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Original Article

Early Assessment of Rheumatoid Arthritis Using the Nørgaard Radiographic Method and Rheumatoid Factor Testing

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Abstract

Background: This comparative study was conducted between July 25 and December 31, 2022, at Abusurra Hospital and Zawia Teaching Hospital in Libya to assess the efficacy of the Norgaard radiographic method versus laboratory analysis in the early detection of rheumatoid arthritis. A total of 64 patients of varying ages and clinical presentations were examined using both diagnostic approaches. **Material and Methods**: Radiographic assessment was performed using the Norgaard method, which focuses on early joint deformities, particularly in the metacarpophalangeal and proximal interphalangeal joints, while blood samples were collected for serological testing, including markers such as Rheumatoid Factor (RF). **Results** showed that 3 cases were identified simultaneously by both methods, 12 cases were exclusively detected using the Norgaard radiographs, and 8 cases were identified through laboratory analysis alone. These findings suggest that the Norgaard method may offer superior sensitivity in the early diagnosis of rheumatoid inflammation, especially when radiographic signs precede serological changes. However, the combination of both methods may enhance diagnostic confidence and reduce false negatives in ambiguous clinical cases. **Conclusion:**. We recommend that future research include broader screening of suspected rheumatoid arthritis cases in outpatient settings using both radiological and laboratory approaches. Emphasis should be placed on standardizing radiographic criteria and correlating imaging findings with serological profiles and clinical symptoms to establish a more comprehensive diagnostic framework.

Keywords: Rheumatoid -Norgaard – Laboratory tests - Rheumatoid factor – Arthritis -Hand injuries - Hand radiography

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INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by symmetrical joint involvement and extra-articular manifestations. The inflammatory process affects synovial joints and periarticular tissues, leading to joint destruction and functional impairment [1]. Early and accurate diagnosis and treatment of rheumatoid arthritis are essential for minimizing patients' disease burden and achieving improved long-term outcomes. Updated guidelines from the National Institute for Health and Care Excellence (NICE) [2] emphasize that initiating therapy within the first three months of symptom onset significantly enhances disease control [3].

RA is the most common form of inflammatory arthritis and is not a single disease but rather a spectrum of clinical presentations arising from synovial joint inflammation [4]. Its incidence increases with age, disproportionately affecting women, especially after the age of 50, and tends to plateau or decrease around age 80 [4]. Globally, RA ranks among the top ten disabling diseases in developed countries and remains a leading cause of pain and disability worldwide [1,5]. The pathogenesis involves a complex interplay of genetic, environmental, and immunological factors, with the HLA-DRB1 gene allele recognized as the most significant genetic risk factor [6]. Epidemiological studies reveal important patterns in RA distribution. The disease affects approximately 0.5-1% of the global population and shows a consistent female predominance (3:1 ratio) with incidence peaking between 50-70 years [7]. Postmenopausal hormonal changes significantly influence disease susceptibility, as supported by large cohort studies demonstrating increased incidence of seropositive RA following menopause [8]. Lifestyle factors, including smoking and dietary patterns, modulate risk, with adherence to a Mediterranean diet associated with lower incidence and milder disease courses [9,10,11,12]. In 1963 and 1965, Flemming Nørgaard introduced a novel radiographic technique aimed at early RA detection. He identified marginal osteoporosis combined with contour defects at the base of the first phalanx of ulnar fingers as common early radiographic findings [13]. The standard posteroanterior (PA) view effectively assesses mineralization and soft tissue changes, while the Nørgaard view - an anteroposterior oblique projection - provides superior visualization of early erosive disease at characteristic sites, including the radial aspect of phalangeal bases, triquetrum, and pisiform bones [14]. Combining both views offers a comprehensive evaluation of hand and wrist pathology [14].

