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Nonossifying Fibromas: A Computed Tomography–based Criteria to Predict Fracture Risk

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Background: Nonossifying fibroma (NOF) is the most common benign osseous lesion in children; however, our understanding of which lesions progress to a fracture remains unclear. In this study, we seek to formulate a classification system for NOFs to assess for fracture risk and determine what this classification system tells us regarding fracture risk of the distal tibia and distal femur NOFs.

Methods: Charts were retrospectively reviewed for patients with NOFs. A 4-point criteria was created and used to calculate fracture risk for distal tibia and distal femur NOFs. The analysis included incidence, specificity, and sensitivity.

Results: One point was given for each of the following findings on computed tomography (CT) scan: (1) >50% width on coronal view; (2) >50% width on sagittal view; (3) any cortical breach; (4) lack of a neocortex. In total, 34 patients with NOFs of the distal tibia had CT scans, of which 14 fractured. Zero with a 0- or 1-point score fractured, 2 with a 2-point score fractured (20%), 4 with a 3-point score fractured (44%), and 8 with a 4-point score fractured (100%). Sensitivities of 1-, 2-, 3-, and 4-point scores were 100%, 100%, 85.7%, and 57.1%, respectively, and specificities were 71.4%, 71.4%, 80%, and 100%, respectively. A total of 41 patients with NOFs of the distal femur had CT scans, of which 5 fractured. Zero with a 0-point score fractured, 1 with a 1-point score fractured (4%), 0 with a 2-point score fractured, 1 with a 3-point score fractured (20%), and 3 with a 4-point score fractured (100%). Sensitivities of 1-, 2-, 3-, and 4-point scores were 100%, 80%, 80%, and 60%, respectively; and specificities were 60%, 87.8%, 90%, and 100%, respectively.

Conclusions: Our 4-point CT criteria is easy to apply and identifies patients at high risk of fracture, helping surgeons make decisions regarding treatment.

Level of Evidence: Level IV—prognostic study.

Key Words: nonossifying fibroma, NOF, NOF classification

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Nonossifying fibroma (NOF) is a common benign lesion of the bone found in children.[1] It was originally described by Dr Jaffe and Dr Lichtenstein[1] in 1942 as a "benign marrow-connective tissue tumor" seen on imaging as an eccentric lesion adjoined to the cortex near the physis on the shaft of a long bone. Our understanding of these lesions has progressed over the last 74 years—whereas all of Jaffe's patients were treated with surgery, we now know that many of these lesions will regress without treatment.[1,2] However, our understanding of when a patient requires advanced imaging and aggressive treatment remains unclear. Although around 30% of adolescents are assumed to have a NOF, to our knowledge no exact incidence of pathologic fracture has been reported. Risk of fracture seems to be associated with the strength of the remaining bone affected by lesion size, location, and aggressiveness and the loads applied to it.[3] In 1981 the Mayo Clinic retrospectively examined the charts of 23 patients who had pathologic fractures as a result of NOFs. They found that 100% of these fractures occurred when the lesion occupied >50% of the cortex, and determined that lesions that are at least 33 mm in length and that occupy at least 50% of the cortex should be closely monitored for impending fracture.[4] However, in 1997 a series of 22 patients with NOFs, each longer than 33 mm and occupying >50% of cortex, showed a pathologic fracture in only 41% of the patients, suggesting that these size parameters are not the only factor at play.[5] Furthermore, in 2010, a prospective study of 58 patients with a variety of benign osteolytic lesions (36 of which were NOFs) also found that lesions with the above size considerations did not necessarily lead to pathologic fracture and suggested more advanced imaging for better evaluation.[6]

Although valuable, the aforementioned studies and others are based on osteolytic lesions with a variety of anatomic locations and etiologies, and thus do not concur on a single best systematic approach to the NOF, and which lesions are likely to fracture and may therefore warrant prophylactic treatment. There is a clear need in the literature for a better stepwise method of the imaging and treatment of NOFs on the basis of their etiology and anatomic location. The purpose of this study is to formulate a new criteria for NOFs of the distal tibia and distal femur that will help aid orthopedic surgeons in determining fracture risk of the patient, and in doing so, help aid their thought process regarding observation versus surgical treatment.

