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REVIEW ARTICLE

Acute changes in knee cartilage and meniscus following long-distance running in habituate runners: a systematic review on studies using quantitative magnetic resonance imaging

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Abstract

Objective Running is among the most popular recreational activities; nonetheless, the acute post-race changes of cartilage or meniscus have rarely been determined. The current study aimed to review the acute changes in knee cartilage and meniscus among habituate runners following long-distance running detected by using quantitative magnetic resonance imaging (MRI).

Materials and methods Systematic literature search was performed on those dominate clinical databases which including MEDLINE, Cochrane, Embase, ScienceDirect, and Web of Science. Included studies should be conducted on healthy marathon runners, and the participants should be examined before and after running by using MRI. Intervention studies were excluded.

Results A total number of 14 studies were finally included in this review which all examined the cartilage or meniscus by using MRI functional sequences. Among them, six studies quantitatively measured the changes regarding volume of the knee cartilage or/and meniscus. Five studies found that the volume would decrease initially after running. Ten studies reported T2 (T2*) would decrease after running and returned to the baseline in a short term, while T1ρ may remain increased in months. Five studies measured subareas for T2 (T2*) value, and found that the superficial and medial subarea changed more vastly than other regions after running.

Conclusion Runners experience transient changes in the volume and signals of knee cartilage and meniscus after long-distance running. A liquid exchange and material interaction in cartilage and meniscus was observed after running. Superficial and medial areas of knee cartilage and meniscus might be more susceptible to mechanical loading.

Keywords Quantitative magnetic resonance imaging · Long-distance running · Knee cartilage · Knee meniscus · Acute changes · Systematic review

Introduction

Running is one of the most popular recreational activities globally, and cartilage and meniscus of the knee joint play essential roles in transferring the mechanical loading to subchondral bone and reducing friction in the joint during the activity. Literatures have suggested that long-distance running will overload the knee joint, thus leading to chronic damage [1]. Previous studies have shown that exercises exert significant impact on the biochemical

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components and microscopic morphology of the cartilage, which may result in deformation [2–4]. In addition, both animal and human studies have found that long-term repetitive mechanical loading could cause health hazards, such as cartilage degeneration in the knee joint and additional chondrocyte apoptosis [5–7]. More importantly, such change could lead to imbalance in the cartilage composition, thus accelerate the development of osteoarthritis (OA) [8].

There is a close spatial relationship between meniscus and cartilage in knee joint; the function of meniscus is to distribute loads in the knee and to lubricate cartilage surfaces [9–11]. Both articular cartilage and meniscus possess type II collagen [2]. Furthermore, meniscus and articular cartilage originate from the interzone [12]. Therefore, they are similar in physiological composition.

Magnetic resonance imaging (MRI) is a valid tool for the quantitative evaluation of microstructural and compositional changes as well as the detection of early-stage knee injuries: specialized MRI quantification techniques can detect changes in water content, proteoglycan, and collagen arrays in cartilage and meniscus to visible imaging changes of OA [13]. T2 value, measured by quantitative MRI, has been widely used to assess changes in water interactions and anisotropy of collagen arrays within the extracellular cartilage or meniscus matrix [14].T2 value of cartilage and meniscus also provides information of water content interaction with each other and with surrounding macromolecules [15, 16]. Compared to T2 value, T2* value takes shorter scanning time and shows higher resolution [17]. The significant positive association between T2 value and T2* value has been reported previously in knee cartilage [18]. T1ρMRI is a noninvasive method to study biophysical condition of in vivo cartilage. T1ρ is used to reflect interactions between motion-restricted water content, especially water and proteoglycan interactions [19, 20]. The slow motion between water and proteoglycan has been reported to be efficiently detected by the T1ρ mechanism [21]. It has been suggested that the increase of T1ρ value represents a decrease in proteoglycan content and tissue hydration in articular cartilage [22]. Therefore, the local macromolecular environment reflected by MRI parameters could potentially indicate cartilage damage and OA risks.

Up to date, the acute post-race changes of cartilage and meniscus are still largely unknown. It is of great clinical significance to elucidate the acute effect of long-distance running on knee cartilage and meniscus. Therefore, the main aim of this systematic review is to consolidate the related publications and to provide robust evidence of the changes in cartilage and meniscus by using T2 (T2*), T1ρ, thickness, and volume parameters from MRI. We also hope this study could give implications on the training distances for recreational runners and athletes to lower the risk of knee damage.

Materials and methods

Systematic review scales

We performed the current systematic review to examine the acute changes of knee cartilage and meniscus by quantitative MRI following long-distance running by two independent reviewers (DBS, SYD). Methodology of the current review was aligned with the Cochrane Handbook for Systematic Review as well as the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [23, 24].

Clinical question of this review was: what are the acute knee and meniscus changes in the post-race phase (within 48 h) when characterized by T2 (T2*) value, T1ρ value, volume and thickness among healthy runners?

Literature search

We searched six major electronic databases systematically, which were PubMed, Cochrane, Embase, ScienceDirect and Web of Science, with the strategy of using keywords "(marathon OR half-marathon OR run OR runner) AND (mri OR magnetic resonance imaging) AND (knee cartilage OR meniscus)." Related articles were identified up to July 1, 2021.

