Review

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Application of Musculoskeletal Ultrasonography in the Diagnosis of Rheumatic Immune Diseases

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Rheumatic immune diseases (RIDs) comprise a heterogeneous group of autoimmune disorders with intricate etiologies, diverse clinical presentations, and challenging diagnostic processes, necessitating additional diagnostic modalities. In recent years, musculoskeletal ultrasonography (MSUS) has been increasingly applied for the evaluation of RIDs and has gradually evolved into a routine auxiliary diagnostic technique. This review highlights recent reports on the utilization of MSUS in the diagnosis and management of patients with RIDs, with particular emphasis on rheumatoid arthritis, gouty arthritis, and osteoarthritis. Special attention was given to its clinical value in improving diagnostic accuracy, guiding therapeutic interventions, and predicting disease progression. The overarching aim was to standardize practices and facilitate the broader adoption of MSUS in routine rheumatology care.

Keywords: rheumatic immune diseases; musculoskeletal ultrasonography; diagnosis; imaging; application

Introduction

Rheumatic immune diseases (RIDs) are a group of autoimmune disorders characterized by nonspecific organ inflammation, primarily affecting bones, joints, and soft tissues [1,2]. There are many types of RIDs, including rheumatoid arthritis, gouty arthritis, and osteoarthritis [3–5]. However, due to diverse etiologies and unclear pathogenesis, the diagnosis of RIDs remains challenging. Without timely diagnosis and treatment, patients with RIDs are at high risk of disability or deformity. With the ongoing development of clinical management concepts, early diagnosis and standardized treatment have become central strategies for RIDs, emphasizing early diagnosis, prompt intervention, and structured therapeutic approaches aimed at remission.

Imaging plays a critical role in clinical diagnosis, evaluation of treatment response, and monitoring prognosis in patients with RIDs [6,7]. Traditionally, X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) have served as the primary imaging modalities for RIDs, while ultrasonography was more commonly applied in the examination of internal organs and vascular structures. Advances in medical technology and increasing clinical demands have expanded the use of ultrasonographic imaging technology to the diagnosis and management of various RIDs [8].

Musculoskeletal ultrasonography (MSUS), an imaging technology developed in recent decades, offers several advantages. It avoids radiation exposure associated with X-ray and CT, is less costly than MRI, and provides point-of-care, non-invasive, non-irradiating, and non-contrast imaging capabilities. MSUS has been utilized in rheumatology since the 1970s, allowing visualization of the synovium, joint effusions, tendon sheaths, tendons, and ligaments. It can also detect bone erosions and assess joint spaces and cartilage [9]. MSUS essentially refers to the ultrasonographic examination of components of the musculoskeletal system. However, because not all ultrasonographic transducers offer sufficient resolution for musculoskeletal imaging and not all sonographers or radiologists are trained in these specialized techniques, it is often designated separately (e.g., "MSKUS" or "MSUS"). Ultrasonography functions by transmitting high-frequency sound waves from piezoelectric elements within the transducer, which interact with tissues. Reflected sound by tissues is captured by the transducer and converted into an image, with highly reflective tissues appearing hyperechoic (brighter) and poorly reflective tissues appearing hypoechoic (dark) [10]. A working schematic of MSUS is shown in Fig. 1. Notably, MSUS has been increasingly incorporated into medical education curricula, with a growing number of medical schools adopting it into their curriculum in recent years [11].

Moreover, MSUS provides additional advantages, including simplicity of operation, absence of significant contraindications, real-time dynamic imaging, cost-effectiveness, and high patient acceptance [12]. The application of MSUS to diagnose musculoskeletal diseases

