

Bone, Exercise, and Stress Fractures

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EPIDEMIOLOGY OF STRESS FRACTURES

Stress fractures are nontraumatic bone fractures caused by repeated application of loads below the fracture threshold, i.e., they are fatigue fractures. They occur in a variety of skeletal locations (femur, tibia, metatarsals, and calcaneus, among others) commonly in physically active individuals (e.g., joggers, soldiers, and ballet dancers). Stress fractures are ranked between the second and eighth most common running injuries [4], with an incidence ranging between 4 [49] and 14.4% [80]. Seventy percent of all stress fractures are reported in runners [76]. Estimates of injury among runners may be too high, because they are based only on those runners who appear in the clinic. Also, estimates rarely include controls for workout intensity or duration, or even for the nature of the physical activity.

The incidence of stress fractures in some of the elite units of the Israeli military are reported as being between 20 and 46% [41, 73, 85, 87, 90]. In a population of 2000 Israeli paratroopers, Milgrom (personal communication) recently found an incidence of 20%.

Rates of occurrence in the U.S. military (1–4%; see ref. 58) are much lower than those reported for Israeli soldiers, although stress fractures still account for more lost duty days among women in the U.S. Army than any other overuse injury [145]. The discrepancy in occurrence in the two military populations may have more to do with the manner in which stress fractures are detected and diagnosed than with inherent differences in the rigor of the training programs [60]. The Israelis diagnose stress fractures based primarily on scintigraphy, whereas the U.S. military relies more heavily on radiographic criteria [124, 154]. The differences in technique could account for a 5-fold higher incidence in the Israeli military, as compared to that in U.S. soldiers [50, 90]. The remaining differences in incidence (about double in the Israeli military) can be accounted for by differences in basic training programs.

Stress fractures most commonly affect the metatarsals, calcaneus, and tibia. The location of the majority of stress fractures has gradually shifted in the past 50 yr from the metatarsals as the predominant site, to the tibia [41, 60]. The incidence of tibial stress fractures in the military now constitutes

between 20 [79, 144] and 72% [40, 154] of all stress fractures, whereas calcaneal stress fractures account for about 25% [53]. Tibial stress fractures account for about 50% of stress fractures in runners [55, 76, 101, 137]. They most commonly occur in the medial tibial plateau or in the distal tibial diaphysis [41, 94], the latter at the junction between the middle and distal thirds of the tibia [31, 124]. The tibia is also the most common site for multiple stress fractures, showing an incidence of 1.5 fractures per affected soldier [41].

The location of fracture may vary, depending on the precise activity. For example, metatarsal stress fractures are more common in ballet dancers [36], whereas tibial stress fractures are common among runners [3, 6, 26, 54, 76, 81, 102, 103, 137, 140] and soldiers [40, 41, 46, 50, 73, 87, 90, 91], although some reports from U.S. forces show that stress fractures of the metatarsals and calcaneus may be at least as common [8, 110]. Metatarsal stress fractures account for fewer of the total number of fractures in women than in men [110, 122].

Stress fractures occur early after the onset of training [41, 46, 90]. Rates of occurrence are generally elevated by the second [43, 122, 146] or third [38, 64, 134] wk of training, although there are reports of peak incidence from 5 to 8 wk [40, 112] after the onset of training. Time of onset may differ slightly between men and women. Pester and Smith [110] reported peaks in men during the 2nd and 4th wk after the beginning of training, whereas stress fractures reported in women are elevated in each of the first 3 wk of training.

RISK FACTORS

Many factors have been reported to be associated with the risk of stress fracture. These can be grouped into several general categories of factors, including: demographic (age, gender, race); biomechanical (hip rotation, knee valgus, pelvic width, bone geometry), physical condition (poor strength and flexibility, previous physical activity, aerobic fitness), and factors related to bone density (weight, family history of osteoporosis, low calcium intake, smoking, age at menarche, amenorrhea). It is not the intention here to review all risk factors for stress fractures, but several important risk factors can be identified.

Physical Activity

There are numerous reports that poor physical conditioning is a risk factor for stress fracture [26, 43, 46, 53, 56, 65], but it is problematic as to whether previous physical activity and improved physical fitness actually can reduce the risk for stress fracture. Reports conflict, and most are poorly controlled or rely on self-reporting for prior physical activity [139], rather than on a

TABLE 7.1.
Physical Activity and Stress Fracture Risk

<i>Level of Previous Activity^a</i>	<i>Stress Fracture Risk (%)</i>		
	<i>Gardner et al.^b</i>	<i>Male</i>	<i>Jones et al.^c</i>
<i>Male</i>	<i>Male</i>	<i>Female</i>	
Very active	0.6	3.4	30.7
Active	0.9	15.7	33.3
Average	1.6	35.1	29.7
Below average/inactive	14.2	42.9	30.0

^aBased on self-reports.

^bData are from ref. 39.

^cData are from ref. 60, which includes all exercise-related injuries.

standardized physical fitness test before the exercise has started. Barrow and Saha [5] reported only one-half of the prevalence of stress fractures in runners that run regularly (29%), as compared to those that are very irregular runners (49%).