The Nørgaard technique demonstrates particular value in detecting subtle radiologic changes associated with rheumatoid joint pain, often before laboratory tests become positive [13]. Stapczynski later validated this projection's utility for detailed bone assessment, including detection of fifth metacarpal base fractures [15]. Clinical studies confirm the Nørgaard view detects erosive changes in up to 70% of early RA patients even with inconclusive serology [16], with De Smet and colleagues demonstrating its superior sensitivity compared to standard PA views [17]. Importantly, this view facilitates earlier diagnosis and treatment when properly implemented [18]. Nevertheless, it requires technical precision and trained interpretation to maximize diagnostic yield. While conventional radiography remains widely accessible, advanced imaging modalities have transformed early detection capabilities. Musculoskeletal ultrasound (MSUS) and magnetic resonance imaging (MRI) demonstrate superior sensitivity in identifying synovitis, tenosynovitis, and bone marrow edema - pathological changes frequently preceding radiographic erosions [19,20]. These techniques are now incorporated in the 2010 ACR/EULAR classification criteria, reflecting their diagnostic importance [21]. Serological testing provides critical diagnostic information, with rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies serving as cornerstone biomarkers. Anti-CCP antibodies exhibit particularly high specificity for RA (70% positivity) and predict disease severity [22,23]. Combined testing achieves 87.1% sensitivity [23], though 20-30% of RA patients remain seronegative, necessitating imaging confirmation [24].Recent studies highlight the complementary value of diagnostic approaches:

- 23-34% of RF-negative undifferentiated arthritis patients show anti-CCP positivity, all progressing to RA [23,25].
- Swedish BARFOT cohort data reveal anti-CCP positivity in 30-31% of non-erosive patients versus 70% of erosive cases [26].
- Routine hand radiographs — which may not consistently include the Nørgaard view or may be performed at very early disease stages — reveal erosions in only 4.4% of newly diagnosed patients [27]. This highlights the limitations of standard

radiographic protocols in early detection when advanced or targeted techniques are not utilized, and underscores the added value of incorporating high-sensitivity views such as Nørgaard into diagnostic workflows.Visser's research [28] emphasizes the need for stepwise approaches combining clinical, laboratory, and imaging data, while Arbillaga et al. [29] demonstrated the reliability of digital x-ray evaluation (0.887 concordance for erosions). Genetic studies by van der Helm-van Mil and Huizinga [30] further elucidate distinct molecular pathways in RA subtypes.Considering all the preceding evidence, rheumatoid arthritis (RA) has no single definitive test, so diagnosis relies on a multimodal approach. Leading reviews note that classical clinical, serologic (RF, anti-CCP) and imaging findings often appear at different times, so all must be considered together [31]. Laboratory markers – especially anti-cyclic citrullinated peptide (anti-CCP) antibodies and rheumatoid factor (RF) – "help in suggesting and confirming" RA [31]. Likewise, current classification criteria explicitly include imaging evidence: for example, erosions seen on hand/wrist X-rays (e.g. the posteroanterior or ball-catcher/Nørgaard view) confirm "joint involvement" and strongly support an RA diagnosis [31]. In practice, a patient's history and exam are combined with blood tests and hand radiographs (often at least PA and oblique/Nørgaard views) to reach a diagnosis.

Serologic markers:

RF and anti-CCP are highly specific for RA. Anti-CCP in particular has "excellent specificity" (often ≥ 90%) and may appear early in disease [32]. Studies show that using both markers together greatly improves accuracy. For example, one review noted that combining anti-CCP and RF *"increases diagnostic specificity"* for RA [33]. In practice, dual positivity (RF+ and anti-CCP+) gives a very high positive predictive value, whereas one or both negative results may prompt closer imaging follow-up. (Conversely, if both antibodies are negative, clinicians still rely on imaging and clinical criteria to avoid missing seronegative RA).

Radiographic imaging:

Conventional hand/wrist radiographs are the standard for documenting joint erosions and narrowing once RA is established. In early RA these changes may be subtle, but even early findings (periarticular osteoporosis, joint-space bulging from synovitis) can hint at RA [31]. Advanced views like the Nørgaard "ball-catcher" projection can reveal small erosions at the metacarpophalangeal joints that are occult on routine views.Importantly, the 1987 ACR criteria *required* erosions on hand X-ray as one of seven items, and even the 2010 ACR/EULAR criteria count "imaging evidence of synovitis/erosion" as a feature [31]. In other words, a finding of juxta-articular erosions on a hand radiograph in a patient with compatible symptoms virtually clinches the diagnosis, especially if serology is positive.

