Healing Predictors of Conservative Treatment for Juvenile Osteochondritis Dissecans of the Talus

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Abstract

Objective: To investigate the healing response of juvenile osteochondritis dissecans (JOCID) of the talus after conservative treatment, identify healing predictors, and develop a predictive model for healing. Design: Retrospective study. Setting: Clinics at a tertiary-level pediatric medical center. Patients: Fifty-five patients (55 ankles) who presented with JOCID. Interventions: Patients were managed with cast immobilization followed by activity restriction. Main Outcome Measures: The primary outcome measure of progressive lesion reossification was determined from the latest radiograph, after at least 6 months of nonoperative treatment. Final clinical evaluation was performed by a questionnaire and complementary telephone interview. Multivariate logistic regression was used to determine the influence of age, sex, lesion size, classification, location, duration of symptoms, containment lesion, and the occurrence of cyst-like lesions on healing potential. Results: After nonoperative treatment, 18 (33%) of 55 lesions had failed to progress toward healing. An older age (P = 0.034) and a completely detached but undisplaced (grade III) lesion (P < 0.001) at the time of diagnosis were predictive for the failure of conservative treatment. A multivariate logistic regression best predictor model that included age and grade resulted in the best predicted healing and yielded an area under the curve of 0.920 (P < 0.001). Conclusion: In two-thirds of skeletally immature patients, conservative treatment resulted in the progressive healing of JOCID of the talus. For older patients with grade III lesions showing a lower healing probability, surgical treatment should be considered.

Key Words: juvenile osteochondritis dissecans of the talus, conservative treatment, prediction model

INTRODUCTION

Osteochondritis dissecans (OCD) of the talus usually occurs in patients aged between 10 and 40 years.1,2 When this disease occurs before physeal closure, it is defined as juvenile osteochondritis dissecans (JOCD) of the talus.3 Spontaneous healing is rarely observed in adult patients with OCD,4 and operative treatment is frequently required to promote healing.5,6 On the contrary, JOCD has been known to have more favorable outcomes with a better long-term prognosis after conservative treatment with protocols that include activity restriction or immobilization.2,7,8

Current management guidelines for JOCD of the talus are commonly based on the Berndt and Harty classification.9–11 Accordingly, grade I to III lesions have been managed conservatively, whereas grade IV lesions should be managed surgically.7 Conservative management is the first step in the treatment of JOCD of the talus, especially for nondisplaced lesions1,4,10; however, the success rates of conservative treatment differ throughout the literature.3,5,7,10–12 Owing to the rarity of JOCD of the talus, most prior studies included a few skeletally mature adolescents.7,10–12 Only one study has investigated JOCD of the talus exclusively in children with open growth plate.3 Furthermore, the literature is scarce regarding the healing predictors of conservative treatment for JOCD, and only one paper investigating the predictors included a mixed population of skeletally mature and immature patients.9

Therefore, the primary aim of this study was to investigate the healing response of JOCD of the talus after conservative treatment. The secondary aim was to identify the healing predictors of JOCD of the talus to provide a prediction model expressed as a nomogram.

METHODS

Study Patients

This retrospective study was approved by our hospital’s institutional review board. We performed a chart review of pediatric patients treated nonoperatively for JOCD of the talus at our hospital between November 2005 and December 2018. The inclusion criteria were as follows: (1) open growth plate of distal tibia and (2) completion of conservative treatment for at
least 6 months at our hospital. Patients were excluded for the following reasons: a history of ankle surgery or deformity and insufficient medical records for review. Patients who did not complete the telephone survey were also excluded.

We identified 68 pediatric patients who were treated conservatively for JOC of the talus and had open growth plate of distal tibia at the initial visit. Of the identified sample population, 13 patients were excluded from the analysis because of insufficient medical records (n = 2), follow-up loss during conservative treatment (n = 5), or inability to complete the telephone survey (n = 6). Thus, 55 patients were included in this study.

