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What is This?

Correlation of MRI Grading of Bone Stress Injuries With Clinical Risk Factors and Return to Play

A 5-Year Prospective Study in Collegiate Track and Field Athletes

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Background: Bone stress injuries are common in track and field athletes. Knowledge of risk factors and correlation of these to magnetic resonance imaging (MRI) grading could be helpful in determining recovery time.

Purpose: To examine the relationships between MRI grading of bone stress injuries with clinical risk factors and time to return to sport in collegiate track and field athletes.

Study Design: Cohort study (prognosis); Level of evidence, 2.

Methods: A total of 211 male and female collegiate track and field and cross-country athletes were followed prospectively through their competitive seasons. All athletes had preparticipation history, physical examination, and anthropometric measurements obtained annually. An additional questionnaire was completed regarding nutritional behaviors, menstrual patterns, and prior injuries, as well as a 3-day diet record. Dual-energy X-ray absorptiometry was performed at baseline and each year of participation in the study. Athletes with clinical evidence of bone stress injuries had plain radiographs. If radiograph findings were negative, MRI was performed. Bone stress injuries were evaluated by 2 independent radiologists utilizing an MRI grading system. The MRI grading and risk factors were evaluated to identify predictors of time to return to sport.

Results: Thirty-four of the athletes (12 men, 22 women) sustained 61 bone stress injuries during the 5-year study period. The mean prospective assessment for participants was 2.7 years. In the multiple regression model, MRI grade and total-body bone mineral density (BMD) emerged as significant and independent predictors of time to return to sport. Specifically, the higher the MRI grade ($P = .004$) and lower the BMD ($P = .030$), the longer the recovery time. Location of the bone injury at predominantly trabecular sites of the femoral neck, pubic bone, and sacrum was also associated with a prolonged time to return to sport. Female athletes with oligomenorrhea and amenorrhea had bone stress injuries of higher MRI grades compared with eumenorrheic athletes ($P = .009$).

Conclusion: Higher MRI grade, lower BMD, and skeletal sites of predominant trabecular bone structures were associated with a delayed recovery of bone stress injuries in track and field athletes. Knowledge of these risk factors, as well as nutritional and menstrual factors, can be clinically useful in determining injury severity and time to return to sport.

Keywords: female athlete triad; MRI grading; bone stress injury; stress fracture

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Bone stress injuries result from chronic repetitive training and can range from a stress reaction to a cortical fracture. These injuries, more common in certain populations of athletes, account for up to 10% of all injuries seen in sports medicine clinics.[27,40,50] Prospective studies suggest an incidence of up to 21% in track and field athletes[9] and 31% in military recruits.[41] Bone stress injuries are an important issue for which the diagnosis and management evolve as our understanding of the multifactorial processes and diagnostic tools develop.

According to Wolff's law,[52] external mechanical forces induce adaptive changes in the internal and external architecture of bone. When the balance between formation and resorption is disturbed, bone weakens and becomes increasingly susceptible to injury. The development of a cortical fracture can occur with consistent stress.[3,30] Johnson and colleagues,[30] in their histological analysis of bone stress injuries by bone biopsies, found that early discontinuation of repetitive stress prevented the progression

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to a fracture. Current understanding suggests that bone stress injuries not identified and managed appropriately can progress to a more serious fracture,[18,22,23,31,32,44] and preventive strategies, including the identification and modification of risk factors, may help prevent the progression to a frank fracture.[22,32]

Historically, radiographs and radionuclide bone scans have been the standard diagnostic tools used to assess and diagnose bone stress injuries. Although standard radiographs may reveal bony changes associated with stress injuries, the findings are often normal.[10,17,47,56] In addition to being affected by the time of onset of symptoms, radiographic abnormalities are also affected by the skeletal location of the bone stress injury.[17] While radiographs are usually the first diagnostic test ordered, their sensitivity is only approximately 10% in the early stages of the injury.[35] If standard radiograph results are negative in the presence of concerning clinical findings, they should be supplemented with diagnostic studies that have greater sensitivity for bone stress injuries. Radionuclide bone scans can detect bone stress injuries as soon as 2 to 8 days after symptoms are first noted.[47] Roub and colleagues,[47] and subsequently Chisin et al[14] and Zwas et al,[56] developed a grading system of a progressive stress injury using radioisotope findings, with a cortical fracture displaying more intense uptake. The use of bone scans as an independent diagnostic tool is, however, limited by low specificity and the lack of visualization of a potential fracture line.[19] Computed tomography (CT) is useful and specific when a fracture line exists, but this occurs at the late stage of a bone stress injury.[18] Ultrasound has been used to assess bone stress injuries in track and field athletes, with a reported sensitivity of 81.9% and specificity of 66.6% compared with magnetic resonance imaging (MRI),[45] but further studies are needed to assess the use of ultrasound as a method of screening.

The application of MRI[24] for the diagnosis of bone stress injuries allows for a sensitivity comparable with, or greater than, scintigraphy and a nonionizing method of detecting and localizing fracture lines.[16] Also, MRI is highly specific and provides useful information about the extent of the bone injury and damage to surrounding tissue.[49] Even at early onset, MRI has the best combined specificity and sensitivity for bone stress injuries and is the recommended diagnostic imaging test to assess the spectrum of bone stress injuries among symptomatic patients.[10,17,21,53]

The full spectrum of bone stress injuries by MRI can be depicted as a periosteal or bone marrow edema pattern of high signals on T2-weighted and short T1 inversion recovery (STIR) sequences and low signals on T1-weighted sequences, with further injury progression demonstrated as a frank cortical fracture.[4,17,18] Fredericson et al[18] described early bone stress injuries on MRI often beginning with periosteal edema and, with worsening of the injury, progressing to include marrow edema. If untreated, the injury can further progress to an identifiable stress fracture. Knowledge of the clinical setting is imperative to the interpretation of MRI findings. Using fat-suppressed T2-weighted sequences on MRI, Fredericson and colleagues[18] clinically correlated this progression in a retrospective review of 33 tibial bone stress injuries and developed an MRI grading system based on the pattern of periosteal and marrow edema. Fredericson et al,[18] in their retrospective study, found that their grading scale correlated with both the extent of clinical findings and time to full return to activity. In a retrospective review of 74 track and field athletes with bone stress injuries, Arendt et al[2] reported similar findings using a modified MRI grading scale that replaced fat-suppressed T2 sequences with STIR sequences. Yao and colleagues,[53] in their retrospective study examining the prognostic value of MRI grading of stress injuries of bone in 24 patients, concluded that the findings of an abnormal cortical signal intensity or a fracture line were of prognostic value, leading to a longer recovery time. However, there was otherwise no prognostic correlation with the bone stress injuries receiving lower MRI grades with recovery time.[53] Beck and colleagues,[7] in their analysis of tibial bone stress injuries in male and female active patients aged 18 to 50 years, found a trend toward a higher MRI grade and longer recovery time, but this did not reach statistical significance. In this same study, radiographic, bone scan, and CT severity of tibial stress injuries were not related to time to healing.[7] Therefore, MRI grading provides a potentially standardized approach to the diagnosis and management of bone stress injuries and appears superior to other imaging modalities.[7]

