

Retrospective quantitative cartilage and semi-quantitative morphological evaluation at 6 years after ACL reconstruction

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Abstract Purpose We analyzed anterior cruciate ligament reconstruction (ACLR) patients in order to evaluate degenerative changes and the effect of meniscal insufficiency at mid-term follow-up.

Methods Sixty subjects (40 patients at 5.9 years after ACLR, 20 healthy controls) underwent 3T MRI. Quantitative cartilage T2 mapping and morphological Whole Organ Magnetic Resonance Imaging Score (WORMS) evaluation were performed. Self-reported questionnaires were used for subjective clinical evaluation. Based on the meniscal status at ACLR, further subdivision within each compartment (lateral and medial) was made: menisci intact and menisci insufficient.

Results The ACLR subjects showed significantly elevated T2 values and higher WORMS scores compared to the control group. T2 values of the anterior lateral femoral subcompartment were significantly higher in menisci insufficient group compared to the control group. In both compartments significantly higher WORMS scores were observed in the menisci insufficient group compared to the menisci intact group.

Conclusions ACLR knees exhibit cartilage matrix and morphological degeneration at mid-term follow-up. Lateral meniscal insufficiency noted at ACLR presents a higher risk of developing degenerative changes than does the

medial meniscus insufficiency; however, this difference may not be detected clinically.

Keywords ACL reconstruction · T2 mapping · Osteoarthritis · Meniscus insufficiency

Introduction

The anterior cruciate ligament (ACL) is an important stabilizer and loss of its function leads to knee instability [1]. Untreated instability may cause further articular injury and may lead to early osteoarthritis (OA), therefore anterior cruciate ligament reconstruction (ACLR) is often recommended [1]. The main goal of ACLR is to restore function and stability, allowing the patient to return to normal activities [2]. Although ACLR restores knee stability, 50–70 % of ACLR patients develop radiological changes of OA at 10–15 years after ACL rupture [1]. This suggests multifactorial etiology of OA in ACLR patients [3].

ACL rupture is a knee injury involving strong compressive forces and is frequently associated with damage to other joint structures [4]. Especially association of ACL injury and meniscus tears has been well established [5]. Recent studies have focused on quantitative cartilage evaluation after ACLR [6–9].

The objective of this study was to evaluate cartilage matrix and morphological degeneration at mid-term follow-up in ACLR knees. Moreover, a longitudinal effect of menisci status at ACLR was studied in order to evaluate its effect on degenerative changes. The primary hypothesis was that ACLR knees would exhibit more degenerative changes than healthy controls and the secondary hypothesis was that meniscal insufficiency is an important risk factor in the development of degenerative changes.

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Materials and methods

Subjects

The National Medical Ethics Committee approved the study (date of issue: 19.8.2014, registration number: 135/08/14) and informed consent was obtained from the subjects after the nature of the study had been fully explained. Forty ACLR patients (26 males) and twenty healthy volunteers (11 males) were recruited for the study (Table 1). The inclusion criteria for the ACLR group were (1) 16–45 years at ACLR; (2) body mass index (BMI) of 18.5–30; (3) preoperative sports activity of at least 4 on Tegner scale. Exclusion criteria were (1) concomitant collateral ligament disruption, (2) concomitant posterior cruciate ligament injury, (3) MR contraindication and (4) total meniscectomy. The healthy control subjects were matched to the ACLR group according to age, sex, BMI and level of sports activity (Table 1). The inclusion criteria for the control group were (1) IKDC score of at least 95 and (2) no history indicative of any knee joint disorder.

Surgically treated subjects were invited from the 3-year period (years 2008–2010). Twenty-three subjects underwent transtibial and seventeen underwent anteromedial

portal ACLR. ACLR procedures were performed by two senior orthopedic surgeons with the same perioperative procedure and same graft type (semitendinosus-gracilis tendon graft), all patients underwent same rehabilitation program. Average time from the ACL injury to the ACLR was 2.1 ± 2.5 years.

Subjective clinical evaluation

Following questionnaires were presented to the study subjects at the MR examination; Knee injury and Osteoarthritis Outcome Score (KOOS), International Knee Documentation Committee Subjective Knee Form (IKDC), Lysholm, Tegner scale and RAND-36 Health Survey [10–14].

Imaging Studies

Preoperative knee radiographs

In the ACLR group, we determined the degree of preoperative OA based on the Kellgren-Lawrence grading system on anteroposterior and lateral radiographs taken at the time of ACLR [15].