METHODS

Institutional review board approval was obtained. A retrospective case series was carried out on patients seen at a single, large-volume academic center between January 2003 and March 2014. ICD-9 codes (M84.859) and CPT codes (27355, 27356, 27357) consistent with NOF and curettage/grafting of bone lesions, respectively, were reviewed. Inclusion criteria encompassed a diagnosis of NOF of the distal femur or distal tibia (the 2 most common locations of NOFs) as determined by radiographic findings and subsequent computed tomography (CT) scan evaluation of the lesion. NOF lesions of these 2 anatomic areas were included in the study, regardless of size. CT's were obtained at the physician's discretion, on the basis of factors including lesion size, apparent etiology, symptoms such as pain, and concern for fracture. Patients without adequate imaging studies were excluded.

Radiographs and CT scans of the distal tibia and distal femur NOFs were reviewed. Imaging that showed fractures was noted. A 4-point NOF criteria was created and utilized, appointing 1 point for each of the following findings on CT scan:

(1) Greater than 50% width on coronal [anterior-posterior (AP)] view.
(2) Greater than 50% width on sagittal (lateral) view.
(3) Any cortical breach.
(4) Lack of a neocortex.

Lesions were analyzed at their large cross-section in each plane (coronal, sagittal, axial). A "neocortex" was defined as an osseous thickening at the central border of the lesions approximating the thickness of the native cortex. It was theorized that such a thickening around the lesion may be protective against pathologic fracture, as opposed to lesions without this thickening where the lesion blends into the medullary canal. A cortical breach referred to any violation of the peripheral cortex of the bone. These 2 factors were evaluated on axial, sagittal, and coronal views (Fig. 1).

CT scans were reviewed by the authors, and a point value was assigned carefully on the basis of the guidelines previously mentioned. Calculations were performed for distal tibia NOFs, and then separately for distal femur NOFs.

Statistical analysis included the incidence of fracture per point value score, and the specificity and sensitivity of each category for fracture at each score. Incidence was calculated as the number of patients with a certain score that fractured divided by the total number of patients with that score. Sensitivity and specificity for 1-point score included patients with 1-, 2-, 3-, and 4-point scores, as these patients all had *at least* 1 point and would be identified by a 1-point process. Likewise, the sensitivity and specificity for 2-point score included patients with 2-, 3-, and 4-point scores, and sensitivity and specificity for 3-point score included patients with 3- and 4-point scores.

Finally, in order to assess the benefit of the CT-based system over simple radiographs, the incidence of fractures using only AP and lateral measurements were compared with the 4-point CT-based system. We assessed the incidence of fractures of patients with lesions $>50\%$ on AP and lateral, and AP or lateral views.

FIGURE 1. An example of a nonossifying fibroma of the distal tibia that fractured. This lesion has a score of "4" on our scale, with > 50% width on both coronal (A) and sagittal (B) views, cortical breach peripherally (C, black arrow), and lack of a neocortex at the central perimeter of the lesion (C, white arrow).

RESULTS

Utilizing CT scans, we were able to formulate 4-point criteria to assess fracture risk in NOFs:
(1) Greater than 50% width on coronal (AP) view.
(2) Greater than 50% width on sagittal (lateral) view.
(3) Any cortical breach.
(4) Lack of a neocortex.

