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The acutely ACL injured knee assessed by MRI: changes in joint fluid, bone marrow lesions, and cartilage during the first year

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Summary

Objectives: To investigate changes in the knee during the first year after acute rupture of the anterior cruciate ligament (ACL) of volumes of joint fluid (JF), bone marrow lesions (BMLs), and cartilage volume (VC), and cartilage thickness (ThCcAB) and cartilage surface area (AC). To identify factors associated with these changes.

Methods: Fifty-eight subjects (mean age 26 years, 16 women) with an ACL rupture to a previously un-injured knee were followed prospectively using a 1.5 T MR imager at baseline (within 5 weeks from injury), 3 months, 6 months, and 1 year. Thirty-four subjects were treated with ACL reconstruction followed by a structured rehabilitation program and 24 subjects were treated with structured rehabilitation only. Morphometric data were acquired from computer-assisted segmentation of MR images. Morphometric cartilage change was reported as mean change divided by the standard deviation of change (standard response mean, SRM).

Results: JF and BML volumes gradually decreased over the first year, although BML persisted in 62% of the knees after 1 year. One year after the ACL injury, a reduction of VC, AC and ThCcAB (SRM −0.440 or greater) was found in the trochlea femur (TrF), while an increase of VC and ThCcAB was found in the central medial femur (cMF) (SRM greater than 0.477). ACL reconstruction was directly and significantly related to increased JF volume at 3 and 6 months ($P < 0.001$), BML volume at 6 months ($P = 0.031$), VC and ThCcAB in cMF ($P < 0.002$) and decreased cartilage area in TrF ($P = 0.010$) at 12 months.

Conclusion: Following an acute ACL tear, cMF and TrF showed the greatest consistent changes of cartilage morphometry. An ACL reconstruction performed within a mean of 6 weeks from injury was associated with increased ThCcAB and VC in cMF and decreased AC in TrF, compared to knees treated without reconstruction. This may suggest a delayed structural restitution in ACL reconstructed knees.

Key words: Knee injuries, Magnetic resonance imaging, Osteoarthritis, Cartilage morphometry.

Introduction

A history of knee injury increases the risk of knee Osteoarthritis (OA) development 7.4 times as compared to non-injured individuals and approximately 50% of those with a history of anterior cruciate ligament (ACL) injury develop radiographic knee OA 10–15 years after injury, regardless of treatment[1,2]. Several studies have suggested good short-term outcomes after non-surgical treatment of knee injuries[3–6]. There have been no short- or long-term results from randomized clinical trials (RCTs) comparing surgical and non-surgical treatment[2,7]. It is not known how knee surgery influences joint fluid (JF), bone marrow lesions (BMLs) or cartilage in the ACL injured joint.

Traumatic BMLs, also described as 'bone bruises', appear on MR images of acutely injured knees and have been suggested to represent a footprint of the injury mechanism[8,9]. A relationship between large volume traumatic BMLs and cortical depression fractures was recently shown supporting post-traumatic BMLs as signs of strong compressive forces to the articular surface[10]. There is no agreement between reports on the longitudinal development of BMLs following joint trauma and quantitative measures from repeated assessment of traumatic BMLs associated with an ACL injury are lacking[11–14].

Magnetic resonance imaging (MRI) is a sensitive non-invasive method for assessing joint morphology[15,16]. New techniques using computer-assisted analysis have made it possible to measure morphometric parameters from calcified as well as soft tissue joint components[15,17,18]. This technique has been used in the assessment of knee OA but we have not found any reports of early changes in cartilage morphometry after knee injury.

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The objectives of this study were twofold: firstly, to investigate changes in the knee during the first year after acute rupture of the ACL of volumes of JF, BML, cartilage volume (VC), cartilage thickness (ThCcAB) and cartilage surface area (AC), and secondly to identify factors associated with these changes.