Data Collection

The following data were obtained: age, sex, laterality, body mass index (BMI), and symptom duration at the time of first presentation. Patients were divided based on symptom duration before the diagnosis, as either acute (<6 weeks) or chronic (>6 weeks). The location and size of the lesion were determined based on the initial imaging studies. Conventional ankle radiographs were made at the time of diagnosis and included anteroposterior, lateral, and mortise views. Magnetic resonance imaging (MRI) of the ankle was performed with the use of a dedicated extremity coil in a 1.5 or 3.0 T scanner [Achieva (Philips Healthcare, Best, Netherlands) or Discovery MR750 (General Electric Healthcare, Milwaukee, WI)] with a 3-mm to 4-mm thick proton density and T1-weighted sequences in the axial, sagittal, and coronal planes. Lesions were graded according to the classification of Berndt and Harty or Kramer on plain radiographs and MRI images. The location of the lesion was described as medial or lateral, based on coronal images, and anterior, center, or posterior, based on sagittal images. The following parameters, which reflect the lesion size, were defined and determined for each patient: coronal width (horizontal extension measured from the coronal image), sagittal length (horizontal extension measured from the sagittal image), and area (as calculated by the ellipse formula, from coronal and sagittal length: \( A = \frac{ab}{2} \pi = \text{coronal width} \times \text{sagittal length} \times 0.79\) (Figure 1). The maximal width and length of the talus were also measured on the coronal and sagittal MRI images. Lesion sizes (length and width) are given as percentages of the maximal length and width of the talus and are, therefore, referred.

Figure 1.

Magnetic resonance images showing a juvenile osteochondritis dissecans of the talus. A, Coronal T1-weighted image showing the width measurement of the lesion, B, sagittal T1-weighted image showing the maximal length measurement of the talus, C, coronal image showing the length measurement of the lesion, and D, sagittal image showing the maximal width measurement of the talus.
to as normalized size measures. The normalized lesion area is reported as the product of normalized width and length. A contained lesion (nonsoulder type) was defined as a cartilage defect that involved the surrounding articular cartilage, whereas an uncontained lesion (shoulder type) did not have a peripheral cartilage border. The occurrence of cystic lesion with high-signal intensity was documented on proton density–weighted images (Figure 2). To avoid potential bias, an independent observer, uninvolved in the care of the patients and blinded to the intention of this study, evaluated the MRI films.

**Treatment Protocol**

All patients received conservative treatment as a first-line treatment for at least 6 months. At the beginning of treatment, the growth plate of distal tibia was open in all patients. All patients routinely underwent follow-up radiography at about 6 weeks, 3 months, 4.5 months, and 6 months after the initial visit. Treatment started with 6 weeks of non–weight-bearing immobilization in a short-leg walking cast, followed by a gradual increase in protected weight-bearing with crutches after removal of the cast. If patients were free of pain after 3 months, regular activities were allowed as tolerated regardless of the degree of radiographic reossification; repetitive-impact sports or other strenuous activities were restricted, however. If the lesion showed total reossification on radiographs, patients were allowed unrestricted activity. After 6 months of conservative treatment, we usually finished the routine follow-up when the patient was able to do all activities without pain and recommended a revisit only if the patient felt pain again or parents wanted a regular checkup. Our institution has taken the approach that MRI acquisition should be considered only when the patient has failed to demonstrate adequate improvement during or after conservative treatment for 6 months or when pain has recurred after completion of conservative treatment.

**Radiographic Assessment**

The final radiographs for each patient were assessed for reossification of the lesion at the latest follow-up visit. Another orthopedic surgeon who was blinded to the MRI and symptomatic data obtained at the time of the initial visit performed the final radiographic evaluation of the lesion.