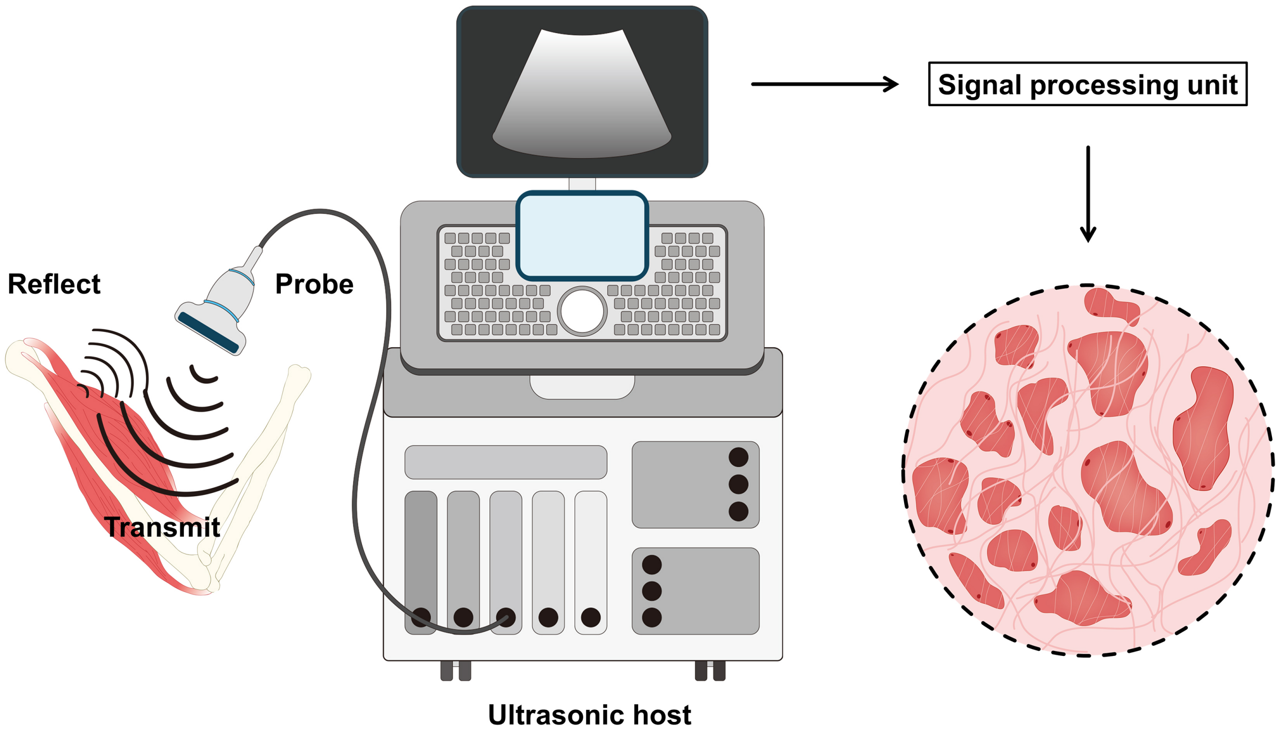

Fig. 1. Schematic diagram of musculoskeletal ultrasonography (MSUS) workflow. The figure was created by Adobe Illustrator v29.0 (Adobe Inc., San Jose, CA, USA).

enables clear visualization of superficial soft tissue structures such as muscles, tendons, ligaments, and peripheral nerves, as well as pathological changes, such as structural abnormalities caused by inflammation, tumors, trauma, or deformities [13]. However, its value in the overall management of rheumatic diseases has not been systematically evaluated. Table 1 outlines the advantages and limitations of commonly used imaging diagnostic methods in RIDs. When combined with the relevant medical history and clinical symptoms, MSUS can accurately diagnose most RIDs. At present, MSUS is widely applied in the diagnosis and management of RIDs. The aim of this review was to summarize the application of MSUS in the diagnosis of RIDs, integrating recent advances across three core domains of these diseases.

Application of MSUS in Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterized by chronic erosive arthritis. In its early stage, synovitis is the primary clinical manifestation, and immune dysregulation plays a central role in the disease progression [14,15]. Epidemiological studies estimate the global prevalence of RA at 0.5%–1% [16]. The most commonly used imaging diagnostic methods in RA include X-ray, MRI, and MSUS [17]. However, conventional X-rays cannot reliably reflect soft tissue injury or articular cartilage damage [14]. MRI, while highly sensitive for detecting synovitis, joint effusion, and early bone erosion [18], is limited by high cost and accessibility constraints. In contrast, MSUS offers a cost-effective, portable, and patient-friendly alternative, making it the preferred imaging method for RA patients. Compared with X-ray, CT, and other imaging methods, ultrasound demonstrates greater sensitivity [19]. Moreover, MSUS outperforms clinical evaluations and laboratory testing in detecting structural abnormalities and diagnosing early RA [20].

