

Biomarkers that Can Predict the Diagnosis of an Anterior Cruciate Ligament Injury on MR Images, Preoperatively

Biomarkery, které mohou předoperačně predikovat diagnózu poranění předního zkříženého vazů na MR obrazu

F. SOY¹, O. PEHLIVAN², B. OKTAŞ³, M. ÇIRPAR³

¹ Kahramankazan State Hospital, Department of Orthopaedics and Traumatology, Ankara, Turkey.

² Beytepe Murat Erdi Eker State Hospital, Department of Orthopaedics and Traumatology, Ankara, Turkey.

³ Kirikkale University Faculty of Medicine, Department of Orthopaedics and Traumatology, Kirikkale, Turkey.

ABSTRACT

PURPOSE OF THE STUDY

The competence of the anterior translation of tibia (ATT), posterior cruciate ligament angle (PCLA), and femorotibial rotation angle (FTRA) measured on MR images in predicting anterior cruciate ligament (ACL) injury was evaluated in this study.

MATERIAL AND METHODS

266 patients who underwent diagnostic arthroscopy between 2015–2020 were included in this study. Age, gender, radiological findings included ATT, PCLA, and FTRA were measured on preoperative MR images of all patients.

RESULTS

ACL tear was detected in 143 of patients and most of them were younger males. In ACL-R group, the ATT was 7 mm (–4–17 mm), PCLA value was 110° (52°–157°), and FTRA value was 5.8° (–5°–18°), while in ACL-I group, the ATT was approximately 5 mm (–4–12 mm), PCLA value was 122° (82°–162°) and FTRA value was 1.6° (–10.9°–10°) ($p < 0.001$). ROC-Curve test results showed that if ATT value was > 6.05 mm (63% sensitivity, 65% specificity) if PCLA value was $< 116.5^\circ$ (65% sensitivity, 70% specificity) and if FTRA value was $> 3.45^\circ$ (73% sensitivity, 72% specificity), these parameters could predict the probability of ACL tear, preoperatively. The Logistic Regression test results revealed that the PCLA and FTRA values could be the best markers to predict the probability of ACL tear, preoperatively.

CONCLUSIONS

This study results showed that the ATT, PCLA, and FTRA values could be used as predictive markers in diagnosis of ACL tear, preoperatively. Among these three values, it was concluded that the FTRA could have the highest sensitivity and specificity ratios and the best predictive value.

Key words: anterior cruciate ligament tear, magnetic resonance imaging, arthroscopy, rotational instability, femorotibial rotation angle, anterior translation of the tibia, posterior cruciate ligament angle.

INTRODUCTION

Anterior cruciate ligament (ACL) injuries are one of the most common ligament injuries of the knee and its incidence has been reported as 85/100.000 (6). Approximately 100.000 ACL reconstructions are performed in the USA each year, and the average healthcare expenditure for these patients is reported to be 1.5 billion dollars (10).

The anterior cruciate ligament plays an important role in rotational stability in addition to anteroposterior stability in the knee joint, and rotational instability develops after ACL injury. Instability leads to joint degeneration in the early period and causes cartilage destruction in the chronic process (1). Today, although arthroscopy is accepted as the gold standard method in the diagnosis of

ACL injury, MRI has also become an important diagnostic tool, which is non-invasive, can be applied safely, and has diagnostic values of up to 96% sensitivity and 96% specificity in ACL tears (13). However, in some cases, it may be difficult to diagnose the ligament injury by examining the ligament structure primarily in MRI scans. Today, extensive research continues on the parameters that can be used in the diagnosis of ACL injury, because the sensitivity and specificity of MRI are reduced in some cases, such as partial ACL tears (4, 5, 15).

In this study, it was aimed to predict the diagnosis of an anterior cruciate ligament injury using the amount of anterior translation of the tibia (ATT), posterior cruciate ligament angle (PCLA), and femorotibial rotation angle (FTRA) values on preoperative MR images of the patient undergoing arthroscopy.

MATERIAL AND METHODS

Patients

Patients aged 16–50 years, who underwent arthroscopy with a pre-diagnosis of ACL tear between 2015 and 2020, were included in this study.