The incidence of stress fractures in U.S. soldiers is higher among those without previous jogging experience [38, 43, 46, 53], although the intensity of the previous physical activity in soldiers who failed to develop a stress fracture is not reported. Garcia et al. [38] report that 72% of the soldiers diagnosed with a stress fracture had no previous running experience, but they do not report how many soldiers who failed to present with a fracture also had no running experience.

In a study of 310 male and female army trainees in which fitness was measured by a battery of tests, including a mile run, push-ups, and sit-ups, Jones et al. [59] found an association between slower mile run times and increased risk for an exercise-related injury in both men and women. The risk of an overuse injury increased as self-assessed activity decreased in men, but there was no relationship between activity levels and injury risk in women. This study reported all overuse injuries, so the specific risk for developing a stress fracture is not reported. However, Gardner et al. [39] found a similar association of physical activity before basic training and stress fracture risk (Table 7.1). Recruits reporting themselves as inactive or below average were nearly nine times more likely to present with a stress fracture, compared to those with average or above-average activity levels.

In the largest study in which physical activity was assessed, 295 infantry recruits between 18 and 20 years old were observed over a 14-wk elite basic training course. No association was found between aerobic physical fitness or pretraining physical activities and risk of later developing a

stress fracture [138]. In a separate study of 279 recruits, 31% of the soldiers presented with stress fractures, regardless of whether they had participated in sports before basic training [41]. In a subpopulation that included only runners, no association was found between the distance run each week and stress fracture incidence. Prior physical activity does not seem to explain the occurrence of stress fractures, which is consistent with the observation that stress fractures occur often in those who have been training for years [16].

Age

Age is probably a risk factor for stress fractures in both men and women, but whether stress fractures increase or decrease in older subjects is controversial. Again, the difficulty is quantifying the amount and intensity of activity in different-aged populations.

In a very small sample of women (six runners reporting a history of stress fracture in the tibia and femur and eight runners with no history of fracture), women reporting stress fractures were significantly ($P < 0.05$) younger than those without a history of stress fracture (26.9 vs. 32.8 yr), even though bone mineral density (BMD) in the stress fracture group was greater than that in the nonstress fracture group [48]. Even though the sample was small, the data support the hypothesis that age is a factor contributing to stress fracture incidence, even in the presence of greater overall bone mass.

Based on self-reports from more than 2000 active duty Army women, Friedl et al. [35] found stress fracture prevalence of 19.6% in women 22–23 yr old but 1.4% for women over the age of 40. Stress fracture incidence between the ages of 18 and 34 was consistently between 15 and 20% but fell rapidly to about 5% by age 38. Although the covariate effects of menstrual history, smoking, ethnic origin, and family history were controlled in this study, it did not account for the change in physical activity among women of these different age groups. Therefore, the effect could have been partly the result of reduced physical activity in the older groups.

In a large prospective study of 783 Israeli military recruits between the ages of 17 and 26, Milgrom et al. [89] reported that recruits more than 20 yr old had only a 2.9% incidence of stress fracture, whereas those recruits younger than 20 had an incidence of 26%. Moreover, each year of increased age above 17 yr reduced the risk of a stress fracture by 28%. This is interesting in light of the observation that bone density increases to a maximum between 20 and 30 yr of age [45, 78, 119], and strength would be expected to increase commensurately [24, 29, 27, 131].

This is in direct contrast to data reported from American Marines [39] in whom stress fracture incidence in recruits older than 21 was nearly double that in recruits younger than 20. It is also at odds with data generated from athletes (runners) or from other American military recruits, which

show an increase from about 1% between the ages of 17 and 22, to more than 5% between the ages of 29 and 34 [8]. Increased incidence with age occurred in both men and women. Jones et al. [59] showed a higher incidence of overuse injuries of all kinds in men over the age of 23 but did not present data on stress fractures alone. Hulkko and Orava [54] showed a greater stress fracture incidence in athletes between the ages of 20 and 29 than in those of age 19 yr or less. However, they also showed that 40% of all stress fractures in athletes occurred between the ages of 16 and 19, with 78% occurring before the age of 30. Similar data were presented by Orava et al. [102]. However, in neither study was the incidence or prevalence of stress fractures within each age range given, so the age-adjusted risk for stress fracture cannot be determined from these studies.

Gender

Gender is a clear risk factor for the occurrence of stress fractures [8, 39, 53, 58, 60, 70, 86, 96, 107, 112, 113, 122, 140], although the role of gender may not be entirely independent of density. Kowal [64] reported that femoral and tibial stress fractures comprised one-third of all musculoskeletal injuries in a group of women undergoing an 8-wk basic training endurance exercise program. Women's smaller body size, lower peak bone density, and tendency to develop menstrual irregularities or even amenorrhea with strenuous and prolonged exercise may be predisposing factors for the occurrence of fracture.

Some studies that suggest that women are more prone to injury than men have not normalized the incidence of injury by using the numbers of male and female runners in the population [56, 104]. Comparisons of men and women undergoing training in the armed forces indicate that rates are much higher in women than in men, although this may be because of a lack of prior physical conditioning and generally lower fitness [4].

