



# Is medial or lateral localization of osteochondral lesions of talus related to foot angles?

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Although the etiology of osteochondral lesions of the talus (OLTs) is multifactorial, they are mostly trauma-related, and a significant percentage of OLTs are non-traumatic.<sup>[1,2]</sup> The OLTs usually involve the medial and lateral corners of the talus.<sup>[3]</sup> Özal et al.,<sup>[4]</sup> on the other hand, examined the relationship between foot angles and OLTs in their study and found a significant relationship between OLTs and lateral talocalcaneal angle (LTCA). Boz et al.<sup>[5]</sup> showed that increased calcaneal inclination angle (CIA) and LTCA were related to OLTs; however, they did not differentiate between medial and lateral localization in their study. These studies support that foot alignment may be one of the etiological factors of OLTs in addition to trauma, hereditary factors,

## ABSTRACT

**Objectives:** This study aims to examine the relationship between foot angles and the presence and localization of osteochondral lesions of the talus (OLTs).

**Patients and methods:** Between January 2014 and January 2019, a total of 152 patients with a diagnosis of medial OLTs (95 males, 57 females; mean age: 28.8±6.4 years; range, 18 to 40 years), 51 patients with a diagnosis of lateral OLTs (36 males, 15 females; mean age: 27.1±6.2 years; range, 18 to 39 years), and 114 patients without known foot-ankle trauma as the control group (56 males, 58 females; mean age: 29.0±6.1 years; range, 18 to 40 years) were included. Magnetic resonance imaging and radiographs of each group were analyzed retrospectively. Lateral talocalcaneal angle (LTCA), calcaneal inclination angle (CIA), Böhler angle (BA), and Gissane angle (GA) were measured on the images and the values were compared among the groups.

**Results:** The CIA had a significant relationship with the localization ( $p<0.001$ ). It was higher in patients with OLTs and had an effect on localization. The mean CIA was 26.6°±3.9° in the medial OLTs group, 23.0°±3.5° in the lateral OLTs group, and 18.5°±3.6° in the control group. There was a significant difference in the LTCA between the control and OLTs groups ( $p<0.001$ ). The LTCA was higher in patients with OLTs, but had no effect on localization. The mean LTCA was 41.1°±4.2° for medial OLTs, 41.3°±4.2° for lateral OLTs, and 35.7°±6.8° for the controls. No significant relationship was found for BA and GA among the three groups.

**Conclusion:** Factors affecting the localization of OLTs are still not fully understood. However, foot morphology seems to play a role in determining medial or lateral localization. The LTCA is not related to the localization of OLTs; however, an increased LTCA may be related to the occurrence of OLTs. Increased CIA may be related to both OLTs localization and OLTs occurrence.

**Keywords:** Calcaneal inclination, foot angles, lateral talocalcaneal angle, osteochondral lesions, talus.

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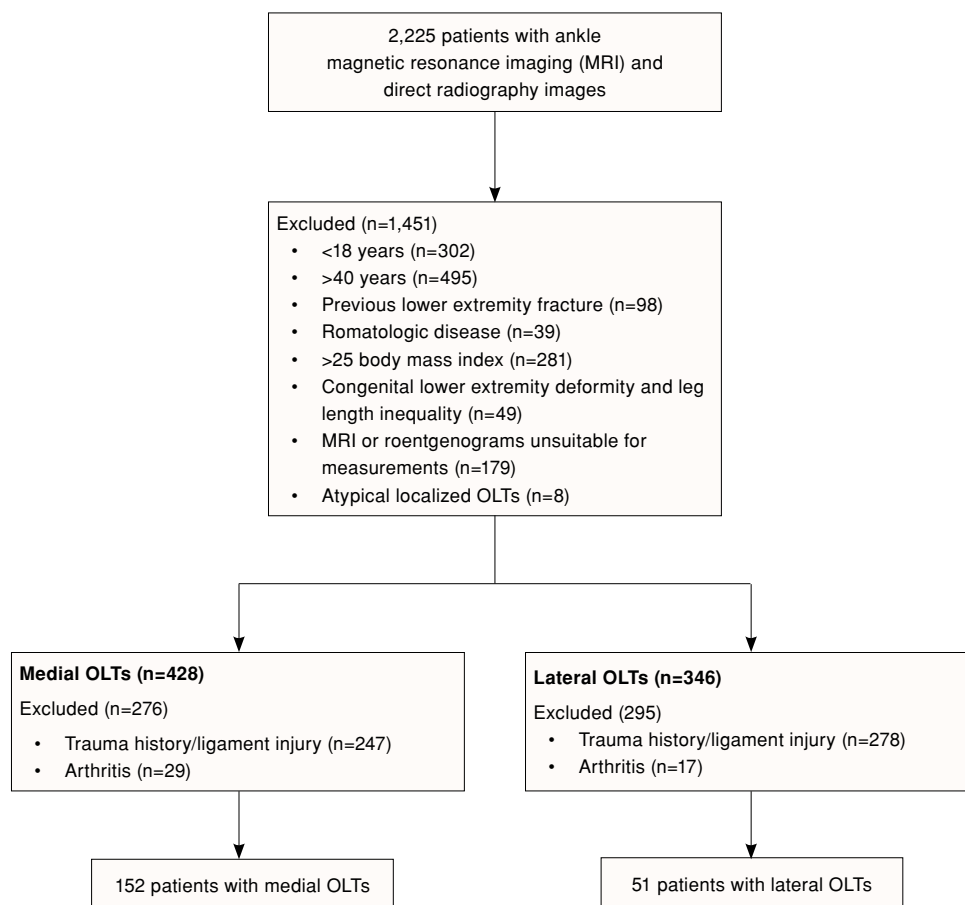
and congenital malformations of cartilage and subchondral bone. The CIA, LTCA, Böhler angle (BA) and Gissane angle (GA) are the angles measured on radiographs and are helpful parameters in diagnosing deformities such as hindfoot varus, congenital talipes equinovarus, and pes cavus.<sup>[4]</sup>