At present, MSUS is widely recognized as an important diagnostic modality for RA, particularly for evaluating synovitis and identifying bone erosions [9]. Its clinical significance lies in the early detection of disease activity and monitoring of RA progression. Rheumatoid arthritis, a chronic and progressive inflammatory disorder, typically presents as symmetrical polysynovitis affecting both small and large joints, potentially leading to bone deterioration and systemic inflammatory complications [21]. Patients with RA frequently experience joint pain and swelling, which results in impaired quality of life. In most cases, the musculoskeletal system is the primary site of disease activity, with progressive regional inflammation, cartilage degradation, and bone erosion [21–23]. Therefore, timely and accurate diagnosis of RA is critical to prevent irreversible joint damage and disability.

Recent research has indicated the value of MSUS in detecting bone lesions in RA patients [24]. One investigation reported that MSUS evaluation is notably valuable in RA patients achieving low disease activity (LDA)

Table 1. Comparative advantages and limitations of common imaging modalities in the diagnosis of RIDs.

Diagnostic method	Advantages	Limitations
X-ray	Traditional auxiliary tool; visualizes bone erosion and joint space changes	Radiation exposure; low sensitivity for early soft-tissue lesions (e.g., synovitis)
CT	High-resolution imaging of bone structure; superior to X-ray	High radiation dose; limited capacity for soft tissue evaluation
MRI	No radiation; clearly visualizes synovium, effusion, tendons, ligaments, cartilage, and other soft tissue lesions	High cost; prolonged examination time; limited patient tolerance (e.g., claustrophobia)
MSUS	Non-invasive, radiation-free, cost-effective; provides real-time dynamic imaging; accurately displays synovium, tendons, ligaments, and bone erosion; simple operation with high patient acceptance	Limited visualization of deep joints (e.g., hip joints); highly operator dependent

RIDs, Rheumatic immune diseases; CT, computed tomography; MRI, magnetic resonance imaging; MSUS, Musculoskeletal ultrasonography.

[25]. Ziegler *et al*. [26] investigated the potential impact of pregnancy on disease activity in RA and psoriatic arthritis (PsA), highlighting the exploratory potential of MSUS as an imaging biomarker in the assessment of these conditions during pregnancy. MSUS provides excellent visualization of synovial proliferation, joint cavity effusion, and bone erosion in the nascent phases of RA, thereby reducing misdiagnosis and inappropriate therapy. Wang *et al*. [27] analyzed the diagnostic value of MSUS in early RA affecting finger joints and found that MSUS had a higher detection rate for joint effusion than MRI. Moreover, MSUS holds diagnostic value for synovitis in wrist and hand lesions [28]. Notably, early guidelines from the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) recommend MSUS as an effective imaging tool for the diagnosis of early RA [29]. Therefore, MSUS examination is regarded as a reliable and practical imaging method to diagnose RA, especially in its early stages, where timely intervention is critical.

At present, the immunologic mechanisms underlying the progression of RA have been preliminarily investigated [30]. The concept of immune dysregulation in RA development was originally identified through the detection of anti-immunoglobulin G autoantibodies, known as rheumatoid factors [31]. With growing insights into immune responses, the notion of autoreactivity has become central in this field. RA is characterized by features of impaired innate immunity, such as immune complex-induced complement activation [31]. Despite therapeutic advances, RA remains an incurable disease. In clinical practice, early diagnosis and prompt intervention are critical for optimal patient outcomes. Furthermore, clinicians must regularly assess disease activity to modify treatment regimens, including drug type and dosage, in a timely manner [32,33].

Nair *et al*. [34] reported a strong correlation between MSUS examination findings and physical examination of joint swelling, as well as disease activity scores in RA patients. The disease activity-related parameters frequently evaluated by MSUS include synovial hypertrophy, synovitis, tenosynovitis, bursitis, and joint erosions [35]. Therefore, MSUS provides an effective means of predicting treatment responsiveness in RA and supports individualized therapeutic decision-making.