The distal tibia group included 48 NOFs in 47 patients, of which there were 34 CT scans for review. There was a male predominance of 1.94:1, and a mean of age at first radiograph of 12.3 years with a range of 6 to 17. Of these patients, 14 presented with fracture, 8 with pain, and 12 presented incidentally. Of the 34 patients, 14 distal tibia NOFs visible on CT scan fractured. In total, 13 of these patients had NOFs at the distal lateral tibia, whereas 1 patient's NOF was at the distal posterior tibia. Of these patients, 0 with a 0- or 1-point score fractured, 2 of 10 patients with 2-point score fractured (20%), 4 of 9 patients with 3-point score fractured (44%), and 8 of 8 patients with a 4-point fractured (100%) (Fig. 1). The sensitivity and specificity of fracture incidence in NOFs of the distal tibia can be visualized in Table 1.

The distal femur group included 68 NOFs in 60 patients, of which there were 41 CT scans for review. There was a male predominance of 2.33:1, and a mean age at first radiograph of 12 years with a range of 4 to 19. Of these patients, 5 presented with fracture, 11 presented with pain, and 25 presented incidentally. Of the 41 patients, 5 distal femur NOFs visible on CT scan fractured. In total, 3 of these patients' NOFs were at the distal medial femur, and 2 were at the distal lateral femur. Of these patients, 0 patient with 0-point fractured, 1 patient with 1-point fractured (4%), 0 patient with 2-point fractured, 1 patient with 3-point fractured (20%), and 3 patients with 4-point fractured (100%). The sensitivities of the scoring system were 100% for 1-point, 80% for 2- and 3-points, and 60% for 4-point. The sensitivities and specificities of fracture incidence in NOFs of the distal femur can be viewed in Table 2.

When only considering AP and lateral measurements, as previous studies have done, there was a decrease in the accuracy of fracture incidence compared with the proposed 4-point system. For distal tibia lesions, there were 19 patients who had > 50% width on AP and lateral views, of which 12 fractured (63%). For the distal femur lesions, there were 10 patients who had > 50% width on AP and lateral views, of which 4 fractured (40%). This is in contrast to a 100% fracture rate of those patients who fulfilled all 4 of our CT requirements for both distal tibia and distal femur NOFs. Also of note, when examining patients who had > 50% width on AP or lateral views, there were 7 patients in the distal tibia category, of which 2 fractured (28.5%) and there were 5 patients in the distal femur group, of which 0 fractured (0%).

TABLE 1. Number and Percentages of Distal Tibia Patients That had Fractured Fitting Each Point Criteria, and Sensitivity and Specificity of Each Point Category for Fracture Risk

Points	No. Fractured/ Total	Percent Fractured	Sensitivity	Specificity
0	0/2	0	—	—
1	0/6	0	—	—
2	2/10	20	100	71.4
3	4/9	44	85.7	80
4	8/8	100	57.1	100

TABLE 2. Number and Percentages of Distal Femur Patients That had Fractured Fitting Each Point Criteria, and Sensitivity and Specificity of Each Point Category for Fracture Risk

Points	No. Fractured/ Total	Percent Fractured	Sensitivity	Specificity
0	0/3	0	—	—
1	1/25	4	100	60
2	0/5	0	80	87.8
3	1/5	20	80	90
4	3/3	100	60	100

DISCUSSION

NOFs are identified in about 30% of children; however, there has yet to be a risk stratification system created that is sensitive, specific, and particular to individual anatomic locations. We present the first study that utilizes a CT-based criteria for NOFs and the first scoring system that isolates NOFs in specific weight-bearing bones. We find that our NOF criteria including > 50% width on coronal (AP) view, > 50% width on sagittal (lateral) view, any cortical breach, and lack of a neocortex provides specific and sensitive results regarding fracture risk, particularly in the tibia.

