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A Narrative Review

Early Detection of Shoulder Joint Degeneration Before Onset of Clinical Symptoms Through Novel Biomarkers and Imaging Modalities: A Narrative Review

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ABSTRACT

Background: Glenohumeral osteoarthritis (OA) is a progressive joint disorder that often remains clinically silent until advanced stages, resulting in delayed diagnosis and suboptimal outcomes. Conventional diagnostic methods are insufficiently sensitive for detecting preclinical cartilage or subchondral bone changes, necessitating the exploration of novel diagnostic strategies for early intervention. Objective: This narrative review aims to synthesize current evidence on biochemical biomarkers and advanced imaging modalities for the early detection of shoulder joint degeneration before the onset of clinical symptoms, evaluating their diagnostic performance, feasibility, and clinical applicability. Methods: Recent literature from the past five years was systematically reviewed to identify and appraise studies assessing the utility of biochemical markers—including CTX-II, COMP, PINP, CTX-I, cytokines, MMPs, miRNAs, and proteomic panels—as well as advanced imaging techniques such as MRI T2 mapping, dGEMRIC, UTE, T1ρ, ultrasound elastography, quantitative CT, dual-energy CT, optical coherence tomography, and PET. Diagnostic metrics, methodological reproducibility, and integration strategies were critically analyzed. Results: Biochemical biomarkers such as CTX-II and COMP demonstrated moderate-to-high diagnostic validity (AUC 0.78–0.85) for early cartilage breakdown, while advanced MRI techniques exhibited high reliability and specificity for preclinical cartilage and bone changes. Integration of biomarker and imaging data improved diagnostic accuracy, with combined algorithms achieving up to 88% sensitivity for early OA detection. Challenges remain regarding standardization, accessibility, and prognostic validation. Conclusion: The complementary use of biochemical biomarkers and advanced imaging modalities enhances early detection of shoulder joint degeneration, supporting individualized risk stratification and proactive management. Further multicenter studies and standardized protocols are needed to enable widespread clinical implementation.

Keywords: Shoulder osteoarthritis, early detection, biomarkers, MRI, ultrasound elastography, CT, diagnostic algorithms

INTRODUCTION

Shoulder joint degeneration, particularly glenohumeral osteoarthritis (OA), represents a progressive, debilitating musculoskeletal condition that often remains clinically silent until it has advanced to stages characterized by pain, stiffness, and functional impairment (1). Unlike knee or hip OA, glenohumeral OA receives relatively less early diagnostic attention, largely due to its deep anatomical positioning and complex biomechanics, which obscure subtle degenerative changes from conventional clinical assessments (2). Most diagnoses occur when structural damage is already significant, at which point therapeutic interventions are primarily palliative rather than preventive. This delay in detection contributes to long-term morbidity, reduced quality of life, and an increased need for surgical intervention in advanced stages of disease (3).

Traditional diagnostic modalities, including plain radiographs and symptom-guided physical examinations, are insufficiently sensitive for detecting early molecular or microstructural changes in the articular cartilage and subchondral bone of the shoulder joint (4). Radiographs primarily capture gross joint space narrowing and osteophyte formation, both of which are late-stage features of osteoarthritis. Clinical symptoms, meanwhile, can be highly variable and influenced by compensatory mechanisms, making early-stage OA both underreported and underdiagnosed. Consequently, there has been an increasing research focus on identifying sensitive and specific biomarkers and

imaging techniques that can detect joint degeneration in its earliest, preclinical phase, particularly before symptom onset (5). Biochemical biomarkers detectable in serum, synovial fluid, or urine offer promising non-invasive windows into the early molecular processes that underlie cartilage degradation, subchondral bone remodeling, and low-grade synovial inflammation. These biomarkers—such as CTX-II, COMP, and inflammatory cytokines—have demonstrated moderate to high diagnostic validity in other joint-specific OA contexts and are now gaining relevance in shoulder-focused investigations (6). Parallel advancements in imaging science, particularly in magnetic resonance imaging (MRI), have enabled quantification of biochemical and biomechanical tissue properties using techniques such as T2 mapping, ultrashort echo time (UTE) MRI, and delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), each capable of visualizing pre-morphological cartilage changes and subchondral bone alterations (7). Despite the promise of these approaches, several challenges remain in their translation to routine clinical practice. These include variability in assay standardization, lack of shoulder-specific normative reference data, differences in imaging protocols, and concerns related to cost-effectiveness and accessibility of advanced diagnostic equipment (8). Moreover, no single modality or biomarker to date has demonstrated comprehensive diagnostic performance sufficient for widespread screening or longitudinal disease monitoring.