To our knowledge, no prospective studies have correlated MRI grading of bone stress injuries at multiple skeletal sites with risk factors and time to return to full sport participation. Therefore, the purpose of this study was to prospectively assess MRI grading of bone stress injuries at various skeletal sites and assess a correlation with risk factors and time to return to sport among male and

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female collegiate track and field athletes. The authors' hypothesis was that higher grade bone stress injuries as assessed prospectively by MRI would be associated with a prolonged recovery. It was also hypothesized that risk factors associated with the female athlete triad would be associated with a prolonged recovery in female athletes.

MATERIALS AND METHODS

Study Participants

A total of 211 male and female collegiate track and field and cross-country athletes from a major Division I university participated in the prospective study over a 5-year period between the fall of 1996 and the spring of 2001. Athletes on the cross-country and track and field teams were asked to participate in the study each year at their preparticipation physical examination before the start of their season and were followed during the duration of the study period. There were 83 athletes on roster year 1, 89 in year 2, 103 in year 3, 98 in year 4, and 88 in year 5. Athlete volunteers consented after appropriate institutional review board approval for human participant research. A self-reported questionnaire on demographic information and general background information (including bone injury history, detailed current and past menstrual history, history of disordered eating/eating disorders, exercise history, general health information, and medications including oral contraceptive pill use) was completed annually by the athlete participant alone at the start of the cross-country and/or track and field season in addition to the standard annual preparticipation physical examination questionnaire that is required at this institution. The questionnaire had not been previously validated. Three-day food diaries were obtained for each athlete participant. For assessment of disordered eating behaviors, data were used from the questionnaire and food diary that were completed by the athlete and a physician interview along with a multidisciplinary assessment including evaluations by the team dietitian and a psychologist utilizing *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition (*DSM-IV*) criteria for eating disorders. Dual-energy X-ray absorptiometry (DXA) studies were administered at baseline and annually for each participant.

Imaging Studies for Suspected Bone Stress Injuries

Athletes on the cross-country and track and field teams were followed prospectively for the occurrence of a bone stress injury throughout their season and until the end of the study period. If an athlete reported pain, he or she was initially evaluated by a certified athletic trainer and then referred to a team physician if a bone stress injury was suspected. Initial plain radiographs were obtained for the majority of suspected bone stress injuries, and if the results were negative, MRI or, in a few instances, bone scintigraphy was performed (Figure 1). Some athletes bypassed standard radiographs and underwent MRI as their initial study.

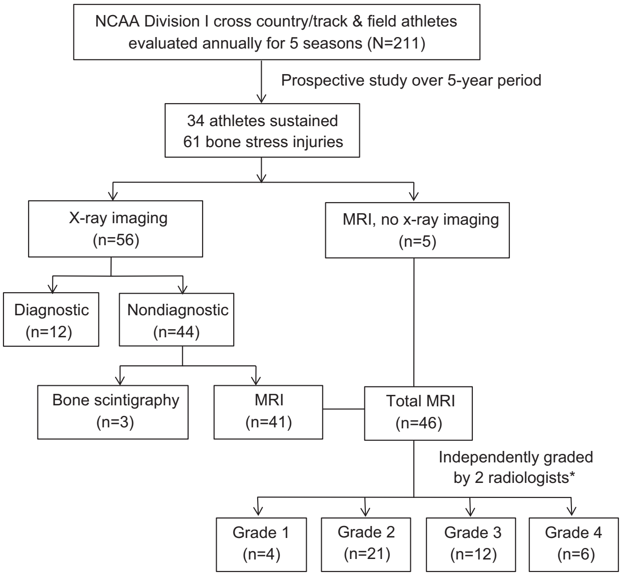

Figure 1. Number of bone stress injuries incurred, diagnostic imaging utilized, and magnetic resonance imaging (MRI) grade results. *Three MRI scans were not graded because of incomplete data on time to return to sport.

Grading by MRI for a suspected bone stress injury in this study was performed independently by 2 fellowship-trained musculoskeletal radiologists (Table 1) using modified versions of the MRI grading scale described by Fredericson and colleagues[18] for tibial bone stress injuries and by Arendt et al[2,4] for bone stress injuries in athletes at all skeletal sites. In defining a grade 1 injury, our grading scale used the presence of mild marrow edema on fat-suppressed T2-weighted images (but not T1-weighted images) or periosteal edema. For grade 2 bone stress injuries at our institution, moderate marrow edema on T2-weighted images (but not T1) or periosteal edema was used and differed from grade 1 in the degree of marrow or periosteal edema. Grade 3 bone stress injuries included the presence of severe marrow edema or periosteal edema on both T2-weighted images and T1-weighted images (in the same location), but without a fracture line. Grade 4 bone stress injuries were similar to grade 3 injuries in the severity of marrow or periosteal edema but included the presence of a fracture line on either T1- or T2-weighted images. Examples of the MRI grading used for our study are illustrated in Figures 2 to 5. On a few occasions only, there was disagreement in MRI grading. In these instances, a consensus was reached between the 2 independent radiologists.

Anthropometric Measurements

The athletes' height and weight were measured and body mass index (BMI) calculated at baseline and annually.