Our scoring system assesses NOF fracture risk, unlike previous studies. The Mayo clinic performed a retrospective chart review over a 49-year period that contained 23 cases of patients with pathologic fractures through NOFs. The anatomic locations of the lesions included the tibia, fibula, and humerus. Of these 23 cases, 100% occurred in the bone that had an NOF occupying > 50% of the cortex on x-ray. They concluded that NOFs that are at least 33 mm in length and occupy > 50% of the cortex on x-ray should be followed for impending fracture.[4] Easley and Kneisl had a case series in 1997 that refuted this claim. Each of their 22 patients had a lesion longer than 33 mm and occupied > 50% of the cortex on x-ray. However, only 41% of these patients fractured. They concluded that size parameters are not the only variable in fracture risk through NOF.[5] In 2010, Leong and colleagues presented a prospective study of 58 patients with a variety of benign osteolytic lesions (36 were NOFs) and also found that a lesion with the above size considerations did not necessarily lead to pathologic fracture and suggested more advanced imaging for better evaluation. They noted that a previous retrospective study at their institution that suggested that in bones with lytic lesions, a 35% reduction in rigidity typically is the point at which fracture occurs. Using these parameters, they created an algorithm to determine the axial, bending, and torsional rigidity of the bones on the basis of CT cuts, and compared them with the contralateral limb, stating that bones with lesions having <65% rigidity were at an increased risk of fracture.[3,6] They were able to obtain sensitive results and were able to successfully avoid surgery in 30 patients who had lesions > 50% of the width of the bone; however, specificity could not be measured as all patients who fell within the high fracture risk category went on to surgery before fracture. Furthermore, it is unlikely that all institutions would be able to utilize such sophisticated programming, so although impressive, a simpler approach would be ideal.

A unique part of our NOF criteria is the concept of the "neocortex," which again, we define as an osseous thickening at the central border of the lesions approximating the thickness of the native cortex and any cortical breach at the peripheral cortex. In the classic biomechanical study by Brooks and colleagues, the authors showed that the presence of a breach in the cortex as small as a 2.8-mm drill hole significantly weakened the bone. This was measured by a decrease in energy-absorbing capacity of 55.2% and an increase in local stress concentration factor by 1.6.[7] We theorized that an intact cortex and/or presence of a neocortex would be preventative against fracture, as opposed to lesions that blend directly into the medullary canal. In Figure 2 we have an example of a NOF that has <50% width on coronal and sagittal views but has a cortical breach and lack of a neocortex. A stress fracture is also visible on CT. This is opposed to Figure 3, which demonstrates a large NOF with > 50% width on coronal and sagittal views, but there is no cortical breach and a neocortex is present. This patient did not fracture.

Roughly half of the pathologic fractures that occur through NOFs are located at the distal tibia.[4] Our results provide a sensitive and specific method for determining fracture risk in patients with NOF of the distal tibia, as shown in Table 1. Incidence of fracture increased in a stepwise manner; 0% of 0- and 1-point patients fractured, 20% of 2-point patients fractured, 44% of 3-point patients fractured, and notably, 100% of 4-point patients fractured. Location within the distal tibia likely did not play a role in fracture risk; 13 of 14 fractures occurred at the lateral aspect of the distal tibia, but 33 of 34 overall tibial NOFs were at this location overall. This prevalence is consistent with previous studies.[8]

Our recommendation would be to avoid surgery in most cases of 1-point patients, as they are unlikely to fracture and to strongly consider prophylactic treatment in patients with 3- and 4-points as they have a high likelihood of fracturing. The question arises with 2-point patients, as they seem to have equivocal sensitivity and specificity, and fractured at a relatively low, but still noteworthy incidence of 20%. These situations will rely strongly on surgeon preference and experience. We would recommend considering symptoms such as patient age, presence or absence of pain and/or swelling, and activity level given that this is a weight-bearing bone, as these factors have been cited previously in regard to function and fracture risk. Notably, many patients have noted playing sports such as football or soccer at the time of fracture, stressing the importance of activity level consideration. Although rare, there are also

FIGURE 2. This patient has a small nonossifying fibroma with a lesion occupying <50% on coronal (A) and sagittal (B) views; however, there is a breach in the cortex peripherally (C, black arrow) and lack of a neocortex centrally (C, white arrow). This lesion has a score of "2" and a fracture line is also identified coming from the lesion.

