

Risk Factors for Osteochondral Lesions and Osteophytes in Chronic Lateral Ankle Instability

A Case Series of 1169 Patients

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Background: Osteochondral lesions (OCLs) and bony impingement are common secondary lesions of chronic lateral ankle instability (CLAI), but the risk factors that predict OCLs and bony impingement are unknown.

Purpose: To analyze the risk factors for the development of OCLs and osteophytes in patients with CLAI.

Study Design: Case-control study; Level of evidence, 3.

Methods: Patients diagnosed with CLAI at our institution from June 2007 to May 2018 were enrolled. The assessed potential risk factors were age, sex, postinjury duration, body mass index, injury side, and ligament injury type (isolated anterior talofibular ligament [ATFL] injury, isolated calcaneofibular ligament [CFL] injury, or concomitant ATFL and CFL injuries). Univariate and multivariate logistic regression analyses were performed to evaluate the association between these factors and the presence of OCLs and osteophytes.

Results: A total of 1169 patients with CLAI were included; 436 patients (37%) had OCLs and 334 (31%) had osteophytes. The presence of OCLs was significantly associated with the presence of osteophytes ($P < .001$). Male sex and older age were significantly associated with the presence of OCLs in the medial and lateral talus. A postinjury duration of 5 years or longer was significantly associated with the presence of OCLs in the medial talus (odds ratio [OR], 1.532; 95% CI, 1.023-2.293; $P = .038$) but not in the lateral talus. ATFL and CFL injuries were both significantly associated with the presence of lateral OCLs. Risk factors for the presence of osteophytes were male sex, older age, postinjury duration 5 years or longer, and CFL injury. Patients with concomitant ATFL and CFL injuries were significantly more likely to have osteophytes than were patients with single-ligament injuries ($P = .018$).

Conclusion: Risk factors for OCLs and osteophytes were postinjury duration of 5 years or longer, older age, and male sex. ATFL injury was associated with the presence of lateral OCLs, whereas CFL injury was associated with the presence of lateral OCLs and osteophytes. Patients with these risk factors should be closely monitored and treated to reduce the incidence of ankle arthritis.

Keywords: chronic lateral ankle instability; postinjury duration; risk factors; osteochondral lesion; osteophytes

Ankle sprain is the most common injury in the athletic and sporting populations and is easily overlooked by both patients and doctors. Although nonoperative treatment of ankle sprains achieves satisfactory outcomes in most patients, up to 40% of patients with a lateral ankle sprain have persistent symptoms, including subjective instability, recurrent sprains, and the development of chronic lateral ankle instability (CLAI).^{13,23}

Patients with CLAI usually have an injured anterior talofibular ligament (ATFL) and/or calcaneofibular ligament (CFL).^{5,11} The loss of these major static lateral ligamentous stabilizers leads to unbalanced loading, causing some patients to develop secondary lesions, including osteochondral lesions (OCLs), osteophytes, intra-articular loose bodies, and intra-articular synovitis,^{6,20} and eventually to develop ankle osteoarthritis.²¹ These secondary lesions are usually associated with poor outcomes and carry an increased risk of arthrodesis or arthroplasty. Patients with intra-articular lesions reportedly have an 8.5-fold higher risk of unsatisfactory outcomes compared with patients

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without these lesions³; furthermore, 68% to 78% of patients with CLAI eventually develop ankle osteoarthritis.^{7,25}

Although OCLs and osteophytes are common lesions in patients with CLAI, there is a paucity of literature about the relationship between ankle injury and the development of posttraumatic ankle arthritis.¹⁴ Thus, it remains unclear which patients with CLAI are at high risk of secondary lesions in the early stages after the initial injury until the development of traumatic arthritis.

The purpose of this study was to analyze the risk factors for the development of OCLs and osteophytes in patients with CLAI. We hypothesized that longer postinjury duration significantly increases the risk of the development of OCLs and osteophytes in the CLAI population. Other factors potentially associated with the development of OCLs and osteophytes were also analyzed, including age, sex, body mass index (BMI), and ligament injury type. The results may help surgeons to identify the appropriate intervention time and identify high-risk CLAI patients who may need more aggressive treatment methods.