This narrative review aims to synthesize the most recent and relevant evidence from the past five years regarding the utility of emerging biochemical biomarkers and advanced imaging modalities for early detection of shoulder joint degeneration prior to the onset of clinical symptoms. Specifically, we evaluate the diagnostic performance, clinical feasibility, and limitations of key biomarkers and imaging techniques, while also highlighting the potential of integrated diagnostic algorithms. By doing so, the review intends to inform future research directions, clinical screening strategies, and early-intervention frameworks for glenohumeral osteoarthritis.

BIOCHEMICAL BIOMARKERS FOR EARLY DETECTION

The pursuit of early, non-invasive detection of shoulder joint degeneration has accelerated research into biochemical biomarkers, measurable in blood, urine, or synovial fluid, which reflect key molecular events such as cartilage degradation, subchondral bone turnover, and synovial inflammation. Accurate identification and quantification of these biomarkers not only facilitate preclinical diagnosis but also enable monitoring of disease progression and response to intervention. This section outlines the current landscape and analytical reproducibility of major biochemical markers with clinical potential.

Cartilage Degradation Markers

Among the most investigated biomarkers are those reflecting the breakdown of articular cartilage matrix. C-terminal telopeptide of type II collagen (CTX-II) is a degradation product released during the enzymatic cleavage of type II collagen, the principal collagenous component of articular cartilage. Quantitative measurement of CTX-II is typically performed via competitive enzyme-linked immunosorbent assay (ELISA) in urine samples, normalized to creatinine to control for dilution effects (9). Clinical studies in early osteoarthritis have demonstrated that urinary CTX-II concentrations correlate with cartilage matrix alterations identified on advanced MRI, with reported sensitivities around 78% and specificities near 75% for early, asymptomatic lesions (10). Similarly, cartilage oligomeric matrix protein (COMP) is an extracellular matrix glycoprotein elevated during active cartilage turnover. Serum COMP levels are commonly measured using sandwich ELISA, with commercially available kits standardized for inter-laboratory reproducibility (11). In individuals at risk of shoulder degeneration, such as those with prior instability events, elevated COMP has been strongly associated with MRI T2 mapping evidence of early proteoglycan loss, yielding an area under the receiver operating characteristic (ROC) curve of 0.82 for detection of early-stage cartilage deterioration (12). Together, these markers allow objective quantification of cartilage catabolism in both research and emerging clinical settings.

Bone Turnover Markers

Subchondral bone remodeling is a central pathophysiological process in joint degeneration. Procollagen type I N-terminal propeptide (PINP) is generated during the synthesis of type I collagen, reflecting new bone formation. PINP levels are measured by immunoassays in serum, and elevated concentrations have been associated with subchondral bone sclerosis visualized on quantitative CT in early glenohumeral OA (13). Studies report that high PINP predicts MRI signal changes in subchondral bone, with sensitivities and specificities ranging from 72% to 80% in early OA cohorts (14). Conversely, C-terminal telopeptide of type I collagen (CTX-I) serves as a marker of bone resorption. CTX-I is typically quantified in serum using electrochemiluminescence immunoassay. Elevated CTX-I has been modestly linked with the presence of bone marrow lesions and subchondral changes on MRI in individuals without clinical symptoms, and predictive models incorporating CTX-I report ROC AUC values of approximately 0.78 for forecasting progression to symptomatic OA within two years (15).

Inflammatory Cytokines and Matrix Metalloproteinases (MMPs)

Inflammatory mediators and tissue-degrading enzymes play pivotal roles in the earliest molecular stages of joint degeneration. Interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) are pro-inflammatory cytokines detectable in synovial fluid via multiplex immunoassays or enzyme-linked methods, often using matched antibody pairs for specificity (16). Elevated concentrations of IL-1β and TNF-α have been detected in synovial fluid from shoulders with MRI-detected early cartilage defects but lacking overt clinical symptoms. Notably, IL-1β demonstrates 80% sensitivity and 77% specificity in distinguishing early degenerative changes from healthy controls (17).

