Relationship Between Quantitative MRI Biomarkers and Patient-Reported Outcome Measures After Cartilage Repair Surgery

A Systematic Review

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Background: Treatment of articular cartilage injuries remains a clinical challenge, and the optimal tools to monitor and predict clinical outcomes are unclear. Quantitative magnetic resonance imaging (qMRI) allows for a noninvasive biochemical evaluation of cartilage and may offer advantages in monitoring outcomes after cartilage repair surgery.

Hypothesis: qMRI sequences will correlate with early pain and functional measures.

Study Design: Systematic review; Level of evidence, 3.

Methods: A PubMed search was performed with the following search terms: knee AND (cartilage repair OR cartilage restoration OR cartilage surgery) AND (delayed gadolinium-enhanced MRI OR t1-rho OR T2 mapping OR dgemric OR sodium imaging OR quantitative imaging). Studies were included if correlation data were included on quantitative imaging results and patient outcome scores.

Results: Fourteen articles were included in the analysis. Eight studies showed a significant relationship between quantitative cartilage imaging and patient outcome scores, while 6 showed no relationship. T2 mapping was examined in 11 studies, delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) in 4 studies, sodium imaging in 2 studies, glycosaminoglycan chemical exchange saturation transfer (gagCEST) in 1 study, and diffusion-weighted imaging in 1 study. Five studies on T2 mapping showed a correlation between T2 relaxation times and clinical outcome scores. Two dGEMRIC studies found a correlation between T1 relaxation times and clinical outcome scores.

Conclusion: Multiple studies on T2 mapping, dGEMRIC, and diffusion-weighted imaging showed significant correlations with patient-reported outcome measures after cartilage repair surgery, although other studies showed no significant relationship. qMRI sequences may offer a noninvasive method to monitor cartilage repair tissue in a clinically meaningful way, but further refinements in imaging protocols and clinical interpretation are necessary to improve utility.

Keywords: quantitative magnetic resonance imaging; cartilage repair surgery; T2 mapping; dGEMRIC

Articular cartilage injuries present a challenging clinical scenario because they can often occur in young patients, and the avascular nature of articular cartilage inhibits spontaneous healing. As a result, surgical management is often required for symptomatic defects. Cartilage procedures are relatively common, with an annual incidence of 90 surgeries per 10,000 patients, and the number of procedures performed is increasing at an average rate of 5% annually.[18] Numerous operative options exist, including marrow stimulation techniques, osteochondral allograft transplant (OCA), osteochondral autograft transfer (OAT), and cell-based techniques such as autologous chondrocyte implantation (ACI), and the field is rapidly evolving.[9] While many of the emerging techniques represent a refinement of already existing treatment options, some novel technologies—such as biologics—are quickly being explored by the field, despite resistance from regulatory barriers.[8] Ultimately, the goals of new treatments are to improve clinical outcomes for patients. In assessing the efficacy of these emerging techniques, it is helpful to establish a reliable method to evaluate the probability of clinical success early in the postoperative period. Magnetic resonance imaging (MRI) has emerged as a promising option for noninvasive assessment

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of the quality of regenerated cartilage and is beginning to garner increased interest.[11]

Qualitative MRI (qMRI) sequences, such as delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), T2 mapping, diffusion imaging, sodium imaging, glycosaminoglycan chemical exchange saturation transfer (gagCEST), and T1-ρ give providers the ability to draw conclusions about the biochemical composition and molecular structure of cartilage through its mechanical properties and appearance on imaging. Through imaging studies on human osteoarthritic cartilage specimens, strong correlations have been established between quantitative imaging parameters and cartilage histologic characteristics.[16] Other investigations have supported these associations and have demonstrated a strong relationship between qMRI and proteoglycan content in cartilage.[13] Ascertaining the early biomechanical properties of regenerated cartilage may enable surgeons to identify patients who are at risk for later deterioration in clinical outcomes and may provide an important method for objective reporting of outcomes after cartilage restoration surgery.