Study selection

Discussions were carried out to make the definitive decision where unanimous agreement could not be reached. After eliminating duplicates, articles were screened according to abstract and title to find all relevant literature for this review according to the inclusion and exclusion criteria as follows: Inclusion criteria: (1) healthy runners without known risk factors of knee injuries; (2) the runners were examined pre and post-race by using quantitative MRI examination; (3) quantitative examination of knee cartilage and/or meniscus were done; (4)the running distance ≥ 5 km and/or the running time ≥ 30 min; (5) English literature; (6) the post-race examination was done within 48 h. Exclusion criteria: (1) review studies, editorials, letters or abstracts only; (2) ultramarathons; (3) intervention studies.

Data extraction

Data extracted of the current review including: the authors of the publication, subject demographics (age, BMI, gender and training stages), time points of MRI examination, grading system, and MRI parameters. All data were extracted by independent investigators (DBS, SYD).

Narrative synthesis

Because of the heterogeneity, it was impossible to perform a formal meta-analysis. Thus, a comprehensive qualitative review of the existing literature was performed.

Quality assessment/risk of bias assessment

Newcastle–Ottawa scale (NOS) was used for the evaluation of the study quality and risk of bias [25]. NOS is one of the most commonly adopted tools for the quality assessment of non-randomized studies included in a systematic review. The scaling results of our included articles are shown in Table 1.

Table 1 Newcastle–Ottawa scale of the articles

Study	Year	Selection	Comparability	Exposure	Quality scores
Esculier et al	2019	4	2	3	9
Cha et al	2012	4	2	2	8
Mosher et al	2009	3	2	3	8
Luke et al	2010	4	2	2	8
Stehling et al	2010	4	2	2	8
Hesper et al	2015	3	2	3	8
Kessler et al	2008	3	2	2	7
Kersting et al	2005	3	1	2	6
Kessler et al	2006	3	2	2	7
Heckelman et al	2020	3	2	2	7
Willwacher et al	2020	4	1	2	7
Wang et al	2020	4	2	3	9
Crowder et al	2020	3	2	2	7
Zhang et al	2020	4	2	3	9

NOS scale has 8 items which are categorized into 3 dimensions (selection, outcome, and comparability). The highest score for each study is nine points: eight to nine points stands for very good study quality, six to seven points stands for good study quality, four to five points stands for satisfactory study quality, zero to three points stands for unsatisfactory study quality

Results

After removing duplicate articles, 652 articles were screened. After reading titles and abstracts, 565 articles were excluded as they were irrelevant. Among the remaining 87 full-text articles, 51 were further excluded for the following reasons: no quantitative testing; neither cartilage nor meniscus was studied; the study participants were not recreational runners.

Finally, a total of 14 studies were included in this systematic review. The detailed screening process is shown in Fig. 1. Demographic characteristics of the involved subjects are shown in Table 2; Table 3 describes the research methods and research instruments; main results of each article are summarized in Table 4.

Qualitative synthesis results

Standard knee MRI examinations pre and post running were performed in all 14 studies. Six studies quantitatively measured the changes in morphology of the knee cartilage or meniscus [26–31]. Ten studies quantitatively measured MRI functional sequences of knee cartilage or meniscus [26, 28, 32–39]. Among them, seven studies measured T2 value [28, 32–36, 38], two studies measured T2* value [26, 39] and four studies measured T1ρ value [32, 33, 36, 37].

MRI parameter changes with time

A number of included studies found that cartilage and meniscus volume or thickness would transiently decrease in a short period of time after running [27–31]. Willwacher et al. examined the volume in cartilage immediately after running and reported a significant decrease [30]; Mosher et al. examined the thickness of cartilage in 15 min after running in both runners and sedentary controls, and the researchers reported a significant decrease [28]; Kersting et al. examined the volume of cartilage and meniscus after running and reported the volume decreased significantly [29]; Kessler et al. reported the volume of cartilage and meniscus decreased immediately after running and then increased to a slightly lower level compared with pre-run ($p > 0.05$) in 60 min [27, 31]..

In terms of quantitative measurement of knee cartilage and meniscus by MRI functional sequence, most studies showed that T2 (T2*) value decreased immediately after running and increased after a convalescence period. The immediate post-run time difference among studies, ranging from one minute to around 20 min, has been clearly addressed in most of the studies. Mosher et al. examined the subjects in 15 min after running and found cartilage T2