Bone Density Measurements

Dual-energy X-ray absorptiometry studies were performed to measure bone mineral density (BMD) using a Hologic QDR

TABLE 1
MRI Grading Scales for Bone Stress Injuries[a]

MRI Grade	Fredericson et al[18]	Arendt et al[2]	Nattiv et al 2013 (Current Study)
1	Mild to moderate periosteal edema on T2; normal marrow on T2 and T1	Positive signal change on STIR	Mild marrow or periosteal edema on T2[b]; T1 normal[c]
2	Moderate to severe periosteal edema on T2; marrow edema on T2 but not T1	Positive STIR plus positive T2	Moderate marrow or periosteal edema plus positive T2; T1 normal
3	Moderate to severe periosteal edema on T2; marrow edema on T2 and T1	Positive STIR plus positive T2 and T1	Severe marrow or periosteal edema on T2 and T1
4	Moderate to severe periosteal edema on T2; marrow edema on T2 and T1; fracture line present	Positive fracture line on T2 or T1	Severe marrow or periosteal edema on T2 and T1 plus fracture line on T2 or T1

[a] Adapted from Table 1 of Fredericson et al[18] and Table 3 of Arendt et al.[2] MRI, magnetic resonance imaging; STIR, short T1 inversion recovery.

[b] Note that periosteal edema is not a necessary criterion for grade 1 or any MRI grade bone stress injury.

[c] Radiograph results are often negative at all grades; they may be normal, or a periosteal reaction may be evident.

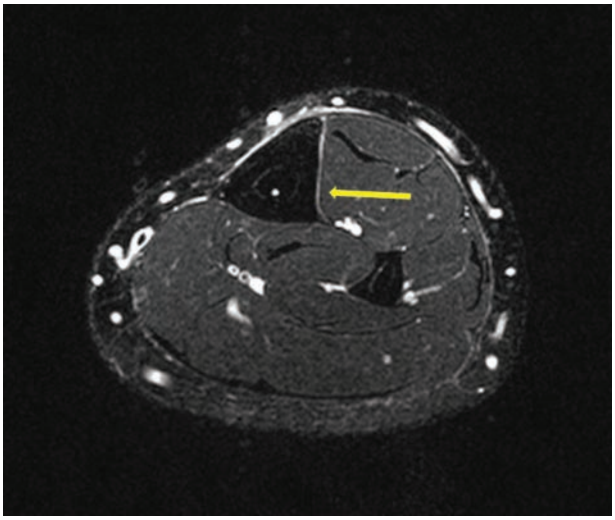

Figure 2. Grade 1 bone stress injury of the tibia on magnetic resonance imaging. Arrow points to mild periosteal edema depicted in this axial image of the posteromedial tibia. Grade 1 includes mild marrow or periosteal edema on the T2-weighted image (but not T1).

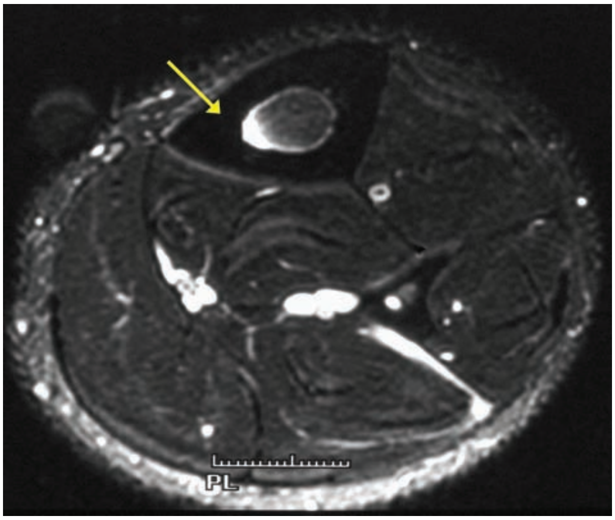

Figure 3. Grade 2 bone stress injury of the tibia on magnetic resonance imaging. Arrow points to moderate marrow edema on the T2-weighted image. Grade 2 includes moderate marrow or periosteal edema on the T2-weighted image (but not T1).

4500A scanner (Hologic Inc, Bedford, Massachusetts). Baseline and follow-up tests were performed on the same DXA scanner by a single certified densitometry technician. The following skeletal sites were measured on each participant scanned: lumbar spine L1 to L4, nondominant total hip and femoral neck, total body, nondominant forearm (one-third radius), and tibia. Percentages of body fat and body composition were also obtained on each participant by DXA.

Weightbearing and Full Return to Sport

For each athlete with a bone stress injury, the details of days and/or weeks of nonweightbearing, partial weightbearing, full weightbearing, and full return to sport were documented in the athlete's chart by the team physician in the athletic training room and supplemented by the certified athletic trainer when needed. For athletes sustaining concurrent bone stress injuries in the same skeletal site (same side or opposite side), the injury with the higher MRI grade was used for time to return to sport. The same team physician evaluated each athlete participant in the study when a bone stress injury was suspected and/or identified and for the majority of the athlete's follow-up visits. The mean follow-up visit interval was every 2 weeks from the diagnosis of a bone stress injury to full return to sport.

Site of Injury

The skeletal site of injury was identified. Bone stress injuries occurring in trabecular versus cortical bone sites were

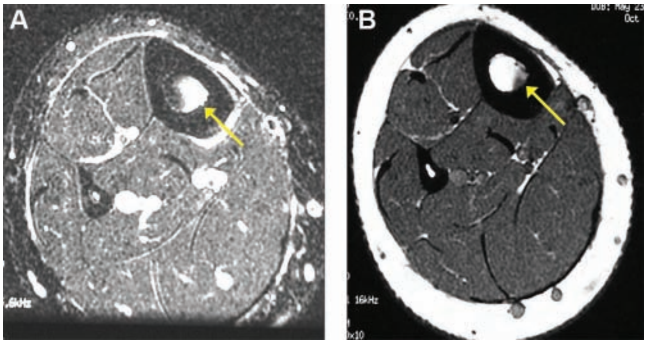

Figure 4. Grade 3 bone stress injury of the tibia on magnetic resonance imaging. (A) Arrow points to severe marrow edema on the T2-weighted image, and (B) arrow illustrates corresponding marrow edema on the T1-weighted image. Grade 3 bone stress injury includes severe marrow edema or periosteal edema on T2- and T1-weighted images.

assessed for time to return to sport and MRI grade. Trabecular bone sites included the femoral neck, sacrum, and pubic bones. Cortical bone sites included the tibia, fibula, metatarsals, navicular, and great toe sesamoids. Bone stress injuries at more than 1 site concurrently were recorded.