Method

MATERIAL

In an RCT (ISRCTN 84752559, http://www.controlled-trials.com) comparing surgical and non-surgical treatment of acute ACL injuries, we included 121 subjects (32 women) with an acute ACL injury in a previously un-injured knee[10,19]. A subset of 63 subjects was followed with MRI over the first year after injury (baseline, 3 months, 6 months and 1 year after injury). Of these 63, five subjects in the non-surgical treatment group were classified as treatment failures according to the RCT protocol because they had an ACL reconstruction within the first year and were excluded from this report. Consequently, 58 subjects with a no more than 5 weeks old ACL injury were included in this study (Table I). Characteristics and self-reported pre-injury activity level according to the Tegner activity scale were collected at baseline[20]. This is not an RCT report and the outcome of the RCT will be analyzed and presented separately. The study was approved by the ethics committee of Lund University (LU 535-01).

SURGICAL TREATMENT GROUP

Subjects treated with ACL reconstruction were operated on within a median of 24 days after randomization or a median of 43 days after injury (Table I). One of three orthopedic surgeons, all with considerable experience in the field, performed the surgery using either Bone-Patella tendon-Bone (BTB) auto-grafts ($n = 15$) or Hamstrings (Semitendinosus and Gracilis) auto-grafts ($n = 19$)[21,22]. Due to clinical symptoms interfering with the rehabilitation protocol, seven subjects underwent additional arthroscopic surgery within the assessment period, performed at a median of 227 (25th, 75th percentile 147, 279) days after the baseline visit: two partial meniscal resections, one meniscal fixation, two synovectomies, one diagnostic arthroscopy, and one notchplasty. One of these subjects had two separate complementary arthroscopies of the index knee over the first year (Table I).

NON-SURGICAL TREATMENT GROUP

In this group, an initial arthroscopy was performed if the following features were present: (1) clinical symptoms interfering with the rehabilitation protocol and/or (2) a concomitant meniscal tear was visualized on MRI and/or (3) symptoms corresponding to meniscal injury at clinical examination. Thus, eight knees were treated with arthroscopic partial resection or fixation of the meniscus using Biofix® arrows within the first year. These procedures were performed at a median of 25 (25th, 75th percentile 14, 125) days after baseline visit. Three subjects in this group had one additional arthroscopy to their index knee during the first year (Table I).

Table I
Characteristics of subjects included in this study (n = *58)*

Characteristic	
Age, mean (SD)	26.7 (4.7)
Female, *n* (%)	16 (28)
Pre-injury activity level	
Tegner, median (range)	7 (5–9)
Days from, median (25th, 75th percentile)	
Injury – randomization	19 (16, 25)
Randomization –	
Surgical reconstruction	24 (20, 28)
3 Months follow-up	114 (112, 119)
6 Months follow-up	211 (210, 213)
1 Year follow-up	366 (365, 373)
ACL reconstruction, *n* (%)	34 (59)
BTB graft, *n* (%)	15 (44)
Hamstring graft, *n* (%)	19 (56)
Cortical depression fracture at baseline, *n* (%)	33 (57)
Arthroscopies during first year	
Knees, *n* (%)	15 (26)

REHABILITATION

Rehabilitation started immediately after randomization, if not already initiated[19]. The rehabilitation protocol was identical for all subjects regardless of treatment, and followed a moderately aggressive training program under the supervision of well-experienced physical therapists. The protocol was based on a consensus report of rehabilitation of ACL injured subjects, developed by the Swedish Association of Sports Medicine and consistent with published literature[23]. Pain, swelling and general discomfort slowed down the progression and thus those treated with ACL reconstruction proceeded at a slower pace through the first 2–3 months after surgery.

CORTICAL DEPRESSION FRACTURES

Subjects reported here were included in a previous report of baseline MRI findings where a definition of depression fracture was presented[10]. Thirty-three of the subjects (57%) included in the present study had a cortical depression fracture at baseline (Table I). These fractures were located centrally in the lateral femoral condyle and/or posterior in the lateral tibial condyle[10].