METHODS

The present study received institutional review board approval from a local ethics committee. Consecutive patients who were diagnosed with CLAI in our institution from June 2007 to May 2018 were considered for study eligibility. To obtain precise information about the ligament injuries, cartilage lesions, and osteophytes, we included only those patients whose surgical records were available. Other inclusion criteria were history of at least 1 serious ankle sprain; ankle instability persisting longer than 6 months (from first sprain to the surgery); feeling of the previously injured ankle joint “giving way” and/or recurrent sprain (>2 sprains in 6 months) and/or “feelings of instability”; and injury of the lateral ligaments (ATFL and/or CFL). Exclusion criteria were history of surgery of the musculoskeletal structures (ie, bones, joint structures, and nerves) in either lower extremity; history of fracture requiring realignment in either lower extremity; acute injury to the musculoskeletal structures of other lower extremity joints in the previous 3 months and periarticular fractures; and other neuromuscular diseases of the lower extremities.

A total of 1169 patients were included (Figure 1). Patient demographics, medical records, and surgical documents were reviewed in detail; the collected data included sex, age at the time of surgery, BMI, injury side, and postinjury

duration from the first ankle sprain. The severity and location of OCLs and osteophytes were detected by arthroscopy. Chondral lesions were defined through use of the Outerbridge staging system, and lesions that had Outerbridge grade 3 or 4 were recorded as OCLs. Chronic ankle ligament rupture was confirmed during open surgery via the observation of a thickened and relaxed ligament.

Statistics

Binary univariate logistic regression was performed to determine the odds ratios with 95% CIs of sex (dichotomous), age (categorical: <20 years, 20 to <40 years, ≥40 years), postinjury duration (categorical: <12 months, 12 months to <2 years, 2 to <5 years, ≥5 years), BMI (categorical: <18.5 kg/m², 18.5 to <23 kg/m², 23 to <25 kg/m², ≥25 kg/m²), injury side (dichotomous), ATFL injury (dichotomous), and CFL injury (dichotomous) for the presence of OCLs on the talus and tibia. Multivariate logistic regression was performed to analyze the risk factors for the presence of OCLs in the medial and lateral talar domes. Binary univariate and multivariate logistic regression analyses were also performed to calculate the risk factors for the presence of osteophytes. The chi-square test was calculated for the association between OCLs and osteophytes. Statistical analysis was performed with SPSS (version 23; IBM).

RESULTS

The patient characteristics are summarized in Table 1.

Osteochondral Lesions

There were 436 (37%) patients with OCLs on the talus or tibia. Arthroscopy was used to identify 747 chondral lesions or OCLs; of these, 478 (64%) lesions were located on the medial talus, 215 (29%) were located on the lateral talus, and 54 (7%) were located on the tibia. There were 49 (7%) lesions classified as Outerbridge 1; 169 (23%) classified as Outerbridge 2; 95 (13%) classified as Outerbridge 3; and 434 (58%) classified as Outerbridge 4.

Univariate logistic regression analysis revealed that the factors significantly associated with the presence of OCLs on both the talus and the tibia were male sex, older age, overweight (BMI, 23 to <25 kg/m²), obesity (BMI, ≥25 kg/m²), and a longer postinjury duration (≥2 years) (Table 2). Multivariate logistic regression analysis revealed that the factors associated with the presence of OCLs on the medial and

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Ethical approval for this study was obtained from Peking University Third Hospital.