In the U.S. Armed Forces, the risk of developing a stress fracture in women is 5–10 times that in men [8, 112, 122], and they may occur earlier [8, 110]. Although the incidence of stress fractures in male soldiers in the U.S. military is reported between 0.9% [8, 51, 110] and 4.8% [134] (mean, 1.8%), that in women in the U.S. military varies between 1.1% [110] and 21% [64] (mean, 9.6%), even with equivalent training regimens [60]. However, these numbers combine racial groups; the relatively low value of 3.4% reported by Brudvig et al. [8] for stress fracture incidence in women, for instance, is increased to 11.83% when only white women are considered. Zernicke et al. [152] report a slightly higher incidence of stress fracture (20–25%) in female collegiate distance runners.

Density

Physical activity can build or maintain bone mass [34]. Greater bone density is positively and exponentially correlated to greater bone strength [27,

28] and stiffness [24, 131]. It is reasonable to conclude from this that greater bone density would reduce the risk for stress fracture.

Some data do, in fact, support this conclusion. Using 50 athletes, one-half of whom had stress fractures and one-half of whom did not and who were matched for sex, age, weight, height, and exercise history, Myburgh et al. [95] found that those with stress fractures had significantly lower bone density in the spine, femoral neck, Ward's triangle, and greater trochanter. However, women in the stress fracture group ($n = 19$ of 25) had a lower calcium intake and lower oral contraceptive use than women in the control group. Moreover, the menstrual status of the women in the stress fracture group was not reported. It is well known that women who are amenorrheic have a higher incidence of stress fractures than that of eumenorrheic women [5, 17, 26, 69]. Pouilles et al. [111] also showed lower BMD in the femoral neck, Ward's triangle, and greater trochanter in 41 military recruits with stress fractures, compared to that of 48 recruits matched for age, height, and weight who did not have fractures.

Grimston et al. [48] found no differences in tibial BMD between runners reporting stress fractures and those without symptoms, even though 7 of the 10 stress fractures reported were localized to the tibia. Although this was an extremely small sample, it is notable that the stress fracture group of women was significantly ($P < 0.05$) younger than that without a history of stress fracture (26.9 vs. 32.8 yr). When age is used as a covariate, BMD in the stress fracture group was greater than that in the nonstress fracture group. These data do not support the hypothesis of a close relationship between low bone density and stress fracture but do support the concept that age is a factor contributing to stress fracture incidence.

In a group of female athletes matched for age, as well as height and weight, Carbon et al. [17] found no significant difference in BMD between women with a stress fracture and those without a stress fracture. Although the authors conclude that bone density does not contribute to the risk for stress fracture, the sample was small, and BMD measurements were not taken at locations where stress fractures occurred. Giladi et al. [41] reported no significant association between tibial bone density and stress fractures at any site ($P > 0.1$) in a study of 295 Israeli military recruits.

Although low bone density can increase the risk for a stress fracture, as demonstrated by irregularly cycling women with low bone mass, stress fracture incidence cannot be explained on this basis in a population in which bone density is within normal limits.

Race

The risk of developing a stress fracture in the U.S. Army is 8.5 times greater for a white woman (11.83%) than for a black woman (1.39%) and about 2.5–4.5 times greater for a white man (1.07–1.56%) than for a black man (0.23–0.60%) [8, 39]. Based on self-reports from more than 2000 active

Army women, 18.5% of white and Asian women reported a history of stress fracture, whereas only 11.3% of black women reported similarly ($P < 0.001$) [35].

Although the data conclusively demonstrate that blacks are less likely to develop stress fractures, this effect is probably not independent of bone mass. It is well known that blacks have higher bone mass and slower turnover than whites [62, 67]. None of the studies demonstrating an effect of ethnicity used bone mass as a covariate in the analysis.

Geometry

Tibial geometry constitutes a risk factor for tibial stress fractures [42, 91]. Tibial width is significantly correlated to stress fracture incidence [42], but the cross-sectional moment of inertia about the anteroposterior axis of bending (IAP), an estimate of bending rigidity, is an even better indicator of risk [91]. Thirty-one percent of recruits with a "low" IAP presented with tibial stress fractures, whereas only 14% of recruits with a "high" IAP presented. No correlation was found between bone mineral content or cortical width of the site and stress fracture [42, 73], although some have proposed that reduced bone mineral content does constitute a risk factor [111, 128]. Shear stresses caused by bending are likely to be a significant causative factor for stress fractures [91, 128], but there are no reported studies in humans comparing the *in vivo* magnitude or distribution of shear strains to variables that determine stress fracture risk.

ETIOLOGY OF STRESS FRACTURES

Role of Repetitive Loading

It is generally conceded that stress fractures are overuse injuries [7, 74, 77, 136, 139] that result when the skeleton fails to respond quickly enough to stresses and strains imposed upon it [46, 128]. They may be more common when bones are repetitively loaded above a certain stress or strain threshold [97–99], but the kind and magnitude of stress required are not known. The risk of developing a stress fracture increases with greater weekly running mileage [56, 63], suggesting that repetitive loads play some role in the pathogenesis.