Combined advantage:

Studies and guidelines emphasize the synergy of tests. For instance, in one early-arthritis cohort the combination of hand-joint erosions plus positive RF/anti-CCP at baseline almost guaranteed progression to RA [33]. In that study, "swollen joint count, morning stiffness, erosions, RF and anti-CCP" together were the strongest predictors of eventual RA; notably, having both RF and anti-CCP (vs. neither) greatly raised the predictive value [33]. Similarly, retrospective analyses show that dual-positive serology (RF+ and anti-CCP+) yields a much higher specificity (fewer false positives) than either marker alone [33]. In clinical practice, a patient with symmetric polyarthritis who has hand-wrist erosions on X-ray and high-titer RF/anti-CCP is treated as RA with high confidence, whereas discordant results (e.g. seronegative but radiographically erosive, or vice versa) prompt close follow-up or alternative diagnoses. In summary, peer-reviewed studies and reviews agree that no single modality suffices: radiographs and serologic tests play complementary roles. Radiography objectively confirms joint damage, and serology provides early immunologic evidence. When used together (as in ACR/EULAR criteria), they substantially improve diagnostic accuracy [31,33]. In practice, rheumatologists routinely order both hand X-rays and RF/anti-CCP tests in patients with suspected RA, because the combination "helps in suggesting and confirming the diagnosis" far better than either approach alone [31,33]. Building on this diagnostic synergy, emerging applications of artificial intelligence (AI) in radiograph interpretation—including the Nørgaard view—show great promise in further enhancing both speed and accuracy. Recent studies have demonstrated that deep learning models can reliably detect early radiographic signs of RA, achieving diagnostic performance that rivals or complements expert

human readers, especially in resource-limited settings [34]. Due to the complexity and challenges in diagnosing rheumatoid arthritis (RA), especially in Libyan clinical settings, this study aims to systematically assess and optimize diagnostic approaches. The investigation will focus on comparing the Nørgaard radiographic technique with serological testing and attempt to develop practical diagnostic algorithms to enhance early intervention outcomes across diverse clinical environments.

This study specifically seeks to:

1. systematically compare Nørgaard radiography with serological testing in Libyan hospitals.
2. evaluate their relative diagnostic performance for early RA detection.
3. contribute to the development of optimized diagnostic protocols by integrating clinical findings with radiographic and serological data."
4. contribute to establishing evidence-based approaches tailored to local resources.

Although anti-CCP testing was not performed in this study, its diagnostic relevance is discussed for comparative and contextual purposes.

MATERIAL AND METHODS:

Study Design: A cross-sectional study was deemed appropriate to fulfill the research objectives, focusing on the diagnostic performance of radiographic and serological methods in the early detection of rheumatoid arthritis.

Study Population: Participants (n = 64) were consecutively recruited from Zawia Medical Center and Abusurra Hospital, both located in Zawia City, Libya.

Diagnostic Tools: Radiographic imaging was performed on all participants using the Norgaard method, which involves a 45° anteroposterior oblique projection of both hands—commonly referred to as the "ball-catcher's view". This technique is specifically intended to detect early radiographic features such as marginal bone erosions, periarticular osteopenia, and deformities in the metacarpophalangeal and proximal interphalangeal joints. Radiographs were interpreted by two experienced radiologists independently, and any discrepancies were resolved by consensus.

In parallel, serological testing was conducted using quantitative measurement of rheumatoid factor (RF), an autoantibody frequently associated with RA. A threshold of > 20 IU/mL was used to determine seropositivity, based on laboratory standards. RF levels were measured using standard hospital laboratory protocols, which typically involve nephelometric or ELISA-based assays.