Statistical Analysis

Frequencies and means (mean ± SEM) were calculated to identify characteristics and sample distribution (eg, sex, ethnicity, track and field event, height, weight, menstrual status, MRI grade) at baseline and time of injury. Analysis of variance (ANOVA) and analysis of covariance (ANCOVA) with Bonferroni correction assessed differences in descriptive traits, bone mass, and time to full return to sport among groups based on MRI grade and fracture location (trabecular vs cortical sites). Chi-square analyses evaluated differences in proportions between groups. Pearson correlations were run to identify factors significantly associated with time to full return to sport. Multiple linear regression assessed variables that significantly contributed to the prediction of time to full return to sport. All analyses were conducted using the Statistical Package for the Social Sciences, version 16.0 (SPSS Inc, Chicago, Illinois).

A power analysis was performed before the initiation of the study using PASS60 (JL Hintz, 1996) and based on a sample size of 80 or 40 athlete participants depending on the possible need to stratify data by sex. It was found that for a linear regression analysis with 80 participants, the power would be at least 84% for detecting covariates that improve the R^2 value by $\geq$0.10. For an analysis based on 40 participants, the power would be at least 74% for detecting increases in R^2 of $\geq$0.15.

RESULTS

Of the 211 National Collegiate Athletic Association (NCAA) track and field and cross-country athletes, 34 (12 men, 22 women) sustained 61 bone stress injuries during the 5-year study period. The mean age at the time of injury was 20.5 ± 0.2 years. All athlete participants with bone stress injuries continued their participation from diagnosis through full return to sport. The mean time of the athlete's prospective participation in the study was 2.7 years. Fifty-six percent of the athletes were white, 29% African American, and 12% Hispanic. Over half (59%) of the athletes who sustained a bone stress injury were cross-country runners who trained and competed in middle- and/or long-distance events. Twenty-three percent of the female athletes reported oligomenorrhea and/or amenorrhea during the 5-year study period. Physical and descriptive characteristics of the 34 athletes who sustained bone stress injuries are reported in Table 2.

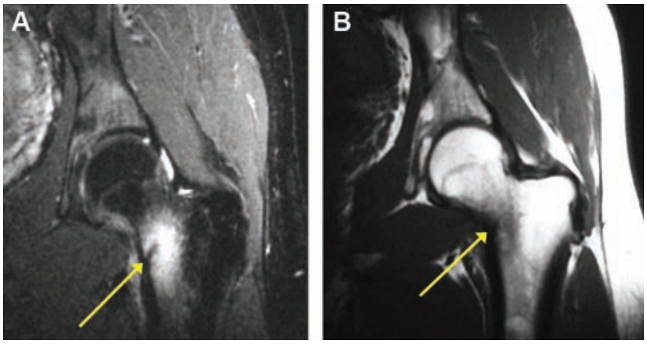

Figure 5. Grade 4 bone stress injury of the femoral neck on magnetic resonance imaging. (A) Arrow points to severe marrow edema on the T2-weighted image plus a fracture line. (B) Arrow points to severe marrow edema on the corresponding T1-weighted image. Grade 4 bone stress injury includes severe marrow or periosteal edema on T2- and T1-weighted images plus a fracture line.

Skeletal sites of the bone stress injury and frequency of injuries are reported in Table 3. The tibia (51% of injuries) and metatarsals (21% of injuries) were the most frequent sites injured. Seventeen athletes (50%) sustained multiple bone stress injuries (11, 2, and 4 athletes had 2, 3, and 4 fractures, respectively) during the study period. Of the athletes with multiple bone stress injuries, 11 (65%) had more than 1 concurrently.

Figure 1 outlines the number of injuries incurred, imaging modality used, and MRI grade distribution. Fifty-six athletes with symptoms consistent with a bone stress injury underwent standard radiographs of the injured site, while 5 were directed to MRI without radiographs. The majority of athletes with bone stress injuries, 44 of 56 (78.6%), had normal plain radiograph findings at the time of initial assessment, with 12 of the 56 (21.4%) injuries diagnosed with plain radiographs alone (Table 4). The skeletal sites at which bone stress injuries were most commonly seen on plain radiographs were in the tibia (47.6%) and metatarsal bones (46.2%). Of the remaining injuries that required a further diagnostic test, 3 (6.8%) underwent bone scintigraphy, and 41 (93.2%) underwent MRI (Figure 1). Of the 46 injuries evaluated by MRI, the frequency of each grade was as follows: grade 1, n = 4;

TABLE 2
Physical and Descriptive Characteristics of Athletes Who Sustained a Bone Stress Injury During the 5-Year Prospective Study[a]

	Female (n = 22)	Male (n = 12)
Ethnicity, n (%)		
White	12 (55)	7 (58)
Black	8 (36)	2 (17)
Hispanic	2 (9)	2 (17)
Asian	0 (0)	0 (0)
Other	0 (0)	1 (8)
Event, n (%)		
Distance	13 (59)	7 (58)
Sprints	5 (23)	2 (17)
Jumps	4 (18)	3 (25)
Height, cm	166.9 ± 1.3	178.4 ± 1.9
Weight, kg	57.7 ± 1.6	67.5 ± 2.0
BMI, kg/m^2	20.5 ± 0.3	21.1 ± 0.4
Lean mass, kg	44.3 ± 0.8	58.5 ± 1.2
Body fat, %	17.2 ± 0.8	12.1 ± 1.1
Menstrual status, n (%)		
Regular	8 (36)	—
Regular/oligomenorrhea/ amenorrhea	6 (27)	—
Oligomenorrhea/amenorrhea	5 (23)	—
History of disordered eating, n (%)	4 (18)	0 (0)
History of fracture, n (%)	12 (55)	4 (36)

[a] Values are expressed as mean ± SEM unless otherwise indicated. BMI, body mass index.

grade 2, n = 21; grade 3, n = 12; and grade 4, n = 6. Three MRI scans were not graded because of missing data on return to sport. The frequency of each grade according to sex is reported in Table 3. Female compared with male participants trended toward a higher MRI grade: 2.6 ± 0.1 versus 2.1 ± 0.3, respectively (*P* = .09). Over half (58.1%) of all MRI scans were evaluated as grade 1 or 2 bone stress injuries. Only 14.0% of all injuries evaluated by MRI were grade 4 (exhibiting a visible fracture line).

Characteristics among athletes with a lower (grade 1 or 2) compared with a higher (grade 3 or 4) MRI grade injury are presented in Table 5. Athletes with a higher MRI grade injury exhibited a lower BMD at the total hip (*P* = .050) and radius (*P* = .047). Among the female athletes, MRI grade was significantly higher among those classified with oligomenorrhea/amenorrhea compared with eumenorrhea: 3.5 ± 0.3 versus 2.5 ± 0.2, respectively (*P* = .009).