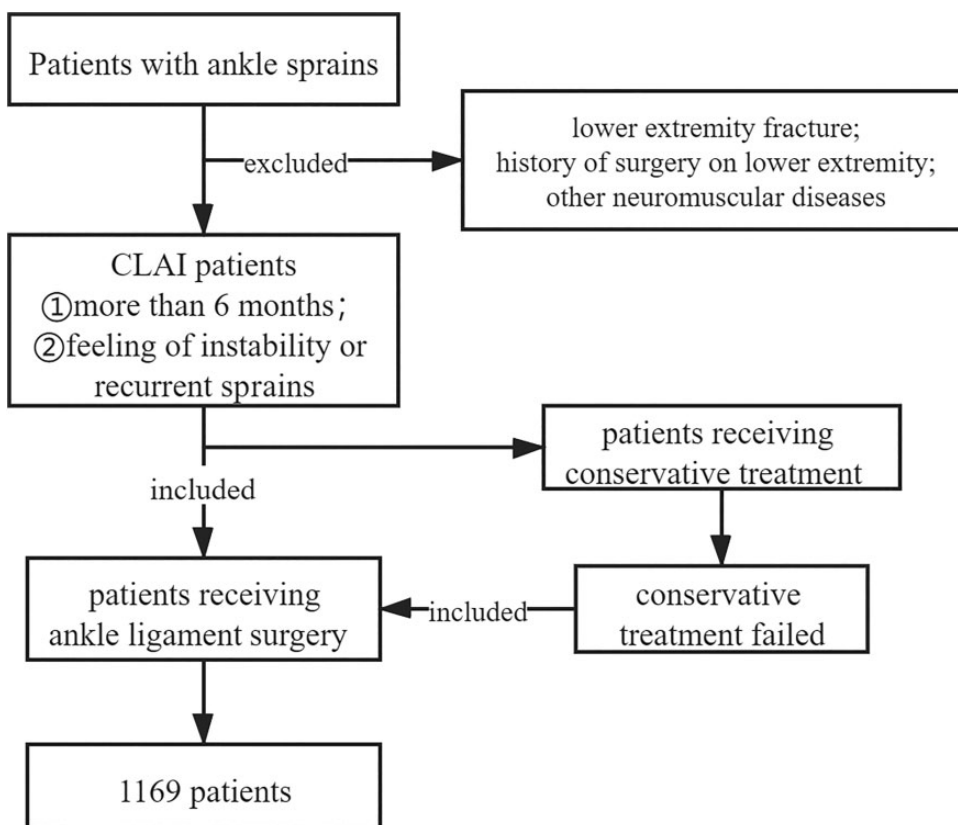


Figure 1. Patient selection diagram. CLAI, chronic lateral ankle instability.

TABLE 1
Patient Characteristics^a

	Overall
Age, y, mean ± SD	30 ± 4
Sex, male/female, n (%)	776 (66)/393 (34)
BMI, kg/m ² , mean ± SD	24.9 ± 3.3
BMI, n (%)	
<18.5 kg/m ²	39 (3)
18.5 to <23 kg/m ²	358 (31)
23 to <25 kg/m ²	233 (20)
≥25 kg/m ²	539 (46)
Side affected, left/right, n (%)	476 (41)/693 (59)
Postinjury duration, mo, mean ± SD	50 ± 30
Postinjury duration, n (%)	
<12 mo	246 (21)
12 mo to <2 y	235 (20)
2 y to <5 y	340 (29)
≥5 y	348 (30)
Ligament injury, n (%)	1169 (100)
Isolated ATFL	309 (26)
Isolated CFL	131 (11)
ATFL and CFL combined	729 (62)

^aATFL, anterior talofibular ligament; BMI, body mass index; CFL, calcaneofibular ligament.

TABLE 2
Univariate Analysis of the Factors Associated With the Presence of Osteochondral Lesions on the Talus and Tibia^a

	OR (95% CI)	P
Male sex	1.618 (1.249-2.096)	<.001
Age		
<20 y	1 ^b	
20 y to <40 y	2.641 (1.764-3.954)	<.001
≥40 y	7.233 (4.537-11.532)	<.001
Postinjury duration		
<12 mo	1 ^b	
12 mo to <2 y	1.268 (0.867-1.856)	.221
2 y to <5 y	1.465 (1.034-2.075)	.032
≥5 y	1.609 (1.140-2.273)	.007
Left side affected	0.948 (0.744-1.207)	.664
BMI		
<18.5 kg/m ²	1 ^b	
18.5 to <23 kg/m ²	1.634 (0.662-4.036)	.287
23 to <25 kg/m ²	3.589 (1.446-8.903)	.006
≥25 kg/m ²	4.975 (2.051-12.069)	<.001
Isolated ATFL injury	0.905 (0.691-1.187)	.472
Isolated CFL injury	0.771 (0.523-1.137)	.189
Combined ATFL and CFL injuries	1.209 (0.945-1.547)	.131

^aBoldface indicates statistical significance. ATFL, anterior talofibular ligament; BMI, body mass index; CFL, calcaneofibular ligament; OR, odds ratio.

^bBaseline value.