Stress fractures can be induced in the tibial diaphysis of an animal model by the repeated application of nontraumatic loads [12]. In this model, the right hindlimb of rabbits is placed in a splint that prevents the contraction of the gastrocnemius and impairs its ability to attenuate tensile loads caused by bending. Skeletally mature rabbits are loaded impulsively at 1 Hz for 40 min/day, 5 days/wk for up to 9 wk. Loads are adjusted to 1.5 times body weight, although because of soft tissue attenuation, loads on the distal tibia are only about 1 times body weight. This loading protocol applies about

FIGURE 7.1.

^{99m}Tc scintigram showing the location of the distal stress fracture site in the rabbit model (arrows). This site corresponds to the site of high shear and compressive stresses in the finite element model shown in Figure 7.4.



12,000 load cycles/wk at a load equivalent to loads placed on the lower limbs during walking. Within 6 wk, 90% of the animals show scintigraphic or radiographic evidence of a stress fracture in the distal tibia (Fig. 7.1).

Mechanical testing of devitalized bone shows that bone can fail with very few loading cycles when tensile strains are large. Bone may fail within 10^3 – 10^5 loading cycles at strain ranges of 5,000–10,000 microstrain [20, 21]. Loading in uniaxial tension at 3000 microstrain causes bone to fail within 10^6 cycles [18–21]. Strains on the craniomedial cortex of the tibia of rabbits loaded impulsively average about -733 (± 233) microstrain, whereas those on the craniolateral cortex average 822 (± 428) microstrain (Table 7.2). These strains are much too low to be the sole cause for stress fractures.

Measurements of strain in the human tibia *in vivo* at a site known to be at risk for stress fracture [13] show that principal compressive strain, even during strenuous physical activities, ranges from -414 microstrain (downhill walk) to -1226 microstrain (zigzag run uphill); principal tensile strain ranges from 381 microstrain (walking on a level surface with a 17-kg pack) to 743 microstrain (zigzag run uphill). Maximum shear strains were greatest for the uphill and downhill zigzag run, reaching nearly 2000 microstrain in each case (Fig. 7.2). Shear strains during sprinting on a level surface were nearly double those during walking with or without a pack (1583 vs. 770 and 871 microstrain). These data show that strains can double or

TABLE 7.2.
Experimentally Measured Strains^a and Strain Rates

Gauge Location	Principle Strain (microstrain)	Shear Strain (microstrain)	Strain Rate (Shear) (microstrain/s)
Stress fracture site			
Craniomedial	-733 (233) ^b	-426 (358)	6083 (1941) ^c
Craniolateral	822 (428) ^b	-459 (383)	5076 (2592)
Posterior	677 (345) ^d	-478 (285) ^b	5862 (3625) ^b
Tibial midshaft			
Medial	-521 (293)	-345 (374)	3933 (1904)
Lateral	490 (280)	-258 (188)	3338 (2356)
Posterior	270 (66)	-253 (118)	3039 (845)

^aStrains at stress fracture site larger than strains at tibial midshaft (one-tailed *t* test; ^b*P* < 0.05; ^c*P* < 0.01; ^d*P* < 0.005.

triple during vigorous exercise, compared to those generated in the tibia during walking.

Strains measured on the human tibia during walking show that strains generated at this site are well below the fracture threshold, even during running. Based on cyclic load to failure studies [20, 21] and linearly extrapolating to the range of strains measured in the human tibia, stress fractures should not occur at this stress fracture site for about 10^6 cycles, if failure is caused solely by the repetitive application of load. In real terms, this means that a person would have to perform vigorous activities, such as running for about 1000 miles before bone failure is likely to occur [71]. However, the relationship between the number of loading cycles and failure in bone at a given strain is not linear [106]. Tensile fatigue tests on primary and Haversian bone at 1500 microstrain, similar to the magnitude of strain measured in the human tibia, and strain rates similar to those developed during running [127] show that healthy bone does not fail in tension by fatigue, defined as a 30% loss of stiffness, even after 37 million loading cycles [133] (Fig. 7.3). (Note that subsequent tests showed that bone would not fail for at least 45 million cycles). Yet, stress fractures occur with repeated high-strain loading, suggesting that momentary high strains or strain rates may occur during more vigorous activities, or that factors in addition to repetitive loading, contribute to pathogenesis (e.g., locally high stresses, muscular fatigue or loss of coordination, high-impact loads, or interactions with the remodeling system).