Sample Size: The study included a total of 64 patients with varying ages and clinical presentations.

Data Collection Period**:** Data collection was conducted over a two-month period, from July 25 to September 30, 2023.

RESULT:

The analysis revealed three distinct diagnostic patterns:

1. Concordant positive cases: 3 patients (4.7%) showed positive findings on both Norgaard radiography and serological testing.
2. Radiography-positive cases: 12 patients (18.8%) were positive exclusively on Norgaard views.
3. Serology-positive cases: 8 patients (12.5%) were positive only in laboratory analysis. The remaining 41 cases (64%) showed no abnormal findings in either modality.

Table 1. Comparative diagnostic yield of Norgaard radiography versus serological testing**.**

Diagnostic Modality	Number of cases	Percentage (%)
Norgaard radiography only	12	18.8
Serological tests only	8	12.5
Both modalities positive	3	4.7
Both modalities negative	41	64

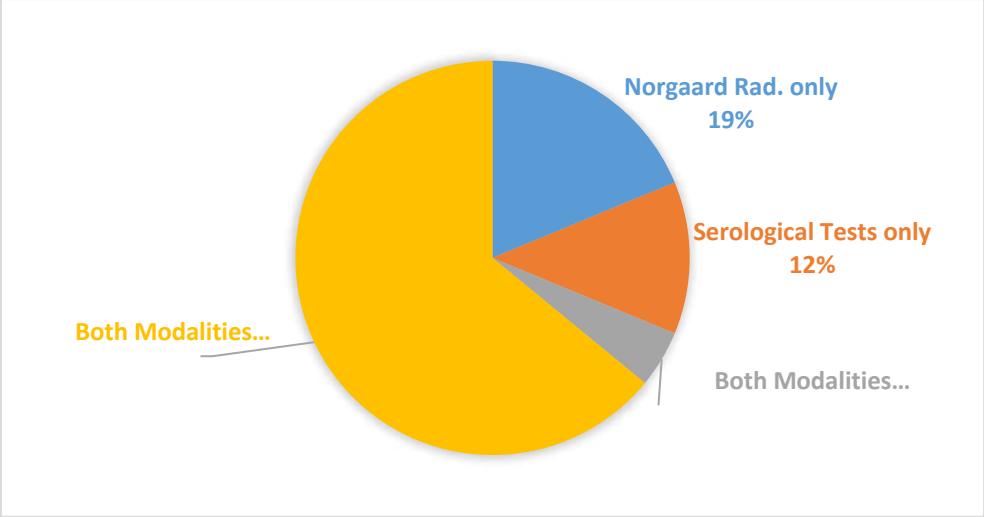

Fig.1. Pie chart representation of diagnostic modality distribution (%).

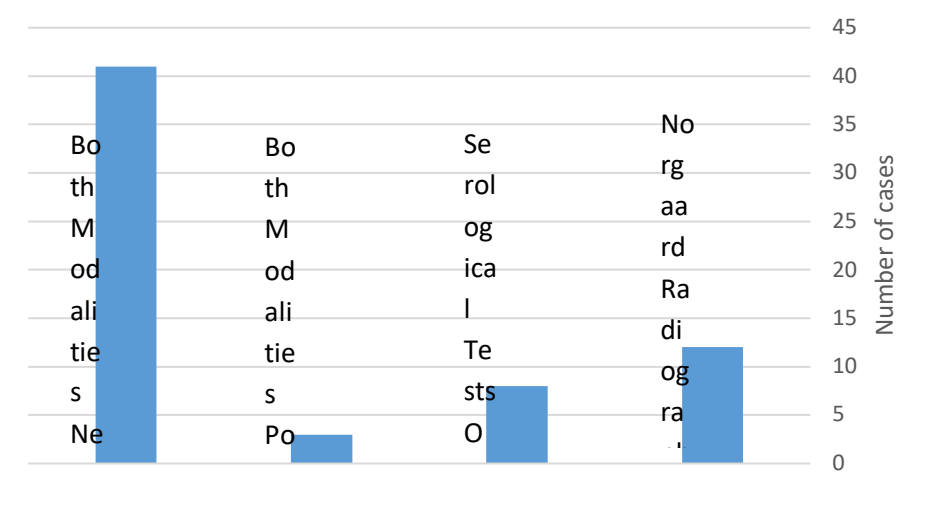

Fig. 2. Bar graph comparing detection rates between modalities.

