ACTA ORTHOPAEDICA et TRAUMATOLOGICA TURCICA
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Research Article

Fracture risk and follow-up indications in lower limb non-ossifying fibromas

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ARTICLE INFO

Article history:
Submitted March 2, 2025
Received in revised form March 3, 2025
Last revision received form January 2, 2026
Accepted January 2, 2026
Publication Date June 12, 2026

Keywords:
NOF
Non-ossifying fibroma
Pathologic fractures

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ABSTRACT

Objective: This study aimed to evaluate the course of non-ossifying fibromas (NOFs) on basis of radiological parameters, determine the risk factors for management and define follow-up strategies.

Methods: A retrospective review was performed on 104 skeletally immature patients who were followed for a minimum of 3 consecutive years. Radiographic evaluations included measurement of lesion size, cortical thinning, and distance from the physis. Lesions were classified according to the radiological maturation stages described by Ritschl et al, and the transition time between each stage was recorded. Fracture risk was assessed using radiographic, computed tomography, and magnetic resonance imaging (MRI)-based criteria, including cortical involvement percentage, cortical breach, lesion size, absence of neocortex, presence of syndesmosis, and the "Pac-Man sign" as defined by Baghdadi et al.

Results: The mean age at diagnosis was 11.3 years. Pathological fractures occurred in 11 patients (10.6%), with 90.9% showing >50% cortical involvement on anteroposterior views and 100% on lateral views. Cortical thinning and disruption were present in all fracture cases. The mean time for radiological progression from Ritschl stage A to B was 17.3 ± 9.9 months, from stage B to C was 24.9 ± 16.2 months, and from stage C to D was 27.3 ± 15.9 months. Overall, the average duration from initial stage A to complete resolution at stage D was 44.9 ± 26.9 months. The fracture risk score in initial radiologic evaluation was significantly higher in patients who presented with fractures (P=.001). In distal tibial lesions, the "Pac-Man" sign was related to fractures (P=.001).

Conclusion: This study demonstrated that stage B lesions, cortical thinning, and involvement of more than 50% of bone markedly increased the risk of pathological fracture, and the presence of the "Pac-Man" sign served as a reliable predictor. These findings held important clinical value, as they supported proactive monitoring and timely intervention in high-risk NOF lesions to prevent preventable fractures.

Level of Evidence: Level III, Prognostic Study.

Introduction

Non-ossifying fibromas (NOFs) are among the most common benign bone lesions in individuals under the age of 15, with reported prevalence rates in the literature ranging from 2.3% to 30%.[1-4] Non-ossifying fibromas are most frequently located in the metaphyseal regions of the femur and tibia and are characterized as multilocular, cortically based lesions with well-defined sclerotic margins.[3,5]

Non-ossifying fibromas are typically asymptomatic and are most often incidentally detected during imaging studies; however, in some cases, they may present with pathological fractures.[2,3] There is no clear data on the exact incidence of pathological fractures associated with NOFs.[3] The management of NOFs is primarily based on the radiological characteristics of the lesion, its staging, and the risk of pathological fracture.[6] The 4-stage classification (Stages A, B, C, and D) introduced by Ritschl in 1988 provides an important reference for monitoring the progression of lesions at different stages, but it does not fully explain the risk of fracture[7] (Figure 1). Fracture risk may vary depending on radiological features and the lesion's impact on the structural integrity of the bone. In this context, the fracture risk scoring system developed by Baghdadi et al represents a valuable tool for assessing NOFs. This scoring system includes radiological findings such as the presence of Ritschl Stage B lesions, lesions occupying ≥50% of the bone diameter, and cortical thinning.[1]

This study aimed to evaluate the course of NOFs on basis of radiological parameters, determine the risk factors for management, and define follow-up strategies.