Table 1 Group Characteristics: demographics, symptoms and function of the ACLR versus control group

	Control group (<i>n</i> = 20)	ACLR group (<i>n</i> = 40)	<i>P</i> value
Demographics			
BMI (mean \pm SD)	23.7 \pm 3.7	25.2 \pm 3.7	0.15
Tegner (median value)	6	6	0.71
Age, years (mean \pm SD)	32.6 \pm 6.7	34.8 \pm 8.3	0.30
Symptoms and function			
Lysholm (mean \pm SD)	99.5 \pm 1.5	89.0 \pm 10.4	<0.01*
IKDC (mean \pm SD)	98.1 \pm 1.5	83.5 \pm 15.4	<0.01*
KOOS pain (mean \pm SD)	99.6 \pm 1.0	91.0 \pm 13.1	<0.01*
KOOS symptoms (mean \pm SD)	94.8 \pm 12.2	87.7 \pm 14.0	0.04*
KOOS activities of daily living (mean \pm SD)	99.9 \pm 0.3	95.1 \pm 10.4	0.04*
KOOS sports and recreation (mean \pm SD)	99.5 \pm 2.2	80.6 \pm 21.1	<0.01*
KOOS quality of life (mean \pm SD)	100.0 \pm 0.0	70.4 \pm 24.9	<0.01*
RAND-36 physical function (mean \pm SD)	99.0 \pm 3.5	93.0 \pm 11.5	0.03*
RAND-36 role limitations, physical health (mean \pm SD)	100.0 \pm 0	90.0 \pm 23.2	0.06 [#]
RAND-36 pain (mean \pm SD)	89.4 \pm 14.1	80.4 \pm 22.0	0.10
RAND-36 general health (mean \pm SD)	90.7 \pm 7.8	79.4 \pm 16.2	<0.01*
RAND-36 energy/fatigue (mean \pm SD)	68.8 \pm 11.5	61.0 \pm 12.8	0.025*
RAND-36 social function (mean \pm SD)	93.9 \pm 12.2	90.3 \pm 19.9	0.46
RAND-36 role limitations, emotional health (mean \pm SD)	98.3 \pm 7.4	91.7 \pm 22.3	0.20
RAND-36 emotional well-being (mean \pm SD)	84.8 \pm 6.9	76.3 \pm 14.7	0.02*

ACLR anterior cruciate ligament reconstruction, BMI body mass index, KOOS Knee injury and Osteoarthritis Outcome Score, IKDC International Knee Documentation Committee Subjective Knee Form

[#] Significant at $P < 0.10$; * significant at $P < 0.05$

MR protocol

MR examinations were performed as a single time intervals capture by using a 3.0 T imager (Magnetom[®] Trio, Siemens, Erlangen, Germany) with an 8-channel transmit-receive knee coil (Invivo, Gainesville, Florida, USA). To minimize the changes of different loading conditions, subjects were instructed to avoid sport activities 1 day prior the MR examination and were scanned after resting at least half an hour. Imaging protocol included proton density (PD) turbo spin echo (TSE) fat saturation (FS) images in the sagittal plane (2230/29 [TR ms/TE ms], 16 cm field of view [FOV], 3 mm/1 mm [slice thickness/interslice gap], 512 × 512 matrix, 120° flip angle [FA], 2 signals acquired) and in the coronal plane (2540/35 [TR ms/TE ms], 15 cm FOV, 3 mm/1 mm [slice thickness/interslice gap], 384 × 384 matrix, 150° FA, 2 signals acquired). PD TSE images were obtained in the sagittal plane (2000/29 [TR msec/TE ms], 16 cm FOV, 3 mm/1 mm [slice thickness/interslice gap], 512 × 512 matrix, 120° FA, 2 signals acquired) and in the axial plane (2230/29 [TR ms/TE ms], 15 cm FOV, 3 mm/1 mm [slice thickness/interslice gap], 512 × 512 matrix, 140° FA, 2 signals acquired). T2 maps were obtained in the sagittal plane (1000/13.8; 27.6; 41.4; 55.2; 69.0; 82.8 [TR ms/TE ms], 16 cm FOV, 3 mm/1 mm [slice thickness/interslice gap], 384 × 384 matrix, 180° FA, 1 signal acquired). Average time from the ACLR to the MR examination was 5.9 ± 0.8 years.

