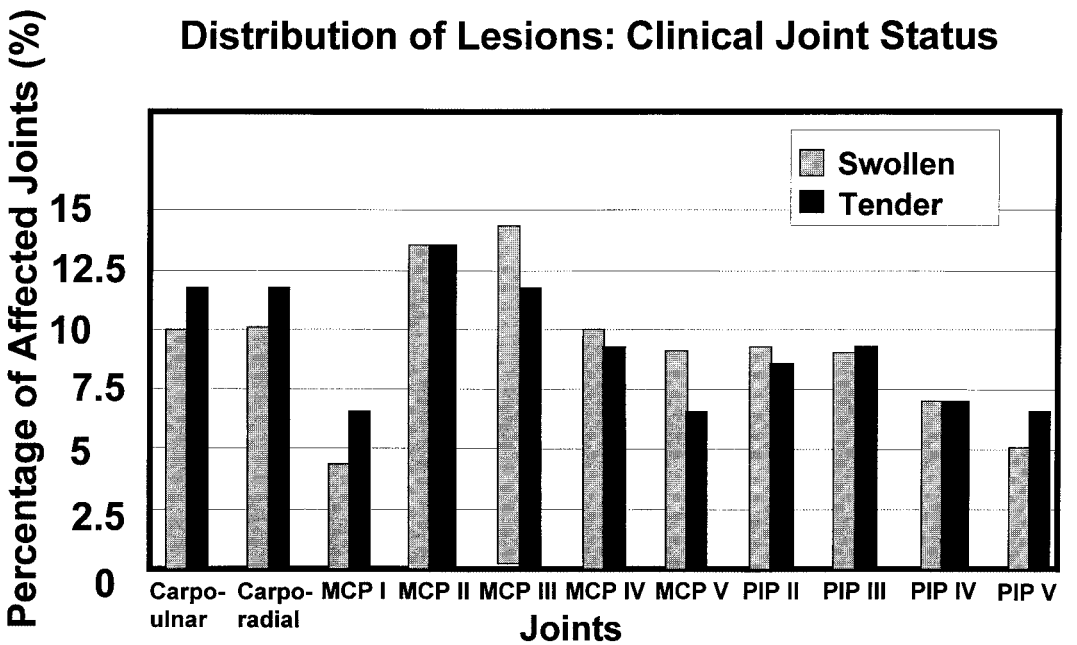

Figure 2. Distribution of swollen and tender joints. MCP = metacarpophalangeal; PIP = proximal interphalangeal.

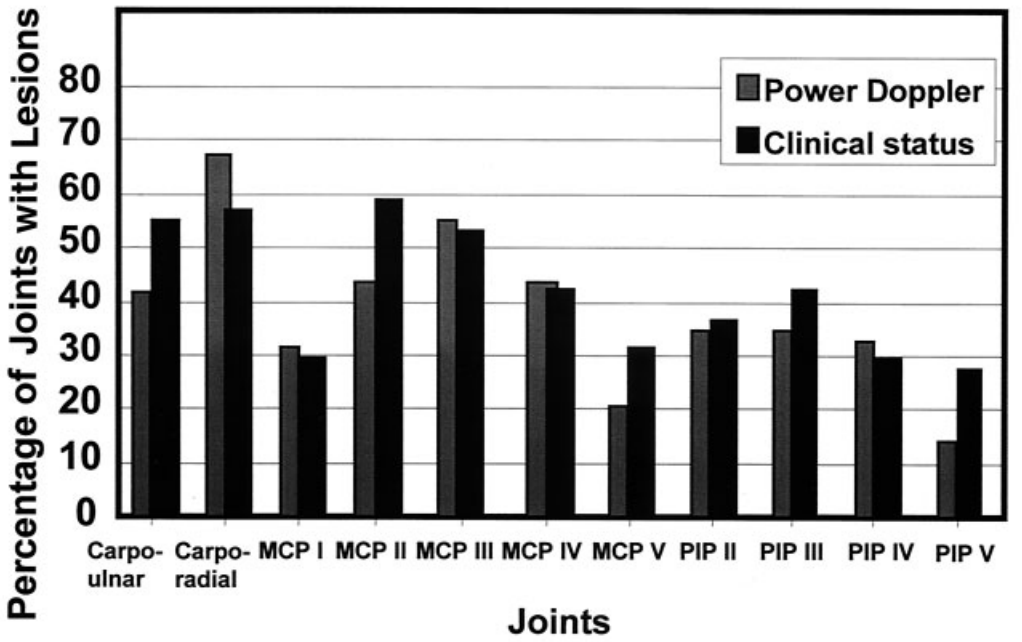

Figure 3. Percentage of involved joints as determined by power Doppler sonography and by clinical evaluation. See Figure 2 for definitions.