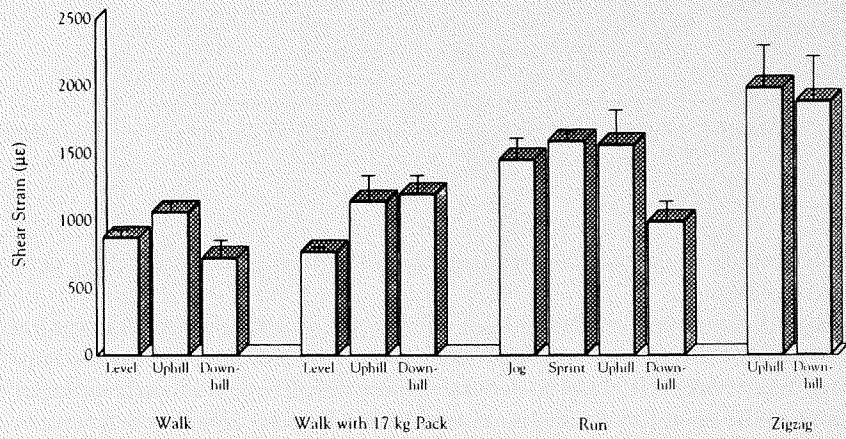
Role of Shear Strain

Milgrom et al. [91] hypothesized that stress fractures occur in regions in which high bending loads are found. This makes bending stress causal and suggests that noninvasive measures of bending rigidity may be one way to

FIGURE 7.2.

Peak engineering shear strains generated on the human tibial midshaft during various activities. Five gait cycles were averaged. In all cases, strains were less than 2,000 microstrain. Error bars represent standard deviations. Reproduced from ref. 15, with permission from Pergamon Press.

MAX. SHEAR STRAIN VS. ACTIVITY



assess risk for fracture. Large bending stresses can create high-shear strains in bone, suggesting the possibility that it is shear that leads to bone failure.

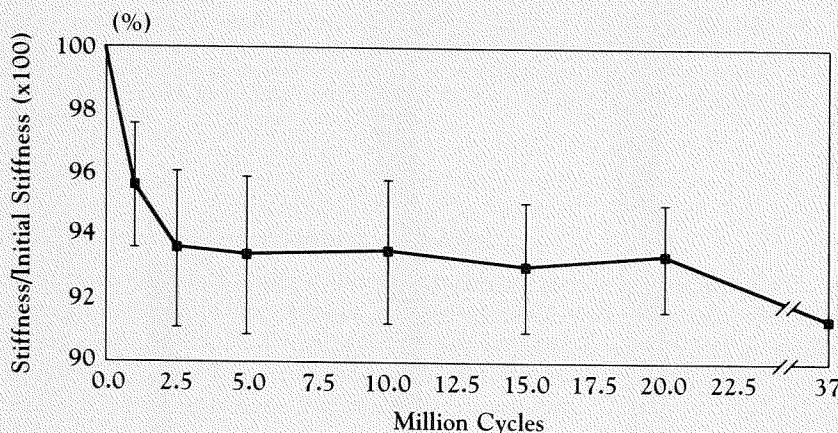
A finite element analysis (FEA) of experimentally produced tibial stress fractures in a rabbit model of stress fractures [12] predicts locally high-shear and compressive stresses on the anterior cortex of the distal one-third of the rabbit tibia, in the identical location that stress fractures occur (Fig. 7.4; Table 7.2). The correspondence between the location of stress fractures in the experimental model and the prediction by FEA of locally high-shear stresses at this location suggest, in combination, that focal pockets of high-shear stress applied at high rates may contribute to fracture risk.

Experiments in which strain was measured in the human tibia *in vivo* [13] show compressive and shear strains, and strain rates can double or triple during vigorous activity, compared to walking at a comfortable speed. Strain gauges were applied at the location in which Israeli military recruits develop symptoms of a stress fracture [41]. The result implies an association between elevation of strain magnitude or rate and subsequent development of a stress fracture.

These data are consistent with the hypothesis that stress fractures occur

FIGURE 7.3.

Fatigue-induced modulus decreases vs. number of loading cycles. When bone is loaded in uniaxial tension at physiological strains (1200–1500 microstrain) and strain rates (0.03/s), there is a rapid stiffness loss to about 3 million cycles, after which no further stiffness loss is observed, at least up to 37 million cycles. Data points represent means for the percentage of original specimen modulus; error bars represent standard deviations. Adapted from ref. 133, with permission from Pergamon Press.



in regions where high bending stresses are found [91]. Shear produced by bending forces is a significant component of the strain induced by normal loading events [129]. Because of varying loading conditions and the complex geometry of the tibia, shear stresses may not be uniform but may be concentrated in specific regions, as the rabbit model suggests. The absolute magnitude of shear strains measured both in the animal model and in humans is low when compared to the fracture strain, however, and may be too low to account for the occurrence of fracture with so few loading cycles.

Bone is generally weak in shear (Table 7.3) [33, 120, 121, 150]. Its transverse breaking strength in shear is similar to that in tension (about 69 mega Pascals (MPa)), which is about one-half of its compressive strength [120, 121]. However, cortical bone shear strength in the longitudinal direction is only about 25% of its strength in tension or transverse shear (17 MPa). Therefore, even relatively small shear stresses may place some bone cortices dangerously close to failure and raises the possibility that shear stresses caused by bending may be partly responsible for some stress fractures.

FIGURE 7.4.

Contour plots of Tresca stress on the anterior cortex of the rabbit tibia. Four of the rabbits for which models were built are shown. The scale is given in MPa. The high shear stress concentrations (> 25 MPa) on the anterior aspect of the distal tibia range from 5 to 30% of tibial length from the distal end, coincident with the region where rabbits presented with stress fractures (see Fig. 7.1).