Quantitative cartilage evaluation

T2 maps were derived using processing package (MapIt, Siemens Medical Solutions, Erlangen, Germany). Image analysis was performed with a Leonardo[®] workstation (Siemens Medical Solutions, Erlangen, Germany).

Knee joint cartilage was manually segmented in accordance with previously reported papers and five compartments were defined: lateral femoral, medial femoral, lateral tibial, medial tibial and patella [7, 8]. These were subdivided into subcompartments with regard to the menisci in a fashion of the regional subdivision used in WORMS (Fig. 1) [16]. Patella was subdivided in the superior and inferior pole. In each subcompartment the zonal (deep zone—adjacent to the subchondral bone; superficial zone—adjacent to the articular surface) T2 values were obtained by undertaking an ROI (Range Of Interest) analysis [8]. Each ROI was manually defined with multiple marker points on two consecutive midsagittal slices in each compartment. The T2 value of each ROI (mean 172 pixels; range 47–573) was expressed as the mean value of two consecutive slices measurements.

Semi-quantitative MR assessment

Whole Organ Magnetic Resonance Imaging Score (WORMS) system was used in the assessment of morphologic degeneration. The final WORMS scores were tabulated and graded in accordance with the paper published by Peterfy et al. [16].

Assessment of the menisci

To evaluate the effect of the meniscal injury at the time of ACLR we have reviewed the arthroscopy records of the patients. Within the medial and lateral compartment we have divided patients according to the meniscal status in two groups: menisci intact and menisci insufficient. In the menisci insufficient group all patients with signs of meniscal injury were included despite the lesion location and the following treatment. In both compartments the groups did not differ significantly in age, follow-up time, BMI at ACLR and BMI at MR examination.

Statistical analysis

Unpaired *t* test was used to compare continuous and Mann–Whitney U test was used to compare categorical variables between two groups. Analysis of variance (ANOVA) was used to assess meniscal status inter-group cartilage T2 values. Post hoc comparisons were made with Bonferroni correction. Pearson correlation coefficient was calculated to evaluate correlation. Significance was set at $P < 0.05$. Statistical analysis was performed with SPSS v.17.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Preoperative radiographs

Nine patients showed radiographic signs of OA. In transtibial group four patients were assigned grade 1, in anteromedial portal group four patients were assigned grade 1 and one patient was assigned grade 2.

Transtibial vs. anteromedial portal technique

No significant differences in preoperative OA were observed between patients undergoing different ACLR technique. Furthermore, at mid-term follow-up no significant differences in subjective clinical evaluation or degeneration changes were observed between these two groups of patients.

Fig. 1 Sagittal T2 map showing the division of the lateral (a) and medial (b) compartment into subcompartments. *sP* superior patella, *iP* inferior patella, *aLF* anterior lateral femoral, *cLF* central lateral femoral, *pLF* posterior lateral femoral, *aLT* anterior lateral tibial, *cLT* central lateral tibial, *pLT* posterior lateral tibial, *aMT* anterior medial femoral, *cMT* central medial femoral, *pMT* posterior medial femoral, *aMT* anterior medial tibial, *cMT* central medial tibial, *pMT* posterior medial tibial