To the best of our knowledge, there is no study examining the relationship between the medial or lateral localization of OLTs and foot angles in the literature. In the present study, we hypothesized that foot angles might affect the medial or lateral localization of OLTs. We, therefore, aimed to examine the angles between non-traumatic medial and lateral OLTs and foot angles.

### PATIENTS AND METHODS

This single-center, retrospective study was conducted at Necmettin Erbakan University, Department of Orthopedics and Traumatology, between January 2014 and January 2019. Magnetic resonance imaging

(MRI) and direct radiography images of symptomatic OLT patients with 152 medial (95 males, 57 females; mean age: 28.8±6.4 years; range, 18 to 40 years) and 51 lateral localizations (36 males, 15 females; mean age: 27.1±6.2 years; range, 18 to 39 years) among 2,225 patients with ankle pain were reviewed. Exclusion criteria were as follows: patients under 18 years of age and over 40 years of age, having a history of major trauma, previous lower extremity fracture, previous lower extremity surgery, lower extremity malalignment (i.e., patients with lateral distal tibial angle values outside the range of 86° to 92°) patients with any limitation of movement in the knee and hip and visual disturbances such as pronounced varus, valgus, recurvatum, procurvatum, or flexion contracture in the systemic lower extremity examination), ankle ligament damage, ankle instability, steroid use, neuromuscular disease, hematological disease, congenital diseases, and patients with a body mass index above 25 kg/m<sup>2</sup>. In addition, throughout the study period, 114 patients



**FIGURE 1.** Study flowchart.  
OLTs: Osteochondral lesions of the talus.

(56 males, 58 females; mean age:  $29.0 \pm 6.1$  years; range, 18 to 40 years) who were admitted to the orthopedics and traumatology outpatient clinic with ankle pain, but did not have any pathology in their imaging and physical examination were included as the control group. Ankle radiographs of all patients were suitable for the measurement of parameters, weight-bearing and with a clear view of the ankle joint line (Figure 1).

The BA was measured by the intersection of the line passing through the highest point of the posterior superior calcaneus and the highest point of the subtalar joint and the two lines passing through the highest point of the anterior process of the talus and the highest point of the subtalar joint (Figure 2).<sup>[6]</sup>

The CIA was measured between the line extending from the inferior border of the calcaneocuboid joint to the posterior inferior of the calcaneus and the line extending from the inferior border of the fifth metatarsal head to the posterior inferior of the calcaneus (Figure 2).<sup>[7]</sup> The normal CIA value range is  $20^\circ$  to  $30^\circ$ . Values above  $30^\circ$  indicate moderate pes cavus, whereas values above  $40^\circ$  indicate severe pes cavus.<sup>[8]</sup>