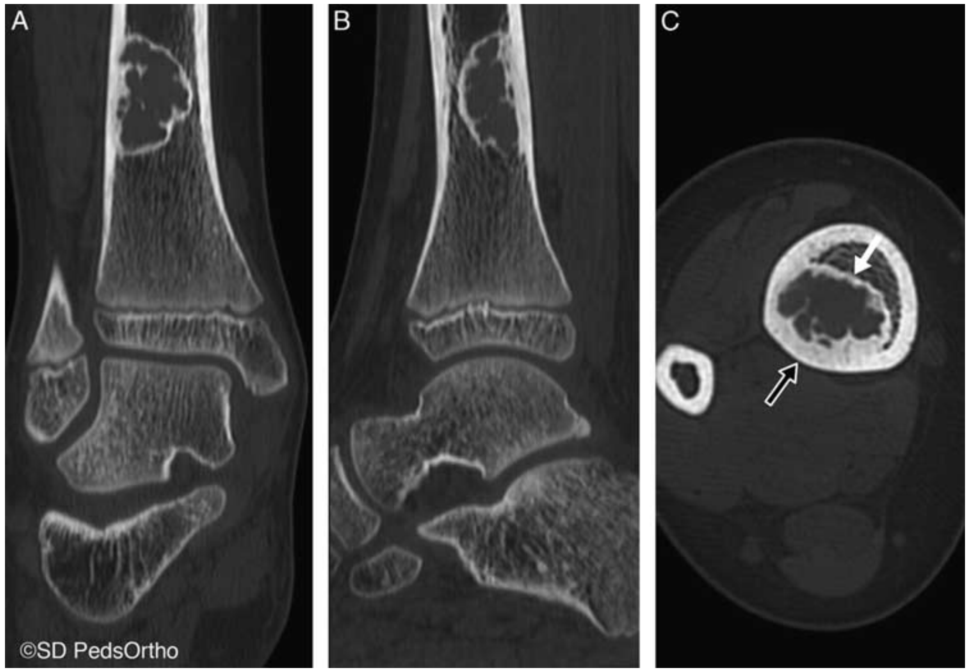

FIGURE 3. An example of a patient with a large nonossifying fibroma on coronal (A) and sagittal (B) views; however, there is an intact cortex peripherally (C, black arrow) and presence of a neocortex centrally (C, white arrow). This patient has a score of "2" and did not have a fracture.

medical issues to consider, including Jaffe-Campanacci syndrome, hypophosphatemic vitamin D-resistant rickets, and osteomalacia.[3,9–11] Finally, Ritschl et al's[12] staging categorization on the natural progression of NOFs can be considered as well; stages A to D describe the formation of the NOF to its natural resolution.[13] Herget and colleagues used these stages in their study and found that the only patients who suffered pathologic fractures were in the "critical" stage B, which lasts on average 21.3 months, and includes NOFs with thin but sclerotic borders, thin cortex that occasionally protrudes, polycyclic shape, and a variable distance from the epiphysis. They concluded that patients in stage B are at higher risk of fracture. They saw the majority of these fractures through NOFs of the distal tibia.[13,14]

Our results were less clear for the distal femur NOFs; this was most likely related to the low number of fractures that presented (5 of the 41 patients). It is not surprising that the number of fractures was low; although the distal femur is the most common place for a NOF to occur, only about 6% of pathologic fractures through NOFs are at this location.[4,15] In this study, sensitivities and specificities progressed in a stepwise manner, as seen in Table 2. Given that 100% of 4-point patients fractured with a specificity of 100%, we would recommend considering prophylactic treatment in these patients. Given a relatively high sensitivity and specificity for 3-point patients, it is reasonable to seriously consider prophylactic treatment as well. Again, surgeon experience and preference should come into play for the lower point scores. The distal femur is a weight-bearing bone, and like the tibia, other risks of fracture should be seriously considered, as previously discussed.[3,9–14] Lesion location also likely did not play a role in the distal femur fracture risk. In total, 60% of the fractures occurred at the posteromedial distal femur and 40% occurred at the posterolateral distal femur in a cohort with 54% of the lesions at the distal posteromedial femur, 30% at the distal posterolateral femur, and 10% at the medial cortex. This is consistent with previously published results.[15]