Material and methods

This retrospective study evaluated the clinical and radiological data of patients diagnosed with lower extremity NOF who were followed up between July 1, 2012, and September 1, 2020. The medical records of a total of 151 patients were reviewed, and demographic information, clinical characteristics, presenting symptoms, and radiological evaluations (X-ray, computed tomography (CT), magnetic resonance imaging (MRI))

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Cite this article as: *İğde N, Aycan OE, Doğan B, Polat B, Sobayapan M, Arslan MC. Fracture risk and follow-up indications in lower limb non-ossifying fibromas. Acta Orthop Traumatol Turc., 2026; 60(3), 0318, doi: 10.5152/j.aott.2026.25318.*

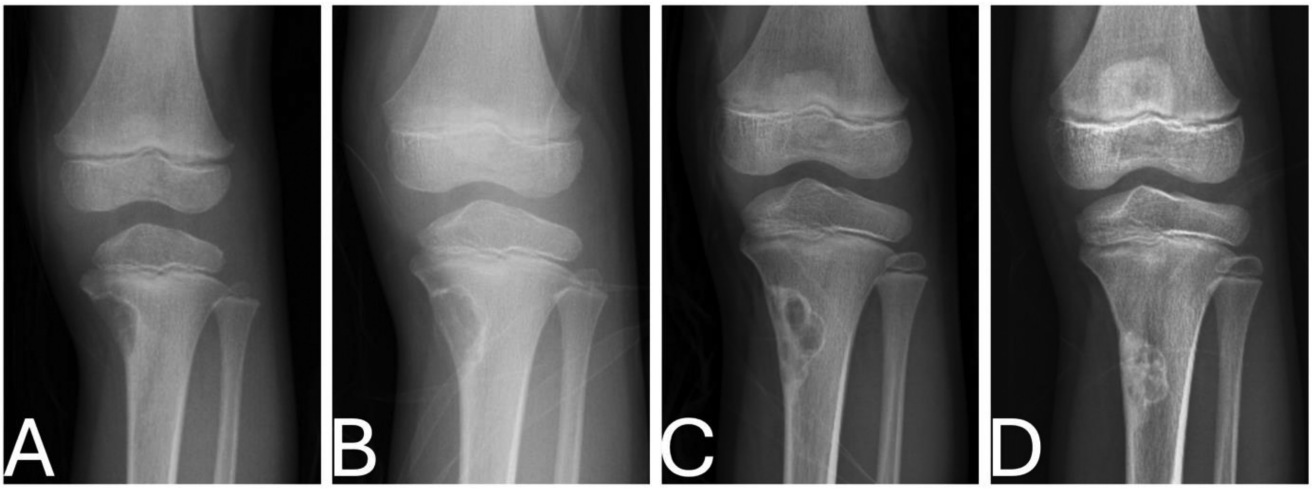


Figure 1. Ritschl Classification. Stage A is characterized by a small, eccentric lesion close to the physeal plate without a sclerotic border; Stage B is defined as a polycystic lesion with thin sclerotic borders and cortical thinning at a variable distance from the physis; Stage C demonstrates increasing sclerosis starting from the diaphyseal side; and Stage D is marked by complete homogeneous sclerosis of the lesion.[7]

were analyzed. The inclusion criteria encompassed patients under the age of 18 with a confirmed diagnosis of NOF based on radiological or histopathological findings, who had not undergone any prior surgical intervention or treatment for NOF, had been regularly followed up, and had complete clinical evaluations. Eight patients who had undergone prior surgical intervention for the lesion, 12 patients with a follow-up period of less than 3 years, 23 patients with insufficient follow-up data including X-ray, CT, and/or MRI, and 4 patients with multiple lesions were excluded from the study. To exclude additional factors that could affect the developmental process, such as genetic disorders, and to avoid confusion in staging the lesions, patients with multiple lesions were excluded from the study. A total of 104 patients (66 males, 38 females) who met the inclusion criteria and were regularly followed up for at least 3 years were included in the study. The study was approved by the ethical committee in accordance with the ethical standards of the institutional and/or national research committee of Metin Sabancı Baltalimanı Bone Diseases Research and Training Hospital and the 1964 Helsinki Declaration (Date: April 10, 2023, Meeting No: 6, Decision No: 53). Informed consent was obtained from all individual participants included in the study or their legal representatives or parents.