The LTCA was measured as the angle between the mid-talar axis and the calcaneal inclination axis

on the radiographs of the weight-bearing lateral foot (Figure 2).<sup>[8]</sup>

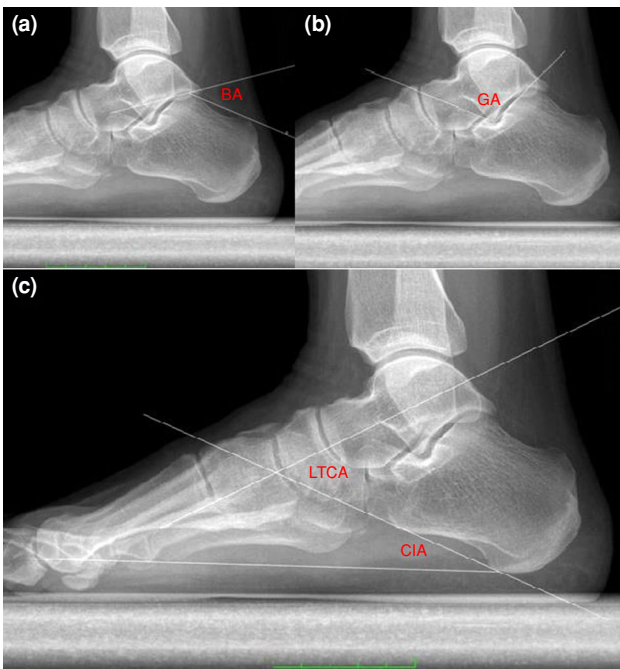
The localization of OLTs was classified by two observers, as described by Raikin et al.<sup>[9]</sup> (Figure 3). The normal LTCA value range is  $35^\circ$  to  $50^\circ$ .<sup>[8]</sup>

The CIA, LTCA, BA, and GA were performed blindly to each other in two separate sessions by two observers (senior orthopedists) on weight-bearing lateral foot lateral radiographs of patients with medial and lateral OLTs detected in standard ankle MRIs.

**Statistical analysis**

The study power and sample size calculation were performed using the G\*Power version 3.1.9.4 software (Heinrich-Heine-Universität, Düsseldorf, Düsseldorf, Germany). It was necessary to have at least 64 patients in each group in the calculation by accepting the effect size as 0.5, alpha 5%, and power at least 80%. The power of the study was rechecked after statistical analysis (post-hoc).

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). The reliability of measurements made by the two blinded observers was analyzed using the intraclass correlation coefficient (ICC). Descriptive data were presented in mean  $\pm$  standard deviation (SD), median (min-max) or number and frequency, where applicable. The normality of the data was analyzed with the Shapiro-Wilk test. One-way analysis of variance (ANOVA) and t-test were used to compare independent variables. The receiver operating characteristics (ROC) analysis was used to calculate sensitivity and specificity and determine



**FIGURE 2.** Angles measured on weight-bearing lateral foot radiography (a) Böhler angle (BA), (b) Gissane angle (GA), (c) lateral talocalcaneal angle (LTCA), and calcaneal inclination angle (CIA).

		Anterior		
		7	1	3
Medial		76	3	44
		69	1	4
		Posterior		
				Lateral

**FIGURE 3.** Distribution of the OLTs localization. OLTs: Osteochondral lesions of the talus.

the cut-off levels with the area under the curve (AUC). A p value of <0.05 was considered statistically significant with 95% confidence interval (CI). The post-hoc (Tukey) tests with Bonferroni correction were used to make pairwise comparisons, decreasing the p threshold to <0.0167.

**RESULTS**

The ICC ranged from 0.85 to 0.93 for all measurements, indicating high within-observation reliability. The power of the study results was rechecked after statistical analysis (post-hoc analysis).

There was no significant difference in the age and sex among the groups (p=0.23 and p=0.42, respectively) (Table I).

In medial OLTs patients, the right side was affected in 71 and the left in 81. In lateral OLTs patients, the right side was affected in 30 and the left in 21. There was no significant difference in the side affected between the medial or lateral localizations (p=0.19) (Table I). In the control group, the imaging was right-sided in 53 and left-sided in 61.

Considering the CIA values, there was a significant difference among the groups (p<0.001) (Table II). When the groups were compared among themselves in pairs, there was a significant difference among them (p<0.001) (Tables II and III). In the medial OLTs group, the mean CIA was 26.6±3.9° (range, 17.1° to 34.2°) (95% CI: 25.5-27.7) (Tables II and III, Figure 4). In the lateral OLTs group, the mean CIA was 23.0±3.5° (range, 16.9° to 29.4°) (95% CI: 21.9-24.1) (Tables II and III, Figure 4). In addition, the mean CIA in the control group was 18.5±3.6° (range, 10.4° to 27.1°) (95% CI: 17.5-19.4) (Tables II and III, Figure 4). The mean CIA was

higher in patients with OLTs and had an effect on localization. The power in the comparison of the control group and the medial OLTs was 100% (d=2.12). The power for the lateral OLTs comparison with the control group was 100% (d=1.23). The power for the medial OLTs comparison with the lateral OLTs was 99.9% (d=0.94) (Table III).