MRI

MRI was performed using a 1.5 T imager (Gyroscan, Intera, Philips, Eindhoven, the Netherlands) with a circular polarized surface coil using identical sequences for all subjects and all time points. The MRI scans consisted of sagittal 3D Water excitation Fast Low Angle Shot (FLASH) with TR/TE/flip angle of 20 ms/7.9 ms/25°, sagittal T2* weighted 3D Gradient Echo (GRE) with TR/TE/flip angle of 20 ms/15 ms/50°. Both series were acquired with 15 cm Field Of View (FOV), 1.5 mm slice thickness, and 0.29 mm × 0.29 mm pixel size. In addition, sagittal and coronal Dual Echo Turbo Spin Echo (DE-TSE), both with TR/TE of 2900 ms/15 ms, 80 ms, 15 cm FOV, 3 mm slice thickness with 0.6 mm gap and 0.59 mm × 0.59 mm pixel size and sagittal and coronal Short Tau Inversion Recovery (STIR) with TR/TE/TI of 2900 ms/15 ms/160 ms, 15 cm FOV, 3 mm slice thickness with 0.6 mm gap and 0.29 mm × 0.29 mm pixel size were acquired. Quality control of the MRI scanner was performed at each scan using volumetric phantoms attached to the knee and monthly using a standardized and calibrated Uniformity and Linearity (UAL) phantom.

QUANTIFICATION AND POST-PROCESSING OF MR IMAGES

Different methods were used for different metrics of joint morphology although all post-processing analyses were performed at the same processing center (VirtualScopics Inc., 500 Linden Oaks, Rochester, NY 14625, USA).

JF and BML – JF volume was computed using the estimated T2 values from the DETSE series. First, the T2 values were computed in each single voxel of the DETSE series by solving the set of linear equations given by the two separate echoes, the mono exponential model and the signal formation. Secondly, a computer algorithm highlighted each voxel with a T2 value similar to the computed T2 values within the FOV. Thirdly, an expert user inspected the highlighted voxels and assigned the appropriate identification only to voxels truly representing JF. This procedure was performed separately for each knee and each time point. Quantification of BML was performed and computed as described[10]. The same procedure was performed for each knee and each time point.

Cartilage – Metric analysis of cartilage was performed following proprietary analysis techniques, in part described previously (VirtualScopics Inc., 500 Linden Oaks, Rochester, NY 14625, USA). Baseline scans were segmented using a computer-assisted approach extracting the bone of femur, tibia and patella as well as the cartilage associated with these regions[24,25]. Further, a feature-based atlas of the knee was used to automatically separate cartilage into regions of interest (ROI)[26]. This segmentation was reproduced in the follow-up scans using a computer algorithm. Thus, all the segmented components from the baseline segmentation were automatically tracked into the follow-up scans using a piece-wise mesh based approach[27]. The tracking algorithm reproduced cartilage segmentation as well as cartilage region definitions that were supervised by an expert user to ensure accurate definition of all cartilage boundaries. The expert user supervision was replaced by a paired trimming algorithm used to remove the edges of the cartilage tissue and thus the need for further manual supervision was unnecessary[28].

PRESENTATION OF CARTILAGE MORPHOMETRIC CHANGE

We present change in cartilage metrics as changes from 3 months as an alternative to change from baseline in this study and there are two major reasons for this. First, there is a possibility of internal bias (b_I) related to differences between baseline image analysis and follow-up image analyses

using the tracking algorithm. Secondly, there is a possibility of artifact bias (b_A) by altered MR signals due to metal artifacts from implants used only in subjects treated with ACL reconstruction. By replacing the values of the actual baseline scan with values from the 3 months scan we correct for both b_I and b_A as all analyses in this study were done only on tracked images, surgery was already performed and consequently any artifacts from implants were present already at the tracked 3-month scan.

ROI

Regions of the knee were reported in conformity with a proposal for nomenclature in MRI studies of knee OA[29]. JF was not regionalized and thus acquired and presented as JF volume within the entire knee joint. BML volumes are reported as total volume of the knee aggregated as published[10]. VC, ThCcAB and AC were acquired as described above for: Femoral condyles (F), central lateral/medial femur (cLF/cMF), posterior lateral/medial femur (pLF/pMF), TrF, lateral tibia (LT), medial tibia (MT), and patella (P). Volume and surface area were summarized for medial femoral condyle (MF) by adding parameters for cMF and pMF, lateral femoral condyle (LF) by adding cLF and pLF, lateral compartment (L comp) by adding LF and LT, and medial compartment (M comp) by adding MF and MT. Thickness was not averaged, and thus only acquired parameters from analyzed regions are presented.