Although MSUS offers significant advantages in RA diagnosis and disease monitoring, its long-term predictive value for joint destruction requires further prospective validation. Emerging advances in high-frequency probe technology are expected to improve MSUS sensitivity for detecting early-stage micro-bone erosion, enabling ultra-early RA diagnosis. Future research should also emphasize precision-guided interventions using MSUS, such as optimizing the outcomes of ultrasound-guided intra-articular injections. Collectively, these developments will further strengthen the clinical utility of MSUS in the diagnosis and management of RA.

Application of MSUS in Gouty Arthritis

Gouty arthritis (GA) arises from abnormalities in the uric acid metabolic pathway, leading to urate deposition and recurrent gout flares. It is classified as a metabolic rheumatic disease with a global prevalence ranging from 0.68% to 3.9% among adults across diverse populations [36,37]. GA is the most prevalent form of crystal-induced arthropathy, accounting for approximately 5% of all arthritis cases [38]. The central pathogenic mechanism during the development of GA is high serum uric acid, which results in the accumulation of monosodium urate crystals in intra- and extra-articular soft tissues and bone tissues, thereby triggering localized inflammatory responses in these sites [39]. Both genetic predisposition and environmental factors contribute to disease onset [40]. Moreover, recurrent or intermittent flares may progress to chronic GA, leading to irreversible cartilage and bone damage.

At present, the most accurate imaging modalities for diagnosing GA are MSUS and dual-energy CT. Other imaging techniques include X-ray and MRI, though they have notable limitations. In both acute and chronic GA, MSUS imaging can detect tophi and their localized destructive impact on adjacent tissues [38]. With advances in ultrasonographic technology, MSUS offers distinct advantages over conventional imaging methods such as X-ray, CT, and MRI, especially in visualizing bones and soft tissues [41]. This advantage is not only reflected in morphological assessment, but more importantly, it enables a dual assessment of "structure and function". MSUS can not only detect early lesions but also provides high sensitivity, ease of use, low cost, absence of radiation, and suitability for long-term follow-up examinations [42]. Additionally, the limitations of dual-energy CT imaging in GA include radiation exposure and high expense, while X-ray lacks sensitivity for detecting early lesions, and MRI findings are often difficult to distinguish from other forms of arthritis. Therefore, MSUS has emerged as the principal imaging modality in clinical practice for diagnosing GA.

MSUS allows multi-angle joint scanning and effectively identifies lesions in small joints (e.g., metatarsophalangeal joints and finger joints), and its availability in primary healthcare institutions further enhances [42]. In recent years, smaller and higher-frequency probes have been applied in MSUS, providing superior resolution and clearer visualization of cartilage, muscle ligaments, and other tissue structures [42,43]. Xue *et al.* [41] observed that MSUS also has diagnostic value in differentiating GA from RA, with the degree of bone destruction showing a positive correlation with disease duration. Therefore, MSUS can be considered the first-choice imaging technique for assessing the degree of joint involvement in GA. In clinical diagnosis and treatment of GA, MSUS findings serve as an important basis for differential diagnosis with other arthritides, thereby improving diagnostic accuracy and guiding appropriate management.

As an effective tool for diagnosing and assessing the severity of GA, MSUS reveals characteristic ultrasonographic findings (such as double contour sign, tophi, bone erosion, and hyperechoic deposits), which serve as valuable indicators of disease activity [41]. Elevated serum uric acid levels in patients with GA present challenges for disease assessment and management [44]. Traditionally, the disease activity of GA has been monitored through serum uric acid concentrations. However, this approach does not fully reflect pathological changes in joint structures, muscle tissues, or synovial membrane tissues. Notably, MSUS has emerged as a powerful diagnostic tool for GA [41,42]. Distinctive MSUS features have been shown to strongly correlate with the disease activity [45,46]. Therefore, given its diagnostic accuracy and potential to evaluate disease severity, MSUS should be integrated into standard clinical protocols, providing a reliable basis for clinical diagnosis, treatment, and nursing interventions. However, during early or intermittent phases of gout, urate deposition in the joint is minimal, and the double contour sign may not be evident, representing a limitation of MSUS in the diagnosis of GA.