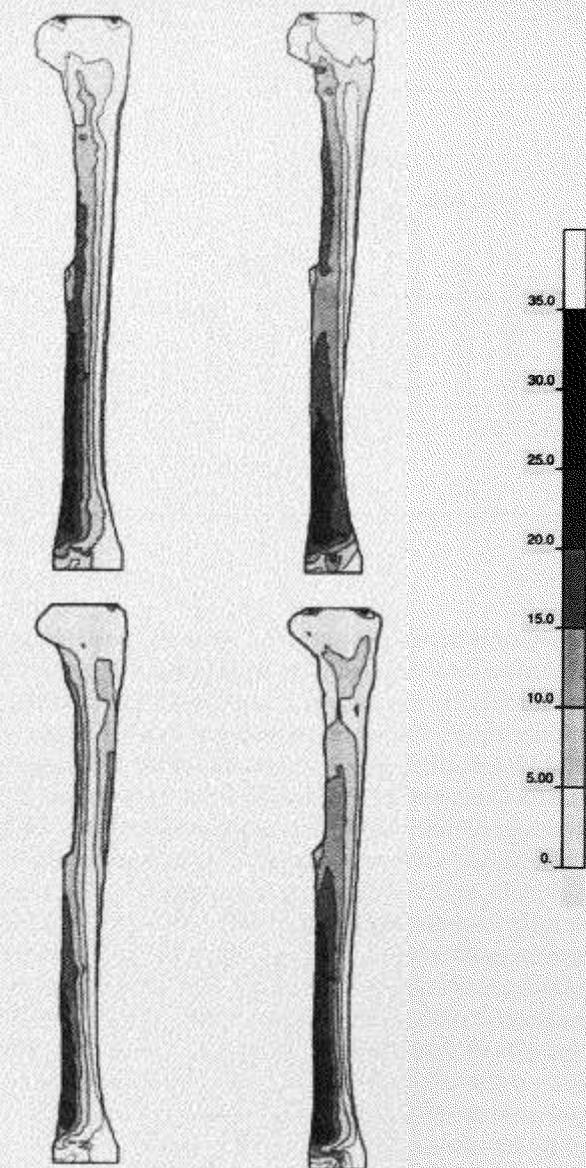


TABLE 7.3.
Bone Strength in Compression, Tension, and Shear

	<i>Transverse Breaking Strength^a</i>	<i>Longitudinal Breaking Strength^a</i>
Compression	133 MPa	193 MPa
Tension	51 MPa	133 MPa
Torsion	58 MPa	
Pure shear ^b	62 MPa (Iosepescu)	18 MPa (Arcan)

^aData on breaking strength in compression, tension, and torsion from refs. 120 and 121.

^bPure shear tests are from quasistatic tests of human femoral midshaft; $n = 12$ in each direction. Pure shear tests in the transverse direction used Iosepescu specimens; those in the longitudinal direction used Arcan specimens. This was necessary because of geometric constraints.

Roles of Musculoskeletal Patterning and Fatigue

During mechanical loading, bones are subject to bending strain [127]. Increased bending of bone causes increased tension and shear, because bending is a combination of compression and tension. Bone is weak in tension and shear [120, 121] and is in the greatest danger of fracturing from high-tensile and shear strains. When muscles on the tensile side of a bone contract, the compression they generate reduces tensile strains [116]. This also reduces shear stress.

Muscles also may dissipate dynamic forces generated in the skeleton by eccentric contraction [52, 83, 108, 109, 115]. They reduce strain rate by absorbing impact energy during movement. Force transients of 5–10 g are produced at heelstrike [68, 108, 135]. These transients send shock waves through the entire skeleton [142, 143, 147, 148]. The leg muscles decelerate the limb before heelstrike [55] and attenuate potentially large ground reaction forces [92, 115, 117, 118]. The time for this reflexive energy-dissipating action of muscles is quick, between 75 and 100 ms [84, 114]. Altered neuromuscular function, such as occurs with muscular fatigue, may slow muscle reaction or otherwise prevent this normal damping mechanism. The transfer of mechanical energy between the eccentric and concentric phases of muscle contraction is reduced during muscular fatigue [44], making the muscle less capable of dissipating impact energy. The absence of appropriate muscle contraction increases the magnitude and rate of application of ground reaction forces at heelstrike [115, 117, 118], and has been linked to the increased risk of fracture in elderly subjects [1, 2, 47, 130].

Clinical observations indicate that stress fractures [32, 63] and other overuse injuries [125, 126] occur most often after muscular fatigue, or with an abrupt change in the normal training routine [26, 56, 81, 82], when the capacity of muscles to protect bone from excessive overloads is compromised. Subjects who have suffered a previous stress fracture produce significantly

greater vertical ground reaction and propulsive forces on impact than subjects who have not [48], although whether the greater ground reaction forces were the cause or are the result of the stress fracture is unknown.