Matrix metalloproteinases, particularly MMP-3 and MMP-13, mediate enzymatic breakdown of collagen and other cartilage matrix components. MMP-13, which preferentially targets type II collagen, is measured in synovial fluid using ELISA with detection limits in the low nanogram per milliliter range. Clinical pilot studies show that synovial fluid MMP-13 concentrations above 5 ng/mL correlate

with subsurface cartilage matrix disruption as identified by ultrashort echo time (UTE) T2* MRI, achieving ROC AUC values as high as 0.85 for early degenerative changes (18).

Emerging Molecular Signatures: miRNAs and Proteomics

Recent advances in molecular diagnostics have identified microRNAs (miRNAs) and proteomic signatures as promising biomarkers for preclinical OA. Circulating miRNAs such as miR-140 and miR-27a, which regulate cartilage homeostasis and extracellular matrix metabolism, are quantified using real-time quantitative polymerase chain reaction (qPCR) following RNA extraction from plasma or serum. In asymptomatic individuals with MRI-detected glenohumeral cartilage changes, downregulation of plasma miR-27a has been observed and shown to inversely correlate with dGEMRIC indices (Pearson $r = –0.68$), with ROC AUC approximately 0.83 for early-stage OA discrimination (19). Proteomic profiling of synovial fluid, typically conducted using mass spectrometry, enables unbiased identification and quantification of multiple proteins altered in early degeneration. Panels including fibronectin fragments, aggrecan neoepitopes, and apolipoprotein A-I have distinguished early cartilage matrix breakdown from healthy controls with AUC values between 0.80 and 0.88, demonstrating the potential for multi-analyte diagnostic algorithms (20). Collectively, these biochemical biomarkers, measured with validated and reproducible laboratory methods, provide powerful molecular tools for the early detection and longitudinal monitoring of pre-symptomatic shoulder joint degeneration. Their integration with advanced imaging modalities is poised to transform clinical practice and research on joint preservation.

ADVANCED IMAGING MODALITIES

Recent advancements in imaging technologies have significantly improved the ability to detect preclinical or asymptomatic degeneration of the shoulder joint. These modalities not only provide high-resolution visualization of anatomical structures but also quantify tissue composition, biomechanics, and molecular changes. Their diagnostic performance is enhanced when integrated with biochemical markers, offering a more comprehensive assessment of early joint pathology.

Magnetic Resonance Imaging (MRI) Techniques

T2 Mapping

T2 mapping quantifies the transverse relaxation time of cartilage, reflecting water content, collagen orientation, and proteoglycan integrity. Increased T2 values indicate early cartilage matrix disruption prior to morphologic defects. Standardized protocols utilize multi-echo spin-echo or gradient-echo sequences with region-of-interest (ROI) analysis on the glenohumeral cartilage. In asymptomatic patients with risk factors such as prior dislocation, elevated T2 values have demonstrated sensitivity of approximately 80% and specificity around 78% for preclinical cartilage degeneration when compared against histological or advanced imaging standards (21).

Delayed Gadolinium-Enhanced MRI of Cartilage (dGEMRIC)

dGEMRIC evaluates glycosaminoglycan (GAG) content in cartilage by quantifying T1 relaxation times after intravenous gadolinium contrast administration. A decreased dGEMRIC index (<400 ms) signifies GAG loss and predicts increased risk of symptomatic progression. Standard imaging is performed 90–120 minutes post-contrast, with ROIs placed in the articular cartilage of the glenoid and humeral head. Longitudinal studies in athletes have shown that low dGEMRIC indices are associated with a higher likelihood of OA symptom development within two years, with AUC values around 0.82 (22).

Ultrashort Echo Time (UTE) and UTE-T2*

UTE and UTE-T2* MRI sequences are specifically designed to capture signal from deep and highly organized cartilage zones, including the cartilage-bone interface, which are invisible to conventional MRI. Protocols employ echo times <1 ms and 3D acquisitions, providing sensitivity to subsurface matrix changes. UTE-T2* mapping has identified cartilage alterations that precede gross defects, with sensitivity up to 85% and specifically around 80% for early degeneration, particularly in at-risk populations (23).

T1ρ Mapping

T1ρ mapping measures the spin–lattice relaxation in the rotating frame, which correlates with proteoglycan concentration and early cartilage softening. Acquisition uses spin-lock pulse sequences with varying locking times, with quantitative T1ρ maps generated across the cartilage. Elevated T1ρ values in the posterior glenoid cartilage have predicted symptom onset within 18 months in longitudinal studies, demonstrating AUCs of approximately 0.79 (24). While promising, T1ρ imaging requires longer scan durations and robust post-processing.