Findings from MSUS examinations also facilitate detailed disease stratification in GA, thus supporting the tailored application of interventions for patients at various disease stages [47,48]. The prompt management of acute GA typically involves nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, corticosteroids, or combinations of these agents. For long-term prevention of recurrent GA, xanthine oxidase inhibitors remain the first-line therapy. Additional therapies aimed at reducing serum uric acid concentration include conventional uricosuric agents and uric acid reabsorption inhibitors. Notably, uric acid control is a cornerstone of GA management to minimize recurrence risk [49]. The guiding principle is to establish individualized therapeutic targets based on serum uric acid levels and the presence or absence of complications.

As a metabolic disorder, the key feature of GA is elevated uric acid levels in the bloodstream. The condition is often overlooked due to its asymptomatic presentation during early stages. However, untreated hyperuricemia may progress to recurrent episodes of acute inflammatory arthritis, tophi formation, and potentially life-threatening complications such as renal damage and cardiovascular disease [50]. Consequently, stringent control and management of uric acid levels are essential to reduce the risk of GA. Current guidelines recommend maintaining serum uric acid levels below 300 μmol/L in patients with GA [51]. Despite these recommendations, many patients remain unaware of the importance of standardized uric acid management, resulting in recurrent flare-ups of GA and a myriad of severe complications.

In recent years, MSUS examination has emerged as a valuable diagnostic tool for detecting urate depositions within joint tissues. Although invisible to the naked eye, these deposits can be visualized using ultrasound technology, thereby allowing clinicians to develop more targeted treatment plans. Collectively, the implementation of standardized uric acid management protocols, together with advanced diagnostic modalities such as MSUS, can significantly improve clinical management of GA.

In the clinical management of GA, the predictive value of MSUS in assessing the risk of acute flare-ups warrants further exploration. With ongoing advances in artificial intelligence-assisted diagnostic technologies, the development of deep learning-based automated classification systems for GA holds promise to significantly reduce operator dependency and improve diagnostic standardization. These research directions are expected to further enhance the clinical value of MSUS in advancing precision medicine for GA.

Table 2. Application of MSUS in the diagnosis of rheumatoid arthritis, gouty arthritis, and osteoarthritis.

Comparison dimension	Rheumatoid arthritis	Gouty arthritis	Osteoarthritis
Diagnostic features	Synovial hypertrophy, synovitis, tenosynovitis, bursitis, and joint damage (erosion)	Double-track sign (urate deposition), bone spurs, bone erosion, hyperechoic deposits (gout tophi)	Cartilage injury, meniscal pathology, ligament damage, joint effusion
Applicable joint range	Small joints of the wrist and hand	Metatarsophalangeal joints and interphalangeal joints	Superficial cartilage
Advantages of early diagnosis	Early identification of synovitis and bone erosion decreases misdiagnosis rates	Detection of urate deposits (even in asymptomatic stages) and evaluation of bone destruction	Early detection of cartilage and soft-tissue lesions, superior to X-ray/CT
Limitations	Other inflammatory arthritides, such as psoriatic arthritis, require differential diagnosis	The early/or intermittent double-track sign may be inconspicuous	Deep joints (e.g., hip joints) poorly visualized; findings heavily on operator expertise
Therapeutic value	Predicts treatment response and guides individualized management	Monitors uric acid deposition and evaluates urate-lowering efficacy	Provides real-time assessment of joint effusion and intra-articular drug delivery outcomes

Application of MSUS in Osteoarthritis

Osteoarthritis (OA), a degenerative joint disorder leading to disability, affects more than half a billion individuals globally [52]. It is a common condition associated with aging, with an estimated prevalence of 10–15% among individuals over 60 years and nearly 500 million people worldwide. In the United States alone, approximately 32.5 million adults are affected, making OA one of the leading causes of disability [53]. Traditionally, OA has been attributed to progressive degeneration of articular cartilage. However, it is now recognized as a chronic, systemic joint disorder driven by biochemical and cellular alterations in synovial joint tissues, ultimately resulting in joint dysfunction [54].