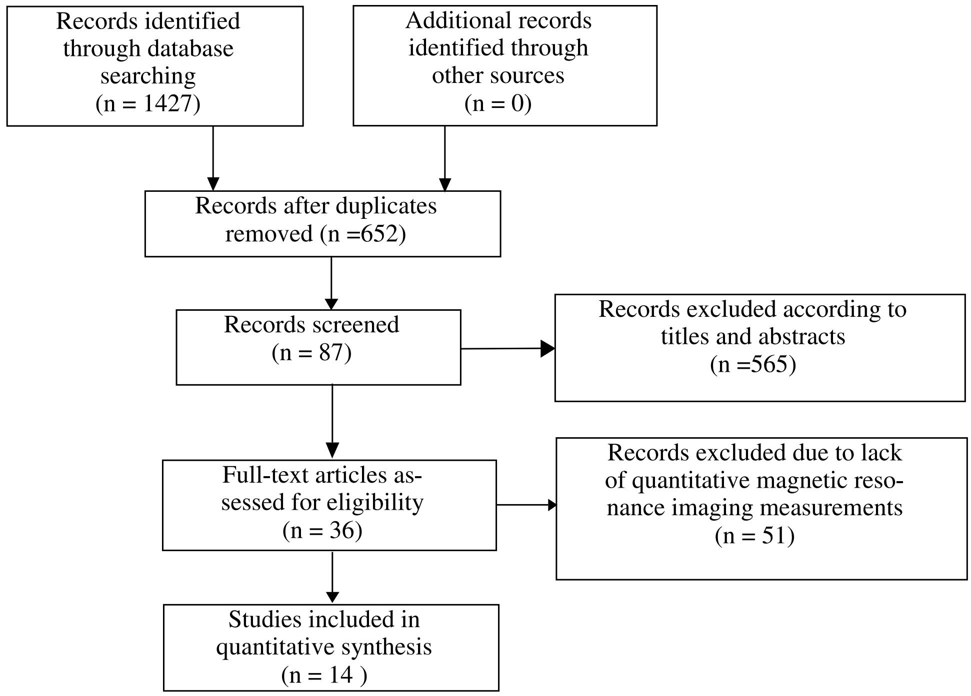

Fig. 1 Flow diagram of the identification of studies

value significantly decreased [28]; Crowder et al. reported a significant cartilage T2 value decrease immediately after running, T2 of superficial femur and superficial patella remained decreased until the 25 min and 15 min, respectively [34]; Esculier et al. observed that T2 values of tibia and femur decrease insignificantly at 19 min after running, but then started to increase at 55 min and 91 min [36]. Cha et al. also reported cartilage T2 value decreased first and increased in 10 min and 2 h after running [35]. Other studies designed a longer convalescence period for another examination and reported T2 (T2*) value increased in 10 h [38], 12 h [26], and 48 h [32, 33, 39].

We encounter a controversial result of T1ρ value changes in the 4 studies examined T1ρ value [32, 33, 36, 37]. Esculier et al. found that in subjects with OA, T1ρ value insignificantly decreased at 31 min after running and increased at 67 min when comparing to pre-run levels. However, the trend is different in healthy controls that T1ρ presented a significant decrease at 31 min and remained at similar level at 67 min [36]. Heckelman et al. reported T1ρ value decreased after running and recovered to pre-run level in 24 h [37]. Luke et al. and Stehling et al. reported T1ρ value in runners significantly increased in 48 h than baseline after running [32, 33]. The recovery periods in each study were different. It is rational to speculate that T1ρ would decrease in a certain period after running, and then increase to a level even greater than baseline.

MRI parameter changes with subarea

Most studies found that the T2 (T2*) value of the superficial and medial subarea of cartilage and meniscus changed vastly in a short period time after running [32, 34, 35, 39]. As for volume and thickness, there were some controversial results: Kersting reported a volume decrease in lateral and medial tibia after running [29]. Zhang et al. has divided the regions into 21 sub-regions by using automatic segmentation and reported that at the time point of 12 h after running, the thickness of lateral central femoral cartilage and the volume of lateral posterior tibial cartilage increased, and at the time point of 2 mon, the thickness and volume of medial anterior tibia significantly decreased [26]. It is worth mentioning that the majority of the included studies segment the cartilage or meniscus manually, two studies used semi-automatic segmentation methods [28, 38], and another two studies used automatic segmentation [26, 32].

Quality assessment/risk of bias assessment

Blinded assessments were carried out to ensure the reliability of MRI reading in some studies. Three studies reported blinded assessments performed by two independent investigators, and the disagreement was resolved by negotiation [26, 32, 33]. In another two studies, the blinded assessments were performed by a panelist [36, 37]. Two studies reported