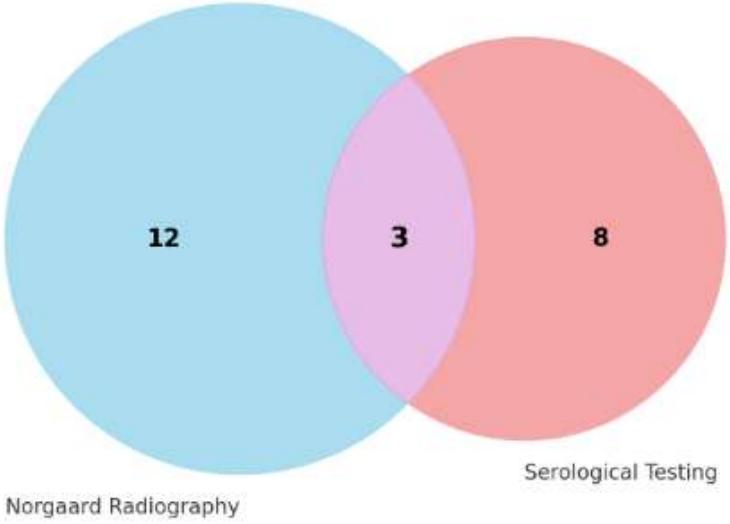

Figure 3. Venn diagram illustrating the distribution of positive cases detected by Nørgaard radiography and serological testing. Overlap indicates patients with concordant positive findings on both modalities.

Integrated Diagnostic Interpretation

The study revealed three primary diagnostic patterns among the 64 patients evaluated using both Nørgaard radiography and serological testing for rheumatoid arthritis. Notably, 3 patients (4.7%) exhibited concordant positive results on both modalities, suggesting a strong diagnostic agreement when both structural and immunological indicators are present. However, 12 patients (18.8%) were identified as positive solely through Nørgaard radiographs, underscoring the radiographic technique's potential to detect early or subtle osseous changes before serological markers become elevated. Conversely, 8 patients (12.5%) were exclusively positive through serological testing, which may reflect early immunological activity in the absence of radiologically visible joint damage. The majority of patients (n = 41, 64%) were negative on both assessments, possibly indicating either absence of disease or preclinical stages below the detection threshold of both modalities. Collectively, Nørgaard radiography yielded positive findings in 15 cases (23.4%), while serological testing identified 11 positive cases (17.2%), suggesting a modestly higher diagnostic yield for the radiographic method within this sample. These findings support the complementary value of combining structural and immunological assessments in early RA detection, particularly in clinical contexts where disease presentation may be atypical or subclinical.

DISCUSSION:

The diagnostic patterns emerging from this study offer significant insight into the early detection profile of rheumatoid arthritis (RA). The predominance of radiography-exclusive positive cases (18.8%) underscores the pivotal role of structural imaging in identifying disease onset, even before seroconversion occurs. These cases likely represent the so-called "erosive window"—a pathophysiological phase in which joint damage, driven by proteolytic activity of synovial fibroblasts, precedes the activation of adaptive immunity. Clinically, this subgroup warrants prompt initiation of disease-modifying antirheumatic drugs (DMARDs) to mitigate the risk of irreversible joint destruction.