Two previous systematic reviews[1,5] identified weak associations between qMRI classification schemes and patient-reported outcomes (PROs) following cartilage repair surgery, but the state of the literature on qMRI and clinical outcomes has not been independently investigated. Compared with qualitative imaging evaluations, quantitative imaging provides a more objective evaluation of tissue and gives insight into the biomechanical properties of regenerated cartilage. The purpose of this study was to investigate the relationships between PRO measures and qMRI results. Our hypothesis was that qMRI sequences will correlate with early pain and functional measures.

METHODS

Search Criteria

A search was conducted of available research studies on the PubMed database until June 12, 2017. To identify articles reporting on the correlation between clinical outcomes and quantitative imaging findings after cartilage surgery, the following search terms were used: knee AND (cartilage repair OR cartilage restoration OR cartilage surgery OR microfracture OR autologous chondrocyte implantation OR matrix-associated chondrocyte implantation OR osteochondral allograft OR osteochondral autograft) AND (delayed gadolinium-enhanced MRI OR t1-rho OR T2 mapping OR dgemric OR sodium imaging OR quantitative imaging). All identified articles were screened initially by title and then abstract by a trained research assistant. Inclusion criteria were articles on patients undergoing cartilage repair surgery of the knee (microfracture, OCA, OAT, or cell-based cartilage therapies), follow-up with PRO metrics, and MRI follow-up. Exclusion criteria included case reports, review articles (including systematic reviews or meta-analyses), biomechanical studies, nonhuman studies, and scientific meeting abstracts or proceedings. The articles that remained after screening by title and abstract were independently reviewed by an orthopaedic sports medicine fellow and a trained research assistant for final inclusion.

Data Extraction

Data were extracted independently by both an orthopaedic sports medicine fellow and a trained research assistant for analysis. Data extracted from each full-text article included the number of total participants, sex of participants, average age (with standard deviation when available), imaging sequences used (dGEMRIC, T2 mapping, 3-dimensional double-echo steady-state, and/or fast low angle shot), scan parameters (scanner used, scanner field strength, and voxel size), type of surgical technique performed (microfracture, ACI, and/or matrix-associated ACI procedures), disease location (patellofemoral, condylar, or both), mean defect size, PRO scores (visual analog scale for pain, Lysholm score, Knee injury and Osteoarthritis Outcome Score [KOOS] subscales, and/or International Knee Documentation Committee [IKDC] score), reported correlations between PRO and MRI findings, and follow-up time points.

RESULTS

A total of 367 articles were initially identified (Figure 1); 284 articles were excluded based on screening by title. A further 51 articles were removed for lack of relevance after reviewing by abstract. A total of 32 full-text articles were reviewed. Five articles were excluded due to lack of reporting of PRO data; 10 articles were excluded because they did not report correlations between PRO data and imaging data; 2 articles were excluded because they did not entail surgical treatment; and 1 article was excluded because it reported only on outcomes after high tibial osteotomy—there was no direct surgical intervention on the knee articular cartilage. Ultimately, 14 articles were included for analysis.

Eight studies[3,6,15,22,23,26,30,33] found a statistical relationship between postoperative quantitative cartilage imaging values and PRO measures following cartilage repair and restoration, while 6 studies[2,7,12,20,25,29] found no statistical