TABLE 3
Risk Factors for the Presence of Osteochondral Lesions on the Medial and Lateral Talus^a

	Medial Talus		Lateral Talus	
	OR (95% CI)	P	OR (95% CI)	P
Sex				
Female	1 ^b		1 ^b	
Male	1.617 (1.151-2.271)	.006	1.856 (1.195-2.882)	.006
Age				
<20 y	1 ^b		1 ^b	
20 y to <40 y	1.789 (1.113-2.874)	.016	2.340 (1.209-4.526)	.012
≥40 y	7.787 (4.518-13.419)	<.001	3.532 (1.691-7.375)	.001
Postinjury duration				
<12 mo	1 ^b		1 ^b	
12 mo to <2 y	1.086 (0.689-1.710)	.723	2.019 (1.140-3.577)	.016
2 y to <5 y	1.446 (0.963-2.172)	.075	1.441 (0.833-2.491)	.191
≥5 y	1.532 (1.023-2.293)	.038	1.662 (0.973-2.840)	.063
BMI				
<18.5 kg/m ²	1 ^b		1 ^b	
18.5 to <23 kg/m ²	0.786 (0.302-2.043)	.621	2.015 (0.261-15.583)	.502
23 to <25 kg/m ²	1.090 (0.413-2.876)	.862	5.129 (0.668-39.355)	.116
≥25 kg/m ²	1.591 (0.617-4.103)	.337	4.917 (0.648-37.310)	.123
ATFL injury				
Not involved	1 ^b		1 ^b	
Involved	1.400 (0.882-2.224)	.154	1.973 (1.063-3.664)	.031
CFL injury				
Not involved	1 ^b		1 ^b	
Involved	1.041 (0.757-1.431)	.805	1.612 (1.064-2.441)	.024

^aBoldface indicates statistical significance. ATFL, anterior talofibular ligament; BMI, body mass index; CFL, calcaneofibular ligament; OR, odds ratio.

^bBaseline value.

lateral talus were male sex and older age (Table 3). A post-injury duration of 5 years or longer was associated with the presence of OCLs on the medial talus, whereas lateral OCLs usually developed in the second year after the initial injury (Table 3). Both ATFL and CFL injuries were associated with the presence of lateral OCLs (Table 3).

Osteophytes

Osteophytes were present in 334 (31%) patients. The incidence of osteophytes was 24.9% (77/309) in patients with isolated ATFL injury, 23.6% (31/131) in those with isolated CFL injury, and 31.0% (226/729) in those with both ATFL and CFL injuries. Univariate analysis revealed that the factors associated with the presence of osteophytes were male sex, older age, overweight (BMI, 23 to <25 kg/m²), obesity (BMI, ≥25 kg/m²), prolonged postinjury duration (≥2 years), and the presence of concomitant ATFL and CFL injuries (Table 4). Multivariate logistic regression analysis revealed that the factors associated with the presence of osteophytes were male sex, older age, postinjury duration of 5 years or longer, and CFL injury (Table 5).

Among the 1169 patients with CLAI, 212 had both OCLs and osteophytes. Osteophytes were present in 50% of the patients with OCLs, whereas OCLs were present in 65% of the patients with osteophytes. The presence of OCLs was

TABLE 4
Univariate Analysis of the Factors Associated With the Presence of Osteophytes^a

	OR (95% CI)	P
Male sex	2.743 (2.020-3.724)	<.001
Age		
<20 y	1 ^b	
20 y to <40 y	2.449 (1.593-3.765)	<.001
≥40 y	3.261 (1.998-5.324)	<.001
Postinjury duration		
<12 mo	1 ^b	
12 mo to <2 y	1.140 (0.742-1.752)	.550
2 y to <5 y	1.577 (1.073-2.316)	.020
≥5 y	2.117 (1.454-3.084)	<.001
Left side affected	0.949 (0.733-1.230)	.693
BMI		
<18.5 kg/m ²	1 ^b	
18.5 to <23 kg/m ²	1.692 (0.579-4.942)	.336
23 to <25 kg/m ²	3.758 (1.287-10.974)	.015
≥25 kg/m ²	5.245 (1.837-14.974)	.002
Isolated ATFL injury	0.779 (0.579-1.047)	.098
Isolated CFL injury	0.752 (0.492-1.150)	.188
Combined ATFL and CFL injuries	1.381 (1.057-1.806)	.018

^aBoldface indicates statistical significance. ATFL, anterior talofibular ligament; BMI, body mass index; CFL, calcaneofibular ligament; OR, odds ratio.

^bBaseline value.