**Clinical Assessment**

Patients were asked to complete a self-reported outcome questionnaire by telephone survey. Subjective outcomes were graded as good, fair, or poor according to the Berndt and Harty8 outcome question. A “good” outcome was defined as no limitation in daily activities. A “fair” outcome was defined as limitations in recreational activities, but no limitation in daily activities. A “poor” outcome was defined as subsequent surgery at our or another institution or severe limitations in both daily and recreational activities requiring the use of an assistive device (crutches, walker, etc). Indications for proceeding with surgery were persistent pain in daily activities even after 6 months of conservative treatment.

**Outcome Measurement**

Patient outcomes were categorized as either “healing” or “failure” according to radiographic and clinical results. Healing was defined as reossification of the lesion on radiographs taken at the last radiological follow-up combined with a “good” clinical outcome at the final phone survey. Failure was defined as “fair” or “poor” clinical outcome at the final phone survey regardless of the presence or absence of reossification of the target lesion.

**Statistical Analysis**

Variables were tested for normality using the Kolmogorov–Smirnov test. Differences between groups (healing vs failure) were detected by the independent sample t test and Mann–Whitney U test for continuous variables or a $\chi^2$ test for categorical variables. Several variables were considered as possible factors that could be related to the healing of JOCD. These factors included (1) age, (2) sex, (3) BMI, (4) symptom duration, (5) classification, (6) location of lesion, (7) lesion...
size, (8) normalized lesion size, (9) presence of containment, and (10) presence of cystic lesion. These predictors were chosen based on our own hypotheses and previous literature.\(^{4,9,16,17,19}\) Univariable logistic regression analysis was performed for each predictor. Multivariable logistic regression with backward (Wald) selection of predictors was used to examine the predictive effects for the independent variables.

The area under the curve (AUC) of the corresponding receiver operating characteristic curve (ROC) was used to quantify the predictive power of the model. The Hosmer and Lemeshow goodness-of-fit test was used to assess the acceptability of the predictive models, as it determined how well the nomogram was calibrated; for instance, close approximation between the observed probability and the predicted probability demonstrated good calibration and confirmed the exportability of the model. A nomogram was produced from the study sample to allow predictions to be made in individual patients. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). \(P\) values < 0.05 were considered statistically significant.

**RESULTS**

A total of 55 patients (55 ankles) were included in this study. There were 30 male and 25 female patients. The mean age at the time of diagnosis was 11.7 (6.7-14.4) years. The mean radiological follow-up was 39.3 (9-157) months. The mean follow-up period for the telephone survey was 6.6 (1.1-17.9) years. All patients were classified as grade I to III lesions at initial presentation, and there was no patient who had grade IV lesion. Descriptive data on the patients are presented in Table 1.

We found the reossification of the lesion in 43 (78%) ankles on radiographic evaluation. Among these, 6 lesions were defined as failure because of “fair” functional outcomes based on the phone survey. Thus, 37 (67%) lesions were defined as healing after at least 6 months of conservative treatment. According to the phone survey, 10 patients defined as failure underwent surgical treatment. Remaining 45 patients did not undergo any subsequent treatment. The descriptive statistics of ankles with and without progression toward healing are provided in Table 2. We found significant differences between groups for age \((P = 0.002)\) and distribution of classification \((P < 0.001)\). With respect to all other variables, there was no statistically significant difference between the 2 groups.

The univariable and multivariable logistic regression models for predicting healing are presented in Table 3. In univariable analysis, healing of JOCD of the talus was associated with younger age \((OR = 0.545, P = 0.004)\) and lower classification \((OR = 0.024, P < 0.001)\). In a subsequent search for the best subset of predictors, age and classification were used to fit a multivariable logistic regression model. The younger age \((OR = 0.515, P = 0.034)\) and lower classification \((OR = 0.024, P < 0.001)\) were related to the healing of the JOCD of the talus. The resulting AUC was 0.920 [95% confidence interval (CI), 0.848-0.991; \(P < 0.001\)] (Figure 3A). An optimal cutoff at 54% healing probability produced a sensitivity of 86.5% (95% CI, 75.5%-97.5%), a specificity of 88.9% (95% CI, 74.4%-103.4%), a positive predictive value of 94.1% (95% CI, 86.2%-102.0%), and a negative predictive value of 76.2% (95% CI, 58.0%-94.4%). The \(P\) value of Hosmer and Lemeshow goodness-of-fit was 0.306, indicating a good fit of our prediction model. Calibration plots showed a close agreement between the predicted and actual probability (Figure 3B). A nomogram represents the healing probability with respect to age and classification (Figure 4).