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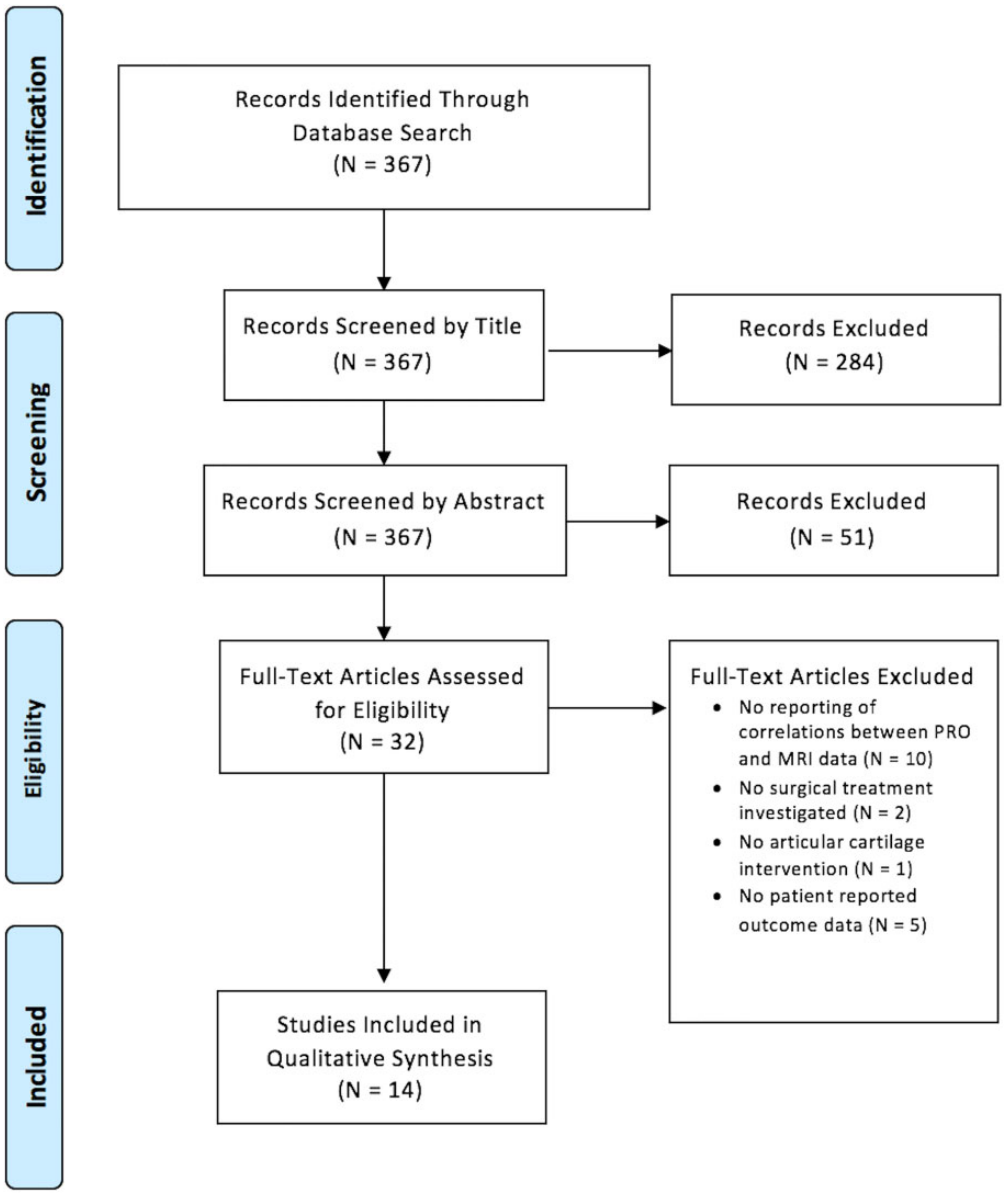

Figure 1. Flowchart demonstrating the systematic review process. MRI, magnetic resonance imaging.