According to the results of the arthroscopy procedure, the patients were divided into two groups as follows:

- ACL-I group (patients without ACL tear after arthroscopy, n=123)
- ACL-R group (patients diagnosed with ACL tear after arthroscopy, n=143)

Patients with a posterolateral corner injury or other extra-articular ligament injuries around the knee that will cause a pivot shift mechanism in preoperative MR imaging, patients with degenerative or inflammatory diseases that will affect the alignment, patients who have undergone knee joint surgery or secondary reconstruction surgery before MR imaging, and children in the childhood age group were excluded from the study.

Materials

The age and gender of the patients were recorded. In addition, ATT, PCLA, and FTRA values measured in MR images of all patients used for preoperative diagnosis were analyzed in the study.

MR examination results used in this study were obtained with a 1.5 Tesla MR device (Philips Medical Systems, Achieva Release 3.2 Level 2013-10-21, The Netherlands). All knee MR images were taken in the supine position, with the knee coil positioned in 15° flexion and 10° external rotation. Sequences routinely used for knee MR included Proton Density (PD)-weighted fat-suppressed sequences in the axial, coronal, and sagittal planes, and T1- and T2-weighted sequences in the sagittal plane (9, 11, 14, 16).

- ATT value was calculated in the mid-sagittal sections of the lateral femoral condyle by measuring the distance between the line drawn parallel to the long axis of the image and tangent to the posterior cortex of the femoral condyle and the line drawn parallel to the previous line on the posterior border of the tibia.

- The PCLA value was calculated by measuring the angle between the lines connecting the midpoints of the proximal femoral and distal tibial attachment areas.
- In FTRA measurement, the angle between the line tangential to the posterior condyles of the femur in the MR axial section and the line tangent to the tibial posterior cortex in the first section where the fibular head is visible was measured (Fig. 1).

Statistical analysis

Statistical Package for Social Sciences (SPSS) Version 20.0 (IBM Corp.) program was used to analyze the study data.

The *Shapiro-Wilk* test was used to test the normal distribution of study data. Categorical data were expressed as N (%) and analyzed with *Pearson's Chi-square* test. Other data were found to be abnormally distributed among the groups. These data were expressed as median (minimum-maximum) and the *Mann-Whitney U* test was used to determine the statistical difference between groups. Spearman-rho Correlation test was used to test the relationship between the data. *ROC-Curve* test was used to find parameters that could predict ACL injury in MR images, and *Logistic Regression* test was used to find out which of these parameters could be the best predictor. In addition, the *Odds Ratio* test was used to predict which parameter might increase the possibility of ACL injury.

RESULTS

Descriptive variables belonging to both groups are presented in Table 1.

Of the 266 patients included in the study, 205 (77.1%) were male and 61 (22.9%) were female ($X^2=11.901$, $p=0.001$). While the number of male patients in the ACL-R group was approximately 6 times the number of female patients, this ratio was found to be 2 times in the ACL-I group. The patients' age was found to be statistically different between the two groups ($Z=-3.718$, $p<0.001$). With this finding, patients with ACL injury were found to be younger males.



Fig. 1. The figure shows the measurement the anterior translation of the tibia (ATT) (1A), and measurement of the posterior cruciate ligament angle (PCLA) (1B) on T1 weighted sagittal MR images; and measurement of the femorotibial rotation angle (FTRA) on T1 weighted axial MR image (1C).

Table 1. The values of the anterior translation of the tibia (ATT), posterior cruciate ligament angle (PCLA), and femorotibial rotation angle (FTRA) which were measured on the magnetic resonance images of the patients of the ACL-I group and patients of the ACL-R group

		ACL-I	ACL-R		
Variable		Median (min-max)/ N (%)	Median (min-max)/ N (%)	Z / X ²	p
Age		35 (16–50)	27 (16–50)	-3.718†	<0.001
Gender	Male	83 (31.2%)	122 (45.9%)	11.901‡	0.001
	Female	40 (15.0%)	21 (7.9%)		
ATT (mm)		5 (-4–12)	7 (-4–17)	-4.544†	<0.001
PCLA (°)		122 (82–162)	110 (52–157)	-7.341†	<0.001
FTRA (°)		1.6 (-10.9–10)	5.8 (-5–18)	-8.863†	<0.001

(†) Z: Z value, Mann-Whitney U test, (‡) X²: chi-square value, Pearson's Chi-square test, p < 0.05

min: minimum, max: maximum, N: number of the participants

When the data measured in the MR images of the patients were compared, it was seen that the amount of ATT (Z=-4.544, p<0.001), PCLA (Z=-7.341, p<0.001), and FTRA (-8.863, p<0.001) values were different between the two groups (Table 1, Fig. 2).