A significantly higher percentage of athletes with trabecular bone injuries (those in the femoral neck, pubic bone, or sacrum) compared with cortical bone sites ran middle and/or long distance, exhibited disordered eating, and had oligomenorrhea/amenorrhea (*P* = .005, *P* = .04, and *P* = .005, respectively) (Table 6). Those with bone stress injuries at trabecular sites had a significantly lower bone mass at the lumbar spine, femoral neck, and total hip (*P* < .001) (Table 6). Time to full return to sport was significantly longer for those with a bone stress injury at a trabecular versus cortical site (*P* < .001), even after adjusting for MRI grade (*P* = .01) (Table 6).

The mean time to full return to sport for grade 4 bone stress injuries (31.7 ± 3.7 weeks) was significantly higher compared with grade 3 (18.8 ± 2.9 weeks; *P* = .055), grade

TABLE 3
Frequency of Injury Site and MRI Grade Among Male and Female Athletes[a]

	Frequency		Total	
	Female (n = 22)	Male (n = 12)	n	%
Injury site				
Tibia				
Anterior	2	1	3	
Posteromedial	18	10	28	
Total	20	11	31	51
Metatarsal				
Second	2	1	3	
Third	3	3	6	
Fourth	2	1	3	
Fifth	0	1	1	
Total	7	6	13	21
Femur				
Femoral neck	1	1	2	
Femoral shaft	2	0	2	
Total	3	1	4	7
Sacrum	3	0	3	5
Sesamoid				
Medial	2	1	3	
Lateral	0	0	0	
Total	2	1	3	5
Fibula	1	2	3	5
Pubic	0	2	2	3
Navicular	2	0	2	3
Total			61	100
MRI grade				
1	3	1	4	9
2	13	8	21	49
3	10	2	12	28
4	6	0	6	14
Total			43	100

[a] MRI, magnetic resonance imaging.

TABLE 4
Bone Stress Injuries Diagnosed by Radiographs (Not Requiring MRI)[a]

Injury Site	n	%
Tibia	10/21	47.6
Metatarsals	6/13	46.2
Sesamoid	1/3	33.3
Fibula	1/3	33.3
Femur[b]	0/4	0
Sacrum[b]	0/3	0
Pubic[b]	0/2	0
Navicular	0/2	0

[a] MRI, magnetic resonance imaging.
[b] Sites high in trabecular bone.

TABLE 5
Characteristics Among Athletes With Lower (Grade 1 and 2) Compared With Higher (Grade 3 and 4) Grade Bone Stress Injuries[a]

	MRI Grade		
	1 and 2 (n = 25)	3 and 4 (n = 18)	*P* Value
Age, y	20.7 ± 0.3	20.2 ± 0.3	NS
Height,[b] cm	168.9 ± 1.0	169.8 ± 1.2	NS
Weight,[b] kg	60.2 ± 1.1	59.0 ± 1.4	NS
BMI[b]	21.1 ± 0.3	20.2 ± 0.3	.068
Body fat,[b] %	14.5 ± 0.9	17.4 ± 1.2	.067
Lean mass,[b] kg	48.6 ± 0.9	46.9 ± 1.1	NS
BMD,[b] g/cm^2			
Spine	1.049 ± 0.032	0.969 ± 0.037	NS
Femoral neck	0.922 ± 0.023	0.882 ± 0.027	NS
Total hip	1.104 ± 0.029	1.015 ± 0.033	.050
Radius	0.450 ± 0.011	0.413 ± 0.014	.047
Tibia	1.013 ± 0.017	1.038 ± 0.022	NS
Total body	1.236 ± 0.022	1.184 ± 0.028	NS
Female, %	64.0	88.9	.065
White, %	56.0	83.0	.059
Distance event, %	60.0	72.2	NS
Oligomenorrhea/amenorrhea, %	0	40.0	.010
History of disordered eating, %	12.0	22.2	NS
History of fracture, %	64.0	55.6	NS

[a] Values are expressed as mean ± SEM unless otherwise indicated. Means were assessed by ANOVA/ANCOVA. χ^2 tests assessed percentages between groups. α = .05. BMD, bone mineral density; BMI, body mass index; MRI, magnetic resonance imaging; NS, not significant.

[b] Adjusted for sex.

2 (13.5 ± 2.1 weeks; P = .001), and grade 1 injuries (11.4 ± 4.5 weeks; P = .008). The mean time to full return to sport for grade 3 and 4 bone stress injuries was significantly higher than for grade 1 and 2 injuries (23.6 ± 2.4 weeks vs 13.1 ± 2.0 weeks, respectively; P = .002) (Figure 6). Among grade 3 and 4 injuries, the mean time to return to sport was significantly longer for those at sites high in trabecular versus cortical bone (38.1 ± 6.4 vs 18.8 ± 2.1 weeks, respectively; P = .005). Among grade 1 and 2 injuries, there was no difference in the mean time to return to sport between injuries at sites high in trabecular versus cortical bone (17.1 ± 9.1 vs 12.7 ± 1.6 weeks, respectively; P = .75) (Figure 7).

The mean time to full return to sport was longer for athletes who were white (20.7 ± 2.0 vs 11.6 ± 2.7 weeks, respectively; $P < .05$), ran middle/long distance (20.0 ± 2.2 vs 13.4 ± 2.7 weeks, respectively; P = .07), and were categorized with an eating disorder (31.3 ± 4.3 vs 15.4 ± 1.7 weeks, respectively; $P < .005$). Fracture history, menstrual status, age at menarche, and sex were not significantly associated with time to return to sport. Pearson correlations identified factors that were positively (MRI grade, r = 0.57; muscle edema, r = 0.43; presence of a fracture line, r = 0.56; $P < .05$) and negatively (BMD of lumbar spine, $r = -0.54$; BMD of femoral neck, $r = -0.54$; BMD of total hip, $r = -0.59$; BMD of radius, $r = -0.51$; total-body BMD, $r = -0.51$; BMI, $r = -0.51$; age at menarche, r = 0.48; $P < .05$) correlated with time to full return to sport.

The multiple linear regression analysis indicated that MRI grade and total-body BMD emerged as significant independent predictors of time to full return to sport among the collegiate athletes (Table 7). The trabecular versus cortical bone site also trended toward significance (P = .063). The model including these 3 factors and BMI accounted for 68% (adjusted R^2 = 0.68) of the variation in time to return to sport (Table 7). Also, MRI grade was a positive predictor, indicating that injuries classified with a higher MRI grade resulted in a significantly increased time to return to sport. Total-body BMD emerged as a significant negative predictor, indicating a protective effect of BMD on time to full return to sport.