relationships between these parameters. The mean level of evidence (LoE) was not different between studies reporting a statistical relationship (LoE = 3.3 ± 0.9) and those that reported no statistical relationship (LoE = 3.0 ± 1.3; $P = .67$). The studies included a mean of 25.9 patients (range, 8-80 patients; total 344 patients) with 60.3% male patients and a mean age of 34.6 years (range of means from 29.7 to 49 years). Matrix-associated ACI was the most common cartilage restoration procedure and was performed in 6 of the studies,[2,7,20,23,30,33] followed by ACI in 3 studies,[22,26,29] microfracture in 4 studies,[6,25,30,33] OAT in 3 studies,[12,15,23] and OCA in 1 study.[3] The Lysholm score was reported in 8 studies,[2,6,12,15,22,23,26,30] followed by IKDC subjective score in 6 studies,[3,6,7,15,20,33] KOOS in 2 studies,[3,29] a visual or numeric analog score in 3 studies,[15,20,22] Western Ontario and McMaster Universities Osteoarthritis Index in 1 study,[25] and Cincinnati knee score in 1 study.[33]

A number of qMRI techniques can be used to characterize the biomechanical properties of cartilage. These include T2 mapping, dGEMRIC, sodium MRI, and gagCEST. T2 mapping measures the variations in matrix content (water, proteoglycan, and collagen), which can be harbingers of early cartilage degeneration.[16] Another imaging type, dGEMRIC, allows quantification of glycosaminoglycan concentration within cartilage through the injection and imaging of gadolinium.[27] Sodium MRI can demonstrate changes in proteoglycan content of cartilage tissue on MRI, which can reveal proteoglycan degradation.[32] Finally, gagCEST allows for endogenous imaging of glycosaminoglycan content in cartilage without the use of contrast injection.[14]

TABLE 1
Relationship Between T2 Mapping Values and Clinical Outcomes[a]

Lead Author (Year)	Level of Evidence	No. of Patients	Cartilage Repair Evaluated	Time Point	Scanner Field Strength	Findings
Brown[3] (2014)	2	9	Osteochondral allograft	1 and 2 y	3.0 T	Superficial T2 values at 2 y postoperative were inversely correlated with IKDC score ($\rho = -0.63$, $P = .09$) and KOOS-QoL score ($\rho = -0.80$, $P = .017$). Deep T2 values at 1 y postoperative were directly correlated with IKDC scores ($\rho = 0.85$, $P = .0077$).
Domayer[6] (2008)	4	24	Microfracture	29 ± 14 mo	3.0 T	T2 index (T2 value of repair tissue relative to normal cartilage) directly correlated with Lysholm score ($\rho = 0.64$, $P < .001$) and IKDC score ($r = 0.55$, $P = .005$). No correlation between IKDC knee examination and T2 values.
Krusche-Mandl[15] (2012)	4	9	Osteochondral autograft	7.9 y	3.0 T	Significant correlation between T2 ratio (repair tissue ROI divided by mean standard deviation of 3 ROIs from signal-free area) and Lysholm score ($\rho = -0.67$; 95% CI, –0.92 to –0.005).
Salzmann[22] (2014)	4	70	ACI	10 y	1.5 T	T2 values of repair tissue were correlated with numeric analog pain score ($r = -0.28$, $P = .04$). No significant relationship between T2 times and Lysholm score.
Salzmann[23] (2009)	2	18	MACI, osteochondral autograft	42 mo	1.5 T	MACI patients had significant correlation between Lysholm score and repair tissue T2 value ($r = 0.73$, $P = .038$). No relationship between T2 value and outcome scores for osteochondral autograft group.
Welsch[30] (2009)	3	20	MACI and microfracture	32.6 mo	3.0 T	Lysholm score weakly but nonsignificantly correlated with T2 index (Pearson $r = 0.30$, $P = .19$).
Eshed[7] (2012)	4	31	MACI	6-49 mo	3.0 T	No statistically significant correlation between IKDC and zonal T2 values ($r = -0.31$, $P = .11$).
Jungmann[12] (2015)	4	20	Osteochondral autograft	9 y	3.0 T	No statistically significant correlations between Lysholm scores and global T2 values or global T2 side-to-side differences.
Niethammer[20] (2014)	4	13	MACI	6, 12, 24, and 36 mo	1.5 T	No statistically significant correlations between T2 values and IKDC scores at 6 mo ($P = .7$), 12 mo ($P = .54$), 24 mo ($P = .66$), or 36 mo ($P = .8$). No correlations between T2 and VAS scores.
Tadenuma[26] (2016)	4	8	ACI	5.9 y	3.0 T	No significant correlations between T2 values and Lysholm score ($r = -0.13$, $P = .71$).
Stanish[25] (2013)	1	80	Microfracture vs BST-CarGel and microfracture	1 and 12 mo	1.5 T	No correlation between T2 values and WOMAC score at 1 y postoperative.