Table 2 Demographic characteristics of all the involving participants

Author	Subjects	Gender (male/female)	Age (years): mean ± SD or (range)	BMI (kg/m^2): average ± SD/ range	Training stages
Esculier et al., 2019	10 runners with symptomatic KOA and 10 without KOA	0/20	With KOA: 52.6 ± 7.6 Without KOA: 52.5 ± 7.8	With KOA: 23.0 ± 3.4; without KOA: 23.5 ± 2.5	With KOA: 20.2 ± 9.9 km/wk; without KOA: 25.3 ± 13.6 km/wk
Cha et al., 2012	10 younger and 10 older amateur athletes	20/0	Older: 51 (46–59.3); younger: 17 (15–18)	NA	Older: 5–9y running experience, younger: 4–5.5y running experience
Mosher et al., 2009	10 older and 12 younger marathon runners; 5 older and 10 younger age-matched sedentary controls	Runners: 7/13; controls: 9:6	Runner: older 52.6 ± 4.8, younger 25.8 ± 5.0; controls: older: 54.0 ± 5.2, younger 28.4 ± 6.3	Runner: older 23.4 ± 3.3, younger 24 ± 2.6; controls: older25.5 ± 3.2, younger 25.4 ± 3.9	Runner: older 28 ± 14mile/wk, younger 19 ± 6mile/wk; controls: older0 ± 0, younger 1 ± 2mile/wk
Luke et al., 2010	10 marathon runners; 10 age, sex, BMI matched controls	Runners: 6/4; controls: 6/4	Runners: 31.4 ± 5.4; controls: 30 ± 5.4	Runners: 23.7 ± 2.7; controls: 23.1 ± 2.2	Runners: taper period ≥ 2 wks before; no marathon training within 3 mon after; Controls: no history of marathon within 5y; exercise < 30 min/d
Stehling et al., 2010	13 marathon runners; 10 physically active controls	Runners: 5/8; controls: 4/6	Runners: 32.3 ± 5.6; controls: 30.5 ± 5.3	Runners: 23.8 ± 2.5; controls: 23.2 ± 2.9	Runners: < 10 miles before test, 1–2 wk tapering period, no marathon training within 3 mon after; controls: do sports other than marathon running
Hesper et al., 2015	10 marathon runners	3/7	28.7 ± 3.97;	NA	NA
Kessler et al., 2008	10 athletes	10/0	26.5 ± 3	22.8 ± 1.5	67.1 ± 35 km/wk
Kersting et al., 2005	18 athletes	11/7	31.6 ± 7.8	22.9 ± 2.8	38.0 ± 15.1 km/wk
Kessler et al.2006	30 athletes	30/0	38 ± 14	22.6 ± 1.6	67.1 ± 35 km/wk
Heckelman et al., 2020	8 runner	8/0	31 (27–40)	23 (18–25)	> 8 km/wk
Willwacher et al., 2020	12 amateur runners	7/5	29 ± 4	NA	NA
Wang et al., 2020	18 amateur marathon runners	16/2	35.6 ± 6.4	22.2 ± 2.2	> 20 km/wk
Crowder et al., 2020	11 amateur runners, 4 controls	0/15	Runners: 33.73 ± 4.22; controls: 27.25 ± 1.38	Runners: 21.35 ± 1.38; controls: 21.85 ± 0.89	Runners: 16.19 ± 1.45mile/wk; controls: 0mile/wk
Zhang et al., 2020	12 amateur marathon runner	5/7	21–37	17.6–27.2	NA

KOA, knee osteoarthritis

Marathon: the distance is 42.196 km

SD, standard deviation

1 mile = 1.609 km

Time units: *min*, minutes; *h*, hour; *wk*, week; *mon*, month

Table 3 Research characteristics of the recruited subjects

Author	Study design	Running type	Time points of testing	MRI type
Esculier et al., 2019	Case control	30 min on treadmill	Pre-run, 19 min, 55 min, 91 min after running for T2, 31 min and 67 min after running for T1r	3 T Philips
Cha et al., 2012	Case control	3.5 mile in 30 min on urethane track	Pre-run, < 10 min, 2 h after running	3 T GE
Mosher et al., 2009	Case control	30 min on asphalt trail	Pre-run, immediately after running (< 15 min)	3 T Bruker
Luke et al., 2010	Case control	Marathon	Pre-run, < 48 h, 10–12wks	3 T GE
Stehling et al., 2010	Case control	Marathon	Pre-run, 48 h, 3mon	3 T GE
Hesper et al., 2015	Longitudinal	Marathon	< 48 h pre-run, < 48 h, around 4wks	3 T Siemens
Kessler et al., 2008	Longitudinal	20 km	Pre-run after 60 min rest, < 3 min, 1 h	1.5 T Siemens
Kersting et al., 2005	Longitudinal	1 h running at maximum speed in a park	Pre-run, post-run	1 T Philips
Kessler et al.2006	Longitudinal	5, 10, 20 km on course	Pre-run after 60 min rest, 3 min and 1 h after running	1.5 T siemens
Heckelman et al., 2020	Longitudinal	3 and 10mile on treadmill	Pre-run, immediately and 24 h after running,	3 T Siemens
Willwacheret al., 2020	Case control	75 min at 2.78 ± 0.38 m/s on treadmill	Pre-run, immediately after running	3 T Philips
Wang et al., 2020	Longitudinal	Marathon	Pre-run, 10 h post-run	3 T Siemens
Crowder et al., 2020	Case control	40 min on flat outdoor terrain	Pre-run, every 5-min interval in 60 min post-run	3 T GE
Zhang et al., 2020	Longitudinal	Marathon	Pre-run, 12 h and 2mon post-run	3 T Siemens

that blinded assessments were performed, however the exact numbers of their evaluators were unclear [27, 31]. In seven studies, assessors and methods were not specified [28–30, 34, 35, 38, 39].