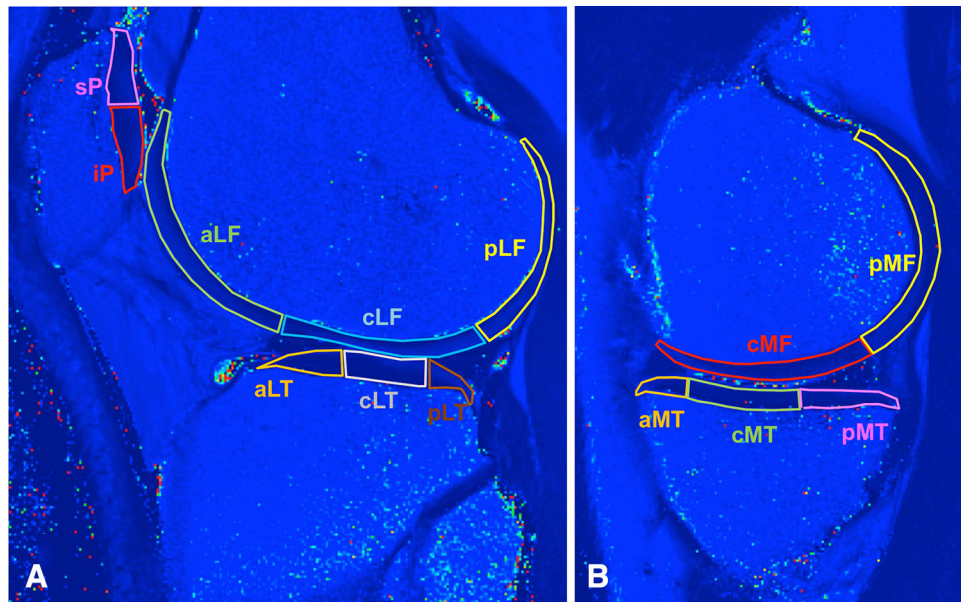


Table 2 Semi-quantitative MR assessment of the ACLR group versus control group

	Control Group					ACLR Group				
	MFTJ	LFTJ	PFJ	S region	Total	MFTJ	LFTJ	PFJ	S region	Total
Cartilage*	/	0.3 ± 0.8	0.3 ± 0.9	/	0.6 ± 1.5	2.6 ± 3.5	2.3 ± 3.2	1.0 ± 1.6	/	5.8 ± 6.6
Marrow abnormality	/	/	/	/	/	0.1 ± 0.4	0.18 ± 0.7	/	0.05 ± 0.316	0.3 ± 0.8
Bone cyst	/	/	/	/	/	0.0 ± 0.2	0.1 ± 0.4	/	/	0.1 ± 0.4
Bone attrition	/	/	/	/	/	0.1 ± 0.5	0.0 ± 0.2	/	/	0.2 ± 0.6
Osteophytes*	/	/	/	/	/	1.1 ± 1.3	1.3 ± 2.4	0.7 ± 1.6	/	2.9 ± 4.3
Compartment total*	/	0.3 ± 0.8	0.3 ± 0.9	/	/	3.5 ± 4.3	3.8 ± 5.5	1.9 ± 3.2	/	8.2 ± 13.0
Menisci*	/	/	/	/	/	1.3 ± 1.7	0.3 ± 0.9	/	/	1.7 ± 1.9
Ligaments	/	/	/	/	/	/	/	/	/	0.1 ± 0.2
Synovitis	/	/	/	/	/	/	/	/	/	0.8 ± 0.5
Total WORMS*	/	/	/	/	0.8 ± 1.7	12.3 ± 12.1	12.3 ± 12.1	12.3 ± 12.1	12.3 ± 12.1	12.3 ± 12.1

ACLR, anterior cruciate ligament reconstruction; MFTJ, medial femorotibial joint; LFTJ, lateral femorotibial joint; PFJ, patellofemoral joint; /, no pathological findings

* Significant at $P < 0.05$

ACLR group vs. control group

Subjective clinical evaluation

Control group showed significantly higher scores than the ACLR group in the knee-specific instruments and RAND-36 items (Table 1).

Semi-quantitative MR assessment

In the control group 14 subjects showed no abnormalities, hence had a total combined WORMS score of 0. However, only two subjects in the ACLR groups showed no abnormalities. Table 2 shows WORMS scores of the ACLR group versus control group.