STATISTICS

Statistical analysis was done using SPSS (version 15.0, SPSS). Age is given as mean (standard deviation, SD) and pre-injury activity level according to the Tegner activity scale is given as median (range). Descriptives of time between injury, MRI scans and surgery are given as median (25th, 75th percentiles), as was JF volumes since this variable was not normally distributed. BML volumes are given as mean (SD) for all time points and morphometric parameters of cartilage (i.e., VC, ThCcAB, AC) are given as mean (SD). Morphometric change of cartilage is given as mean change (SD), percent (mean, SD) and standard response mean (SRM). SRM was defined as the mean change divided by the standard deviation of that change. Factors tested for association with morphometric change were: age, sex, pre-injury activity level (Tegner score), ACL reconstruction (yes/no), complementary arthroscopy (yes/no), cortical depression fracture (yes/no), JF volumes after 12 months (mm^3) and persistent BML after 12 months (yes/no). JF volumes were logarithm transformed and analyzed for all above factors using General Linear Models with adjustment for baseline volumes. BML volumes were analyzed for all above factors using the Pearson correlation coefficient and the *T* test, respectively. Change in cartilage morphometry was correlated to baseline values for some regions and thus all factors were analyzed using General Linear Models with adjustment for baseline values. All factors and regions with an influence at a significance level of less than 5% are presented, although a significance level of 1% was considered as significant morphometric change.

Results

JF VOLUMES

Median JF volume at baseline was 19,500 (25th, 75th percentiles 9100, 31,200) mm^3 and 4000 (2400, 6900) mm^3 after 1 year. There was a gradual decrease over the assessment period, and median JF volume had decreased to 7092 (3103, 13,521) mm^3 already after 3 months. After 3 months, knees treated with an ACL reconstruction had more than threefold larger JF volumes than knees not reconstructed (95% confidence interval, CI 223−455%, $P < 0.001$), after 6 months the difference was more than twofold (95% CI 153−345%, $P < 0.001$) (Fig. 1). No differences were found after 1 year ($P = 0.730$) and no other factor was related to JF volumes at any time during the first 12 months after an ACL injury ($P > 0.108$).

TRAUMATIC BML VOLUMES

All knees were affected by traumatic BML at baseline, where the total mean BML volume of the knee joint was 25,923 (SD 16,784) mm^3. A gradual decrease of BML volume, similar to the development of JF volumes, was found over the assessment period and mean BML volume after 1 year was reduced to 3550 (SD 7596) mm^3. A complete resolution of traumatic BML was found in 22 (38%) knees 1 year post-injury. The first year changes of BML were heterogeneous, where the majority of knees followed a decreasing pattern but 17 (29%) of the knees showed increased BML volumes at one or more follow-up visit. Knees treated with an ACL reconstruction had a mean of 4693 (434−8952, 95% CI) mm^3 larger BML volumes after 6 months, compared to knees treated without reconstruction ($P = 0.031$) (Fig. 1). Knees with a cortical depression fracture had significantly larger BML volumes at baseline as compared with those without depression fractures ($P < 0.001$), but no relation between presence of cortical depression fractures and follow-up BML volumes was found ($P > 0.180$). No other risk factor was related to BML volume at any time during the assessment period ($r < 0.161$, $P > 0.170$).

CARTILAGE

Changes of VC, ThCcAB and AC during the assessment period are presented in Table II. SRMs (negative sign indicates cartilage loss) were generally small and varied across different regions of the knee. The largest consistent reduction was found in the TrF where $-0.588 < \text{SRM} > -0.440$ for all morphometric parameters. A consistent increase in cartilage morphometry values was found in the cMF where $0.477 < \text{SRM} > 0.567$ for VC and ThCcAB (Table II).