The correlation analysis results applied to all data of all patients revealed a positive correlation between the ATT and FTRA values (r=0.319, p<0.001). On the other hand, a negative correlation was found between the FTRA values and age (r=-0.196, p=0.001), between the FTRA values and gender (r=-0.150, p=0.014), between the FTRA and PCLA values (r=-0.206, p=0.001) and between the ATT and PCLA values (r=-0.373, p<0.001) (Table 2).

The ROC-Curve test results applied to all data of all patients revealed that if the ATT value was measured >6.05 mm, it was found that this parameter could be 63% sensitive and 65% specific in predicting the diagnosis of ACL injury (area=0.661, p<0.001). In addition, if the PCLA value was <116.5°, it was found that this parameter could be 65% sensitive and 74% specific in predicting the diagnosis of ACL injury (area=0.239, p<0.001). Furthermore, if the FTRA value was meas-

Table 2. The correlation among the values of the anterior translation of the tibia (ATT), posterior cruciate ligament angle (PCLA), and femorotibial rotation angle (FTRA) measured on the magnetic resonance images in all participants

Variable		Gender	ATT	PCLA	FTRA
Age	r	0.052	0.000	0.063	-0.196
	p	0.400	0.999	0.307	0.001
Gender	r	1.000	-0.108	0.049	-0.150
	p		0.079	0.430	0.014
ATT	r		1.000	-0.373	0.319
	p			<0.001	<0.001
PCLA	r			1.000	-0.206
	p				0.001

r: correlation coefficient value, Pearson's rho correlation test, p<0.05

ured >3.45°, it was found that this parameter could be 73% sensitive and 72% specific in predicting the diagnosis of ACL tear (area=0.815, p<0.001). However, the Logistic Regression test results showed that the parameters of the PCLA (B=1.546, Wald=25.397, p<0.001) and FTRA (B=1.826, Wald=36.542, p<0.001) were the best markers in predicting the diagnosis of ACL injury (Table 3, Fig. 3).

The Odds Ratio test showed that if the ATT value was >6.05 mm, it was associated with more than a three-fold risk of ACL tear (OR=3.159, 95% CI=1.911–5.222, p<0.001). In addition, if the PCLA value is <116.50°, it was associated with more than a five-fold risk of ACL tear (OR=5.455, 95% CI=3.209–9.274, p<0.001). Furthermore, if the FTRA value is >3.45°, it was associated with more than a six-fold risk of ACL tear (OR=6.980, 95% CI=4.068–11.978, p<0.001) (Table 3, Fig. 3).

DISCUSSION

In this study, the data of the patients diagnosed with ACL injury (ACL-R group) using the arthroscopic ACL examination method, which is accepted as the gold