It is possible that muscle fatigue, or a change in muscle recruitment patterns associated with fatigue, can increase strain magnitude or rate on a bone significantly. Using a canine model, Yoshikawa et al. [154] showed that muscle fatigue (measured by a shift to lower median electromyogram (EMG) frequencies) was associated with increased peak principal and shear strains on the tibia. Bone strain increased when muscles became fatigued but did not increase when muscles failed to become fatigued. Shear strains increased at a greater rate after muscle fatigue than did either principal tensile or compressive strains. Just as importantly, the *distribution* of strain within the tibia changed.

The magnitude of these changes after fatigue is consistent with those found in human studies. Muscular fatigue leads to a 50% increase in tibial acceleration [141]. This is probably related to an inability of the fatigued muscles to control knee extension and flexion in a way that attenuates impact at heelstrike. Knee extensor/flexor muscle activity is delayed after muscular fatigue. Knee flexion tends to occur earlier [100], reducing stride rate [25] and increasing the amplitude of the heelstrike impact [141]. This increases peak vertical ground reaction forces by about 25% (from 2.35 body weight (BW) to 2.97 BW) [100].

In vivo strain measurements made on seven male subjects between the ages of 23 and 50 yr at a site known to commonly undergo stress fracture indicate that the nature of the change in bone strain after fatigue may vary with age [37]. The subjects walked at 5 km/hr on a treadmill while prefatigue strains were collected for 20 s. Subjects then participated in a 2-hr session of strenuous outdoor exercise that included rapid walking, running up and down hills, and stair climbing. After the outdoor exercise, subjects ran on the treadmill at 11 km/hr until exhausted while muscle activity was monitored using EMG. Strains were measured immediately postfatigue while the subject walked on the treadmill at 5 km/hr.

After fatiguing exercise, tibial strain rates *increased* in younger subjects but *decreased* in older subjects, whereas strain magnitude was *unchanged* in younger subjects but *increased* in older subjects. These data are consistent with previous studies that have examined the effects of age [89] and strain rate [10, 88]. They suggest that (a) the age dependence of stress fracture may result from the age dependency of changes in strain and strain rate after fatiguing exercise and (b) strain rate rather than strain magnitude is implicated in the etiology of stress fracture in subjects younger than 35 yr of age.

Role of Strain Rate and Impact

These data show that alterations in musculoskeletal patterning, coordination, or muscle force production can have a significant effect on the me-

chanical stimulus to bone. Carter [20, 21] showed that bone fails quickly at strains and strain rates above those normally generated during activities of daily living. Because of the nonlinear relationship among strain magnitude, microdamage accumulation, and bone failure [14, 20, 21, 23], any increase in strain magnitude or rate caused by a reduction of muscular protective reflexes can reduce bone's fatigue life exponentially.

Indeed, high-impact activities generally will be associated with stress fractures. Increased time spent running on concrete or other hard surfaces is correlated with a higher incidence of stress fractures [56]. Because bone is a viscoelastic material, higher loading rates may increase its elastic modulus and material stress [149]. This is correlated with decreased fatigue resistance of compact bone [61, 72, 132]. Relatively few studies have specifically examined the effects of high strain rates on the development of stress fractures. However, measurements at the stress fracture site in the rabbit model show that average shear strain rates on all tibial cortices were >50% higher at the stress fracture site than at midshaft (Table 7.2) [12].

Strain rates can double or triple in the human tibia during strenuous physical activity, reaching 50,000/s. Because these measurements were made at a site at risk for stress fracture, this implies an association between the elevation of strain rate and subsequent development of a stress fracture. Although these strain rates are higher than those previously recorded in humans [66], they are still within the range of strain rates reported for running horses [30] and dogs [127], which can range up to 80,000/s.

However, if strain rate is implicated, it may be possible to reduce the risk of a stress fracture through a modification of the training regimen or through the proper use of orthotics. Military training programs that have attempted to eliminate continuous high-impact activities have resulted in a 13% decrease in stress fracture incidence (7% in women and 16% in men) [46]. A randomized prospective study of different types of orthotics on stress fracture incidence in elite infantry recruits ($n = 410$) showed that orthotics could reduce stress fracture incidence to less than one-half of that without orthotics (C. Milgrom and A. Finestone, personal communication). In this case, the use of custom polypropylene modules with neutral rearfoot posts, or with neutral hindfoot posts molded of Pelite reduces stress fracture incidence from 33 to 15%.

This study indicates that a custom-molded orthotically fabricated from a neutral subtalar position, either fabricated from a semirigid or soft material, can significantly lower the incidence of stress fracture. Whether protection afforded by orthotics is the result of a reduction in strain magnitude or rate is not known. However, among athletes at high risk for stress fracture, a polypropylene or Pelite orthotic with neutral hindfoot posts fabricated from neutral subtalar position casts may be warranted.

BIOLOGICAL BASIS FOR STRESS FRACTURES—PATHOGENESIS

The data imply that muscular fatigue may lead to a situation in which locally high shear stresses or impact strains are elevated to the point at which stress fractures can occur but also suggest an interaction with biological processes. Two hypotheses about the pathophysiology of stress fractures are prevalent.