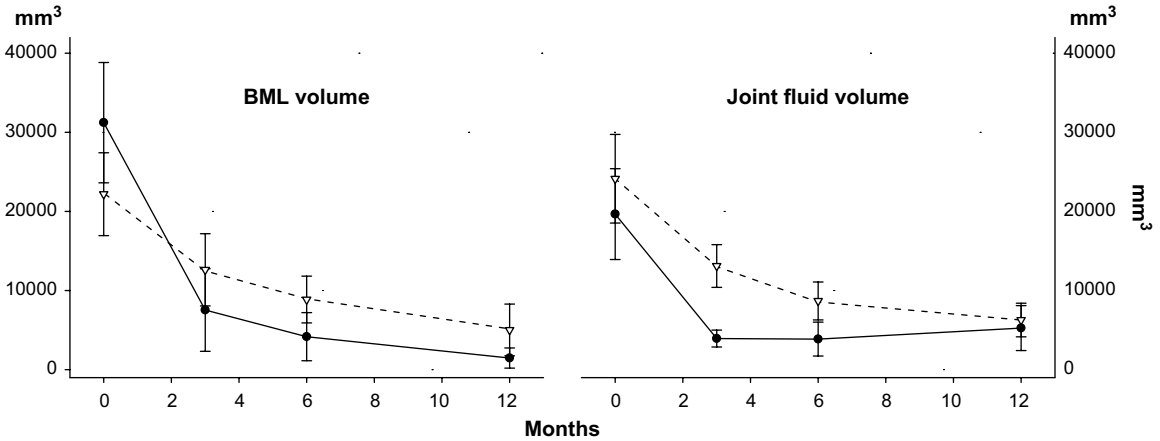

Fig. 1. Mean (95% CI) BML volume (left) and JF volume (right) development over the first year after ACL injury in subjects treated with ACL reconstruction ($n = 34$, unfilled triangles, dashed lines) and without ACL reconstruction ($n = 24$, filled circles, solid lines).

Table II

Development of VC, AC and ThCcAB for all 58 subjects in this study. Mean metrics at 3 months (SD) and mean change between 3 and 12 months (SD) as well as mean change in percent (SD) are presented. SRM was calculated as mean change divided by the standard deviation of that change. Regions of the knee presented in agreement with a previous publication[29]

Region	VC				AC				ThCcAB			
	3 Months mean (SD), mm^3	Mean change (SD), mm^3	SRM	Percent change (SD), %	3 Months mean (SD), mm^2	Mean change (SD), mm^2	SRM	Percent change (SD), %	3 Months mean (SD), mm^3	Mean change (SD), mm^3	SRM	Percent change (SD), %
MT	2132.6 (526.2)	−26.0 (110.4)	−0.236	−1.2 (5.2)	1180.5 (187.6)	−2.9 (29.2)	−0.099	−0.2 (2.6)	1.93 (0.22)	−0.022 (0.090)	−0.244	−1.1 (4.4)
LT	2562.8 (665.9)	24.5 (116.1)	0.211	1.0 (4.6)	1181.9 (200.6)	−0.1 (28.7)	−0.002	0.0 (2.4)	2.45 (0.28)	0.019 (0.094)	0.202	0.8 (3.9)
F	11684.6 (2768.8)	−122.9 (380.3)	−0.323	−0.8 (3.2)	6146.0 (876.4)	−29.5 (79.4)	−0.372	−0.5 (1.3)	2.23 (0.25)	−0.016 (0.064)	−0.250	−0.6 (2.9)
MF	3214.0 (856.7)	23.7 (167.7)	0.141	1.0 (5.3)	1812.7 (346.7)	2.8 (49.7)	0.056	0.2 (2.8)				
cMF	1669.8 (482.7)	49.8 (104.3)	0.477	3.3 (6.3)	874.3 (174.8)	3.5 (29.3)	0.119	0.5 (3.4)	2.20 (0.28)	0.059 (0.104)	0.567	2.8 (4.8)
pMF	1544.3 (427.9)	−26.1 (106.1)	−0.246	−1.4 (6.5)	938.4 (198.5)	−0.7 (29.5)	−0.024	0.1 (3.1)	2.00 (0.22)	−0.028 (0.110)	−0.255	−1.2 (5.5)
LF	3219.9 (820.7)	−38.9 (165.3)	−0.235	−0.9 (4.9)	1794.5 (295.5)	−7.1 (44.2)	−0.161	−0.3 (2.8)				
cLF	1496.6 (375.6)	−12.5 (100.6)	−0.124	−0.3 (6.1)	813.2 (123.7)	−5.8 (31.1)	−0.186	−0.6 (4.1)	2.08 (0.26)	0.001 (0.123)	0.004	0.2 (5.8)
pLF	1723.3 (510.8)	−26.4 (99.0)	−0.267	−1.0 (6.5)	981.3 (198.1)	−1.3 (36.6)	−0.036	0.1 (4.7)	2.16 (0.27)	−0.029 (0.097)	−0.299	−1.2 (4.5)
TrF	4684.0 (1199.8)	−109.1 (202.6)	−0.538	−2.2 (4.0)	2071.8 (307.4)	−28.7 (48.8)	−0.588	−1.4 (2.4)	2.48 (0.34)	−0.037 (0.084)	−0.440	−1.4 (3.4)
P	3117.0 (855.6)	−18.5 (150.2)	−0.123	−0.7 (3.8)	1532.6 (224.4)	−7.2 (36.7)	−0.196	−0.6 (2.4)	2.96 (0.34)	−0.009 (0.096)	−0.094	−0.3 (3.2)
L comp	5782.3 (1427.3)	−14.4 (182.3)	−0.079	−0.1 (3.3)	2976.3 (475.2)	−7.6 (54.7)	−0.139	−0.2 (2.0)				
M comp	5346.6 (1332.9)	−2.3 (215.1)	−0.011	0.1 (4.2)	2993.1 (515.2)	−0.2 (62.9)	−0.003	0.0 (2.1)				