In the routine follow-up protocol, patients under the age of 12 were evaluated radiologically every 6 months, while those aged 12 and above were evaluated annually. In lesions with a risk of fracture—particularly those occupying more than 50% of the cortical diameter in either the anteroposterior or lateral plane—X-ray imaging was performed every 3 months. Large lesions, as well as those that could be confused with other pathologies such as aneurysmal bone cyst or giant cell tumor in the differential diagnosis, were assessed using MRI. In the series, MRI did not reveal any features suggestive of an alternative diagnosis; all lesions evaluated with advanced imaging showed characteristics consistent with NOF. Additionally, CT was utilized when necessary in patients with a high risk of fracture. The treatment of pathological fractures involves a conservative approach for non-displaced fractures, while displaced or unstable fractures require intervention. Following histopathological confirmation via biopsy, the lesion is treated with curettage, the resulting defect is filled with either autograft or allograft, and the fracture is stabilized using appropriate internal fixation techniques.

HIGHLIGHTS

- The natural course and stage transition times of non-ossifying fibromas were analyzed to provide evidence-based recommendations for follow-up strategies.
- Pathological fractures showed >50% cortical involvement in 90.9% of cases on anteroposterior views and 100% on lateral views.
- The "Pac-Man" sign was identified as a significant predictor of pathological fractures in distal tibial lesions (P=.001).
- Baghdadi fracture risk score, cortical thinning, and >50% bone involvement were found to be crucial in predicting fracture risk.
- Patients with Ritschl stage-B lesions are at high risk of fractures and should be monitored every 3 months, with surgical intervention considered for high-risk cases.

All imaging studies (X-ray, CT, and MRI) were directly evaluated by 2 orthopedic surgeons specialized in musculoskeletal tumor oncology independently, and reports prepared by radiologists were reviewed. In cases where there was any doubt as to whether the lesion represented a NOF, histopathological findings were consulted when available. In the series, the radiographic appearance was typical for NOF in all cases; no lesion required a separate biopsy for diagnostic confirmation. Biopsy was performed only as part of surgical management for pathological fractures to confirm the diagnosis for medicolegal purposes. Radiographs were analyzed for cortical thinning, cortical expansion, the distance of the lesion from the physeal plate, initial cortical involvement, and whether the lesion occupied more than 50% of the bone diameter on both anteroposterior (AP) and lateral views. Cortical thinning was defined as a clear decrease in the thickness of the bone cortex over or around the lesion, compared to the normal cortex seen above and below the lesion in the same bone. This was evaluated by visually comparing the affected area to the nearby normal bone. Cortical expansion was defined as outward bulging of the bone beyond its normal shape. It was considered present if the cortex in the lesion area was more than 2 mm wider than the normal cortex above and below the lesion.[1]

The lesions were classified according to the Ritschl classification system based on radiological features (Figure 1). The transition times between Ritschl stages were assessed by determining the radiological stage of each lesion at the time of the patient's initial presentation. During follow-up visits, the stage was re-evaluated based on updated imaging studies. If a stage change was identified at any follow-up, the time interval between the last visit without a stage change and