These findings align with the seminal work of Nørgaard [13], who emphasized the diagnostic superiority of the oblique bilateral hand radiograph in early RA. The Nørgaard technique has demonstrated the ability to detect microerosions and fine cortical irregularities, particularly at the base of the fifth metacarpal (associated with the little finger), which often elude detection through conventional radiographic views [15]. This reinforces the utility of structural imaging as an early and sensitive diagnostic modality, especially in seronegative cases.In contrast, serological testing alone identified 8 positive cases (12.5%), with a mean biomarker value of 11.36 ± 1.89. Notably, these patients lacked classical clinical manifestations such as joint stiffness or functional impairment. This cohort likely reflects the "pre-erosive phase" of RA, in which autoantibodies such as anti-CCP may promote subclinical synovitis in the absence of radiographic evidence. These patients are prime candidates for early immunomodulatory therapy aimed at halting immunological progression before structural damage becomes evident. Interestingly, the overlap between radiographic and serologic positivity was minimal (4.7%), highlighting the temporal asynchrony between immunological and structural manifestations in early RA. This diagnostic discordance underscores the limitations of relying on a single modality and supports the necessity for a multimodal diagnostic approach—combining high-resolution radiographic imaging with targeted serological panels—to achieve comprehensive disease characterization.

Collectively, the data affirm that radiographic evaluation using the Nørgaard method provides an invaluable window into early joint pathology, complementing but not substituting serological assessment. Integration of both modalities offers a more nuanced and temporally sensitive diagnostic framework, enhancing the likelihood of timely therapeutic intervention and improved long-term outcomes

Table 2. Management Protocol Based on Diagnostic Patterns.

Patient Subgroup	Immediate Action	Monitoring Protocol
Radiography-only positive	Start DMARDs (e.g., methotrexate)	Clinical + radiographic assessment every 6–8 weeks
Serology-only positive	Short-course steroids ± DMARDs	Serological testing every 8 weeks; baseline radiography

Double-negative		Rule out mimics (US/synovial fluid); symptom diaries		Re-evaluate in 3 months or if symptoms worsen