**DISCUSSION**

A principal finding of the present analysis was that a grade III lesion (detached but undisplaced fragment) at the time of...
diagnosis and an older age of the patient are predictive factors for the failure of conservative treatment. Only one study had investigated the predictors for the failure of nonoperative treatment, and their findings are in agreement with ours; however, they did not describe whether or not the growth plate of included patients were open and did not either include other potential predictors such as the size of the lesion and the presence of cystic lesion which were suggested as the influencing factors in adults. In this study, we included all possible factors that may affect the treatment outcome and created a nomogram to predict the success of conservative treatment for JOCD of the talus.

There are several limitations to our research. First, a limitation in any study that includes a nonoperative treatment is patient compliance. However, we chose cast immobilization as the initial form of treatment to enforce compliance with

| TABLE 2. Comparison of Patient Characteristics With Regard to Outcome |
|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Variables               | Failure (18 Ankles)     | Healing (37 Ankles)     | P           |
| Age, yr                 | 12.9 ± 1.5              | 11.2 ± 1.8              | 0.002       |
| Sex, n (%)              |                         |                         | 0.607       |
| Male                    | 9 (50)                  | 21 (56.7)               |             |
| Female                  | 9 (50)                  | 16 (43.3)               |             |
| Side, n (%)             |                         |                         | 0.916       |
| Right                   | 10 (55.6)               | 20 (54)                 |             |
| Left                    | 8 (44.4)                | 17 (46)                 |             |
| BMI                     | 23.3 ± 7.3              | 21.5 ± 4.8              | 0.328       |
| Follow-up period, mean (range), mo | 47.9 (9-157) | 35.1 (9-100)               | 0.188       |
| Follow-up period at the phone survey, mean (range), yr | 76.2 (1.1-15.6) | 81.2 (1.2-17.9) | 0.744 |
| Symptom duration, n (%) |                         |                         | 0.462       |
| Acute                   | 13 (72.2)               | 23 (62.2)               |             |
| Chronic                 | 5 (27.8)                | 14 (37.8)               |             |
| Classification, n (%)   |                         |                         | <0.001      |
| I                       | 1 (5.6)                 | 5 (13.5)                |             |
| II                      | 1 (5.6)                 | 26 (70.3)               |             |
| III                     | 16 (88.8)               | 6 (16.2)                |             |
| Location, n (%)         |                         |                         | 0.281       |
| Coronal view            |                         |                         |             |
| Medial                  | 15 (83.3)               | 29 (78.4)               |             |
| Central                 | 0 (0)                   | 5 (13.5)                |             |
| Lateral                 | 3 (16.7)                | 3 (8.1)                 |             |
| Sagittal view           |                         |                         | 0.079       |
| Anterior                | 2 (11.1)                | 2 (5.4)                 |             |
| Middle                  | 11 (61.1)               | 32 (86.5)               |             |
| Posterior               | 5 (27.8)                | 3 (8.1)                 |             |
| Lesion size, mean (SD)  |                         |                         |             |
| Length, mm              | 12.3 ± 2.5              | 11.1 ± 3.2              | 0.170       |
| Width, mm               | 8.2 ± 1.7               | 7.7 ± 2.5               | 0.400       |
| Area, mm²               | 84.4 ± 29.2             | 68.7 ± 33.7             | 0.098       |
| Normalized lesion size, mean (SD) |                     |                         |             |
| Length, %               | 34.6 ± 6.6              | 31.2 ± 7.8              | 0.113       |
| Width, %                | 28.6 ± 5.4              | 27.6 ± 11.4             | 0.749       |
| Area, %                 | 10.0 ± 2.8              | 8.8 ± 4.9               | 0.351       |
| Containment, n (%)      |                         |                         | 0.160       |
| Contained, nonshoulder type | 0 (0)                  | 5 (13.5)                |             |
| Uncontained, shoulder type | 18 (100)               | 32 (86.5)               |             |
| Cystic lesion, n (%)    |                         |                         | 0.639       |
| Yes                     | 8 (44.4)                | 14 (37.9)               |             |
| No                      | 10 (55.6)               | 23 (62.1)               |             |