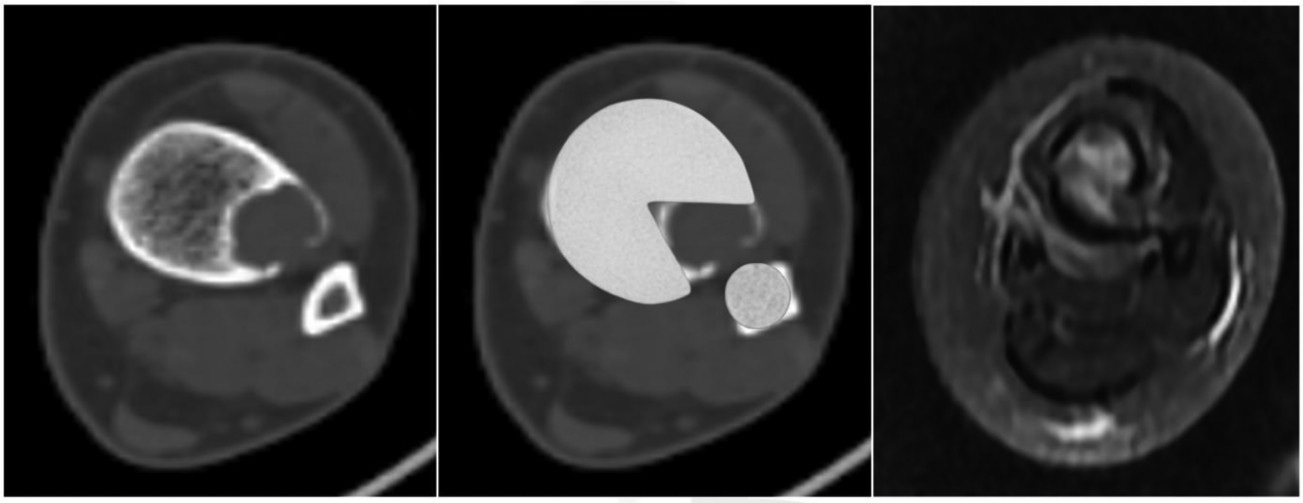


Figure 2. Axial computed tomography and magnetic resonance imaging images of the distal tibia showing the Pac-Man sign.

the visit at which the change was first detected was recorded as the transition time for that specific stage. These individual intervals were then used to calculate the mean transition time between each Ritschl stage.

The fracture risk scoring system developed by Baghdadi et al for NOFs in the distal tibia was analyzed for NOFs located in different bone regions. The presence of Pac-Man sign on axial MRI and CT slices of distal tibial NOFs was recorded. The "Pac-Man sign" was defined as cortical bone proliferation and remodeling observed anterior and posterior to the syndesmosis insertion on axial CT or MRI images. This configuration creates a visual resemblance to the Pac-Man character and is considered a specific radiological indicator of increased fracture risk (Figure 2). This scoring system evaluates fracture risk based on clinical and radiographic features. The criteria include Ritschl stage B (1 point), a lesion occupying ≥50% of the bone diameter on AP radiographs (1 point), the presence of cortical thinning on AP radiographs (1 point), a lesion occupying ≥50% of the bone diameter on lateral radiographs (1 point), and the presence of cortical thinning on lateral radiographs (1 point). Each criterion is assigned 1 point if present, with a maximum total score of 5.[1]

In this study, statistical analyses were performed using SPSS version 27. Quantitative variables were summarized using mean, standard deviation, median, minimum, and maximum values, while qualitative variables were summarized using frequency and percentage. The Shapiro–Wilk test was used to assess the normality of the data distribution.

For comparing quantitative variables between 2 groups that did not follow a normal distribution, the Mann–Whitney *U*-test was applied. For comparing qualitative data, the Chi-Square test or Fisher's Exact test was used, as appropriate. The results were evaluated with a 95% CI, and statistical significance was set at $P < .05$.

Table 1. Distribution of clinical features by stages at the time of diagnosis

	Stage A n=52 Mean ± SD	Stage B n=47 Mean ± SD	Stage C n=5 Mean ± SD
Average age (years)	10.7 ± 4.3	11.9 ± 3.2	12.4 ± 2.6
Average length (mm)	26.3 ± 13	41.5 ± 19.7	34.6 ± 9.6
Average AP involvement (%)	32.3 ± 16.3	55.5 ± 23.1	44.6 ± 13.9
Average Lat involvement (%)	36.7 ± 19.3	57.8 ± 23.3	46.5 ± 15.3

AP, anteroposterior.

Results

The mean age of patients at initial presentation was 11.33 ± 3.76 years, with 63.5% being male (n=66). The mean follow-up duration was 62.69 ± 23.25 months. The distribution of lesion locations was as follows: distal femur in 43 patients (41.3%), proximal tibia in 29 patients (27.9%), distal tibia in 25 patients (24%), proximal fibula in 6 patients (5.8%), and distal fibula in 1 patient (1%). Among the patients presenting to the outpatient clinic, 19 (18.3%) reported pain as a symptom, and 11 (10.6%) presented with non-displaced fractures (These patients were managed non-operatively). In contrast, 74 patients (71.1%) were referred following the incidental detection of the lesion during imaging studies. At the time of initial diagnosis, 52 patients were classified as stage A, 47 as stage B, and 5 as stage C (Table 1).

Radiological evaluation at the time of diagnosis revealed that cortical thinning was present in 37 patients (35.6%), cortical expansion was observed in 15 patients (14.4%). The mean distance from the physis was 26.8 ± 17.6 mm. Cortical involvement was measured as 43.4 ± 22.8% on AP views and 46.8 ± 23.6% on lateral views. The mean maximum longitudinal length of the lesions was 33.9 ± 17.8 mm (Table 2).