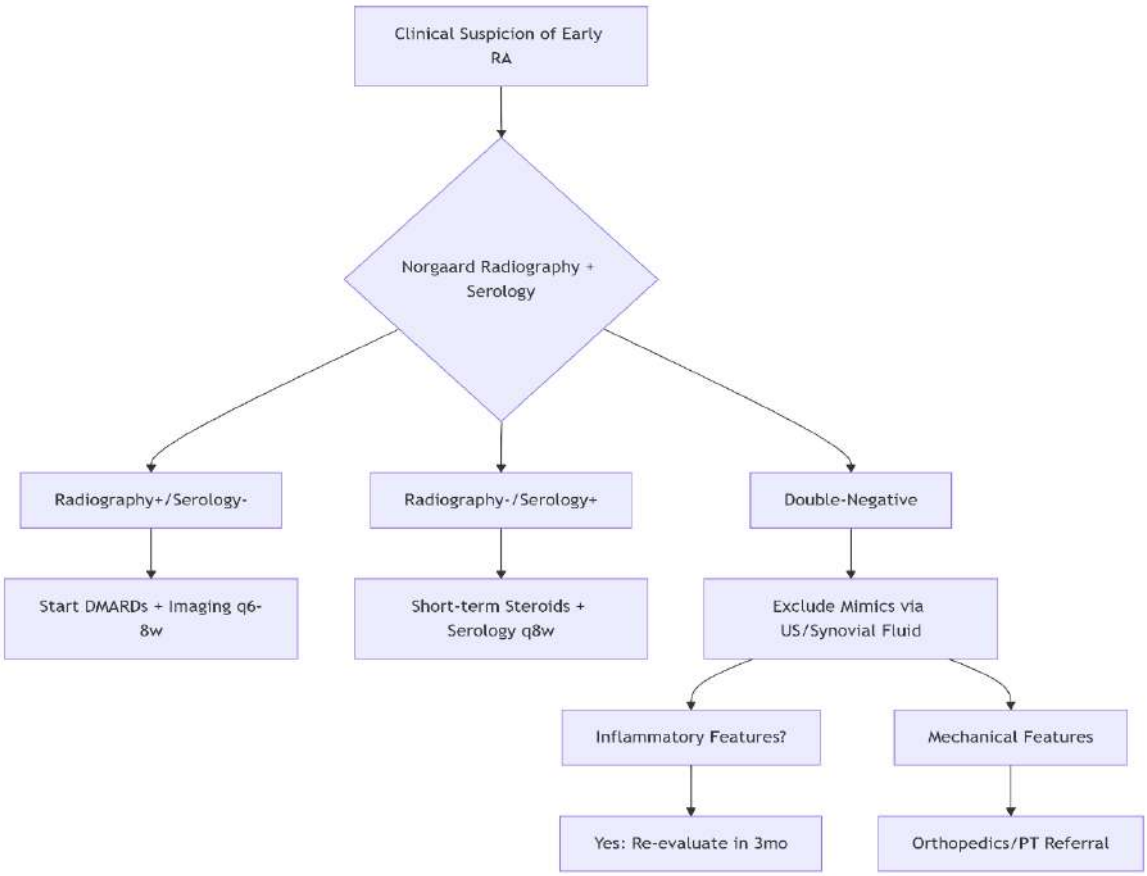

Figure 4. Integrated Diagnostic Protocol.

Key Recommendations

1.Adopt tiered diagnostics:

- First-line Norgaard radiography for seronegative patients.
- Reserve MRI/US for double-negatives with persistent inflammation.

2.Streamline referrals:

- Mechanical symptoms → Orthopedics/Physical Therapy.
- Inflammatory features (symmetric swelling, stiffness) → Rheumatology re-evaluation.

3. Patient empowerment**:** Digital symptom trackers to differentiate inflammatory/mechanical pain.

Table 3. Future Research Imperatives

Initiative	Expected Impact
Larger cohorts (n > 300)	Identify demographic/genetic predictors of "diagnostic delay" patterns.

Longitudinal tracking	Quantify progression rates of radiography-only vs. serology-only subgroups.
AI-assisted image analysis	Automate erosion detection in Norgaard views to reduce operator dependence.
High-sensitivity serological panels	Explore novel antibodies (e.g., anti-CarP) in seronegative radiography-positive cases.

Recommendations for Clinical Practice

1. Adopt Norgaard radiography as a first-line tool in early arthritis clinics, particularly where advanced imaging is unavailable.
2. Tailor monitoring intervals based on initial patterns:
   - Radiography-positive: 6-week clinical/imaging follow-ups.
   - Serology-positive: 8-week serological retesting.
3. Develop rapid-access pathways for double-negative high-risk patients to exclude mimics (e.g., psoriatic arthritis via dermatology referral).

Limitations

This study is subject to several limitations. First, the relatively small sample size (n = 64) may limit the generalizability of the findings and reduce statistical power for subgroup analysis. Second, serological evaluation was limited to rheumatoid factor (RF) without assessment of anti-cyclic citrullinated peptide (anti-CCP) antibodies, which are known to have higher specificity for early RA. Third, the cross-sectional nature of the study precludes longitudinal evaluation of disease progression, treatment response, or conversion from subclinical to overt RA. Future research should incorporate larger, multicenter cohorts, expanded immunological panels, and prospective follow-up to validate and expand upon these findings.

CONCLUSION:

This study validates Nørgaard radiography as a superior structural tool for early RA detection (23.4% yield), whereas serology identifies pre-erosive autoimmune activity. The 64% double-negative cohort should not be viewed as a diagnostic dead-end but rather as an opportunity for precision stratification—differentiating preclinical RA from mimicking conditions through targeted assessment.

Integrating standardized radiographic imaging with symptom-specific follow-up protocols may help bridge current detection gaps. Future research should focus on developing reliable biomarkers to identify "at-risk" subgroups within the double-negative population, thereby turning diagnostic ambiguity into a path for therapeutic intervention.

Furthermore, the application of artificial intelligence—trained on radiographic and serological data—holds great promise for advancing early RA detection. Machine learning models could identify subtle, otherwise imperceptible, patterns to improve patient stratification, detect high-risk seronegative cases, and support timely, personalized treatment decisions.

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