Currently, no definitive cure exists for OA, partially due to a limited understanding of the intricate mechanisms underlying its onset and progression. In clinical practice, MSUS has shown high diagnostic accuracy for OA. Compared with X-ray, CT, and MRI, MSUS demonstrates superior capability in identifying early abnormalities such as cartilage damage, meniscal degeneration, and ligament injury, thereby supporting timely intervention and management [55]. The portability and relatively low cost of MSUS highlight its potential as the “first line of defense” for early OA screening, particularly in primary medical healthcare settings. Recently, MSUS has gained wider recognition and clinical application due to its capacity to detect early lesions, joint effusions, synovitis, bone destruction, bone erosions, and vascular changes [56]. Furthermore, given its non-invasive nature, remarkable sensitivity, and capacity to provide real-time information, MSUS stands out as an effective diagnostic and evaluative tool for OA.

As an advanced form of ultrasound technology, MSUS has emerged as a valuable tool for monitoring osteoarthritis progression and evaluating treatment efficacy [57]. The role of MSUS in assessing disease activity and therapeutic outcomes is multifaceted [58]. Firstly, MSUS enables precise and objective evaluation of treatment response by monitoring synovial fluid and accumulation and joint cavity effusions in osteoarthritis patients. This non-invasive technique provides a reliable alternative to conventional radiography, allowing clinicians to assess clinical outcomes more accurately. Secondly, MSUS permits multi-site examinations, thereby enhancing diagnostic reliability and clinical discrimination. Moreover, MSUS facilitates precise intra-articular drug delivery under real-time visualization, which will not only enhance therapeutic administration but also maximize treatment effectiveness [59].

From the perspective of disciplinary development, the advances in MSUS technology are transforming the diagnostic and therapeutic paradigm of osteoarthritis. Previous studies have applied MSUS to monitor disease activity in patients with rheumatoid arthritis and hand osteoarthritis, as well as to serve as a screening tool in rheumatology programs targeting rheumatoid arthritis and osteoarthritis [57,60]. Furthermore, MSUS has demonstrated utility in assessing functional changes after total knee arthroplasty (TKA). In a study examining muscle thickness (MT) and echo intensity (EI) in patients with knee osteoarthritis (KOA) with or without TKA, reduced skeletal muscle mass was observed in the TKA group [61]. This finding suggests that MSUS may serve as a key tool for postoperative rehabilitation monitoring.

Despite its broad potential, challenges remain in the clinical adoption of MSUS. The application of MSUS in osteoarthritis is limited by several factors that necessitate integration with complementary imaging or clinical methods to improve diagnostic accuracy. First, MSUS has limited capacity to visualize deep joint cartilage (e.g., in the hip and knee joints), restricting its use primarily to superficial cartilage assessment. Second, differentiating OA from RA remains challenging. Finally, the accuracy of ultrasound-guided arthroscopic evaluation is highly dependent on operator expertise. Future developments, including multimodal imaging integration, standardized scanning protocols, and AI-assisted analysis, may significantly improve diagnostic precision and clinical utility.

The application of MSUS in the diagnosis of rheumatoid arthritis, gouty arthritis, and osteoarthritis demonstrates both universal advantages and significant variations depending on disease pathophysiology. To systematically compare the diagnostic value of MSUS across these three conditions, Table 2 summarizes key aspects, including primary diagnostic features, advantages of early diagnosis, applicable joint ranges, and limitations.

Conclusion

In summary, MSUS significantly enhances the accuracy of early diagnosis in RIDs and allows dynamic monitoring of disease progression, thereby providing crucial evidence for personalized therapeutic strategies. However, existing findings remain heterogeneous due to insufficient procedural standardization and inconsistent diagnostic criteria across studies, potentially limiting widespread clinical adoption. Additionally, high technical training requirements, disparities in equipment availability, and ongoing debates on cost-effectiveness present potential barriers.

Future research should prioritize the development of standardized MSUS protocols and validate their long-term clinical value through large-scale multicenter clinical trials. Simultaneously, the integration of AI-assisted interpretation, telemedicine applications, and streamlined training frameworks may help address current implementation challenges. This review offers evidence-based support for the rational application of MSUS in RID diagnosis and management, highlights future research priorities, and lays the foundation for its eventual inclusion into clinical practice guidelines.

Availability of Data and Materials

Not applicable.

Author Contributions

Substantial contributions to conception and design: XYS. Formal analysis and visualization: JL, FL. Drafting the article or critically revising it for important intellectual content: All authors. Final approval of the version to be published: All authors. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved: All authors.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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