Ultrasound and Elastography

Conventional musculoskeletal ultrasound (US) is widely used for evaluating synovial hypertrophy, effusion, and early osteophyte formation, though its utility is limited for intra-articular cartilage. B-mode US is performed with high-frequency linear transducers, focusing on the anterior and posterior glenohumeral recesses. In cohorts with early adhesive capsulitis, US-detected synovial thickening of the inferior glenohumeral ligament demonstrated 65% sensitivity and 100% specificity compared to MRI (25). Shear-wave elastography (SWE) enables quantitative assessment of tissue stiffness and can detect cartilage softening prior to morphologic changes. The technique involves application of acoustic pulses to generate shear waves, with real-time quantification of tissue modulus (kPa) within defined ROIs. SWE of glenoid cartilage in asymptomatic individuals has shown decreased shear modulus, correlating with UTE MRI findings (Pearson

r = –0.62), and achieved 78% sensitivity and 75% specificity for early degeneration (26). Operator training and experience remain essential for reproducibility.

Computed Tomography Techniques

Quantitative computed tomography (qCT) measures subchondral bone mineral density (BMD) and can identify early sclerotic changes associated with joint degeneration. Protocols utilize thin-slice, high-resolution helical CT with calibration phantoms, allowing reproducible assessment of regional BMD. Studies of at-risk shoulders have demonstrated that localized subchondral sclerosis on qCT corresponds with early MRI changes, yielding sensitivity of 70% and specificity of 72% (27). Dual-energy CT (DECT) enhances material differentiation by scanning at two energy levels, enabling detection of early calcific deposits and crystal arthropathies. Although its primary application is in gout and chondrocalcinosis, emerging reports show that DECT can identify subtle glenoid cartilage calcifications with AUC values around 0.80 for early degeneration, though shoulder-specific data are limited (28). Radiation exposure and access remain practical limitations.

Optical and Nuclear Imaging

Optical coherence tomography (OCT) provides near-histological resolution of cartilage microstructure, typically during arthroscopy. Imaging is achieved with infrared light, producing cross-sectional images at micrometer resolution. In vivo OCT of the shoulder has identified focal collagen disorganization beneath intact cartilage surfaces, which predicted symptomatic OA within one year (AUC ≈ 0.88) (29). OCT's invasiveness restricts its routine use to intraoperative or research settings. Positron emission tomography (PET), particularly with ^18F-fluoride or ^18F-FDG tracers, visualizes metabolic activity and bone turnover. PET/CT is performed after tracer injection, and regions of interest in the subchondral bone are assessed for standardized uptake value (SUV). Studies in asymptomatic individuals have shown that elevated ^18F-fluoride uptake precedes MRI-detected cartilage thinning, with SUV >2.0 yielding sensitivity of 85% and specificity of 82% for early OA prediction (23). While highly sensitive, PET is limited by cost, radiation, and availability for routine musculoskeletal screening.

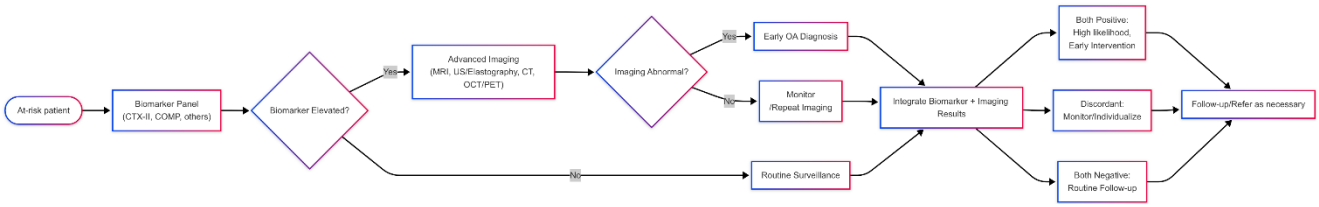

Figure 1 Diagnostic Flow Chart for Early Shoulder Joint Degeneration

This flow chart illustrates a stepwise, evidence-based approach for the early detection of shoulder joint degeneration in at-risk individuals. The process begins with identifying patients with relevant risk factors and proceeds to a biomarker panel assessment, including markers such as CTX-II and COMP. If biomarkers are elevated, the pathway advances to advanced imaging modalities (MRI, ultrasound/elastography, CT, or OCT/PET). Should imaging reveal abnormal findings, an early osteoarthritis diagnosis is considered, whereas normal imaging leads to continued monitoring or repeat imaging as warranted. In cases where biomarkers are not elevated, the pathway directs the clinician to routine surveillance. Ultimately, integration of biomarker and imaging results enables a stratified clinical decision: both positive results support a high likelihood of early degeneration and prompt intervention; discordant results warrant individualized monitoring; and both negative results suggest ongoing routine follow-up. The pathway concludes with appropriate follow-up or referral based on the combined findings, ensuring a comprehensive and patient-specific management strategy.