F = Femoral condyles, MF = Medial Femoral condyle, LF = Lateral Femoral condyle, L comp = lateral compartment (LF + LT), M comp = medial compartment (MF + MT).

Factors associated with change in cartilage morphometry were only assessed in TrF and cMF as these regions were the only regions of consistent change. ACL reconstruction was a risk factor for a decrease of AC ($P = 0.010$) in TrF as well as an increase of VC ($P = 0.001$) and ThCcAB ($P = 0.002$) in cMF at 12 months after adjustment for the 3 months values. No other factors were significantly related to cartilage change ($P < 0.010$) at 12 months after an ACL injury (Table III). An un-adjusted graphic comparison of SRMs for the 3–12 months period between subjects treated with or without ACL reconstruction is shown in Fig. 2.

Discussion

Using a state-of-the-art quantitative MRI technique, we have shown that knee joint effusion, as measured by JF volume, and traumatic BML volume decreased gradually during the first year after ACL injury. In general, JF volumes were normalized after 3 months while a total resolution of traumatic BML was only found in 38% of the knees 1 year post-ACL injury. The changes in cartilage morphology after 1 year suggested reduction in volume, thickness and surface area for most regions of the knee except for the cMF where an increase was found. An ACL reconstruction was a direct and significant risk factor for increased JF volumes after 3 and 6 months, a prolonged resolution time of BML volumes and greater changes in cartilage morphometry variables within TrF and cMF.

We have not found any previous report assessing the short-term development of knee effusion after ACL injury. JF volumes reported here were quantified based on signal intensity on MR images and although no intra-venous contrast was used the signal intensity of fluid is different from that of synovium. It is possible, but not likely, that JF volumes reported here incorporate unknown quantities of synovial tissue[30]. JF volumes were high at baseline in spite of all knees having been aspirated for hemarthrosis in the acute phase of injury. Thus, early aspiration of JF does not prevent recurring effusion within the first 4 weeks of injury. A normalization of JF volumes, within a wide range, was found after 3 months where median volumes were comparable to JF volumes of healthy controls (data not shown). A slower reduction of median JF volumes continued until 12 months after injury indicating that some knees followed a different pattern or even increased their JF volume over the assessment period.

There are several reports assessing the development of traumatic BML after knee injury[11,12,14,31,32]. A median healing time of 42 weeks was reported in a prospective study of traumatic BML development of the knee[31]. In that study BMLs were assessed semi-quantitatively, a method suggested to be less sensitive than the one used here[10], different knee traumas were grouped together, and only one out of four knees had an ACL tear. Our findings of 62% knees with persistent BMLs after 1 year are considerably higher than the 28% reported previously[31], perhaps related to our study including only ACL injuries.