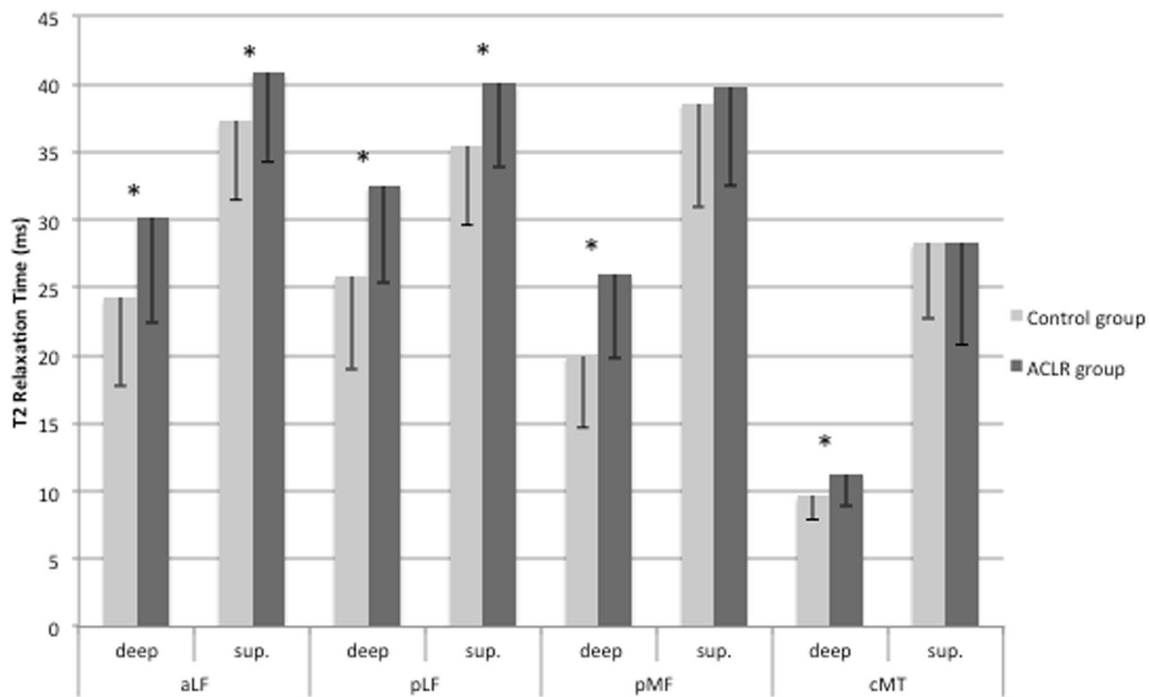


Fig. 2 Cartilage MR relaxation time quantification of the ACLR group versus control group. *ACLR* anterior cruciate ligament reconstruction, *aLF* anterior lateral femoral subcompartment, *pLF* posterior

lateral femoral subcompartment, *pMF* posterior medial femoral subcompartment, *cMT* central medial tibial subcompartment, *sup.* superficial

Quantitative cartilage evaluation

The ACLR group showed significantly elevated T2 values compared to the control group in four subcompartments (Fig. 2).

Meniscal status subdivision and inter-group comparison

Subjective clinical evaluation

In both compartments (lateral and medial) no significant differences were found between the menisci insufficient and menisci intact group.

Semi-quantitative MR assessment

23 patients showed meniscal lesions at the time of the ACLR. 16 patients showed medial meniscus lesions, 9 patients showed lateral meniscus lesions and 2 patients showed lesions in both menisci. Table 3 shows subdivision of patients according to the specific compartment meniscal status at ACLR and WORMS scores.

Quantitative cartilage evaluation

In 4 subcompartments significant differences were observed when dividing groups according to the meniscal

status. Figure 3 shows cartilage T2 values according to the meniscal status in the lateral and medial compartment.

Correlations

No significant correlations were observed between demographic characteristics (age and BMI) and degenerative changes or between subjective clinical evaluation and degenerative changes. In the ACLR group T2 values of only one subcompartment showed significant correlations with WORMS: deep and superficial zone of the anterior lateral femoral subcompartment showed significant correlation with lateral compartment cartilage, lateral and patellofemoral compartment total, and total combined WORMS score.

Discussion

In this study a quantitative and semi-quantitative evaluation of the ACLR knees was employed to characterize degenerative changes and to evaluate the effect of meniscal lesions at mid-term follow-up.

The focus of most papers evaluating knee cartilage in ACLR patients has been on the early postoperative cartilage matrix changes [7–9, 17]. Only one study reported a follow-up with 11 years after ACL injury; however, T2 mapping sequences were limited to the lateral compartment

Table 3 Semi-quantitative MR assessment of the menisci intact versus insufficient menisci group

	MFTJ			LFTJ		
	MINT group (<i>n</i> = 24)	MINS group (<i>n</i> = 16)	<i>P</i> value	MINT group (<i>n</i> = 31)	MINS group (<i>n</i> = 9)	<i>P</i> value
Cartilage	2.4 ± 3.7	2.8 ± 3.3	0.74	1.2 ± 1.8	5.8 ± 4.3	<0.01*
Marrow abnormality	0.1 ± 0.4	0.1 ± 0.3	0.74	0.1 ± 0.5	0.4 ± 1.0	0.17
Bone cysts	0.1 ± 0.2	/	0.42	0.0 ± 0.2	0.2 ± 0.7	0.15
Osteophytes	0.5 ± 0.9	1.8 ± 1.5	0.002*	0.7 ± 1.1	3.3 ± 4.0	<0.01*
Compartment total	2.7 ± 4.3	4.7 ± 4.3	0.16	2.0 ± 2.6	9.9 ± 8.2	<0.01*
Menisci	0.6 ± 1.3	2.4 ± 1.8	0.001*	0.0 ± 0.4	1.1 ± 1.5	<0.01*
Total WORMS	11.7 ± 13.9	13.3 ± 9.0	0.69	9.6 ± 7.1	21.7 ± 19.7	<0.01*