To date, quantification of power Doppler sonography has not been standardized by a scale adequate for differentiation; thus, we established a classification using a newly created 4-point scale, ranging from 0 to 3.

Correlation with clinical and radiographic data. Thirty-one of the patients were RF positive, and 16 were seronegative; the average RF titer was 594.1 (Table 1). No significant differences in sonographic abnormalities were observed between patients who were positive and those who were negative for RF, nor did the RF level show any significant correlation with radiologic findings ($P > 0.05$ for Pearson's correlation coefficient). ESR (mean ± SD 53 ± 32 mm/hour), ANA (13 patients positive), and CRP (mean ± SD 4 ± 3 mg/dl) showed no significant influence on sonographic findings. Fifteen patients were taking disease-modifying antirheumatic drugs (DMARDs), 22 were taking nonsteroidal antirheumatic drugs, and 14 were taking steroids.

On enrollment, 39% of the joints were classified as swollen and 35% as tender. The mean (±SD) number of swollen joints was 9 ± 6, and that of tender joints was 7 ± 6. Minor differences between the 2 criteria (swelling versus tender upon pressure) were apparent. Fourteen percent of the swollen joints were third MCP joints, 13% were second MCP joints, and 10% were radiocarpal joints. Five percent of the swollen joints were fifth PIP joints. The joint most frequently involved in terms of tenderness was the second MCP (13%), followed by the third MCP and the radiocarpal and carpoulnar joints (12% each). The joints with the lowest frequency of tenderness were the first MCP and the fourth PIP (both 6.3%), and the fifth PIP (6%) (Figure 2).

When sonography (power Doppler application), scored with the new scale (Figures 1A–D), was compared with the clinical findings, there was a significant correlation (Pearson $P < 0.01$). On average, power Doppler showed 4–7% fewer joints to be involved, but the tendency for the PIP joints to be less frequently involved was seen with both methods (Figure 3).

For each joint, the scores for lesion severity were added to obtain a grade and to show the difference between sonographic findings (joint erosions and changes of soft tissue accompanied by hypervascularization) and radiographic findings of abnormalities. With sonography, more severe lesions were detected primarily in the radiocarpal joint (12%), the carpoulnar joint (12% with B-mode application and 10% with power Doppler application), and in the third MCP joint (11%) and second MCP joint (10%). Low-grade involvement was demonstrated in the fifth PIP joint (6%). Lesion severity paralleled the distributions of joint involvement found on sonography: a higher frequency of involvement was observed in the wrist and the second and third MCP

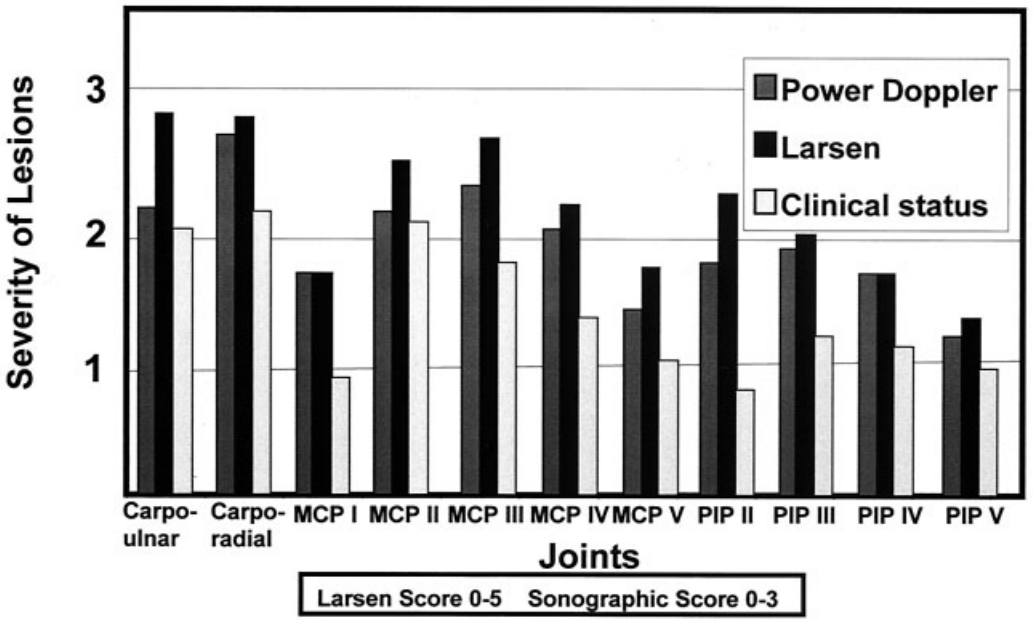

Figure 4. Sonographic, Larsen, and clinical scores. See Figure 2 for definitions.

joints, whereas the fifth PIP and the fifth MCP joints showed the lowest frequency of involvement (Figure 4).