MRI-derived morphometric measures of cartilage, as measured in this study, were reduced in the majority of sub-regions of ACL injured knees 1 year after ACL injury. SRMs were generally small and for most regions no consistent change was found. VC was reported to decrease at between 1% and 8% per year in knees suffering from OA[15], although a recent report, using a methodology similar to ours, found only minor annualized changes in subjects with high risk for OA development[33]. cMF was found to be an area of consistent change of VC in both the latter study and our study, although the direction of change differed (SRM = −0.394 vs SRM = 0.477)[33]. The increase in VC of this region in the present study was largely explained by an increase of ThCcAB (SRM = 0.567), suggesting a hypertrophy of the cartilage of this specific region. The short- and long-term significance of such cartilage hypertrophy as well as the genesis of these findings remains to be determined. Animal models have suggested that cartilage hypertrophy precedes cartilage breakdown[34–36]. We suggest that TrF and cMF regions should be specifically monitored for changes in cartilage morphology in the early phase of ACL injury, and for early signs of knee OA.

The long-term consequences of a prolonged knee effusion are not known. Hemarthrosis was shown to activate inflammatory pathways of the joint and suggested as a risk factor for knee OA development[37,38]. We did not analyze JF samples and it is therefore not clear if increased JF volumes found in this study represent hemarthrosis,

Table III

Risk factors associated with changes in cartilage morphometry over the first 3–12 months after an ACL rupture. All variables were adjusted for baseline values and only variables with a statistically significant ($P < 0.05$) relation to a specific region are presented. Regression coefficient (β), 95% CI of β, P-value of association and each variables contribution to the coefficient of determination (R^2) as well as the total R^2 with the risk factor present is given for each model

Morphometric parameter	cMF				TrF			
	β	95% CI	*P*-value	R^2	β	95% CI	*P*-value	R^2
VC, mm^3								
3-Month value	*1*	*1, 1*	*<0.001*	*95.3*	*1*	*1, 1*	*<0.001*	*97.3*
ACL reconstruction	90	39, 141	0.001	0.9 (96.2)	−111	−210, −12	0.028	0.2 (97.5)
Tegner activity score (5–9)	4	−19, 27	0.739	0.1 (95.4)	41	1, 81	0.044	0.2 (97.5)
AC, mm^2								
3-Month value	*1*	*1, 1*	*<0.001*	*97.2*	*1*	*1, 1*	*<0.001*	*97.5*
ACL reconstruction	13	3, 28	0.102	0.1 (97.3)	−33	−60, −8	0.010	0.3 (97.8)
ThCcAB, mm								
3-Month value	*1*	*1, 1*	*<0.001*	*86.7*	*1*	*1, 1*	*<0.001*	*94.1*
ACL reconstruction	0.085	0.034, 0.136	0.002	2.2 (88.9)	−0.037	−0.006, 0.080	0.087	0.3 (94.4)
Cortical depression fracture	−0.057	−0.111, −0.004	0.036	1.1 (87.8)	−0.026	−0.069, 0.018	0.243	0.1 (94.2)

In dichotomous variables the regression coefficient (β) gives the difference between two groups. In non-dichotomous variables and continuous variables (such as pre-injury activity level according to the Tegner Activity Score), an increase of one step in the independent variable (here activity level) is related to β units of change of the dependent variable.