[a]ACI, autologous chondrocyte implantation; BST-CarGel, commercially available chitosan scaffold for cartilage repair; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MACI, matrix-associated autologous chondrocyte implantation; QoL, quality of life; ROI, region of interest; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

However, gagCEST and sodium MRI are limited by lower resolutions, potential need for higher field strength scanners, additional imaging time requirements, and lack of clearly established clinical relevance compared with traditional MRI.[17,31]

We found that T2 mapping was the most frequently used imaging sequence, reported in 11 studies (Table 1). Other imaging sequences included dGEMRIC in 4 studies (Table 2), sodium imaging in 2 studies, diffusion imaging in 1 study, and gagCEST in 1 study (Table 3). Eight studies used a 3.0-T MRI scanner,[2,3,6,7,12,15,26,30] 5 studies used a 1.5-T scanner,[20,22,23,25,29] and 1 study was performed with a 7.0-T scanner.[33] An 8-channel knee coil was used most frequently, in 9 studies,[2,3,6,7,12,15,22,23,30] while a 28-channel coil was used in 1 study[33] and a single channel coil was used in 1 study.[20] Three studies did not specify the type of coil used. In 12 studies,[§] the surrounding cartilage served as an internal control to compare with repair tissue, while 2 studies imaged the contralateral knee as an internal

[§]References 2, 3, 6, 15, 20, 22, 23, 25, 26, 29, 30, 33.

TABLE 2
Relationships Between dGEMRIC and Clinical Outcomes[a]

Lead Author (Year)	Level of Evidence	No. of Patients	Cartilage Repair Evaluated	Time Point	Scanner Field Strength	Scan Before Gd?	Exercise Time, min	Gd Dose	Findings
Brown[3] (2014)	2	9	Osteochondral allograft	1 and 2 y	3.0 T	Yes	15	0.2 mg/kg	Inverse correlation between relative relaxation rate and IKDC score ($r = –0.75$, $P = .019$), KOOS Pain ($r = –0.86$, $P = .003$), KOOS Symptoms ($r = –0.66$, $P = .052$), KOOS ADL ($r = –0.89$, $P = .001$), KOOS Sports ($r = –0.72$, $P = .03$), KOOS QoL ($r = –0.73$, $P = .026$) at 1 y after surgery.
Tadenuma[26] (2016)	4	8	ACI	5.9 y	3.0 T	Yes	10	0.2 mmol/kg	Significant correlation between dGEMRIC T1 value and Lysholm score ($r = –0.82$, $P = .002$).
Brix[2] (2013)	2	11	MACI	40.6 mo postoperative and again 12 mo after that	3.0 T	No	20	0.2 mmol/kg	Trend toward correlation between Lysholm score and rT1 at initial scan ($r = –0.57$, $P = .067$). No other correlations.
Vasiliadis[29] (2010)	3	31	ACI	12.9 y	1.5 T	No	15	30 ml (0.5 mmol/ml)	No correlation between dGEMRIC and KOOS scores.