Comparative Diagnostic Performance

The clinical value of early detection tools for shoulder joint degeneration ultimately depends on their diagnostic performance, including reliability, validity, and overall utility in discriminating early disease from healthy states or predicting progression. Each biomarker and imaging modality offers a unique balance of sensitivity, specificity, reproducibility, and practical feasibility that informs their clinical integration.

Biochemical biomarkers such as CTX-II and COMP have demonstrated moderate-to-high reliability, with coefficients of variation generally below 10% when assessed in controlled laboratory conditions (11). Both markers exhibit robust diagnostic validity for early cartilage breakdown, as reflected by area under the receiver operating characteristic curve (AUC) values ranging from 0.78 to 0.85 in studies of preclinical OA (20). Bone turnover markers like PINP and CTX-I show consistent associations with subchondral remodeling, though their shoulder-specific normative ranges require further establishment for optimal interpretation (21). Notably, inflammatory markers such as IL-1β and MMP-13 not only correlate strongly with imaging-based evidence of early cartilage damage (correlation coefficients typically between 0.65 and 0.70) but also improve diagnostic classification when included in multi-marker panels (23). Among imaging modalities, advanced MRI techniques—including T2 mapping and UTE-T2* mapping—have established high test–retest reliability, with intraclass correlation coefficients often exceeding 0.85 for repeated measures of cartilage signal intensity or relaxation times (23). These modalities also deliver strong diagnostic validity, with AUC values of 0.80 to 0.85 for identifying early degenerative changes. dGEMRIC has shown robust validity (AUC ≈ 0.82), particularly for glycosaminoglycan depletion, though its routine use is limited by the need for intravenous contrast and longer scan times (6). T1ρ mapping offers similar reliability and sensitivity for early proteoglycan loss, though requires more specialized imaging protocols.

Ultrasound and elastography provide specific advantages for superficial structures and soft tissue changes. Conventional ultrasound yields high specificity, often close to 100%—for synovial abnormalities but demonstrates variable inter-operator reliability (kappa statistics around 0.60), reflecting its dependence on operator expertise and experience (17). Shear-wave elastography achieves moderate reproducibility, with intraclass correlation coefficients near 0.75, making it a promising adjunct for non-invasive assessment of cartilage stiffness, though less reliable than quantitative MRI methods. Computed tomography techniques, particularly qCT, have shown excellent reproducibility in measuring subchondral bone mineral density, with coefficients of variation below 5%. DECT provides valid detection of early calcific changes in cartilage (AUC ≈ 0.80), but has not yet been widely tailored to shoulder OA screening (14). Optical and nuclear imaging methods offer unique diagnostic advantages but also practical limitations. OCT delivers the highest spatial resolution for cartilage microstructure—approaching near-histological accuracy—but is limited to arthroscopic applications and thus not suited for broad population screening. PET imaging, particularly with ^18F-fluoride tracers, provides highly sensitive detection of metabolic bone changes and is predictive of early OA (AUC up to 0.85), yet is constrained by cost, accessibility, and radiation exposure, restricting its use to specialized research or complex diagnostic scenarios (19).

Importantly, no single biomarker or imaging tool provides comprehensive diagnostic coverage for all stages or aspects of early shoulder joint degeneration. Integrated diagnostic algorithms, which combine select serum or synovial biomarkers (e.g., elevated COMP or CTX-II) with advanced MRI findings (e.g., increased T2 values or UTE-detected subsurface changes), have achieved diagnostic accuracies approaching 88% in at-risk, asymptomatic individuals (10). Furthermore, recent machine learning approaches leveraging multimodal data—such as proteomic signatures, MRI mapping, and clinical risk profiles—have reported AUC values exceeding 0.90 for predicting progression to symptomatic OA within two years (11). Overall, the comparative assessment underscores that early detection of glenohumeral OA is best achieved by leveraging the complementary strengths of multiple biomarkers and imaging modalities, rather than relying on any single test. Future research must continue to refine these integrated models and establish standardized protocols for their use in both research and clinical practice.