One hypothesis proposes that stress fractures are solely a mechanical result of repeated large-magnitude loads on the bone, i.e., many loading cycles will lead to fatigue failure of the structure. This seems unlikely in view of recent *in vivo* strain data on the human tibia, which show that strains at a stress fracture site rarely or never exceed 2000 microstrain. Even given the worst case scenario in which there is a linear relationship between strain magnitude and cycles to failure, bone should not fail for at least 10^6 cycles at this strain magnitude [20]. Assuming that 1000 loading cycles are placed on a bone per mile of running [71], 10^6 load cycles would be equivalent to 1000 miles of running (and more of walking). Documentation of training activities in recruits during basic training estimate that they march 70 miles and run 130 miles over 12 wk [60]. The number of loading cycles placed on the lower limb during the entire basic training period is less than 20% of that required to cause fracture solely from bone fatigue. Because we know that there is not a linear relationship between strain magnitude and cycles to failure [133] and that at strains of 2500 microstrain exponentially more cycles are required to cause failure than at 2000 microstrain [106], the discrepancy between the actual training intensity or duration and the fracture threshold is likely to be much greater than this. The majority of fractures occur between 3 and 7 wk in the training regime, when even fewer cycles have been placed on the skeleton, making it even less plausible that loading alone is the cause for stress fractures.

A second hypothesis views the stress fracture as positive feedback between the bone's attempt to adapt to increased strain by remodeling and the continued loading applied to the bone. In this view there is a transient reduction in bone mass caused by the acceleration of remodeling, and fracture is the result of continued repetitive loading superimposed on a significant decrease in bone mass caused by more and larger resorption spaces [57, 128]. Accelerated bone remodeling and increased skeletal fragility may be the consequence of the gradual accumulation and growth of microcracks within the bone [20–22, 24, 27, 153] and their repair [9, 11, 93]. Alternatively, accelerated remodeling may be induced by high strain levels without the introduction of obvious microdamage [15].

Positive Feedback between Loading and Bone Remodeling

It is possible that the “adaptive” response of the bone to repeated loading may accelerate the presentation of a stress fracture. Bone remodeling is strain mediated. Remodeling begins with resorption, and each time a new

remodeling unit is begun, it temporarily creates a new resorption space, which increases porosity and reduces bone mass. This decreases bone stiffness and strength exponentially [24, 123, 131]. Because there is less bone to sustain loading, strains on the remaining bone increase, a new remodeling cycle can begin, and more bone is lost. Over time, this leads to a gradual loss of bone and, with repeated overuse, could eventually lead to fracture.

Martin [75] simulated the effects of positive feedback between increased porosity resulting from remodeling, damage accumulation in bone, and repetitive loading. The model showed that, as strain magnitude or the number of load cycles per day increases, a critical threshold is reached at which porosity, damage, and strain begin to grow at a rapidly accelerating rate and without limit. Although periosteal woven bone, in some instances the only radiographic evidence that a stress fracture has occurred, strengthens the bone, this new bone periosteally does not remove the instability. The model shows that porosity introduced by remodeling can contribute via a positive feedback mechanism to an unstable situation in which a stress fracture will occur.

This hypothesis has not been fully tested but is consistent with both the epidemiological and experimental data that exist. In those cases in which it is possible to know, most stress fractures begin within 3 to 7 wk after the initiation of vigorous training [38, 64, 134]. This is coincident with the period when the first phase of bone remodeling (resorption) occurs after the introduction of a higher-than-usual strain stimulus but before new bone formation would be very well established. Generally, after a change in a training regimen, the activation of new remodeling requiring the proliferation and recruitment of new cells will take 5–7 days. The resorption period follows for about 3 wk, whereas the formation phase occurs over the following 3 mo [105]. Thus, fractures occurring between 3 and 7 wk would be well into the resorption phase of bone remodeling and before formation and mineralization caused by the accelerated activity is complete.

Experimental studies with the rabbit model also suggest that positive feedback between loading and remodeling may be a feature of the pathogenesis of stress fractures in this model. Rabbits loaded for 32,400 cycles over the course of 1 day showed no biological evidence of skeletal damage (M. B. Schaffler, personal communication). Rabbits loaded for 36,000 cycles over 3 wk presented with bone microdamage and increased porosity. Eighty percent of these rabbits also have evidence of a stress fracture, and 48% of them showed severe lesions [12]. These data implicate either a damage response or a biological remodeling response, or both, via positive feedback with continued loading, in the pathogenesis of stress fractures.

CONCLUSION

Stress fractures preferentially may occur in regions of high local stress concentration created by repetitive impact loads uncontrolled by synergistic

muscle action. Loading alone, at least at magnitudes consistent with normal human activity, is insufficient to cause the development of a stress fracture. It is likely that positive feedback with the normal adaptive remodeling system is a component of the pathogenesis of stress fractures. Any change in training routine, which can lead to uncontrolled remodeling in a region of stress concentration or the loss of muscle coordination, which prevents the normal attenuation of impact loads, will increase the risk for a stress fracture.

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