The most optimal cut-off value in the ROC analysis performed for CIA between the control group and the lateral OLTs group was 20.3°, and this value showed 72.7% sensitivity and 73.7% specificity (likelihood ratio [LR]=2.76). The most optimal cut-off value in the ROC analysis for CIA between the lateral and medial OLTs groups was 24.5°, giving a sensitivity of 66.7% and specificity of 66.1% (LR=2.06) (Figure 5). Regardless of medial or lateral distinction, all patients with OLTs and the control group were compared with the ROC analysis for CIA. A cut-off value of 21.05° showed 81.5% sensitivity and 75.4% specificity (LR=3.31). A cut-off value of 24.1 showed 55.4% sensitivity and 94.7% specificity (LR=10.53, AUC: 0.875).

Considering the LTCA values, there was a significant difference among the groups (p<0.001) (Table II). When the groups were compared among themselves, the LTCA values of the control group were significantly lower than those of the medial OLTs and lateral OLT groups (p<0.001 for both) (Tables II and III). There was no significant difference in the LTCA between the medial OLTs and lateral OLTs groups (p=0.99) (Tables II and III). In the medial OLTs group, the mean LTCA was 41.1±4.2° (range, 30.7° to 49.4°) (95% CI: 39.9-42.3) (Table III, Figure 6). In the lateral OLTs group, the mean LTCA was 41.3±4.2° (range, 29° to 47.2°) (95% CI: 39.3-41.8) (Table III, Figure 6). The mean LTCA in the control group was 35.7±6.8° (range, 21.5° to 48.9°) (95% CI: 33.9-37.6)

**TABLE I**  
Demographic characteristics of patients

	Medial OLTs (n=152)			Lateral OLTs (n=51)			Control group (n=114)			p
	n	Mean±SD	Min-Max	n	Mean±SD	Min-Max	n	Mean±SD	Min-Max	
Age (year)		28.8±6.4	18-40		27.1±6.2	18-39		29.0±6.1	18-40	0.23
Sex										0.42
Male	95			36			56			
Female	57			15			58			
Side										0.19
Right	71			30			53			
Left	81			21			61			

OLT: Osteochondral lesions of the talus; SD: Standard deviation.

**TABLE II**  
Table showing the intergroup comparison of CIA, LTCA, BA, and GA

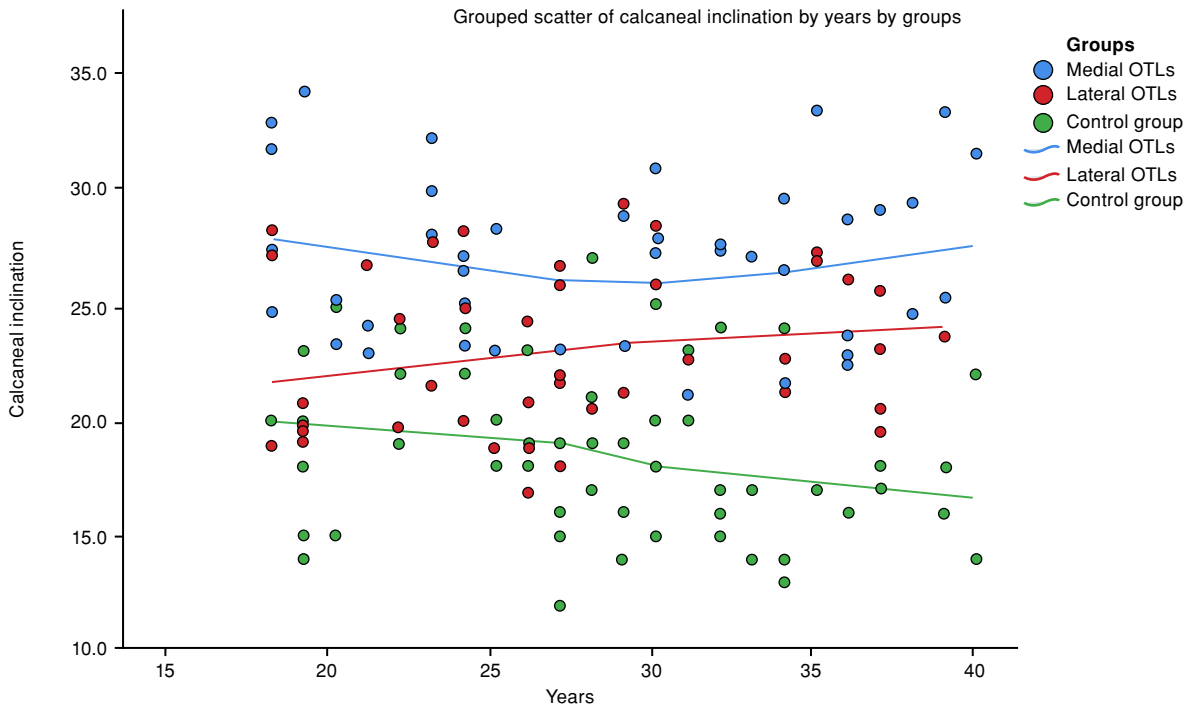
Parameter	Medial OLTs					Lateral OLTs					Control group				
	Mean±SD	Median	Min-Max	95% CI	p	Mean±SD	Median	Min-Max	95% CI	p	Mean±SD	Median	Min-Max	95% CI	p
CIA (°)	26.6±3.9	27.1	17.1-34.2	25.5-27.7	<0.001*	23.0±3.5	22.7	16.9-29.4	21.9-24.1	<0.001*	18.5±3.6	18.0	10.4-27.1	17.5-19.4	<0.001*
LTCA (°)	41.1±4.2	41.3	30.7-49.4	39.9-42.3	<0.001*	41.3±4.2	40.6	29.0-47.2	39.3-41.8	<0.001*	35.7±6.8	36.0	21.5-48.9	33.9-37.6	<0.001*
BA (°)	32.9±6.5	32.1	19.2-46.9	31-34.9	0.91	33.4±7.2	32.4	20.4-47.6	31.1-35.6	0.91	33.4±4.9	34.0	22.0-46.1	32.1-34.7	0.91
GA (°)	112.1±7.4	111.3	98.8-129.6	109.9-114.2	0.76	111.3±8.1	112.2	96.4-132.4	108.9-113.8	0.76	112.5±8.5	113.2	91.3-131.1	110.2-114.8	0.76