Discussion

The current systematic review study is trying to provide solid evidence for the transient structural changes of knee cartilage and meniscus after long-distance running. Healthy runners without known risk factors of knee injuries can experience transient changes in T2 (T2*), T1ρ, volume, and thickness of knee cartilage and meniscus after running. There would be a liquid exchange period in cartilage and meniscus after running, which indicates an interaction between water and cartilage matrix.

Volume of knee cartilage and meniscus

Five studies assessed volume of cartilage and meniscus reported controversial results with various convalescence period. However, it is not hard to find a certain trend when comparing to T2 and T1ρ values that volume would decrease immediately after running and recover to baseline after a certain period of rest. Due to the limited number of the included studies in this systematic review, we were unable to conclude the exact time points for the changes. The cartilage deformation might be caused by high impact load mainly [40], and the recovery of cartilage volume in a short period of time after running may be due to its adaptability to loading.

Moreover, the volume or thickness cartilage subarea changed differently. Willwacher et al. reported the volume decreased in medial tibia [30]; Zhang et al. reported the thickness of lateral central femoral cartilage and the volume of lateral posterior tibial cartilage increased at the time point of 12 h after running, the thickness and volume of medial anterior tibia significantly decreased after two months [26]; Kersting et al. reported that the volume of lateral tibia cartilage decreased the most after running [29]; Kessler et al. reported lateral and medial meniscus significantly decreased after running in the studies done in 2006 and 2008; in 2008 they also observed an significant increase after 60 min recovery[27, 31]. The decreased thickness and volume of medial cartilage could be explained by the large contact area of the medial cartilage during exercise. It has been suggested that the medial cartilage transmitted most of the knee loading [26]. The increased thickness and volume of cartilage might be due to the vacuum effect caused by the uneven stress. In this phenomenon, the pressure in the cartilage compression area increases and accumulates, while the pressure in the adjacent cartilage structure decreases. At this time, the cartilage structure in the compression area deformed, water was extruded, and the content of proteoglycan and collagen in the cartilage increased accordingly [41]. This different result of decreased volume of lateral tibial cartilage after running might be due to the uneven loading caused by the runner's different postures. Willwacher et al. found the reduction was more significant in the group with

Table 4 Summary of the results from the included publications

Author	Region	ROIs	Index	Results
Esculier et al., 2019	Cartilage	lF, lT, mF, mT	T2	T2 of TFOA: lF↓† from pre-run (50.4) to time 19 min (50.3), ↑* at time 55 min (53.1) and time 91 min (53.9); lF↓† from pre-run (31.6) to time 19 min (31.3), ↑† at time 55 min (33.6), ↑* at time 91 min (34.5); mF↑† from pre-run (51.1) to time 19 min (51.3), ↑* at time 55 min (53.8), ↑* at time 91 min (54.6); mT↓† from pre-run (34.8) to time 19 min (34.6), ↑† at time 55 min (38.0), ↑* at time 91 min (38.6)
				T2 of controls: post-run values showed no significant difference with pre-run values; lF: pre-run (49.6), time 19 min (48.7), time 55 min (49.6), time 91 min (52.0); lT: pre-run (33.8), time 19 min (33.6), time 55 min (33.7), time 91 min (35.2); mF: pre-run (48.5), time 19 min (47.1), time 55 min (48.6), time 91 min (50.0); mT: pre-run (34.1), time 19 min (31.5), time 55 min (32.6), time 91 min (3.8);
			T1ρ	TFOA: lF from pre-run (52.5)↓† to time 31 min (51.4), had no difference with time 67 min (52.5)†; lT from pre-run (33.8) ↓† at time 31 min (32.8) ↑† at time 67 min (33.3); mF: from pre-run (53.4) ↓† at time 31 min (51.7), ↑† at time 67 min (53.6); mT from pre-run (30.9) ↑† at time 31 min (31.0), ↓† at time 67 min (30.7); TFOA > *controls in mT;mF:
				Controls: lF from pre-run (50.4)↓* to time 31 min (48.8), ↓† time 67 min (48.8); lT from pre-run (35.8) ↓† at time 31 min (34.3), ↓† at time 67 min (34.6); mF: from pre-run (49.1) ↓* at time 31 min (46.9), ↓† at time 67 min (49.0)†; mT from pre-run (32.1) ↓† at time 31 min (31.7), ↓† at time 67 min (30.9)
Cha et al., 2012	Cartilage	mF (a,m,p), lF, mT (a,m,p), lT	T2	T2post/T2pre and T2delay/T2post in mF and lT of older group > younger group. In younger group, mF T2post/T2pre > Tdelay/Tpost. T2post/T2pre ≤ Tdelay/Tpost in F of younger group and in T of both groups. Changes in T2post/T2pre and Tdelay/Tpost ratios were significant, no significant difference between younger and older groups; smF of the anterior zone*: older group > younger group the superficial medial femoral cartilage, For the sT of the anterior and posterior zones*: older group > younger group. dmT in the middle zone*: older group < younger group
Mosher et al., 2009	Cartilage	cmF condyle, pmF condyle, cmT, pmT, clF condyle, plF condyle, clT, plT	T2	sF↓ 2 to 4 ms; T↓ 1 to 3 ms; pre-run T2: F > T. At all ROIs: older groups > younger groups†, young marathoners > young sedentary controls; older marathoners > older sedentary controls. At time0: different in F and T layers (d, middle, s). change of T2: s zone* > middle zone* > d zone†, no significant difference age or physical activity level;ROIs: cmF condyle↓*, pmF condyle↓*, cmT↓*, pmT↓†, clF condyle↓*, plF condyle↓*, clT↓*, plT↓*
			Thickness	Change of thickness: marathoners > sedentary controls; F↓** and T↓* in young marathoners and sedentary controls, F↓† and T↓† in older marathoners and sedentary controls;