[a]ACI, autologous chondrocyte implantation; ADL, activities of daily living; dGEMRIC, delayed gadolinium-enhanced magnetic resonance imaging of cartilage; Gd, gadolinium; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MACI, matrix-induced autologous chondrocyte implantation; QoL, quality of life; rT1, relative T1.

control.[7,12] Ten of the reviewed studies included 1 postoperative scan of the knee,[‖] while imaging was performed at 2 time points in 3 studies[2,3,25] and at 4 time points in 1 study.[20]

T2 Mapping

Of the 11 studies that reported relationships between T2 mapping values and PROs (Table 1), 5 studies found a significant relationship between T2 values and outcome measures while 6 studies did not. No clear differences were noted between studies with a positive relationship and those without regarding scanner field strength, type of cartilage repair procedure, time point of imaging, or number of patients included. Nine of the studies reported imaging sequence parameters, with echo spacing ranging from 6 to 13.9 milliseconds and the number of echoes ranging from 5 to 16. In those studies with a significant correlation between T2 values and clinical outcomes, 2 studies showed a direct relationship, with increasing T2 values associated with better outcome measures[6,23]; 2 studies showed an inverse relationship, with lower T2 values correlated with better outcome scores[15,22]; and 1 study showed a difference in the correlation in the superficial cartilage zone, which was negatively correlated with the IKDC score, while the deep T2 values were directly correlated with increasing outcome scores.[3]

dGEMRIC Imaging

Four studies reported on the relationships between dGEMRIC imaging and clinical outcome scores (Table 2). Two of these showed a significant statistical relationship between these measures.[3,26] A statistical trend was noted in 1 study,[2] while 1 study[29] showed no relationship between dGEMRIC measures and KOOS scores. Two of these studies performed preinjection and postinjection scans and calculated a change in the T1 values, both of which found strong correlations.[3,26] The 2 studies that found no relationship or only a trend had a single postinjection scan and compared T1 values between repair cartilage and normal surrounding tissue.[2,29] The 3 studies that showed a significant relationship or trend toward a significant relationship found a negative correlation between dGEMRIC values and clinical outcomes.[2,3,26]

[‖]References 6, 7, 12, 15, 22, 23, 26, 29, 30, 33.

TABLE 3
Relationships Between Sodium, gagCEST, and Diffusion-Weighted Imaging and Clinical Outcomes[a]

Lead Author (Year)	Level of Evidence	Sequence	No. of Patients	Cartilage Repair Evaluated	Time Points	Scanner Field Strength	Findings
Welsch[30] (2009)	3	Diffusion-weighted imaging	20	MACI and microfracture	32.6 mo	3.0 T	Lysholm score significantly correlated with diffusion index (Pearson $r = –0.56, P = .011$).
Zbyn[33] (2012)	3	Sodium imaging	18	Microfracture and MACI	33 mo	7.0 T	Trend toward association between ratio of repair-to-reference sodium signal intensity to IKDC score ($r = –0.50$, $P = .14$) and Cincinnati score ($r = –0.55$, $P = .10$).
Krusche-Mandl[15] (2012)	4	Sodium imaging and gagCEST	9	Osteochondral autograft	7.9 y	3.0 T and 7.0 T	No significant relationship between sodium or gagCEST and IKDC, Lysholm, or VAS scores.

[a]gagCEST, glycosaminoglycan chemical exchange saturation transfer; IKDC, International Knee Documentation Committee; MACI, matrix-associated autologous chondrocyte implantation; VAS, visual analog scale.

Sodium, gagCEST, and Diffusion-Weighted Imaging

Three studies reported on sodium, gagCEST, or diffusion-weighted imaging (Table 3). Two studies that included sodium imaging were performed with a 7.0-T scanner,[15,33] as was the gagCEST study,[15] while the diffusion-weighted imaging was performed on a 3.0-T scanner.[30] Welsch et al[30] found a significant relationship between the diffusion index and Lysholm score following matrix-associated ACI and microfracture. One study that included sodium imaging showed a trend toward a significant relationship,[33] while the other study showed no significant relationship between either sodium or gagCEST and any outcome measure.[15]