TABLE 5
Multivariate Analysis of the Factors Associated
With the Presence of Osteophytes^a

	OR (95% CI)	P
Sex		
Female	1 ^b	
Male	2.675 (1.891-3.785)	<.001
Age		
<20 y	1 ^b	
20 y to <40 y	1.872 (1.192-2.941)	.006
≥40 y	3.102 (1.814-5.305)	<.001
Postinjury duration		
<12 mo	1 ^b	
12 mo to <2 y	1.086 (0.694-1.700)	.719
2 y to <5 y	1.378 (0.921-2.060)	.119
≥5 y	1.783 (1.199-2.652)	.004
BMI		
<18.5 kg/m ²	1 ^b	
18.5 to <23 kg/m ²	1.154 (0.382-3.486)	.799
23 to <25 kg/m ²	2.114 (0.696-6.423)	.187
≥25 kg/m ²	2.464 (0.825-7.358)	.106
ATFL injury		
Not involved	1 ^b	
Involved	1.511 (0.959-2.381)	.075
CFL injury		
Not involved	1 ^b	
Involved	1.380 (1.004-1.897)	.047

^aBoldface indicates statistical significance. ATFL, anterior talofibular ligament; BMI, body mass index; CFL, calcaneofibular ligament; OR, odds ratio.

^bBaseline value.

significantly correlated with the presence of osteophytes ($P < .001$; Pearson correlation coefficient = 0.342).

DISCUSSION

The most important findings of the present study are that the significant risk factors for both OCLs and osteophytes in patients with CLAI were postinjury duration of 5 years or longer, older age, and male sex. ATFL injury was associated with the presence of lateral OCLs, whereas CFL injury was associated with the presence of lateral OCLs and osteophytes.

OCLs are among the most common complications of CLAI, and the presence of OCLs is the most important predictor of poor long-term outcomes. Ankle instability aggravates OCLs.^{3,9} Chondral lesions are reportedly found in 89% of acutely injured ankles and 95% of ankles with chronic injuries.¹⁸ A study of 148 patients with CLAI reported that cartilage lesions were present in 66% of patients with lateral ligament injuries versus 98% of patients with deltoid ligament injuries.⁸ Another study reported that OCLs were detected in 77% of chronically unstable ankles, and 58% of these lesions were located at the tip of the medial malleolus.¹⁷ Our study found that the prevalence of OCLs in patients with CLAI was as high as 53%, and 64% of these OCLs were located on the medial side, which is consistent with most previous studies.

The present results indicate that the characteristics of medial and lateral OCLs might differ. The presence of medial talar OCLs was associated with a postinjury duration of 5 years or longer in the present study, which contrasts with the results of a previous study that indicated that the latency of symptoms did not affect the grade of the chondral damage.¹⁷ OCLs on the medial side might be caused by long-term degenerative changes. Deficiency of the lateral ligaments increases the anterior translation and internal rotation of the talus and increases the peak strain on the medial side of the talus; this is because of the curved surface of the cartilage on the medial portion of the tibial cartilage.^{1,2,6} Thus, OCLs gradually develop, and the fissures of the subchondral bone plate and continuous high fluid pressures can further lead to osteolysis and cyst formation.^{10,22} Therefore, we suggest that a postinjury duration of 5 years should be considered an important clinical risk for the development of medial OCLs.

In contrast with the present findings regarding medial OCLs, the risk of lateral OCLs was not associated with postinjury duration. This might be because a lateral OCL is more likely to develop as a result of a single traumatic injury rather than as a chronic degenerative lesion, as with a medial OCL. The incidence of lateral OCLs was higher in patients with a postinjury duration of 1 to 2 years, whereas a postinjury duration of longer than 2 years did not increase the risk of lateral OCLs. During surgery, the characteristic lesion seen on the lateral side was a thin and sliced-off cartilage chip. Furthermore, lateral talus OCLs have been significantly associated with the presence of concomitant ATFL and CFL injuries, which mainly occur as a result of violent trauma. CFL injuries primarily occur in inversion when the ankle is dorsiflexed,⁴ and traumatic impacts to the lateral half of the talus cause cartilage damage. Although Sugimoto et al¹⁷ did not distinguish between medial and lateral OCLs, those investigators suggested that a larger talar tilt angle and varus inclination of the tibial plafond were risk factors for the development of OCLs after ankle sprain.