Table 4 (continued)

Author	Region	ROIs	Index	Results
Luke et al.., 2010	Cartilage	m/l T, m/ l F (weightbearing and non-weightbearing), trochlea, P	T2	Runners: T2 from pre-run to time 48 h: P↑* (31.7 to 33.3), trochlea↑** (32.6 to 34.6), mF condyle ↑* (29.1 to 30.3), mT↑* (25.7 to 27.7), lF condyle↑†(29.5 to30.5), lT↑†(25.9 to 27.5); T2 from pre-run to time 3 months:P↑† (31.7 to 32.6), trochlea↑† (32.6 to 32.9), mF condyle ↑* (29.1 to 30.1), mT↓* (25.7 to 25.3), lF condyle↑†(29.5 to 30.5), lT↓†(25.9 to 25.4);
				non-runners: T2 from pre-run to time 3 months:P† (30.4 to 30.4), trochlea↓† (32.6 to 31.7), mF condyle ↓† (29.2 to 29.0), mT↓† (26.0 to 25.9), lF condyle↑†(29.8 to 30.0), lT↑†(25.4 to 25.7);
				T2 relaxation times at pre-run:runners (29.4) and controls (28.9) had no difference†; T2 at 3 months: runners (29.4) > †controls (28.9)
			T1ρ	runners: T1ρ from pre-run to time 48 h: of all ROIs↑*** from pre-run (37.0) to time 48 h (38.9), trochlea↑* (41.3 to 43.6), P↑** (38.4 to 40.1), mF condyle↑* (35.9 to38.4), mT↑** (32.4 to 34.9), lFC↑† (39.0 to 39.9), lT ↑† (35.3 to 36.3); T1r from pre-run to 3 months: trochlea↑* (41.3 to 43.7), P↑** (38.4 to 40.3), mF condyle↑** (35.9 to 38.2), mT↑* (32.4 to 34.4), lFC↓† (39.0 to 39.4), lT ↑† (35.3 to 36.7)
				non-runners: T1ρ from pre-run to 3 months: trochlea↓† (40.9 to 40.6), P↓† (38.8 to 38.5), mF condyle↓† (36.4 to 36.3), mT↓† (32.3 to 31.8), lFC↑† (38.0 to 38.5), lT↑† (34.3 to 34.7)
				T1ρ at pre-run: runners (37.0) and controls (36.8) had no difference†; T1ρ at time 3 months: runners (39.0) > **controls (36.7);
Stehling et al.., 2010	Meniscus	Six compartments were segmented (ma, m body,mp, la, l body, lp)	T2	Control: no differences in T2 values of pre-run (11.3) and time 3 months (11.06). No difference of T2 of pre-run between marathoners (11.15) and controls (11.3); T2 of marathoners ↑*** (11.15 to 13.36) at time 48 h to 72 h, and ↓*** at time 3 months (13.36 to 11.47). T2 at time 3 months: no difference between marathoners (11.47) and controls (11.3)
			T1ρ	T1ρ at pre-run: no difference between marathoners (14.73) and controls (15.36); T1ρ: marathoners ↑*** (14.73 to 17.28) at time 48 h to 72 h and remained high (17.36) at time 3 months which > * baseline; T1ρ at time 3 months: marathoners > ***controls
Hesper et al., 2015	Cartilage	clF condyle, cmF condyle; lT plateau, mT plateau, P, trochlea; s, d and bulk zone, and full-thickness in each region	T2*	T2* values: bulk cartilage ↑** from pre-run (29.84) to after marathon within 48 h (30.47); no difference between pre-run (29.84) and after convalescence (29.81); s layers > *** d and s layers; mT plateau ↓ after convalescence (24.2 to 21.6)
Kessler et al., 2008	Cartilage	T, P	Volume	At time0: P↓** of 7%, T↓* of 5.1%; after 60-min recovery: P↑** of 5.3%, T ↑* of 4.3%; at time 60 min to pre-run: P↓† of 2.1%; T↓† of 1.2%

Table 4 (continued)