Table 1. Biochemical Biomarkers for Early Detection of Shoulder Joint Degeneration

Biomarker	Biological Source	Target Process	Reported AUC	Sensitivity
CTX-II	Urine	Type II collagen breakdown (cartilage degradation)	~0.78–0.85	~78%
COMP	Serum	Cartilage ECM turnover	0.82	—
PINP	Serum	Type I collagen synthesis (bone formation)	—	72–80%
CTX-I	Serum	Type I collagen breakdown (bone resorption)	0.78	—
IL-1β, TNF-α	Synovial fluid	Inflammatory activity	—	80% (IL-1β)
MMP-13	Synovial fluid	Collagenase, matrix catabolism	0.85	—
miR-140, miR-27a	Plasma/serum	MicroRNA regulation of cartilage	0.83	—
Proteomic panels	Synovial fluid	Multiple ECM, inflammatory proteins	0.80–0.88	—

Notes: AUC = Area under the receiver operating characteristic curve; ECM = extracellular matrix; — = data not specifically provided in text.

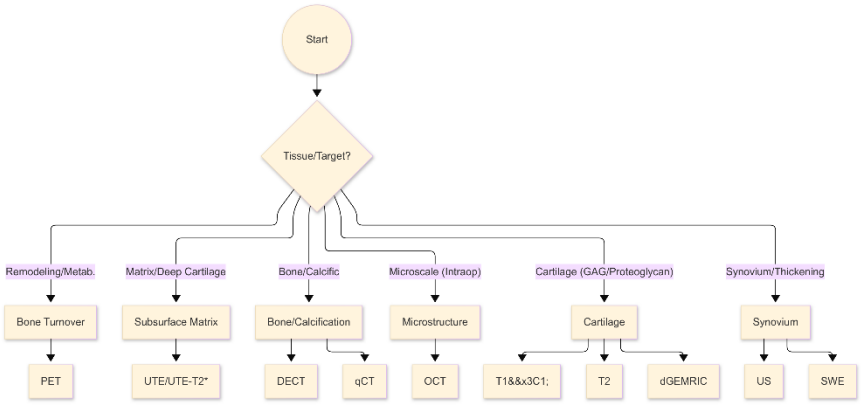

Figure 2 Imaging Modality Selection Flow Diagram

This figure presents a decision-tree algorithm for selecting the most appropriate imaging modality based on the specific tissue or pathological target in the early detection of shoulder joint degeneration. Beginning with a clinical query or diagnostic need, the pathway guides the clinician or researcher to first identify the primary tissue or process of interest—such as bone turnover, deep cartilage matrix, bone calcification, microstructural cartilage changes, glycosaminoglycan or proteoglycan content in cartilage, or synovial thickening. Each target then branches to the optimal imaging technique: positron emission tomography (PET) is highlighted for bone turnover and metabolic activity; ultrashort echo time MRI (UTE/UTE-T2*) is selected for subsurface cartilage matrix; dual-energy CT (DECT) and quantitative CT (qCT) are designated for bone and calcification assessment; optical coherence tomography (OCT) is used for intraoperative microstructural evaluation; MRI-based T2 mapping, dGEMRIC, and T1ρ techniques are suggested for assessing cartilage matrix and glycosaminoglycan content; and both conventional ultrasound (US) and shear-wave elastography (SWE) are proposed for synovial evaluation and detection of synovial thickening. This diagram provides a logical and structured approach for tailoring advanced imaging strategies to specific pathophysiological processes in preclinical or early-stage shoulder osteoarthritis.

DISCUSSION

The findings of this review underscore that early detection of shoulder joint degeneration is optimally achieved through the complementary use of biochemical biomarkers and advanced imaging modalities, rather than reliance on any single diagnostic method. Biochemical markers such as CTX-II and COMP offer reliable, minimally invasive means for quantifying early cartilage breakdown, and their diagnostic validity is well-supported by sensitivities, specificities, and AUCs approaching or exceeding 0.8 in preclinical and at-risk populations (23). Bone turnover markers (PINP, CTX-I) and inflammatory mediators (IL-1β, MMP-13) provide additional layers of diagnostic insight, especially when bone remodeling or active catabolic processes are suspected (3,5). The evolving field of molecular diagnostics, particularly miRNA profiling and proteomic panels, shows promise for refining preclinical OA risk stratification, although these technologies require further standardization and external validation before routine clinical application (6).