CIA: Calcaneal inclination angle; LTCA: Lateral talocalcaneal angle; BA: Böhler angle; GA: Gissane angle; OLT: Osteochondral lesions of the talus; CI: Confidence interval.

**TABLE III**  
Table showing pairwise comparisons of medial OLTs, lateral OLTs, and control groups for CIA, LTCA, BA, and GA

Parameter	Medial OLTs-Lateral OLTs				Medial OLTs-Control group				Lateral OLTs-Control group			
	MD±SE	95% CI of MD	Power (effect size d)	p	MD±SE	95% CI of MD	Power (effect size d)	p	MD±SE	95% CI of MD	Power (effect size d)	p
CIA	3.54±0.53	2.50-4.59	99.9% (0.94)	<0.001*	8.11±0.51	7.01-9.10	100% (2.12)	<0.001*	4.56±0.50	3.54-5.55	100% (1.23)	<0.001*
LTCA	0.54±0.61	-0.66-1.75	<80% (0.06)	<0.99	5.27±0.8	3.75-6.86	100% (1.28)	<0.001*	4.73±0.83	3.09-6.37	100% (1.32)	<0.001*
BA	-0.41±1.0	-2.44-1.60	<80%	0.99	-0.47±0.79	-2.03-1.07	<80%	0.99	-0.06±0.86	-1.76-1.63	<80%	0.99
GA	0.75±1.1	-1.48-3.0	<80%	0.99	-0.4±1.1	-2.58-1.76	<80%	0.99	-1.16±1.17	-3.48-1.15	<80%	0.917

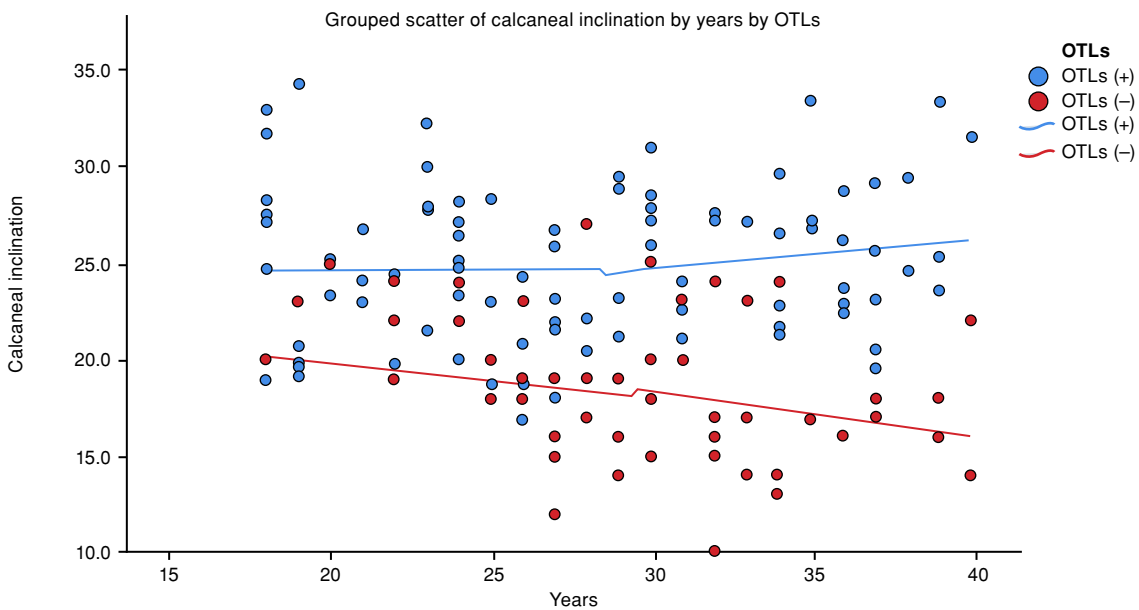
OLTs: Osteochondral lesions of the talus; CIA: Calcaneal inclination angle; LTCA: Lateral talocalcaneal angle; BA: Böhler angle; GA: Gissane angle; MD±SE: Mean difference ± standard deviation; CI: Confidence interval.