The mean transition time from stage A to B was 17.3 months (n=33), stage B to C in 24.85 months (n=68), and stage C to D in 27.3 months (n=44). Overall mean time to change from stage A to D was 44.89 months (n=28). There was no stage change in 5 patients within 47.2 months follow-up in the series (Figure 3).

Among the 11 patients with pathological fractures at the time of presentation, 9 were stage B, while 2 were stage A. There were no cases of fracture observed during follow-up in the patients.

Table 2. Radiological features of patients at the time of diagnosis

		n (%)
Cortical thinning	Present	37 (35.6)
	Absent	67 (64.4)
Cortical expansion	Present	15 (14,4)
	Absent	89 (85.6)
		Mean ± SD
Distance from the physis (mm)		26.8 ± 17.6
Cortical involvement on AP view (%)		43.4 ± 22.8
Cortical involvement on Lat view (%)		46.8 ± 23.6
Max longitudinal length (mm)		33.9 ± 17.8

AP, anteroposterior.

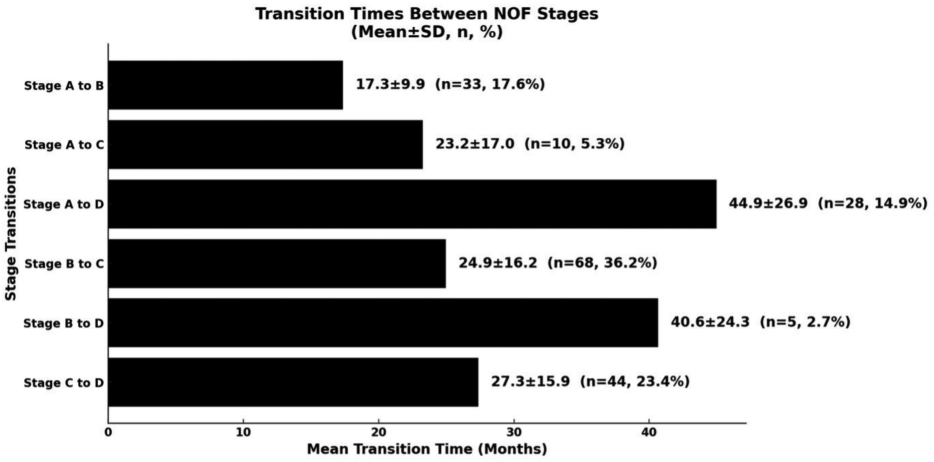


Figure 3. Transition times between non-ossifying fibromas stages.

In patients with pathological fractures, more than 50% cortical involvement was observed in 10 cases (90.9%) on AP views, whereas more than 50% involvement was detected in all cases (100%) on lateral views. All patients with pathological fractures (100%) exhibited cortical thinning and cortical disruption. Cortical expansion was observed in 6 patients (54.5%). Among the 11 patients with pathological fractures, 8 had lesions located in the distal tibia, while 3 had lesions in the distal femur. Among the 25 patients with NOF located in the distal tibia, fractures developed in 8 cases, and the Pac-Man sign was observed in 5 of these cases. However, none of the 17 non-fractured patients exhibited this sign (P=.001) (Table 3).

Discussion

This study provides guidance for NOF follow-up by determining the transition periods between different stages of NOFs and identifying those with a risk of pathological fracture. The analysis demonstrated that, in Ritschl stage-B lesions, cortical thinning or expansion, more than 50% bone involvement on anteroposterior and lateral radiographs, and the presence of the "Pac-Man" sign in distal tibial lesions were all associated with an increased risk of pathological fracture. Moreover, the average transition times between stages were calculated as 17.3 months from A to B, 24.9 months from B to C, and 27.3 months from C to D, clearly indicating the expected progression interval at each stage.

The study, based on real-life data, contributes to the literature by offering insights into the optimal follow-up duration and frequency of these lesions and identifying situations that require increased vigilance. The lesions in the cohort were predominantly located in the distal femur (41.3%), proximal tibia (27.9%), and distal tibia (24.0%), with the majority being metaphyseal (68.3%), consistent with previous studies.[4,7,8]

Pain is one of the primary symptoms in patients with bone tumors. However, a large epidemiological study involving 6222 children with a mean age of 11.6 years reported that the presence of pain in NOF patients is not directly related to the lesion itself.[2] Similarly, in the study, the mean age was 11.3 years, and most lesions were incidentally detected (71.1%), whereas a smaller proportion of patients presented with pain (18.3%) or fractures (10.6%), consistent with the existing literature.