Statistically meaningful variables are expressed in bold. Values are expressed as the means ± SD unless otherwise indicated.
activity rest in this active population, and none of the patients removed their cast prematurely. The patients and parents were queried on activity compliance at each visit, and the rationale for treatment was reinforced. Second, we did not perform follow-up MRI for all patients, and even those who showed good radiographic evidence of healing or progression toward healing still might show signal changes in articular cartilage on their follow-up MRI scans. If we were to analyze this cohort of patients with MRI data, we would likely find a greater number of failures than is reflected by the 33% rate. Third, telephone surveys were used to evaluate patient functionality. As such, objective functional outcomes, such as severity of pain or sport activity level, using validated scoring systems and up-to-date radiographs were not available, which prohibited us from

| Factor          | Univariable Odds Ratio* | P     | Multivariable Odds Ratio* | P     |
|-----------------|-------------------------|-------|---------------------------|-------|
| Age             | 0.545 (0.358-0.828)     | 0.004 | 0.515 (0.280-0.953)       | 0.034 |
| Sex             |                         |       |                           |       |
| Male vs female  | 0.682 (0.220-2.118)     | 0.508 |                           |       |
| BMI             | 0.948 (0.851-1.056)     | 0.333 |                           |       |
| Symptom duration|                         |       |                           |       |
| Acute vs chronic| 1.582 (0.464-5.397)     | 0.463 |                           |       |
| Classification  |                         |       |                           |       |
| III vs I and II | 0.024 (0.004-0.134)     | <0.001| 0.024 (0.004-0.145)       | <0.001|
| Coronal location|                         |       |                           |       |
| Lateral vs medial| 0.525 (0.094-2.925)    | 0.462 |                           |       |
| Sagittal location|                        |       |                           |       |
| Anterior        | 2.909 (0.365-23.198)    | 0.313 |                           |       |
| Middle          | 0.600 (0.053-6.795)     | 0.680 |                           |       |
| Lesion size     | 0.985 (0.968-1.003)     | 0.102 |                           |       |
| Normalized lesion size | 0.940 (0.827-1.070) | 0.351 |                           |       |
| Containment     | 6.226 (0.249-157.465)   | 0.265 |                           |       |
| Cystic lesion   | 1.314 (0.419-4.121)     | 0.639 |                           |       |

* The values are given as coefficient with the 95% CI in parentheses.

Figure 3. A. Receiver operating characteristic curve resulting in an area under the curve of 0.920 (blue line). B. Calibrated plots demonstrating a close agreement between predicted probability and actual probability.
commenting in detail on these outcomes. Finally, we acknowledge that there were some limitations associated with the retrospective design of this study, including the variability of follow-up periods and the reliability and accuracy of the study measures.

Despite a minimum of 6 months of nonoperative treatment that included an initial 6 weeks of weight-bearing cast immobilization, a 33% failure rate was noted in our series. A 6-month timeframe for the trial of nonoperative treatment was decided on, as it is commonly used to judge the success of nonoperative healing of JOCD of the knee.\textsuperscript{20,21} We defined “healing” as the presence of radiographic evidence of healing (reossification) of the lesion on the latest radiographs and no restriction of daily activity without pain, as determined by a phone survey. To the best of our knowledge, although we did not perform a validated clinical evaluation, this is the first study to re-evaluate the functional results of conservative treatment by a phone survey after a relatively long follow-up period (mean of 6.6 years).