DISCUSSION

Although retrospective studies have supported the importance of MRI evaluation and grading of bone stress injuries,[2,18] this study serves as the first large prospective analysis of MRI grading, its correlation with risk factors, and association with time to return to sport. Our primary finding was that MRI grade and total-body BMD emerged as significant and independent predictors of time to full return to sport. This clinically relevant observation and evidence-based model can potentially be used to help physicians guide athletes in their recovery and rehabilitation. In addition, these findings suggest that optimizing bone mass may not only reduce the risk of sustaining a stress injury to bone but also contribute to an improved healing potential and reduced recovery time. Further studies would be needed, however, to assess this hypothesis.

TABLE 6
Descriptive Characteristics, MRI Grade, and Time to Return to Sport Among Athletes With Bone Stress Injuries at Cortical and Trabecular Sites[a]

	Cortical (n = 36)	Trabecular (n = 7)	*P* Value
Age, y	20.5 ± 0.2	20.4 ± 0.5	NS
BMI	20.8 ± 0.2	20.1 ± 0.9	NS
MRI grade	2.3 ± 0.1	3.1 ± 0.4	.02
BMD, g/cm^2			
Lumbar spine	1.058 ± 0.021	0.828 ± 0.048	<.001
Femoral neck	0.933 ± 0.015	0.785 ± 0.042	<.001
Total hip	1.101 ± 0.021	0.913 ± 0.040	<.001
Radius	0.442 ± 0.009	0.399 ± 0.033	.10
Tibia	1.018 ± 0.018	1.049 ± 0.018	NS
Total body	1.223 ± 0.017	1.147 ± 0.054	.09
Return to sport, wk	14.9 ± 1.4	31.1 ± 6.4	<.001
Adjusted MRI grade	15.8 ± 1.5	26.7 ± 3.8	.01
Female, %	77.8	57.1	NS
White, %	61.1	100.0	.045
Distance event, %	58.3	100.0	.005
Oligomenorrhea/amenorrhea, %	12.5	75.0	.005
History of disordered eating, %	11.1	42.9	.04
History of fracture, %	69.4	14.3	.006

[a] Values are expressed as mean ± SEM unless otherwise indicated. Data presented are for those athletes with MRI data. Means were assessed by independent *t* test and ANCOVA. χ^2 tests assessed percentages between groups. $\alpha = .05$. Trabecular fractures include those of the sacrum, pubic, and femoral neck. BMD, bone mineral density; BMI, body mass index; MRI, magnetic resonance imaging; NS, not significant.

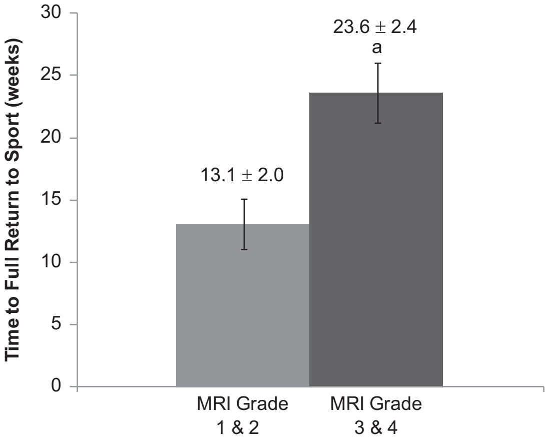

Figure 6. Time to full return to sport (weeks) for injuries evaluated using magnetic resonance imaging (n = 43): comparison between grades 1 and 2 (n = 25) versus grades 3 and 4 (n = 18). [a]Grade 3 and 4 injuries were significantly longer than grade 1 and 2 injuries (23.6 ± 2.4 vs 13.1 ± 2.0 weeks, respectively; *P* = .002, independent *t* tests).

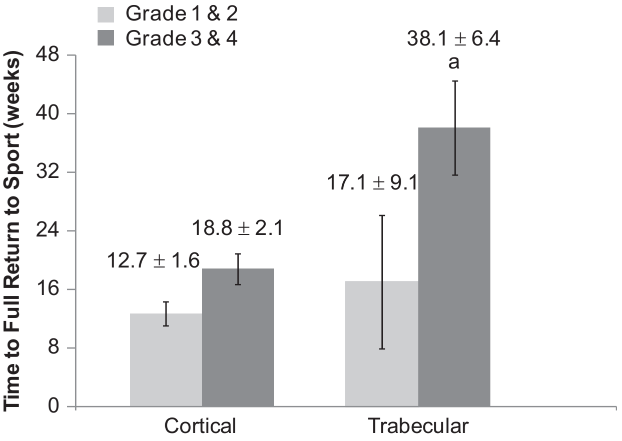

Figure 7. Time to full return to sport (weeks) for injuries evaluated using magnetic resonance imaging (n = 43): comparison between grades 1 and 2 (n = 25) versus grades 3 and 4 (n = 18) for injuries occurring at cortical (n = 36) and trabecular (n = 7) bone sites. [a]Grade 3 and 4 trabecular bone stress injuries were significantly longer than grade 3 and 4 cortical bone stress injuries (38.1 ± 6.4 vs 18.8 ± 2.1 weeks, respectively; *P* = .005). No differences were observed between grade 1 and 2 trabecular bone stress injuries versus grade 1 and 2 cortical bone stress injuries (*P* = .75, independent *t* tests).

Early diagnosis of bone stress injuries can aid in their effective management and treatment, particularly with use of MRI. In a recent prospective comparison of imaging modalities in 42 athletes with a clinically suspected tibial stress injury and negative radiograph findings, the sensitivity of MRI, CT, and radionuclide bone scans were 88%, 42%, and 74%, respectively.[21] Also, MRI was highly specific, equaling CT at 100%.[21] In the current study, 49% (21/43) of the MRI-graded bone stress injuries were grade 2, and only 14% (6/43) were actual stress fractures (grade 4, with

TABLE 7
Multiple Regression Model of Variables Contributing to the Prediction of Time to Full Return to Sport Among Bone Stress Injuries With MRI Grade (n = 43)[a]

	Unstand *B* (Error)	Stand *B*	95% CI	*P* Value	R^2
Model					0.68
MRI grade	6.8 (2.1)	0.44	2.5 to 11.1	.004	
Trabecular vs cortical	8.5 (4.3)	0.26	–0.5 to 17.5	.063	
Total-body BMD, g/cm^2	−40.7 (17.4)	−0.35	−77.0 to −4.3	.030	
BMI	–0.90 (1.2)	–0.10	–3.5 to 1.7	.476	

[a] For injuries evaluated using MRI and with complete data on time to return to sport. BMD, bone mineral density; BMI, body mass index; MRI, magnetic resonance imaging.

a visible fracture line) (Figure 1), indicating that with use of MRI, bone stress injuries can be identified before a fracture occurs and thus facilitate treatment and recovery.