In the study, the coronal plane length of the lesion was significantly higher in cases with pathological fractures compared to those without fractures, measuring 43 mm (38-82.2) and 30 mm (5.2-95.5),

Table 3. Comparison of radiographic features in patients with pathological fractures

		Pathological fracture		
		Absent (n=93)	**Present (n=11)**	***P***
Cortical thinning	Absent	67 (72)	0 (0)	[a].001
	Present	26 (28)	11 (100)	
Cortical expansion	Absent	84 (90.3)	5 (45.5)	[a].001
	Present	9 (9.7)	6 (54.5)	
Expansion of diameter on AP X-ray (%)	Mean ± SD	40.4 ± 21.5	68.8 ± 6.8	[b].001
	Med (min-max)	37.2 (4.3-99.2)	71.2 (50.4-99)	
Expansion of diameter on Lateral X-ray (%)	Mean ± SD	43.4 ± 21.9	75.6 ± 17.3	[b].001
	Med (min-max)	41.8 (4.8-99)	76.8 (53.4-100)	
Longitudinal length (mm)	Mean ± SD	32.0 ± 17.5	48.6 ± 13.5	[b].001
	Med (min-max)	30 (5.2-95.5)	43 (38-82.2)	
Baghdadi fracture risk score (initial)	Mean ± SD	1.8 ± 1.7	4.6 ± 0.7	[b].001
	Med (min-max)	2 (0-5)	5 (3-5)	
		Distal tibial fracture		
		Absent (n=17)	**Present (n=8)**	
Pac-Man sign	Absent	17	3	[c].001
	Present	0	5	

AP, anteroposterior.
[a]Pearson chi-square test.
[b]Mann–Whitney *U*-test.
[c]Fisher's exact test.

respectively (P=.001). When reviewing the literature, 1 study reported that in all patients who experienced fractures, the lesion length exceeded 33 mm, suggesting an increased risk of fracture in these cases.[9]

A previous study found that all pathological fractures occurred in stage B and associated the risk of pathological fractures with this stage.[4] In the study, 9 of the patients who experienced fractures were in stage B, while 2 had fractures in stage A. However, the presence of fractures in stage A in the study supports the hypothesis that fracture risk should not be overlooked in other stages and that a follow-up scale should be established based on risk factors.

Baghdadi et al reported the presence of the Pac-Man sign in 47% of distal tibial lesions and emphasized its 95% specificity in predicting fracture risk.[1] Consistent with the literature, the study also identified the Pac-Man sign as a significant predictor of fracture risk in distal tibial NOFs (P=.001). However, according to the data, while the Pac-Man sign was present in 5 patients who sustained pathological fractures due to distal tibial lesions, 3 fractured patients did not exhibit this sign. This indicates that although the Pac-Man sign is a significant predictor of fracture, its absence does not completely rule out the risk. Therefore, clinical and radiological risk factors should be considered collectively in the assessment.

In the study, consistent with the literature, Baghdadi fracture risk score, bone involvement exceeding 50%, and cortical thinning were found to be significantly higher in patients with pathological fractures (P=.001). Based on these findings, when evaluating parameters predictive of fracture risk, the study, which includes the largest patient cohort in the literature, identified that patients with more than 50% bone involvement, cortical thinning, and Ritschl stage B lesions have a high risk of fracture. Therefore, regular follow-up was recommended at 3-month intervals for this patient group. Additionally, surgical intervention should be considered in patients with a high fracture risk score or the presence of the Pac-Man sign.