WORMS, Whole Organ Magnetic Resonance Imaging Score; /, no pathological findings

* Significant at $P < 0.05$

at the site of initial bone bruise [5]. In our study cartilage evaluation of all 3 compartments was performed with the time from the ACLR of 5.9 years. With longer follow-up time we proposed the differences between ACLR patients and controls would be more pronounced than in the previous papers, since a process of cartilage degeneration is accelerated at 5–7 years after ACL injury [5]. Most of the previous studies have shown prolongation of the cartilage relaxation time over the follow-up time after ACLR [5, 18, 19]. In our study cartilage relaxation time prolongation was observed in four subcompartments. Interestingly, the anterior lateral femoral subcompartment was the only subcompartment in our study in which higher T2 values were associated with meniscal status. This is consistent with a previous study that found significantly elevated $T_{1\rho}$ values in the anterior lateral femoral subcompartment in patients with associated lateral meniscal tears compared to the respective regions in the contralateral knee [8].

In primary OA morphological degeneration is seen predominantly in the medial compartment; however, in ACLR patients equal distribution between both femorotibial compartments is observed [20]. Injury mechanism has been proposed as the underlying cause for this, since ACL rupture predominantly inflicts trauma in the lateral compartment [20]. Similar observation has been made in our study with ACLR group showing equal distribution of morphological degeneration changes between compartments. However, when the ACLR group was sub-analyzed according to the meniscal status at ACLR significant differences were observed between compartments. In the lateral compartment significantly higher scores in WORMS features of cartilage, osteophytes, total compartment and total WORMS were observed in menisci insufficient group compared to menisci intact group. However, this was not the case in the medial compartment, where menisci insufficient group showed significantly higher scores in only one WORMS feature—osteophytes. It is well established that meniscus insufficiency increases

the risk of knee OA both in isolation and in combination with an ACL rupture [3]. However, the results of our study suggest that lateral meniscus insufficiency in ACLR patients presents higher risk of developing morphological degeneration than does the medial meniscus insufficiency.

Despite the differences in WORMS scores between the menisci intact and menisci insufficient group, no such differences were found for subjective clinical evaluation and cartilage relaxation time. Similarly Li et al. reported no significant differences in clinical evaluation between subjects with intact and insufficient menisci [17]. Observation for the cartilage relaxation time is in agreement with the study by Hirose et al.; however, other studies reported longer cartilage relaxation times in patients with insufficient menisci than in patients with intact menisci [6, 17, 19]. Moreover, we found no correlation between WORMS menisci score and cartilage relaxation times, a finding that is consistent with previous studies [17, 18]. Studies report good correlation between T2 values and WORMS in OA knees; however, in our study this finding was observed only in the anterior lateral femoral subcompartment [21].

There are few limitations to the study. Firstly, only preoperative radiographs were obtained; thus, direct longitudinal MR evaluation of degeneration changes could not have been performed. Secondly, the arthroscopic records were reviewed retrospectively and more attentive arthroscopic exploration may have been undertaken in prospective study. The incidence of medial meniscus tears at the time of ACLR rupture varies from 25 to 45 %; and for the lateral meniscus from 31 to 62 % [5]. Similar rate for the medial meniscus was observed in our study; however, lower rate was observed for the lateral meniscus than in the previous studies. The lower rate may have been attributed to the fact that the arthroscopic records were reviewed retrospectively; however, good association between meniscal status at ACLR and WORMS menisci score was observed in both compartments, which suggests accuracy