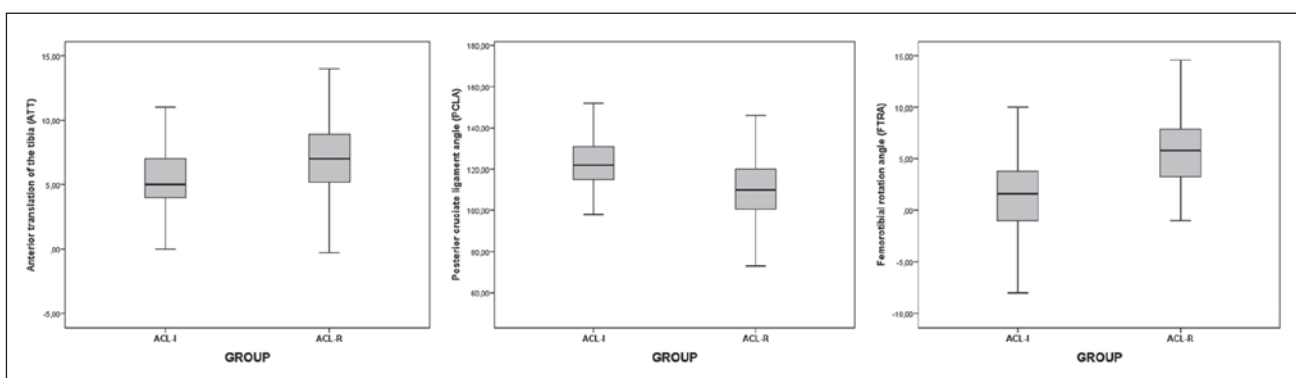


Fig. 2. Each error bar shows the values of the anterior translation of the tibia (ATT), posterior cruciate ligament angle (PCLA), and femorotibial rotation angle (FTRA) measured on the magnetic resonance images in ACL-I and ACL-R group patients.

Table 3. The parameters that can predict the anterior cruciate ligament tear in patients who performed diagnostic arthroscopy: the Odds Ratio test results and its corresponding 95% confidence intervals for the direction and strength of the association between the patients' data and the anterior cruciate ligament tear risk

ROC Curve test							
Variable			Area	p	"Cut-off" value	Sensitivity	Specificity
ATT			0.661	<0.001	>6.05 mm	%63	%65
PCLA			0.239	<0.001	<116.50°	%65	%74
FTRA			0.815	<0.001	>3.45°	%73	%72
Odds Ratio test							
					95% CI		
Variable	"Cut-off" value	ACL-I	ACL-R	OR	Lower	Upper	p
ATT	<6.05 mm	80 (30.1%)	53 (19.9%)	3.159	1.911	5.222	<0.001
	>6.05 mm	43 (16.2%)	90 (33.8%)				
PCLA	<116.50°	91 (34.2%)	49 (18.4%)	5.455	3.209	9.274	<0.001
	>116.50°	32 (12.0%)	94 (35.3%)				
FTRA	<3.45°	89 (33.5%)	39 (14.7%)	6.980	4.068	11.978	<0.001
	>3.45°	34 (12.8%)	104 (39.1%)				
Logistic Regression test							
Variable					B	Wald	p
PCLA					1.546	25.397	<0.001
FTRA					1.826	36.542	<0.001

p < 0.05

ACL-R: anterior cruciate ligament-ruptured, ACL-I: anterior cruciate ligament-intact, ATT: anterior translation of the tibia, PCLA: posterior cruciate ligament angle, FTRA: femorotibial rotation angle, OR: Odds Ratio value, CI: confidence interval. ROC-Curve test, Odds Ratio test, and Logistic Regression test, *p* < 0.05.

standard method in the diagnosis in the literature, were compared to the data of the patients without ACL injury (ACL-I group). The main purpose of using this method was to separate the two groups with the highest possible accuracy and to minimize the possibility of false-positive and false-negative diagnoses in the groups. As a matter of fact, it has been reported in the literature that adhesions can often occur on the posterior cruciate ligament (PCL) when ACL injuries are left to their natural course without treatment. As a result, it was thought

that patients with an ACL tear, who were reported to have ACL intact in MR reports, but did not give a tear signal in MR images after this natural course process, might cause deviations in the accuracy of statistical analyzes if the MRI results were examined without arthroscopic confirmation. In this respect, the fact that all patients diagnosed with ACL tear or reported as intact ACL was also confirmed arthroscopically, further increased the value of our study and made it superior to other studies that did not have this feature.