Ritschl et al analyzed 107 NOFs and proposed that these lesions could be classified into 4 stages (A, B, C, D), each of which could be identified using a single radiograph.[7] In his study, 22 lesions were monitored for an average of 7.3 years using multiple radiological evaluations, while 18 lesions were followed for an average of 6.8 years with at least 2 radiographs. However, the study did not report specific data on the average duration of each stage.[7] In a study conducted by Herget et al, the average duration of each stage was reported as follows: Stage A lasted approximately 23 months, Stage B 21 months, Stage C 16 months, and Stage D 11 months.[4] Additionally, in another study conducted by Ritschl in 1990, the transition times between stages were reported as follows: A→B transition occurred in 7 lesions with an average duration of 19.7 months, B→C transition in 9 lesions with an average duration of 21.3 months, C→D transition with an average of 45.4 months, and A→D transition (in 4 patients) with an average of 69.2 months.[10] Although various studies in the literature have reported on the duration of each stage, there is no standardized approach for patient follow-up protocols.[4,7,10] In the study, the transition time from Stage A to Stage B was calculated as 17.3 ± 9.9 months (n=33), from Stage B to Stage C as 24.9 ± 16.2 months (n=68), and from Stage C to Stage D as 27.3 ± 15.9 months (n=44). The total transition time from Stage A to Stage D was found to be 44.9 ± 26.9 months (n=28). In the study, patients in Stage B, who had a high risk of pathological fracture, were followed up with AP and lateral radiographs every 3 months, while patients in other stages were monitored at 6-month intervals. This approximate 2-year period of close follow-up for Stage B lesions was chosen because Stage B lesions in the cohort took around 25 months on average to progress to Stage C, and because 2 years often coincides with patients approaching skeletal maturity. Once a high-risk lesion transitions to a later stage (Stage C or D) or the patient's growth plates close, the fracture risk is markedly reduced. Therefore, 3-month interval imaging is maintained for Stage B lesions until the lesion progresses to a lower-risk stage or until physis closure, after which follow-up can be extended or concluded. As a real-life data study presenting the largest case series on stage transition times in the literature, the research provides valuable guidance for clinicians in establishing stage-specific follow-up strategies, given the lack of a standardized protocol for NOF monitoring. The findings offer an important roadmap for determining the appropriate follow-up frequency based on NOF stages and facilitating the early identification of high-risk patients.

This study has several limitations. First, due to its retrospective design, patient follow-up durations and imaging frequencies were not standardized. Additionally, since the entry and exit stages of the lesions varied among patients, stage transition times could not be uniformly evaluated for all cases. Although 104 patients were analyzed, the number of patients who experienced pathological fractures (n=11) was limited, which restricted the statistical power of fracture risk factor analysis. Furthermore, the presence of lesions in different anatomical locations may limit the generalizability of the results. Although all cases were diagnosed as NOF, their localization within different bones of the lower extremity may have a differential impact on the risk of pathological fracture. Lastly, as this study was conducted in a single center, its findings may not be fully generalizable to other populations. Future studies should address these limitations by incorporating larger sample sizes, multicenter designs, and standardized protocols.

In conclusion, this study provides valuable insights into the natural course of NOFs, stage transition durations, and the risk of pathological fractures. The findings demonstrate that Ritschl stage B lesions, when accompanied by cortical thinning and more than 50% bone involvement, significantly increase the risk of fracture. Additionally, the Pac-Man sign is an important predictor of fracture risk in distal tibial lesions. In high-fracture-risk lesions, regular follow-up combined with timely surgical evaluation can help prevent complications effectively.

Based on these findings, the following practical follow-up strategy was proposed:

Stage B lesions with high fracture risk (presence of cortical thinning, >50% cortical involvement, or a high Baghdadi score): Should be monitored with AP and lateral radiographs every 3 months for an average of 2 years (or until the lesion transitions to a lower-risk stage). Surgical intervention should be considered in patients with multiple risk factors.

Stage A, C, and D lesions without high-risk features: Follow-up can be performed every 6 months or annually, depending on the patient's age and lesion characteristics.

Lesions with atypical features or diagnostic uncertainty should be evaluated using MRI or CT to clarify the diagnosis and assess fracture risk.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Metin Sabancı Baltalimanı Bone Diseases Research and Training Hospital (Approval no: 53/6, Date: 10.04.2023).

Informed Consent: Written informed consent was obtained from all individual patients or their legal representatives who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.İ., O.E.A., B.D.; Design – N.İ., O.E.A., B.D.; Supervision – O.E.A.; Materials – B.P., M.S.; Data Collection and/or Processing – B.D., B.P., M.S.; Analysis and/or Interpretation – N.İ.; Literature Search – N.İ., B.P.; Writing – N.İ., M.S.; Critical Review – N.İ., O.E.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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