Author	Region	ROIs	Index	Results
	Meniscus	lM, mM	Volume	at time0: mM ↓** of 8.2%, lM ↓** of 9.3%; after 60-min recovery: mM↑* of 2.7%, lM ↑* of 6.8%; at time 60 min to pre-run: mM ↓† of 5.9%, lM↓† of 3.2%
Kersting et al., 2005	Cartilage	F, mT, lT, P	Volume	Volume at time0: whole cartilage volume↓** (25,114 to 24,373 mm^3) of 3%, F↓*(14,351 to 13917mm^3), T↓*(5985 to 5829mm^3),lT↓***, mT↓†, P↓** (4778 to 4625 mm^3); volume change correlated positively with resting COMP* (r = 0.469) and negatively with COMP change* (r = −0.487);time span of co-activation correlates with F* and total volume change*, m-l shear force and the flexion–extension torque correlate with T** and P* volume change
Kessler et al., 2006	Cartilage	T, P	Volume	5 km at time0: P↓* of 6.6%, T↓** of 3.6%; 10 km at time0: P↓** of 6.1%, T↓** of 5.0%; 20 km at time0: P↓** of 8.1%, T↓** of 6.1%
	Meniscus	lM, mM	Volume	5 km at time0: mM↓* of 5.2%, lM↓** of 5.5%;10 km at time0:mM↓** of 7.5%, lM↓** of 8.2%;20 km at time0: mM↓** of 10.1%, lM↓** of 7.7%;
Heckelman et al., 2020	Cartilage	T, F, P	T1ρ	3 mile distance: difference*** of T (49 ms), F (65 ms), P (79 ms); T,F,P↓ at time0 than pre-run (65 to 62 ms)*; knee cartilage ↓ of 4%*; T,F,P change at time hour24 than pre-running (65 to 65 ms)†; T,F,P↑ at hour 24 than time0† (p-value = 0.07) 10 mile distance: difference*** of T (79 ms), F (67 ms), P (83 ms)*; T,P,F↓ at time0 than pre-running (69 to 62 ms)***; knee cartilage ↓ of 11%*; T,F,P change at time hour24 than pre-running (69 to 67 ms)†; T,F,P↑*** at hour 24 than time0
Willwacher et al., 2020	Cartilage	P, mT, lT, mF, lF,cmF, cfF	Volume	mT↓** at time0; volume↓ in mT*, mF*, P* ROIs: high > low HMP deviation runners; HMP deviation correlated with mT* (R^2 = 0.43) and mF* (R^2 = 0.35)
Wang et al., 2020	Cartilage	PFJ (lP, mP, trochlea); TFJ (lF condyle, mF condyle, mT plateau), each TFJ divided into 4 sub-area: with a meniscus, with m meniscus, with p meniscus, not with meniscus	T2	PFJ: PFJ ↑* at time0 (32.6 to 34.1 ms), P ↑* of at time0 (mP↑***: 31.8 to 34.4 ms (+8.2%); lP↑***: 32.0 to 33.8 ms (+5.6%)); trochlea ↑** 33.2 to 34.1 ms (+5.8%)); TFJ: mT plateau↑* at time0 34.6 to 35.6 ms (+2.9%), mF condyle↓† 35.5 to 35.2 ms (−0.8%), lF condyle ↑† 35.2 to 35.9 ms (+2%); mTFJ ↑* (amT plateau↑*: 3 ms (9.2%), mF condyle↑*: 3 ms (9.2%)); middle mT plateau↓† (35.8 to 35.4); pmT plateau↑† (35.3 to 35.9 ms); alF condyle↑**(32.7 to 34.8 ms, 6.4%) at time0; Change in amT plateau at time 0 correlated with body weight* (r = 0.6746) and BMI**(r = 0.6989); change in amF condyle correlated with BMI* (r = 0.7089). T2 values did not correlate with marathon time, height, age, or sex in any of the subareas

Table 4 (continued)

Author	Region	ROIs	Index	Results
Crowder et al., 2020	Cartilage	F: width m/l, length a/c/p, depth s/d, total 12 regions; T: width a/p, length a/c/p, depth s/d, total 12 regions; P: width m/l, depth s/d, total 4 regions	T2	Runners: no significant difference between control; difference of F (right: 30.39, left: 30.75), P (right: 25.63, left: 26.30), T (right: 28.82, left: 28.85)between right and left knee; sF↓** of 3.2%–4.6% at baseline (37.32 ms) to from Time 0 (35.86 ms) to time25min; sT↓* of 2.6%–3.3% at baseline (33.00 ms) to Time 0 (32.03 ms); sP↓* of 3.3%–3.8% between baseline (34.85 ms) and Time 15 min (33.62 ms)
Zhang et al., 2020	Cartilage	F: laF; lcF; lpF; maF, mcF, mpF; cF trochlea; lF trochlea; mF trochlea;; P: liP, lcP, lsP, miP, mcP, msP; T: lpT, lcT, laT, mpT, mcT, maT	T2	Difference among pre-run, time 12 h and time 2 months*: mcF, mF trochlea, lpF, mcP, msP, maT; ↑*at time 12 h: mcF, maF, lpF, lcF, laF, lcP, miP, mcP;↓*at time 12 h: mcT; ↑*at time 2mon: mcF, mF trochlea, lpF; ↓*at time 2mon maT
			Thickness	Difference of thickness among pre-run, time 12 h and time 2 months*: mF trochlea, lF trochlea, lcF, lpT; lcF↑*at time 12 h; maT ↓* at time 2mon;
			Volume	Difference of volume among pre-run, time 12 h and time 2 months*: lcF, laF, lpT, maT; lpT↑*at time 12 h, laF ↓* at time 2mon, maT ↓* at time 2mon