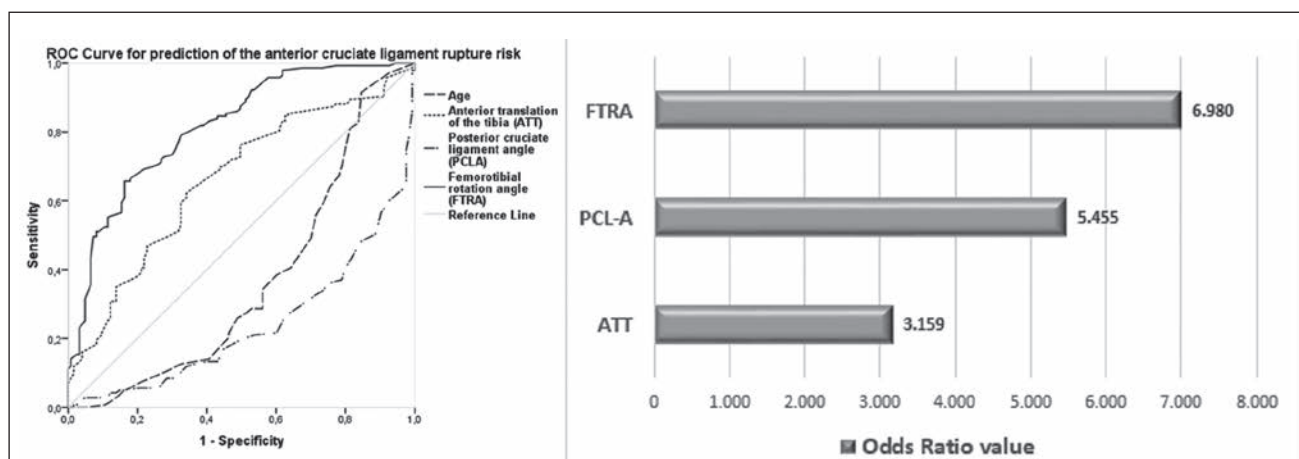


Fig. 3. The ROC-Curve plot shows the parameters that can predict the diagnosis of the anterior cruciate ligament tear in patients undergoing arthroscopy, and the Odds Ratio test plot shows the parameters that can be associated with the anterior cruciate ligament injury.

Vahey et al. reported that subluxation of more than 5 mm could be a secondary finding an ACL tear with a sensitivity of 58% and a specificity of 93%, and all patients with subluxation of 7 mm or more had a ACL tear, definitely (7). In other studies, it has been reported that subluxation of the tibia greater than 5 mm may be sensitive and specific in diagnosing ACL tear (2, 3, 7). In the present study, the *ROC-Curve* analysis results showed that if the amount of ATT is > 6.05 mm, this parameter could be 63% sensitive and 65% specific in predicting the diagnosis of ACL tear. However, contrary to the literature, it was observed that the diagnostic value of the amount of ATT might be limited in ACL tear, and as a result of the *Logistic Regression* analysis, it was found that it did not have a predictive value compared to the other two parameters (PCLA and FTRA). Besides, the *Odds Ratio* analysis results revealed that the probability of the ACL tear could be more than a three-fold increase in patients with an ATT value > 6.05 mm. It was thought that these results might be due to the detection of ATT values up to 12 mm in individuals in the ACL-I group who were confirmed to have no ACL injury arthroscopically. Therefore, it was concluded that the value of the ATT would not be sufficient to predict the diagnosis of ACL tear, preoperatively.

It has been reported in the literature that the PCLA value can be measured at an average of 95° in the chronic period in ACL tear, and this value can be measured as an average of 109° in acute tear and 123° in healthy individuals (3, 8, 9). In this study, PCLA value was determined as 110° in the ACL-I group and 122° in the ACL-R group. However, at the end of *ROC-Curve* analysis, the cut-off value of the PCLA was found to be 116.50° , and it was found that the PCLA values measured below this value could be able to predict the diagnosis of ACL tear with 65% sensitivity and 74% specificity. Besides, the *Odds Ratio* analysis results revealed that the probability of the ACL tear could be more than a five-fold increase in patients with an PCLA value $< 116.50^\circ$. Furthermore, the *Logistic Regression* test revealed that the PCLA value could be the best parameter to predict the diagnosis of an ACL tear. With these results, it was concluded that the PCLA value obtained from MR images can be used as a marker to predict the diagnosis of an ACL tear, preoperatively.