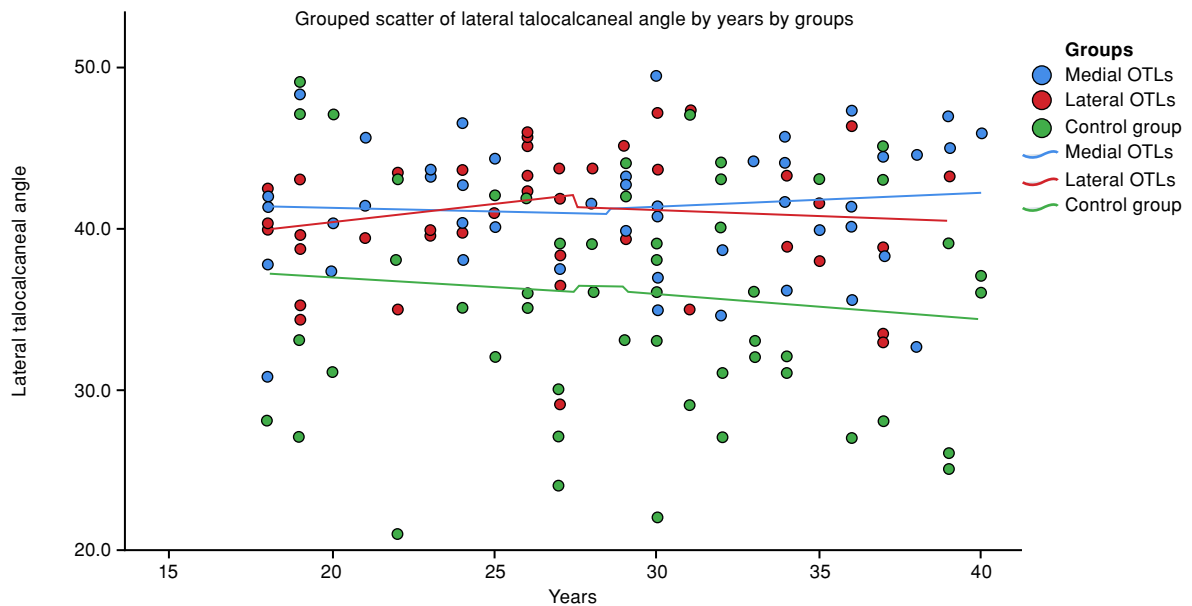
**FIGURE 4.** Graph showing the distribution of CIA and age by medial OLTs, lateral OLTs, and control groups. CIA: Calcaneal inclination angle; OLTs: Osteochondral lesions of the talus.

(Table III, Figure 6). The LTCA was higher in patients with OLTs but had no effect on localization. In addition, the power in the comparison of the control group and the medial OLTs was 100% (d=1.28).

The power for the lateral OLTs comparison with the control group was 100% (d=1.32). Finally, the power for medial and lateral OLTs groups' comparison was <0.80.



**FIGURE 5.** Graph showing the CIA and age distribution in patients and control groups with OLTs without distinction of medial or lateral. CIA: Calcaneal inclination angle; OLTs: Osteochondral lesions of the talus.



**FIGURE 6.** Graph showing the distribution of LTCA and age by medial OLTs, lateral OLTs, and control groups. LTCA: Lateral talocalcaneal angle; CIA: Calcaneal inclination angle; OLTs: Osteochondral lesions of the talus.

All patients with OLTs and the control group, regardless of medial or lateral distinction, were compared with the ROC analysis for LTCA, and the most optimal cut-off value showed a sensitivity of 69.6% and a specificity of 68.4% (LR=2.20) at 39.2°. When the cut-off value was taken as 44.1, it showed 21.7% sensitivity and 91.2% specificity (LR=2.47, AUC: 0.720).