↓Decrease

↑Increase

* p-value < 0.05

** p-value < 0.01

*** p-value < 0.001

† p-value > 0.05

time0: immediately after running

P, patella; *F*, femur; *T*, tibia; *M*, meniscus

d, deep; *s*, superficial; *a*, anterior; *c*, central; *m*, medial; *p*, posterior; *l*, lateral; *i*, interior

PFJ, patellofemoral joint

TFJ, tibiofemoral joint

COMP, serum cartilage oligomeric matrix protein

TFOA, runner group with symptomatic tibiofemoral osteoarthritis larger deviation of habitual motion path (HMP) [30]. They suggested that uneven local stress could be an important factor in cartilage volume reduction. Future studies are strongly suggested to clarify the relationship between longer recovery time and the changes of cartilage subarea after running.

T2 value and T2* value of knee cartilage and meniscus

A certain trend was observed in the T2 value and T2* value of cartilage and meniscus during running: T2 value or T2* value would decrease initially after running and started to increase to baseline in months. Nag et al. suggested that water was squeezed out from the cartilage matrix during running and would exchange back after the race [42]. Thus, the possible mechanism could be the cartilage still in a compressed condition after running, and the increased T2 value indicates the water absorbing after running, which could be the repairing process. The alternative mechanism for the increase of T2 value can be the enhanced post-race inflammatory response in cartilage matrix. The rapid increase of T2 value may be resulted from the articular cartilage of the elders that was more intolerable to long-term running load, leading to the enhanced inflammatory response in cartilage matrix. Future trials with larger sample sizes and longer follow-up period would be needed to understand the exact mechanisms.

Most studies found that the T2 (T2*) value of the superficial and medial subarea of cartilage and meniscus changed most in a short period time after running [28, 32, 34, 35, 39]. This might be that superficial and medial cartilage was more vulnerable to mechanical loading. Previous study has suggested that the degeneration of type II collagen associated with aging starts from the shallow layer, which might be led by repeated mechanical loading. As mentioned above, the medial cartilage might transmit most of the knee loading [26]. Luke et al. observed similar trend as T2 value and T1ρ value increased in the medial part of knee cartilage after running [32]. Hesper et al. found that T2* value of superficial cartilage layers changed more significant after running [39], and Zhang et al. found that the T2 value of medial knee cartilage increased 12 h after running [26]. The detection time after running was longer than 12 h in the abovementioned three studies, which is 10–12 weeks, 4 weeks, and 8 weeks, respectively. It is reasonable to consider the long recovery period as the rising period of liquid exchange.

T1ρ value of knee cartilage and meniscus

There was a similar post-race change trend of T1ρ value, volume and T2 value, except for T1ρ value, which changed slower than volume and T2 value. A similar interactive physiological change is speculated between the change of T1ρ value and T2 value after running. T2 value of cartilage and meniscus decrease after running and could start to rise in about 24 h after running, whereas T1ρ value increased in about 48 h after running. However, very limited studies reported T1ρ values. More studies are suggested to provide thorough information at more frequent examination time points.

The shorter running time and distance may also have an essential influence on the rapid recovery of T1ρ value. Heckelman et al. reported that T1ρ value of knee cartilage decreased of 4% and 11% with 3 miles and 10 miles running, respectively. After running, the cartilage of knee joint recovered up to 2% of its baseline value within 24 h after running (no significant difference) [37]. They regarded the recovery as a normal physiological change, thus suggested running within this distance range would be safe. It was worth mentioning that Luke et al. and Stehling et al. found T1ρ value stayed higher after marathon than pre-run level after 3 months [32, 33]. The difference in test distance would be a possible reason for the T1ρ value changes. Esculier et al. found that runners showed better tolerance to the load with the running time of 30 min than those without running habits [36]. Therefore, running and training distance may play an important role in the change of T1ρ value. And in the studies of Luke et al. and Stehling et al. on T1ρ [32, 33], it might still be in the rising period of liquid exchange period 3 months after running. Future trial with longer follow-ups and consistent design are recommended to study the clinical significance of T1ρ value and the recovery time of T1ρ value in the knee cartilage and meniscus of runners.

Conclusions

A fluid exchange period in knee cartilage and meniscus has been observed by using MRI parameters after long-distance running among runners. The exchange has been speculated as the interaction between water molecules and cartilage matrix. In general, the values of those MRI parameters would decrease initially after running, and then experience an increase to the baseline level. The volume of cartilage and meniscus and the collagen arrays represented by T2 (T2*) changes more rapidly than the proteoglycan represented by T1ρ changes after running. Superficial and medial areas of knee cartilage and meniscus are more susceptible to mechanical loading. More studies are needed in superficial, medial and deep sub-areas using MRI parameters more than T2 values, especially volume and T1ρ values in at more frequent time intervals in order to draw a picture on a clear picture of the trend.

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Declarations

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