Currently, a wide range of success rates, ranging from 42% to 100%, for conservative treatment in JOCD are reported in the literature.\textsuperscript{3,7,9–11} A high success rate of 100% was reported in one study that incorporated only 6 patients.\textsuperscript{7} Letts et al\textsuperscript{11} reported 26 cases with a mean patient age of 13.3 years and a success rate of 42%. Heyse et al\textsuperscript{9} reported a similar success rate of 40% in 77 ankles with a mean age of 11.4 years. In this study, we experienced a higher success rate of 67%, and this may be explained by our exclusive inclusion of the juvenile patients with open physes, whereas most of the previous literature used heterogeneous populations with adolescent patients with closed growth plates. In line with this, our findings were similar with those of Perumal et al\textsuperscript{3}; the only study that exclusively investigated JOCD of patients with open physes. Our results confirm that conservative management should be the first-line treatment for JOCD of the talus in children with open physes.

We found that a grade III lesion at the time of diagnosis was the prognostic variable for the failure of conservative treatment. A possible explanation for this might be or could be the fact that a grade III lesion is defined by complete disconnection of the affected area from the host bone. Although the fragment has not been displaced yet, the disconnection may represent a severe obstacle for healing, indicating that a definite assessment of lesions is very important to predict the possibility of healing. However, this may not necessarily mean that surgery is the optimal treatment of grade III lesions; conservative management was still favorable, as a delayed time to surgery has been shown to not affect the final outcome in younger ages.\textsuperscript{9,22} Nevertheless, evaluating the continuity of lesions can be helpful in predicting the success of conservative treatment for JOCD of the talus.

Our regression analysis showed that age had a significant effect on the prognosis of JOCD of the talus. To date, only one study has reported that an older age was predictive for the failure of conservative treatment.\textsuperscript{9} Although further research is needed, this result indicates that the residual potential of growth plate, even in children with open growth plate, affects the healing of JOCD. Distal tibial physeal closure is generally completed by the age of 14 years in girls and 16 years in boys, and minimal longitudinal growth of the distal tibia occurs after the age of 12 years in girls and 14 years in boys.\textsuperscript{23} Therefore, conservative treatment may not be effective in patients near closing of the growth plate of distal tibia.

Location of lesion and symptom duration was not related to the success of conservative treatment. Similar results were obtained in one study, in that the location of the lesion, locking symptoms, and instability were shown to have no significant effect on the result of nonoperative treatment.\textsuperscript{9} Lesion size and the presence of cystic lesions were also not healing predictors of conservative treatment despite those factors were reported as an important prognostic factor in OCD of the talus in adults.\textsuperscript{16,19} Although a direct comparison is not appropriate, our results were different from those in adults. Unlike adult OCD of the talus, we suspect that JOCD of the talus may show a different healing integrity.

A nomogram developed from multivariate logistic regression analysis based on the Berndt and Harty\textsuperscript{8} or Kramer\textsuperscript{14} classification of the lesion and age at the time of diagnosis may provide an objective algorithmic tool to aid clinicians in
determining the relative prognosis of conservative treatment for JOCD of the talus. Nomograms can be useful tools for the prediction of ordinal outcomes on the basis of clinical signs at the time of diagnosis. Figure 5 presents an example of the nomogram-predicted outcome based on the classification of the lesion and age in an actual patient. For patients with a lower healing probability, alternative therapeutic regimens should be applied.

CONCLUSIONS

In patients with JOCD, two-thirds of the lesions experienced healing after nonoperative treatment, including cast immobilization and activity restriction. A thorough evaluation of patients with JOCD at the time of the initial presentation, to evaluate the articular surface of the lesion, is important in deciding on the method of treatment and predicting the prognosis for healing. Furthermore, our nomogram that incorporates the classification of the lesion and age at the time of presentation may aid in the prediction of the healing potential in individuals with JOCD.

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