DISCUSSION

Quantitative cartilage imaging uses the abilities of MRI to probe the biochemical composition and structure of tissue. This noninvasive tool can provide useful information on proteoglycan content, collagen structure, and water content, in addition to providing a qualitative assessment of the joint, subchondral bone, and surrounding soft tissues. Qualitative assessment scores such as MOCART (magnetic resonance observation of cartilage repair tissue), and other factors such as defect fill, are commonly evaluated after cartilage repair, and a systematic review found limited correlations between these parameters and clinical outcome scores.[5] Qualitative MRI schemes provide a global overview of regenerated cartilage tissue but are limited by a degree of inter- and intraobserver reliability. Comparatively, quantitative measures focus directly on the biomechanical properties of regenerated cartilage. Instead of a second-look arthroscopy or biopsy of repair tissue, which can provide inconsistent samples and limited information on surface appearance and tactile evaluation by probing, quantitative imaging may prove to be the optimal method to track patients following cartilage repair and restoration, although the relationships between specific imaging sequences and PROs have not been completely defined. The purpose of this systematic review was to determine those relationships for the application of quantitative cartilage imaging after surgical treatment of chondral defects. Variable relationships were observed; significant relationships were reported by 5 of 11 studies on T2 mapping, 2 of 4 studies on dGEMRIC imaging, and 1 of 3 studies on other imaging sequences (sodium, gagCEST, and diffusion-weighted imaging).

T2 mapping was the most frequently studied sequence and inconsistently correlated with PROs. Interestingly, T2 values were both positively and negatively correlated with PROs. T2 mapping values are related to the concentration of water and the organization of collagen within cartilage, with higher values seen with greater concentration of free water.[28] Low T2 values can be indicative of poorly hydrated fibrous repair tissue, which may reflect less durable repair tissue and may explain the positive relationship observed by Domayer et al.[6] The intermediate-term follow-up in this investigation (29 ± 14 months) likely resulted in T2 imaging of fibrocartilage repair tissue, a known product of microfracture surgery that demonstrates inferior biomechanical properties.[6] Conversely, high T2 values are observed with cartilage degeneration seen in early osteoarthritis.[4] This finding may explain the inverse correlation reported by Salzmann et al[22] and Krusche-Mandl et al,[15] two long-term follow-up studies ($\geq$8 years) in which T2 imaging likely characterized the results of long-term breakdown of repair tissue and the corresponding osteoarthritic changes rather than the properties of the repair tissue itself. Additionally, the T2 relaxation times show zonal variation within normal hyaline cartilage, given the differential organization of cartilage in the deep and superficial zones.[24] Different relationships with PROs and T2 values were reported by Brown et al,[3] who observed an inverse relationship in the superficial layer and direct correlations in the deep layer. A previous systematic review on primarily qualitative MRI found weak to moderate correlation

between T2 values and clinical outcome across 5 studies that reported T2 values after cartilage repair surgery.[5] Overall, the information contained within T2 mapping is complex, and deviations in either direction from normal cartilage may represent abnormal tissue following cartilage repair, leading to the differential results observed in the various studies included here. Variations in tissue quality from short-term (acute-phase fibrocartilage or hyaline cartilage repair tissues) to long-term (degraded repair tissue with associated osteoarthritic changes) time points may further confound the interpretation of these imaging studies. Additional research is required to clarify appropriate time points and imaging algorithms for advanced cartilage imaging to support more standardized clinical interpretation.