In contrast, the number of lesions found on radiographs was mainly concentrated in the second MCP joint (16%) and the radiocarpal joint (14.5%). Radiography revealed lesions in only 6% of the first and fifth MCP joints and 7% of the second and fifth PIP joints (Figure 5).

Sonography in the B-mode and power Doppler application detected 20% more erosions and hypervascularization than did conventional radiography. With sonography, 43% of the 704 investigated joints were found to be definitely involved, resulting in a score of >1 by B-mode and power Doppler sonography, and were

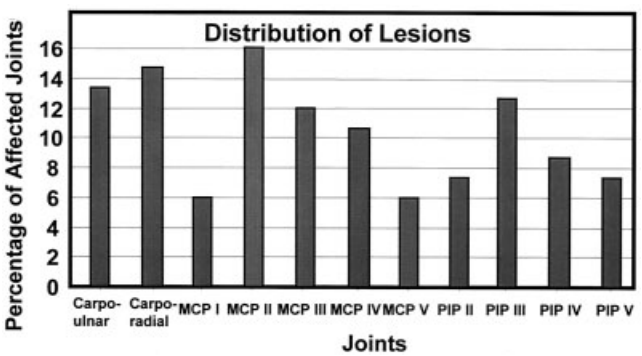

Figure 5. Distribution of erosions by conventional radiography. See Figure 2 for definitions.

therefore found to be abnormal. Erosions were detected by radiography in 23% of joints and by sonography in 43%. Hypervascularization was found in 34% of 704 joints, using power Doppler.

Sonographic quantification. Objective quantification of the grade of vascularization, performed by Doppler shift, did not yield relevant results, because investigation and quantification of the blood flow in small or curved vessels are difficult. Thus, a scoring system for the quantification of the vascularization of the affected joints (range 0–3) was useful.

The data on lesion severity according to the Larsen score and the sonography score, as described above, revealed a strong correlation between sonographic and radiographic findings ($P < 0.001$). The B-mode and power Doppler investigation scores were almost identical to the Larsen score (Figure 6). However, it should be noted that we used 2 different score scales for the sonographic and radiographic methods. To match the 0–3-point sonographic score (Figures 1A–D) to the standard Larsen score, we had to normalize the sonographic scores to the 0–5-point scale of the Larsen score. We plotted the Larsen and sonographic scores as function over the different joints.

DISCUSSION

Depending on the characteristic anatomic distribution of inflammatory tissue, effusions, and erosions, a

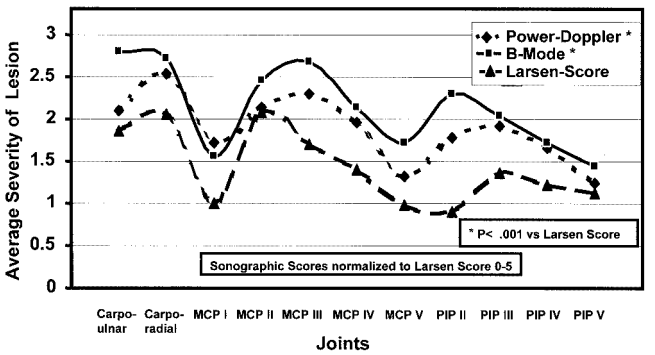

Figure 6. Comparison of sonographic scores and Larsen score. Sonographic scores (3-point scale) were normalized to the Larsen score (5-point scale). The data were plotted as function over different joints. See Figure 2 for definitions.

specific sonographic approach is necessary to detect and document abnormalities in RA. The general radiologic concept of image interpretation in rheumatology that has developed in the past few decades relies primarily on allocation (i.e., the analysis of the anatomic distribution of lesions among and within the affected joints) (7,9,29,30). Using high-resolution sonography, this concept must be developed further with regard to the typical location and distribution of inflamed synovium in joints and tendon sheaths. Documentation should be extended by including more regions (the interphalangeal joints) if corresponding clinical symptoms or signs are present. In this study, we used sonography to investigate the hands of patients with RA, including not only the soft tissues of the joints but also the tendon sheaths, because the PIP and MCP joints of the hand and the wrist are preferential sites, although any joint can be involved (12).

Vascularization is characterized by power Doppler (1,16,18) to support the diagnosis of RA. In general, power Doppler has been used to detect hypervascularization and to differentiate it from edema. Currently, effusions of >1 ml can be detected by ultrasound examination (31). With prominent vascularization, there is a correlation between the disease process, including inflammation, and increased blood flow of the vessels.