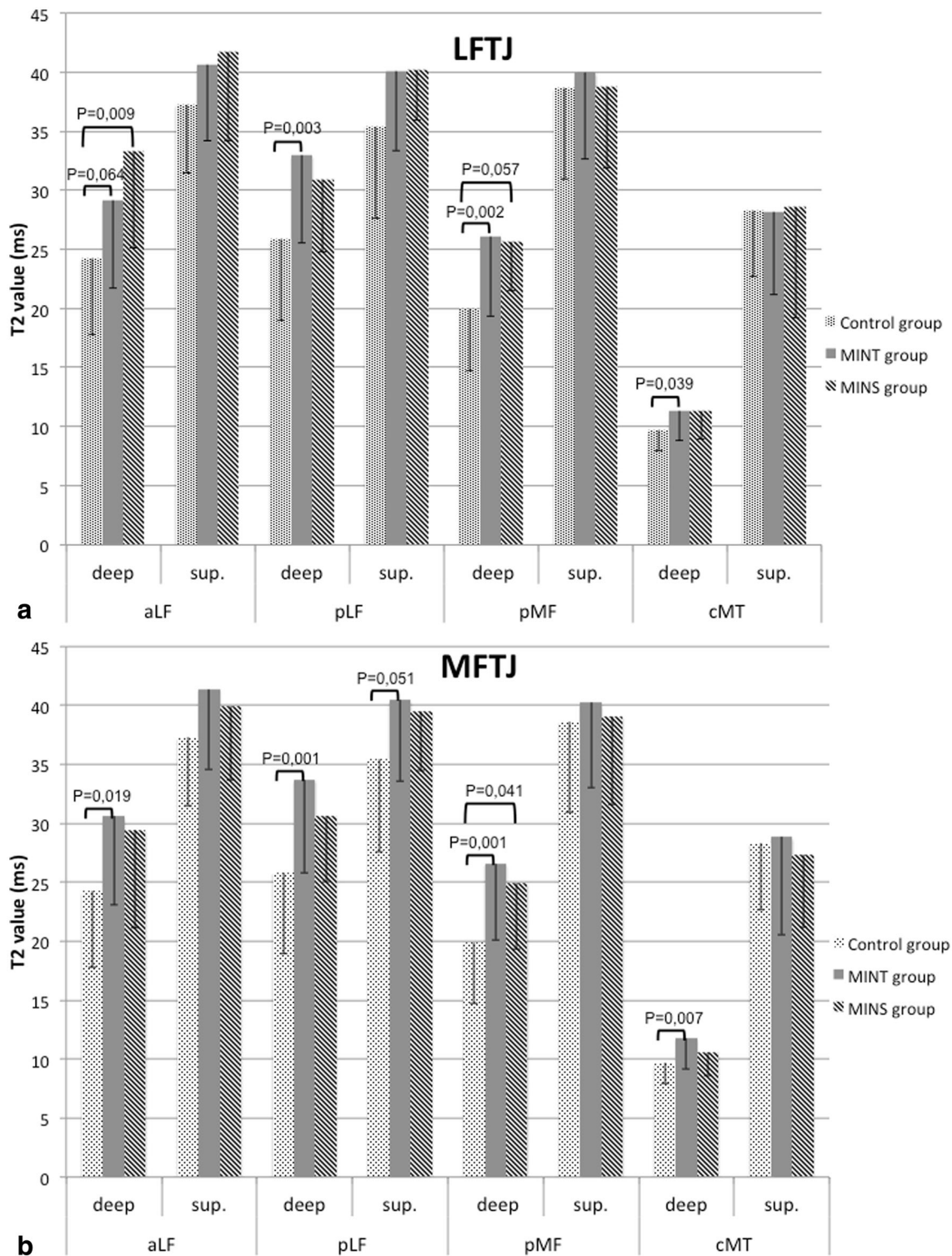


Fig. 3 Cartilage MR relaxation time quantification according to meniscal status **a** in the lateral femorotibial joint (LFTJ) and **b** in the medial femorotibial joint (MFTJ). *aLF* anterior lateral femoral

subcompartment, *pLF* posterior lateral femoral subcompartment, *pMF* posterior medial femoral subcompartment, *cMT* central medial tibial subcompartment, *sup.* superficial, *asterisk* significant at $P < 0.05$

of arthroscopic records. Thirdly, clinical evaluation with only self-reported questionnaires was performed without objective clinical evaluation or evaluation of clinical knee

laxity. Finally, the range of time between ACL injury and ACLR is quite large and both chronic and acute ACLR were included in the study.

In conclusion, the present study showed cartilage matrix and morphological degeneration of ACLR knees at mid-term follow-up. Meniscal lesions noted at ACLR contribute to morphologic degeneration with lateral meniscus insufficiency presenting a higher risk of cartilage matrix and morphologic degeneration than does the medial meniscus insufficiency.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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