It has been reported that FTRA measurement can be used as a parameter in the evaluation of rotational knee instability and diagnosis of an ACL tear. Recent studies have shown that the mean FTRA value in patients with ACL tear was found to be significantly higher than in patients with intact ACL, and it was reported that 4.9° value could be the optimal threshold value and could be 93% sensitive and 80% specific in predicting the possibility of ACL tear (16). In the present study, the FTRA value in the ACL-R group was found significantly higher than in the ACL-I group. The *ROC-Curve* analysis results showed that if the FTRA value was $> 3.45^\circ$, this parameter could be 73% sensitive and 72% specific in predicting the possibility of ACL tear. On the other

hand, the *Odds Ratio* analysis results revealed that the probability of the ACL tear could be more than a six-fold increase in patients with an FTRA value $> 3.45^\circ$. In addition, the *Logistic Regression* analysis results suggested that the FTRA value may be the best parameter to predict the diagnosis of the ACL tear, preoperatively. On the other hand, since the FTRA value is an angle value, it was thought that it would be easier to use in daily practice compared to the length values, and its measurement would be less affected by the differences between the systems than the length values.

At the end of this study, it was found that the amount of ATT, PCLA, and FTRA values could be used as predictive markers in differentiating the patient group with ACL tear from individuals with ACL intact. Among these three values, FTRA and PCLA values had the highest sensitivity and specificity ratios in predicting ACL injury. Thus, it was concluded that the three values studied, especially FTRA, could be used in the patient group with suspected anterior cruciate ligament damage and in whom a definitive diagnosis could not be reached, especially in the primary findings of ACL tear on MR images. As a result, it was suggested that the FTRA value, which had better result than the other two values, and the threshold value of this angle, could be kept in mind and used routinely in daily practice in predicting ACL tear.

Limitations

This study had some limitations. *Firstly*, this study was a retrospective case-control study. For this reason, sufficient information could not be reached about the occupational characteristics, relations with sports, and education levels of the individuals, and therefore, the etiological causes of ACL injury could not be clearly revealed in this study. However, at the end of the study, it was found that most of the patients with ACL injuries were male, and it was thought that this difference might be due to the fact that the individuals probably engaged in professional and amateur sports activities may be predominantly male gender (12). *Secondly*, healthy individuals and their MR images could not be included in this study. For this reason, the results of ATT, PCLA, and FTRA values evaluated in healthy subjects could not be revealed. However, in this study, diagnostic arthroscopy, which is the gold standard method for diagnosing ACL tear, was used to establish the patient and control group. To the best of our knowledge, this is the first study in the literature to exclude patients with injuries of other anatomical structures that will contribute to the rotational stability of the knee, and whose injury status was determined using arthroscopy. *Thirdly*, patients with damaged posterolateral corner structures and anterolateral ligaments that contribute to rotational stability, except for the ACL, were not included in this study. Furthermore, because the other secondary findings such as the deep lateral femoral notch finding, bone contusion, and segment fracture could not give us a numerical value, they were not included in this study, and

therefore, only these three parameters were examined in the study. *Finally*, the results of this study could not provide an answer as to whether the high FTRA value in the ACL-R group was an etiological cause of ACL injury or the result of ACL tear. However, when the current correlation analysis results were evaluated in this study, it was thought that the FTRA value increased as a result of the biomechanical changes that occurred after ACL tear due to the interrelationship of the findings. It was thought that an answer to this question could be found in future studies created with contralateral knee MR imaging.

CONCLUSIONS

It was found that the amount of ATT, PCLA, and FTRA values could be used as predictive markers in differentiating the patients with ACL tear from individuals with intact ACL. Among these three values, FTRA and PCLA values had the highest sensitivity and specificity ratios in predicting ACL injury. As a result, it was argued that PCLA and especially FTRA threshold values could be the best predictors for the diagnosis of the ACL injury preoperatively, and therefore, they could be used routinely in practice.