The general limitations of ultrasound (i.e., acoustic shadowing or deviation of the ultrasound beam) are of no importance when imaging superficial structures. In our study, all sonographic investigations were performed successfully, although it should be noted that power Doppler sonography is extremely sensitive to tissue movement, especially at low PRF. This artifact should be recognized as such and not be confused with true signal.

Magarelli et al showed that with power Doppler sonography with contrast medium a qualitative increase in signal from synovial vessels could be demonstrated and that this correlated with synovial changes in inflammatory diseases, concordant with the findings of MRI (32). Microbubble-based sonography contrast agents might improve the detection of blood flow signal within small finger joints and support the early diagnosis of RA and the differentiation between active and inactive inflammation (33). However, the cost of the microbubble-based contrast agent is approximately $60 per patient. In our study, performed with B-mode and power Doppler sonography, we did not use expensive contrast agent.

In general, the advantages of sonographic investigation are the fast and easy application, the superior spatial resolution, the ability to perform the examination with the patient in a comfortable position, and the lack of additional x-ray exposure. Furthermore, sonography as a diagnostic method is cost effective compared with other modalities, such as MRI. Often, patients with RA must endure uncomfortable positioning inside the magnet for MR investigations of the hand and wrist. According to a previous report by Wakefield et al, lesion extent and severity can be delineated to better advantage with sonography compared with radiography. In that study, sonography detected 6.5-fold more erosions than did radiography in the early stages of RA (34). Our results do not differ from those reported by those investigators. In our study, sonography detected 20% more lesions in the B-mode application than did conventional radiography and thus had more sensitive diagnostic value. This can be explained by the late detection of bone lesions using conventional radiography. The lesions found on radiographs correlated significantly not only with those detected by sonography using the B-mode application, but also with cumulative scores for clinical joint inflammation (35).

With power Doppler, we observed that 34% of the joints were involved, and that 16% of lesions were located in the radiocarpal joints. When these results were compared with clinical findings, clinical examination was associated with a slightly higher detection rate with regard to joint swelling (39%), whereas the rate of detection of tenderness was about the same (35%) for the 2 methods. There was a significant correlation between the distribution and number of inflamed joints. However, it should be noted that the medication taken by patients before sonographic examinations may have had an antiinflammatory effect on the joints and thus reduced the inflammation signs expressed as hypervascularization and edema. Stone et al demonstrated that

steroid treatment resulted in significant improvement in synovitis activity assessments (17). This could explain the more severe inflammation of the joints before use of medication, as characterized by tenderness on pressure and swelling on the day of admission; in patients receiving medication, superficial inflammation, such as edema and hypervascularization, was reduced according to sonographic criteria. This effect is illustrated in Figure 3: the carpoulnar joint, the second and fifth MCP joints, and the third and fifth PIP joints show a statistically significantly higher percentage of lesions detected by clinical examination.

Increased vascularization of the joints could be a marker for the early diagnosis of RA or could indicate a need for institution of low-dose medication (36). Expanded diagnosis using ultrasound could enable monitoring of medication levels (17). Therefore, followup of patients receiving medication that suppresses inflammatory processes could lead to a better prognosis for RA. The question remains as to whether a suitable method to quantify the increased vascularization in the joints of RA patients can be developed.

A scoring system necessitates a thorough examination of the patient, with an evaluation of the destructive disease process. A treatment regimen can be developed based on these objective findings (13). In contrast to the standardized technique of conventional radiography, a standardized method for the quantification of changes on sonographic evaluation does not currently exist. Therefore, we created a new scoring scheme ranging from 0 to 3, which can differentiate 4 levels of severity of joint damage caused by inflammation, including erosions, effusion, synovial thickening, expanded tendons, joint space narrowing, and "rheumatic nodules" (26,27).

Beneficial effects on the rate of joint erosion have been reported with low-dose prednisone, combination therapy with >1 DMARD (37), and combination therapy with a DMARD and prednisone (38). With early detection of RA, the appropriate medication could be initiated at an early stage, which could slow or stop the inflammation and prevent severe destruction of the joints.

In conclusion, sonography can be used to support the diagnosis of RA of the hand, and it is more sensitive than conventional radiography for detecting lesions of the small joints. Early detection of the disease and an evaluation of the disease process could help prevent further joint destruction. We suggest routine monitoring of patients with possible RA. This study also presents the basis for a concise sonographic protocol for imaging in RA. Despite the relatively small number of patients, we believe our findings offer the potential for standardized instrumentation and documentation as an adjunct to further research in this field, which will lead to a reliable method for lesion quantification in RA.

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