Fredericson and colleagues[18] previously identified an MRI grading scale for tibial bone stress injuries based on a pattern of bone marrow and periosteal edema. The grading scale of Fredericson et al[18] correlated with both the extent of clinical findings and time to full return to activity for bone stress injuries of the tibia. Arendt et al[2] also performed a retrospective study using a similar grading scale and further confirmed the correlation between MRI grade and full return to sport. Our MRI grading scale differed from that of Fredericson et al[18] in that periosteal edema was often, but not always, present and therefore not a necessary feature in the diagnosis of a bone stress injury. Muscle edema was often associated with higher MRI grade injuries but was also not a necessary criterion. A comparison of the MRI grading scales can be found in Table 1. Yao and colleagues,[53] in their retrospective study of MRI grading and recovery time, also found that periosteal edema was not always present and found no association with periosteal edema and a quicker return to sport.

Of note is that in our study, radiograph results were negative the majority of the time (78.6%) in the initial assessment of bone stress injuries, regardless of the injury grade. Contrary to the description by Arendt et al[2] of a periosteal reaction present on plain radiographs in bone injuries of MRI grades 3 and 4, we found that although a periosteal reaction may be present, plain radiograph findings are usually negative even at the higher MRI grades.

Using our grading scale prospectively, time to full return to sport was positively correlated with MRI grade ($r = 0.6$; $P < .05$). From the multiple regression model for every 1-unit increase in MRI grade, time to full return to sport increased by approximately 48 days ($P = .004$). Also, with a mean recovery time of approximately 8 months, time to full return to sport for grade 4 injuries was significantly longer compared with all other grades (Figure 6). Therefore, when a bone stress injury has progressed to the point where there is cortical disruption (fracture) noted on MRI (grade 4 bone stress injury), it considerably disrupts the athletes' ability to train and compete, and return to sport is significantly delayed. These findings are consistent with those in retrospective studies by Arendt et al[2] and Fredericson et al.[18] Among collegiate athletes, prolonged injury and limited training contribute to an array of consequences, including muscle loss, aerobic deconditioning, and significant psychological distress[48] that may continue to affect their remaining athletic career. Therefore, it appears prudent to employ methods for diagnosing bone stress injuries at the earliest onset. These findings provide support for the utility of MRI and the MRI grading scale to identify the earliest signs of stress injuries to bone and thus allow for improved treatment outcomes.

In addition to MRI grade, total-body BMD and bone stress injuries of trabecular bone structures (specifically in the femoral neck, pubic bone, and sacrum) were associated with time to return to sport in our study. These findings suggest that when a bone stress injury is suspected and/or identified, management of the injury can be more accurately determined when the clinician is provided with information about the severity of injury as determined by MRI grading of the bone stress injury as well as the location of the injury (trabecular vs cortical sites). Performing DXA provides valuable prognostic information that can help predict recovery time. When these variables were combined with BMI, we were able to account for more than 68% of the variation in time to return to sport. Other prospective studies in female track and field and cross-country athletes have found that lower BMD is associated with an increased risk for stress fractures,[9,33] but to our knowledge, it has not been previously reported that lower BMD is predictive of return to sport outcomes (longer recovery time) in athletes with bone stress injuries. With future research, this type of a model can be further developed and used as a tool to guide clinicians in their management of patients' return to sport activities.

Similar to prior reports, the most frequent skeletal sites for bone stress injuries were the tibia (51%) and metatarsals (21%)[2,9,29,40,42] (Table 3). Distance runners sustained a higher percentage (59%) of injuries compared with athletes participating in other sprint and field events. It has been previously noted that distance runners exhibit high rates of stress injuries to bone.[2,12,42] Arendt et al[2] reported that cross-country runners compared with all track and field athletes had the highest yearly incidence of bone stress injuries over a 10-year period (incidence rates of 6.4% vs 1.6% and 3.9% vs 0.8%, among male and female participants, respectively). Matheson and colleagues,[40] in their evaluation of 320 stress injuries in a sports medicine clinic, reported the highest number of injuries among long-distance runners. Additionally, the incidence of stress fractures has been associated with an increase in long-distance running training among female military recruits.[1,46] In contrast to the current study, however, Bennell et al,[9] who prospectively evaluated male and female track and field athletes for 1 year, did not report a higher prevalence of bone stress injuries among athletes running long-distance events, although the distance runners sustained more long bone and pelvic fractures. The difference in the study duration and diagnostic imaging used (CT vs MRI) to define bone stress injuries between the study of Bennell et al[9] and the current study may account for the discordant results. Long-distance runners are at a higher risk of sustaining stress injuries to bone as a result of their high training volume (and thus increased exposure of bone to repeated stress), potential biomechanical imbalances (such as pes planus, leg length discrepancy, or increased Q angle),[19,54] and risk of undernutrition.[5,6,20,38]

Of the 34 athletes with bone stress injuries in this study, 22 (65%) were female (Table 2), suggesting that women in the study were at higher risk. Multiple prior studies have reported similar findings.[2,13,29,55] In a larger study of 914 athletes, Johnson et al[29] reported an overall incidence of stress fractures of 2% per year in men compared with 7% per year in women. Furthermore, female athletes incurred higher grade bone stress injuries than their male counterparts (Table 3). Approximately half of female bone stress injuries were grade 3, and all of the grade 4 injuries were sustained by women (Table 3). This greater severity of injury among women may be caused by anatomic factors, such as the smaller body size in women, physiological differences in women compared with men, psychological or social factors, and/or factors associated with the female athlete triad.[8,9,34,43]