dGEMRIC is an imaging protocol that uses a gadolinium contrast agent, which distributes through the extracellular matrix of cartilage in inverse proportion to negatively charged glycosaminoglycans.[28] Therefore, dGEMRIC values reflect the proteoglycan content of cartilage, which is an important parameter to monitor after cartilage repair surgery because proteoglycan decrease is related to decreased chondral stiffness and early chondral degeneration.[10,28] Two of the 4 included studies that used dGEMRIC imaging found a relationship between lower proteoglycan content and inferior clinical results.[3,26] Importantly, these 2 studies used the dGEMRIC technique of scanning before and after intravenous injection of gadolinium rather than comparing postinjection repair values with surrounding normal cartilage. Future high-quality studies should investigate whether pre- and postinjection scanning influences results for dGEMRIC after cartilage repair surgery. The only study that showed no relationship between dGEMRIC and outcome scores was conducted on a 1.5-T scanner.[29] This finding may highlight the importance of using higher field strength (3.0 T) when following patients after cartilage repair. From the studies reviewed here, it appears that proteoglycan content as measured by dGEMRIC correlates with clinical outcomes, although these results were not consistent across all studies. Additional investigations are required to draw concrete conclusions regarding the importance of magnetic field strength, coil differences, and the timing of gadolinium injections on the clinical applicability of results.

Sodium imaging also measures the proteoglycan content of cartilage based on the negative charge of glycosaminoglycans, although it requires specialized equipment and generally a high-field-strength scanner (7.0 T).[21] The included studies on sodium imaging showed no clear association between this measurement and PROs. Due to the need for scanners and equipment that are not routinely available in clinical practice and the lack of clear relationships in the reviewed studies, there was no evidence to support the use of sodium imaging to monitor clinically relevant changes after cartilage repair surgery. Similar to T2 mapping, diffusion-weighted imaging provides information on the structure of cartilage by measuring the organized diffusion of water within a defined region.[19] More studies should be performed to further explore diffusion-weighted imaging and its relationship with clinical outcomes, although the single study[30] included in this review did support its correlation with patient outcomes.

This systematic review carries some limitations. The included studies had small sample sizes and incorporated several possibly confounding variables, including a range of disease processes, treatments, and follow-up durations. The imaging protocols and scanner equipment were not standardized across the studies, which may lead to variation in the observed results. Due to this limitation and multiple potential confounding variables, we do not believe that the results are amenable to a meta-analysis. Finally, the qMRI results did not account for important qualitative findings, such as defect fill, the subchondral bone, or the state of the surrounding joint.

Current qualitative classification systems, such as MOCART and the Henderson score, incorporate gross assessments of cartilage regeneration such as percentage fill and border integration. While these qualitative scoring systems provide important data points, the quantitative scoring techniques outlined in this study provide insight into the biochemical properties of regenerated cartilage. These biochemical measurements can objectively evaluate repair tissue and show the importance of both proteoglycan content, through dGEMRIC, and collagen organization, through T2 mapping and diffusion-weighted imaging. Future studies using these imaging modalities should consider the zonal differences of T2 signal, as this may contribute to variability in the studies reviewed here, and preinjection and postinjection scans for dGEMRIC imaging, as those studies showed the strongest relationship with outcome measures. No studies were reviewed that used T1-ρ as an imaging biomarker, although this sequence allows for the assessment of proteoglycan content without exogenous contrast material and could prove useful in monitoring repair tissue after cartilage surgery.[16] Ultimately, new scoring systems that integrate gross properties of regenerated cartilage, such as percentage fill, and quantitative assessments of the quality of regenerated cartilage may provide improved correlation to clinical outcomes compared with either scheme alone. Further research should also evaluate the ability of these imaging biomarkers to predict long-term symptoms and function after cartilage surgery.

CONCLUSION

Multiple studies on T2 mapping, dGEMRIC, and diffusion-weighted imaging showed inconsistent relationships between quantitative imaging parameters and PRO measures after cartilage repair surgery. Given the limitations of small sample sizes, with only 3 studies including more than 30 patients, and differing imaging protocols between studies, it is difficult to draw strong conclusions from the currently available body of literature; this emphasizes the need for future high-quality prospective studies to clarify the role of advanced imaging in monitoring patients after cartilage repair. While T2 mapping, dGEMRIC, and diffusion-weighted imaging can provide important insights into the chemical composition of cartilage, further refinements in imaging algorithms and clinical interpretation are required to improve the utility of these studies.

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