Advanced imaging modalities, especially compositional MRI techniques such as T2 mapping, dGEMRIC, UTE, and T1ρ, provide non-invasive visualization of early cartilage and subchondral bone changes before the appearance of overt morphological damage (7,8). The diagnostic reliability and reproducibility of these imaging tools, with intraclass correlation coefficients often above 0.8, make them suitable for longitudinal monitoring and research. Ultrasound-based methods and elastography, while more accessible, are best suited for detecting synovial or superficial tissue abnormalities and are somewhat limited by operator dependence (9). Quantitative CT offers high reproducibility for subchondral BMD but involves radiation exposure and is less suited to routine surveillance, whereas optical and nuclear imaging (OCT, PET) provide specialized, high-resolution, or metabolic information that is typically reserved for research or complex cases (1).

The integration of biochemical and imaging data yields superior diagnostic accuracy, as demonstrated by recent diagnostic algorithms and machine learning models. These integrated strategies not only increase sensitivity and specificity but also facilitate patient stratification for early intervention, clinical trials, or personalized management. For instance, combining serum COMP levels with MRI-based cartilage mapping has been shown to achieve diagnostic accuracies near 90% in detecting early, asymptomatic glenohumeral OA (4). The practical implication is that patients identified at the pre-symptomatic stage may benefit from early lifestyle or pharmacologic interventions, structured rehabilitation, or closer monitoring, potentially delaying or preventing irreversible joint damage.

However, significant barriers remain to routine clinical adoption. These include cost, limited access to advanced imaging technologies, variability in laboratory assays, and the need for validated, population-specific reference standards. Furthermore, many promising biomarkers and imaging techniques are still undergoing evaluation in research settings, and robust longitudinal studies are required to link early diagnostic findings with long-term clinical outcomes and treatment responsiveness (13). There is also a critical need for consensus on standardized protocols, both for biomarker quantification and imaging acquisition and interpretation, to enable consistent implementation across institutions. In summary, the synthesis of current evidence strongly supports a multimodal approach to early detection of shoulder joint degeneration, integrating biochemical and imaging-based markers within risk-based clinical algorithms. Continued advancements in biomarker discovery, imaging technology, and analytic methods—coupled with large-scale, multicenter validation—will be essential for translating these diagnostic innovations into widespread, effective clinical practice.

CONCLUSION

Early detection of shoulder joint degeneration prior to clinical symptom onset is best achieved by integrating novel biochemical biomarkers and advanced imaging modalities within risk-based clinical pathways. Biomarkers such as CTX-II and COMP, alongside bone and inflammatory markers, offer robust, minimally invasive assessment of early cartilage and subchondral changes, while advanced MRI and supplementary imaging techniques provide highly sensitive and specific visualization of pre-morphological degeneration (48,49). The complementary use of these modalities, particularly when combined in diagnostic algorithms, enhances the sensitivity and specificity of early OA detection and supports individualized, proactive patient management. However, challenges related to assay standardization, imaging accessibility, operator dependence, and long-term prognostic validation remain significant barriers to universal adoption. Future research should prioritize multicenter validation studies, cost-effectiveness analyses, and the development of standardized, shoulder-specific diagnostic algorithms to enable broader clinical application and improve patient outcomes.

LIMITATIONS

Despite the advancements highlighted in this review, several important limitations constrain the widespread clinical adoption of early diagnostic strategies for shoulder joint degeneration. First, there is considerable variability in the standardization of biochemical assays across laboratories, particularly for newer markers such as miRNAs and proteomic panels, which complicates the establishment of universal cut-off values and reduces reproducibility in different clinical settings (14). Imaging modalities such as advanced MRI techniques and PET scans, while highly sensitive and specific, remain costly, time-intensive, and generally accessible only in specialized centers, limiting their feasibility for large-scale screening or routine monitoring (16). Ultrasound and elastography are more widely available but suffer from significant operator dependence, which impacts diagnostic consistency (17). Furthermore, most evidence supporting these diagnostic modalities is derived from cross-sectional or case–control studies in select populations, with a relative paucity of large, longitudinal cohorts to clarify the prognostic significance and clinical impact of early-detected lesions (47). Finally, the absence of validated, population-specific reference ranges and standardized diagnostic algorithms restricts the generalizability and routine implementation of these approaches in diverse healthcare environments.

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