References

1. Barrack RL, Bruckner JD, Kneisl J, Inman WS, Alexander AH. The outcome of nonoperatively treated complete tears of the anterior cruciate ligament in active young adults. *Clin Orthop Relat Res.* 1990;259:192–199.
2. Chan WP, Peterfy C, Fritz RC, Genant HK. MR diagnosis of complete tears of the anterior cruciate ligament of the knee: importance of anterior subluxation of the tibia. *AJR Am J Roentgenol.* 1994;162:355–360. doi: 10.2214/ajr.162.2.8310927.
3. Gentili A, Seeger LL, Yao L, Do HM. Anterior cruciate ligament tear: indirect signs at MR imaging. *Radiology.* 1994;193:835–840. doi: 10.1148/radiology.193.3.7972834.
4. Gianotti SM, Marshall SW, Hume PA, Bunt L. Incidence of anterior cruciate ligament injury and other knee ligament injuries: a national population-based study. *J Sci Med Sport.* 2009;12:622–627. doi: 10.1016/j.jsams.2008.07.005.
5. Hewett TE, Myer GD, Ford KR, Heidt RS Jr, Colosimo AJ, McLean SG, van den Bogert AJ, Paterno MV, Succop P. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med.* 2005;33:492–501.
6. Kaeding CC, Léger-St-Jean B, Magnussen RA. Epidemiology and diagnosis of anterior cruciate ligament injuries. *Clin Sports Med.* 2017;36:1–8. doi: 10.1016/j.csm.2016.08.001.
7. Kalegowda A, Ahmed J, Mehetri G. Anterior translation of the tibia at MR imaging as a predictor of degree of anterior cruciate ligament tear. *IJARS.* 2018;7:RO12–RO16.
8. Lee K, Siegel MJ, Lau DM, Hildebolt CF, Matava MJ. Anterior cruciate ligament tears: MR imaging-based diagnosis in a pediatric population. *Radiology.* 1999;213:697–704. doi: 10.1148/radiology.213.3.r99dc26697.
9. McCauley TR, Moses M, Kier R, Lynch JK, Barton JW, Jokl P. MR diagnosis of tears of anterior cruciate ligament of the knee: importance of ancillary findings. *AJR Am J Roentgenol.* 1994;162:115–119. doi: 10.2214/ajr.162.1.8273648.
10. Miyasaka KC, Daniel D, Stone ML, Hirshman P. The incidence of knee ligament injuries in general population. *Am J Knee Surg.* 1991;4:3–9.
11. Ozkan I, Cullu E, Savk O, Aydogdu S, Alparslan B. Akut ve kronik ön çapraz bağ lezyonlarında sekonder manyetik rezonans görüntüleme bulguları. *Acta Orthop Traumatol Turc.* 2000;34:28–33.
12. Parkkari J, Pasanen K, Mattila VM, Kannus P, Rimpelä A. The risk for a cruciate ligament injury of the knee in adolescents and young adults: a population-based cohort study of 46 500 people with a 9 year follow-up. *Br J Sports Med.* 2008;42:422–426. doi: 10.1136/bjsm.2008.046185.
13. Samitier G, Marciano AI, Alentorn-Geli E, Cugat R, Farmer KW, Moser MW. Failure of Anterior Cruciate Ligament Reconstruction. *Arch Bone Jt Surg.* 2015;3:220–240.
14. Vahey TN, Hunt JE, Shelbourne KD. Anterior translocation of the tibia at MR imaging: a secondary sign of anterior cruciate ligament tear. *Radiology.* 1993;187:817–819. doi: 10.1148/radiology.187.3.8497637.
15. Van Dyck P, De Smet E, Veryser J, Lambrecht V, Gielen JL, Vanhoenacker FM, Dossche L, Parizel PM. Partial tear of the anterior cruciate ligament of the knee: injury patterns on MR imaging. *Knee Surg Sports Traumatol Arthrosc.* 2012;20:256–61. doi: 10.1007/s00167-011-1617-7.
16. Vassalou EE, Klontzas ME, Kouvidis GK, Matalliotaki PI, Karantanas AH. Rotational knee laxity in anterior cruciate ligament deficiency: an additional secondary sign on MRI. *AJR Am J Roentgenol.* 2016;206:151–154. doi: 10.2214/AJR.15.14816.

Corresponding author:

Furkan Soy, MD
Kahramankazan State Hospital
Department of Orthopaedics and Traumatology
Ankara, Turkey
E-mail: dr.furkansoy@gmail.com