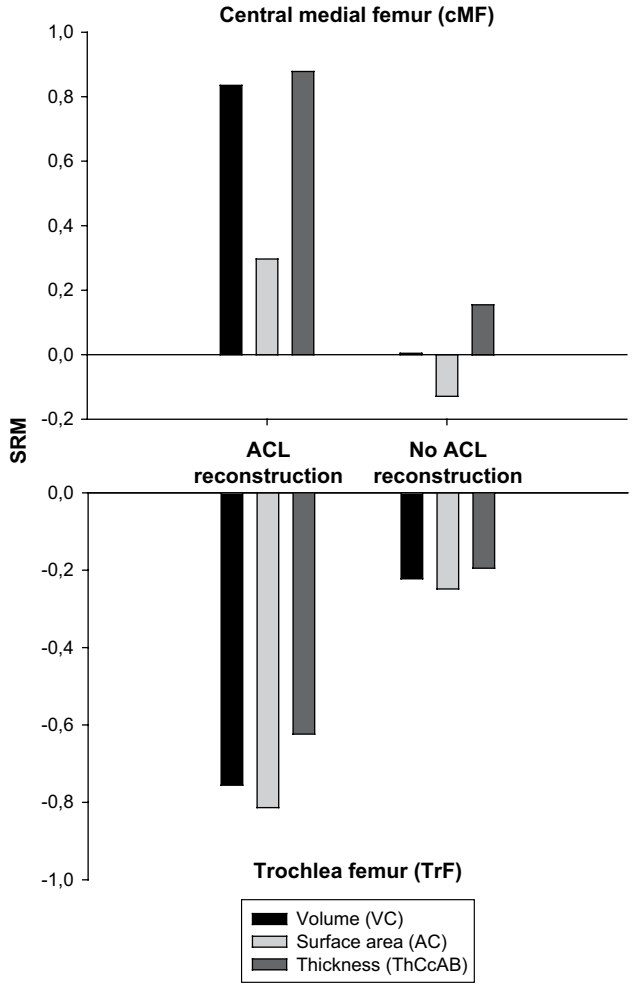

Fig. 2. SRMs of 3–12 months change in VC (black bars), ThCcAB (dark grey bars) and AC (light grey bars) in the cMF (top) and TrF (bottom) for knees treated with ACL reconstruction ($n = 34$) and without ACL reconstruction ($n = 24$).

synovitis or increased volumes of normal JF. Inflammatory processes secondary to trauma and structural recovery of the injured/operated joint are likely to occur in these knees and studies of inflammatory markers in samples from these patients may shed some light on this issue. Resolution of traumatic BML only reflects the disappearance of an MRI-derived signal and previous considerations of BML 'healing' remain speculative[31]. Histology is needed to confirm what is happening in areas of traumatic BML before resolution of increased MRI signals could be regarded as features of a healing process. Little is known about changes in MRI-derived morphometrics of cartilage and the present study is to our knowledge the first describing early changes in human cartilage morphology following an ACL injury. The long-term consequences of our findings with regard to joint structure or patient symptoms are unclear. Further monitoring, replication of our findings and correlations to other biomarkers and patient-relevant outcomes are needed.

This study has some limitations. The methodology of quantifying MRI-derived joint morphology is new and reference data for comparison are lacking. We identified and corrected for b_I and b_A when analyzing cartilage morphometric variables by presenting change from 3 to 12 months. This correction improved the quality of our results but we lost the ability to discover any cartilage change during the first 3 months after injury. JF and BML volumes were segmented separately for each follow-up and were thus unlikely to be subject to method bias. BML volumes were summarized for the entire knee and regional differences could not be detected. Metric change of cartilage morphology was not analyzed due to the given limitations and the fact that we did not assess reproducibility of the method. However, we used SRM, which also includes variation caused by a possible reproducibility error, and thus the results of this study give a valid estimate of the size and direction of change in cartilage metrics. Risk factors assessed in this study were only generally tested for associations. The patients included were a subset from an ongoing RCT, limiting the statistical power and generalizability of any comparisons between the two treatment groups. Cortical depression fractures and BMLs were not regionalized and arthroscopies were not related to time of surgery. The role of ACL reconstruction as a risk factor for early changes in cartilage morphology needs to be further explored in prospective studies, preferably in studies using an RCT design.

We found that an ACL reconstruction performed within a mean of 6 weeks after injury was associated with a reduction of AC in TrF, as well as increased VC and ThCcAB in cMF. Insufficient statistical power prevented us from adequately testing risk factors found on the 5% level, although a high pre-injury activity level and cortical depression fractures should be considered as potential risk factors for morphologic cartilage change. We showed that knees treated with ACL reconstruction had larger BML volumes 6 months after injury compared to knees treated without ACL reconstruction, but no treatment dependent differences in BMLs persisted after 12 months. On the one hand, this could reflect a normal response to surgical intervention. On the other hand, the combination of increased JF volumes, slowly resolving BMLs and changes in cartilage morphology could indicate an ongoing structural remodeling of the traumatized knee where early return to strenuous activities could have a negative influence on the morphologic restitution of the joint with unknown long-term consequences. Thus, we may speculate that knees treated with ACL reconstruction could benefit from a longer period of recovery than knees treated without reconstruction.

Conflict of interest

The authors have no conflict at interest.

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