Osteophytes are another common complication of CLAI.¹⁶ In the present study, 31% of the patients with CLAI had osteophytes. The development of osteophytes is closely associated with joint instability and is considered an adaptive response aimed at increasing the stability of the ankle. Thus, osteophyte removal may not necessarily improve the long-term outcomes.¹⁵ In the present study, those patients with injuries to both ligaments were significantly more likely to form osteophytes than were patients with injury to only 1 ligament. Our results also showed that osteophytes were more frequently found in patients with a higher BMI, which leads to a greater amount of stress on the ankle joint. Thus, the microtrauma theory, in which osteophyte formation is considered to be a response of the skeletal system to intermittent stress and injury that causes bone remodeling,²⁰ might also apply to the nonathletic population.

The greater prevalence of osteophytes in male patients in our study is consistent with findings from smaller clinical studies of patients with osteophytes.^{12,20} A study of 670 ankle specimens from 344 cadavers found osteophytes in

21% of specimens, and spurs were significantly more prevalent in male than female and in older versus younger cadavers.¹⁹ Sex-based differences in the incidence of osteophytes require further research. Similar to OCLs, osteophytes were significantly increased in patients with CLAI with a postinjury duration of more than 5 years. Thus, the high-risk group of male patients of older age with a postinjury duration of 5 years or longer and injuries to both the ATFL and CFL ligaments requires close monitoring for the development of osteophytes.

In the present study, 65% of the patients with osteophytes had OCLs, and 50% of the patients with OCLs had osteophytes. This result was similar to those of a previous study in which the degree of cartilage lesions was found to increase in tandem with the size of the spurs.¹² The loss of balance of the biomechanical system of the ankle affects both the congruence of the articular surface and the state of the cartilage as well as its dynamic stability.¹⁵

Aging and trauma are risk factors for the development of osteoarthritis.²⁴ The present study also found that older patients with CLAI were more likely to develop both OCLs and osteophytes. Senescent cells reportedly accumulate in the articular cartilage and synovium after trauma and cause further progression of osteoarthritis.⁹ Ankle sprain might trigger degenerative changes in the ankle joint, and older patients with senescent cells would more easily develop OCLs and osteophytes than younger patients. However, because older individuals are more likely than younger individuals to have chronic degenerative changes independent of any injury, the evaluation of age-matched control participants without injury is required to better understand the role of age as a risk factor for the development of OCLs and osteophytes.

The strengths of the present study include the relatively large sample size with complete and accurate data regarding patient characteristics, ligament rupture types, and concomitant lesions, which were obtained from the surgical records and confirmed during intraoperative evaluation. However, these strengths also entail bias because all of the included patients had ATFL and/or CFL injury and had undergone surgery, which limits the generalization of the present conclusions. These patients were chosen because their ligament injuries, cartilage lesions, and osteophytes could be definitively diagnosed only by arthroscopy. In contrast, healthy individuals and patients receiving nonoperative treatment are unlikely to accept arthroscopic surgery. Thus, the risk factors for individuals lacking symptoms or CLAI patients receiving nonoperative treatment should be further studied. Another limitation of the present study is that the analysis did not account for recurrent sprains, as these data would have been subjectively reported by the patients and might not have been accurate. In addition, the present study did not include other potential risk factors for the presence of OCLs and osteophytes, such as patient activity level, generalized joint laxity, limb alignment and range of motion of the ankle-foot complex, muscle strength, and muscle reaction time.

Despite these limitations, the present study provides valuable information regarding the risk factors for cartilage dysfunction in symptomatic ankles requiring lateral

ankle ligament repair or reconstruction. The integrity of these factors may aid in the analysis of their correlation with secondary lesions in CLAI. Patients with these risk factors may require early aggressive treatment, even surgery, to reduce the occurrence of ankle arthritis. Future research is needed to develop a consensus regarding all risk factors for ankle injury. This will allow for the design of future intervention studies to identify treatment methods that will reduce the incidence and severity of traumatic arthritis after ankle sprain.

CONCLUSION

Risk factors for OCLs and osteophytes were postinjury duration of 5 years or longer, older age, and male sex. ATFL injury was associated with the presence of lateral OCLs, whereas CFL injury was associated with the presence of lateral OCLs and osteophytes. Patients with these risk factors should be closely monitored and treated to reduce the incidence of ankle arthritis.

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