An argument can be made to lessen radiation exposure by only using radiographs. However, we found that the predictive value of fracture incidence is much greater when we combine the 4-point CT method, compared with just looking at AP and lateral views on x-rays. This agrees with the findings of Easley and Kneisl,[5] as discussed above. However, given that we found a higher percentage of patients who fractured with both AP and lateral findings than just a single finding, we would recommend that patients who do have both AP and lateral findings be considered for CT scan, as these patients are at higher fracture risk. We would also recommend a CT scan in settings with lesions where there is a concern for a cortical defect, as the presence of a defect and/or a neocortex can be better visualized on CT. An example where this was prudent can be seen again in Figure 2, where the CT was obtained because of concern for a cortical defect, and the CT later revealed a stress fracture. Furthermore, although it is impossible to know for sure that a cortical defect occurred before a fracture in this retrospective study, there were 13 tibias and 30 femurs with cortical defects that did not have fractures. From this we can assume that the majority of these lesions cause these cortical defects before fracture.

There were limitations in our study, including its retrospective nature. A prospective study would be more valid in terms of the scoring system's predictive value. Particularly, we evaluated patients who had already fractured on a CT scan. However, we do not think that this effects our study results, as our data show that the lesions that had fractured tended to have these findings on CT, and therefore one can infer that there would be a high risk of fracture in these patients, as there were zero patients in our population who had all 4 points and did not fracture. Pre-CT symptoms such as pain could also be better characterized in a prospective study. Another weakness is the increased radiation exposure with CT scans compared with radiographs. Although radiographs may be sufficient for small lesions in non–weight-bearing bones, it is our opinion that for larger lesions in weight-bearing bones that are at higher risk of fracture, a CT scan can provide valuable information in terms of better detail of the bone defect, and this opinion is supported in the literature.[3,6,10,16,17] Our statistical analysis was thorough with the inclusion of fracture incidence, sensitivity, and specificity of the scoring system; however, it should be noted that this study was not powered a priori to establish statistically significant differences between criteria groups. Selection bias should also be considered in this study. As it was retrospective in nature, the patients who had CT scans were those that the ordering surgeon likely thought was more likely to fracture and/or become symptomatic. Patients with smaller and painless NOFs were likely to have a lower probability of fracture. However, given that the patients who fractured typically had larger lesions on the basis of our NOF criteria, this likely does not change the overall conclusions of its utility.

In conclusion, our 4-point CT-based NOF criteria is easy to apply to any patient with the appropriate imaging and identifies patients at high risk of fracture. For tibia NOFs, the 4-point NOF criteria predictably correlates with fracture risk, as those scoring 0 and 1 point in this series did not fracture, and those scoring 3 and 4 points fractured at a high rate. We recommend that for NOFs of the distal tibia with a score of at least 3 points there should be strong consideration of preemptive surgical intervention, as nearly half of the patients with this score fractured, and the score presents a sensitivity and specificity of 85.7% and 80%, respectively. In total, 2-point scores approach a gray-zone for the distal tibia, as 20% of the patients in this group fractured. In a 2-point situation, surgeon discretion is recommended on the basis of additional symptoms. For the distal femoral NOFs, the 4-point NOF criteria was not as predictive, likely because of the low number or fractures that presented. However, within the femur group, this series demonstrated a 100% fracture incidence with a score of 4 points, so this should be strongly considered in the decision of whether to treat a patient prophylactically. For patients who do not yet have a CT scan, we would recommend that patients with lesions that are >50% width in both AP and lateral views, or those with questionable cortical defects obtain CT scans because of higher fracture risk. This is the first study to present a 4-point CT-based risk stratification scheme for NOFs. The 4-point scale gives orthopaedic surgeons additional information when deciding the appropriate course of treatment for patients with NOFs in their weight-bearing bones.

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