The CIA and LTCA were significantly positive correlated ( $r=0.458$ ,  $p<0.001$ ). In the medial OLTs group, there was no significant difference between the anteromedial centromedial and posteromedial subgroups in terms of both CIA and LTCA ( $p=0.62$  and  $p=0.91$ , respectively). In the lateral OLTs group, there was no significant difference between the anterolateral, centrolateral and posterolateral subgroups in terms of both CIA and LTCA ( $p=0.78$  and  $p=0.96$ , respectively).

When the three groups were compared in BA, there was no significant relationship between them ( $p=0.91$ , Table II). In the medial OLTs group, the mean BA was  $32.9\pm 6.5^\circ$  (range,  $19.2^\circ$  to  $46.9^\circ$ ) (95% CI: 31.1-34.9) (Table III). The mean BA in the lateral OLTs group was  $33.4\pm 7.2^\circ$  (range,  $20.4^\circ$  to  $47.6^\circ$ ) (95% CI: 31.1-35.6) (Table III). In addition, the mean BA in the control group was  $33.4\pm 4.9^\circ$  (range,  $22^\circ$  to  $46.1^\circ$ ) (95% CI: 32.1-34.7) (Table III). The power between pairwise comparisons were  $<80\%$  (Table III).

When the three groups were compared in terms of GA, they showed no significant relationship ( $p=0.76$ , Table II). The mean GA in the medial OLTs group was  $112.1\pm 7.4^\circ$  (range,  $98.8^\circ$  to  $129.6^\circ$ ) (95% CI: 109.9-114.2) (Table III). In the lateral OLTs group, the mean CIA was  $111.3\pm 8.1^\circ$  (range,  $96.4^\circ$  to  $132.4^\circ$ ) (95% CI: 108.9-113.8) (Table III). In addition, the mean CIA in the control group was  $112.5\pm 8.5^\circ$  (range,  $91.3^\circ$  to  $131.1^\circ$ ) (95% CI: 110.2-114.8) (Table 3). Power between pairwise comparisons were  $<80\%$  (Table III).

## DISCUSSION

In the present study, we investigated the angles between non-traumatic medial and lateral OLTs and foot angles. The main finding of this study was that increased CIA and LTCA values were related to OLTs and that the increase in CIA was related to the medial and lateral localization of OLTs.<sup>[10]</sup>

In a recent study including 55 patients with OLTs and 118 controls, Boz et al.<sup>[5]</sup> found significantly higher CIA and LTCA values in the OLTs group (CIA:  $23.5^\circ$  vs.  $17.1^\circ$ , LTCA:  $40.3^\circ$  vs.  $23.5^\circ$ , respectively). The results obtained by Boz et al.<sup>[5]</sup> support the results of our study. In addition, the aforementioned authors showed that Achilles tendinitis was more common in the OLTs group with high CIA and LTCA, indicating that foot

alignment may also be associated with pathologies other than OLT. However, there was no data on the localization of OLTs in their study. In our study, we observed that increased LTCA might have an effect on the formation of OLTs, but not on their localization. Increased CIA was related to OLTs localization. The CIA values between 20.3° and 24.5° were related to an increased risk of lateral OLTs, whereas values greater than 24.5° were related to an increased risk of medial OLTs. Özal et al.<sup>[4]</sup> compared CIA, LTCA, BA and GA on 25 OLTs and 29 control patient groups. Their study reported that LTCA increased significantly ( $p=0.032$ ) in patients with OLTs. In this respect, our study and Özal et al.'s<sup>[4]</sup> study support each other. Özal et al.<sup>[4]</sup> found in their study that there was no significant relationship between the groups in terms of CIA. In our study, CIA was significantly higher in the patient group with OLTs. In this respect, the two studies do not support each other. Indeed, patients with medial and lateral OLTs in our study significantly differed among themselves regarding CIA, but in the study of Özal et al.,<sup>[4]</sup> no distinction was made regarding medial and lateral localization of OLTs. Yang et al.,<sup>[11]</sup> in their daily practice, found that the severity of OLTs increased in some of the patients who underwent calcaneal osteotomy due to lateral malleolus impingement in feet with valgus deformity, although the symptoms regressed, this was attributed to the increase in the hindfoot varus caused by osteotomy. Then, the distal tibial varus syndrome in these patients were described. Their study divided the distal tibial varus syndrome into three groups by measuring the distal tibial anterior surface angle (TAS) and distal tibial tilt angle (TTA) on anteroposterior X-ray. They reported that, in type 1 (non-reactive type) group, there was pain in the lateral side on examination, no pathology was observed on MRI, and the patients were treated conservatively. Additionally, edema around the peroneal tendon at the level of the calcaneus on MRI in type 2 (proliferative type) was reported. Finally, in the type 3 group (osteochondral lesion type), 27 of 28 patients had medial OLTs, and one had lateral OLTs. Based on these results, they reported that OLTs originated from the hindfoot varus. There was no significant difference among the three groups regarding TAS and TTA. The medial OLTs group in our study and the type 3 group in Yang et al.'s<sup>[11]</sup> study show similarities. From this point of view, it can be thought that OLTs that occur with the predictive effect of hindfoot varus may be related not only to distal tibial alignment abnormalities, but also to foot alignment abnormalities.