The inverse association found between total-body bone mass and recovery is consistent with previous reports of postmenopausal osteoporotic women and estrogen-depleted osteoporotic animals exhibiting delayed bone healing. Additionally, a study that utilized in vivo micro-CT analysis to evaluate bone healing reported impaired neurovascularization, bone formation, and bone remodeling and a lower restoration of mechanical properties in ovariectomy-induced osteoporotic mice compared with sham-operated controls.[25] It is also important to note that athletes with higher MRI grade injuries had a significantly lower bone mass at the total hip and radius, suggesting that lower bone mass may be associated with the development of more advanced stress injuries to bone. Together, these findings underscore the importance of optimizing bone mass to facilitate the processes of healing from a stress injury to bone. While genetic factors significantly influence bone mass and strength, regular bone-building exercises and adequate nutrition maximize the genetic potential to accrue and mineralize bone.[26,36]

It has been established that functional hypothalamic amenorrhea in athletes results from insufficient energy intake in comparison with the calories expended from exercise activity.[43] A chronic period of undernutrition leads to the suppression of metabolic processes and a reduction in various hormone levels that affect bone turnover.[28,51] Lower estradiol levels, as seen in functional hypothalamic amenorrhea, negatively affect bone mass through a variety of mechanisms, including reduced calcium absorption, increased processes of bone resorption, and suppressed bone formation. Among the women in the current study, oligomenorrhea/amenorrhea was associated with sustaining a higher grade bone stress injury. This was not an unexpected finding particularly because the athletes with oligomenorrhea/amenorrhea in the study had a significantly lower bone mass. Furthermore, oligomenorrhea/amenorrhea did not emerge as a significant predictor of time to return to sport in the multiple regression analysis. Although not significant in the regression model, oligomenorrhea/amenorrhea may have indirectly influenced the athlete's recovery time and healing potential because of its (1) relationship with the development of a higher MRI grade injury and (2) association with lower bone mass. Furthermore, menstrual irregularity was noted to be present in 75% of all female athletes with injuries at trabecular bone sites and only 12.5% at cortical bone sites (Table 6). Thus, functional hypothalamic menstrual disturbances may predispose women to bone stress injuries with a higher MRI grade at skeletal sites of predominantly trabecular bone.

The important clinical finding that trabecular bone stress injuries (including femoral neck, sacral, and pubic bone stress injuries) were associated with a significantly longer time to full return to sport participation than cortical bone stress injuries should help guide clinicians to utilize a more gradual progression of activity and cross-training in athletes with injuries in these skeletal sites, while addressing important nutritional, hormonal, and bone health preventive measures. Marx and colleagues,[39] in their retrospective cross-sectional study, found that female athletes with stress fractures in regions of mostly trabecular bone had lower BMD than those with stress injuries of cortical bone sites. In a biomechanical laboratory study assessing the fatigue properties of trabecular and cortical bone tissue of the human tibia, Choi and Goldstein[15] found that trabecular specimens had significantly lower moduli and lower fatigue strength than cortical specimens. Different fracture and damage patterns were identified between these 2 types of bone based on mechanical and qualitative analyses. These findings reinforce the important role that optimal bone health plays in the prevention and management of bone stress injuries and have significant clinical implications.

High-risk stress fractures as defined by Boden and Osbahr[11] represent a subset of bone stress injuries that have a propensity to progress to a complete fracture, delayed union, or nonunion. Specific sites for these types of stress injuries include the femoral neck (tension side), anterior tibia, medial malleolus, navicular, fifth metatarsal (proximal diaphysis, distal to tuberosity), talus, patella, and great toe sesamoids.[11] In our study, there were no statistically significant differences with regard to MRI grading patterns or time to return to sport with these specific high-risk injuries grouped together, although this was likely because of too few bone stress injuries at these sites in this population of athletes. Progression of a bone stress injury into a complete fracture at these higher risk skeletal sites can have a devastating outcome (eg, a complete hip fracture), can be career ending, and/or result in surgical fixation if not managed and treated appropriately.

All of the collegiate athletes assessed in this study had clinical symptoms that correlated with their bone stress injuries on MRI. However, it should be noted that asymptomatic grade 1 bone stress injuries have been found to be common in elite military recruits,[34] and asymptomatic bone stress injuries have been documented in runners, with no known clinical significance.[10,37] These studies emphasize the importance of correlating MRI findings with clinical symptoms before making diagnostic and treatment decisions.

This study was limited by the relatively small sample size of athletes with injuries. Additionally, self-reporting of certain data such as demographic information and general background information (bone injury history, detailed menstrual history of current and past menstrual patterns, nutritional history, history of disordered eating/eating disorders, exercise history, general health history, medications including oral contraceptive pill use) was, in some instances, subject to participants' memory and therefore may be limiting because of potentially inadequate or inaccurate reporting. Lastly, baseline BMI and BMD were used for the statistical analyses rather than at the time of an identified injury.

The protocol for the study did not include the use of high-resolution CT, in addition to MRI, for the assessment of bone stress injuries receiving MRI grades 1 to 3 to further assess if a fracture was present. This would have added additional costs and radiation exposure and was not believed to be clinically indicated. In addition, other than for femoral neck and tarsal navicular bone stress fractures (higher grade injuries at higher risk sites), and additional trabecular bone sites of the sacrum and pubic bone, MRI was generally not repeated during healing if the athlete was pain free and improving clinically. Of the MRI studies that were repeated before full return to sport, there was no evidence of a higher MRI grade bone injury or progression of a fracture line. Although data were gathered over a decade ago, it should be noted that MRI technology has not significantly advanced for musculoskeletal imaging with regard to the assessment of bone stress injuries.

CONCLUSION

In this prospective study, we found that MRI grading severity, total-body BMD, and location of the bone injury (trabecular vs cortical bone) were important variables associated with time to full return to sport. A notable difference in our MRI grading scale from that used by Fredericson et al[18] is that periosteal edema was not a necessary criterion for any grade injury and was not associated with return to sport. We also identified nutritional and menstrual status as important factors affecting MRI grading severity, location of the bone stress injury, and the athlete's BMD. These results support the important contribution of risk factors of the female athlete triad[43] and relationship to bone stress injury and recovery.

In conclusion, when a bone stress injury is suspected and/or identified, we recommend utilizing MRI and an evidence-based grading scale, measuring BMD, identifying the injury site as trabecular or cortical bone, and obtaining a careful history of nutritional and menstrual status. With this information, a clinician can better predict time to return to sport participation and ultimately improve the management of bone stress injuries. Further research is warranted to develop clinical algorithms of risk and/or risk stratification scores that may help clinicians with decisions involving athlete clearance and return to play that may lead to improved bone health and decrease the incidence of bone stress injuries, especially in the high-risk athlete.

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