In previous studies, it has been shown that cavus deformities are associated with increased CIA, and they result in hindfoot varus with the addition of the secondary inverter effect of Achilles to the calcaneal inversion, which occurs due to the superiority of the medial muscle group to the peroneal muscle group in cavus deformities.<sup>[8,12]</sup> It has also been demonstrated that the subtalar joint, which is sufficiently mobile, has a compensatory function to come to eversion to provide a plantigrade gait and to normalize the hindfoot varus.<sup>[8]</sup> However, the subtalar joint, which does not have sufficient mobility, cannot show the compensatory effect to prevent the hindfoot varus; therefore, hindfoot alignment results in varus, and prolonged posterior foot varus causes contracture of the medial soft tissues, leading to increased anteromedial ankle joint pressure.<sup>[8,13]</sup> If this data is interpreted together with the results related to CIA in our study, CIA values in the lateral OLTs group, which is between the control group and the medial OLTs group, may cause lateral OLTs by increasing the lateral pressure with the compensatory eversion effect of the subtalar joint to prevent varus. On the other hand, in the medial OLTs group with the highest CIA, the subtalar joint's compensatory effect is insufficient, and the hindfoot varus is relatively dominant; therefore, medial OLTs may occur. However, despite this hypothesis, we believe that the effect of foot alignment on OLTs has not been clear yet, since it is not known how mobile the subtalar joint is and how much compensatory effect it has on the hindfoot varus.

Krause et al.,<sup>[14]</sup> in their biomechanical study on cadavers, placed 15° and 30° custom-made aluminum wedges on the dorsal side of the first tarsometatarsal joint and fixed them with tubular plates to create cavovarus foot models. In the serial pressure measurements, they made at the tibiotalar joint, the mean pressure was significantly higher, and the pressure center was shifted significantly anteromedially in the foot model placed on the 30° wedge compared to the control group, while they could not find a significant increase in pressure and displacement in the 15° wedge group's pressure center. Krause et al.,<sup>[14]</sup> on the other hand, did not cause any significant pressure increase and medial displacement of the pressure center with the first 15° wedge they placed on the tarsometatarsal joint, but when the wedge angle was increased by 15°, the increase in tibiotalar pressure and the medial displacement of the central pressure increased disproportionately, resulting in significant changes. In our study, the group with the highest CIA and LTCA values, which



were shown to be associated with the cavovarus, was the medial OTLs group. In these aspects, the two studies support each other. Thus, increased CIA and LTCA values, which increase the tendency of a normal foot to be a cavovarus foot, may move the pressure center in the talotibial joint anteromedially, *albeit* in small amounts, and may increase the risk of medial OTLs. In addition, the mean CIA value of the lateral OTLs group in our study was between the control and medial OTLs groups. They do not support each other with the study of Krause et al.<sup>[14]</sup> We believe that the reason for this may be related to the long-term subtalar joint compensation and/or lateral ligament adaptations in naturally occurring mild cavovarus feet, unlike the cavovarus foot obtained in the cadaver model, as mentioned in the study of Krause et al.<sup>[14]</sup>

Although the clinical significance of this basic radiological study is unclear, it is the first in the literature to show that CIA can be a predictive factor in affecting the etiologies of medial and lateral non-traumatic OLTs with separate mechanisms. We believe that biomechanical studies evaluating the subtalar compensation mechanism, medial and lateral tibiotalar joint pressures on osteotomy cadaver models are needed to further elucidate the etiology of non-traumatic OTLs. The retrospective nature of this study is a limitation. Another limitation is that although the trauma history of the patients was questioned in detail, the patients could not remember the traumas they experienced.

In conclusion, factors affecting the localization of OLTs are still not fully understood. However, foot morphology seems to play a role in determining medial or lateral localization. The LTCA is not related to the localization of OLTs; however, an increased LTCA may be related to the occurrence of OLTs. Increased CIA may be related to both OLTs localization and OLTs occurrence.

**Ethics Committee Approval:** The study protocol was approved by the Necmettin Erbakan University Pharmaceutical and Non-Medical Device Research Ethics Committee (date: 16.09.2022, no: 160). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

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