Age and Female Sex Are Important Risk Factors for Stress Fractures: A Nationwide Database Analysis

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Background: Stress fractures are caused by micro-trauma due to repetitive stress on bone, common in active individuals and athletes. Previous studies demonstrate that the weightbearing bones of the lower extremities incur stress fractures most often, especially in women and older adults.

Hypothesis: Prior literature does not quantify the difference in frequency of stress fractures among different genders, age groups, or body mass indices (BMIs). We hypothesized that older female patients would have higher rates of lower extremity stress fractures than male patients.

Study Design: Epidemiological research.

Level of Evidence: Level 3.

Methods: Records of female and male patients with lower extremity stress fractures from 2010 to 2018 were identified from the PearlDiver administrative claims database using the International Classification of Diseases (ICD)-9/ICD-10 codes. Stress fractures were classified by ICD-10 diagnosis codes to the tibial bone, proximal femur, phalanges, and other foot bones. Comorbidities were incorporated into a regression analysis.

Results: Of 41,257 stress fractures identified, 30,555 (70.1%) were in women and 10,702 (25.9%) were in men. Our sample was older (>60 years old) (37.3%) and not obese (BMI <30 kg/m^2, 37.1%). A greater proportion of female patients with stress fracture were older ($P < 0.001$) and had foot stress fractures ($P < 0.001$), while a greater proportion of male patients with stress fracture were younger than 19 years ($P < 0.001$) and had metatarsal ($P < 0.001$), hip ($P = 0.002$), and tibia stress fractures ($P < 0.001$).

Conclusion: Stress fractures commonly occur in women and older adults with low BMIs. Metatarsal and tibia stress fractures were the most common, and a greater proportion of women had foot stress fractures.

Clinical Relevance: Our study examined the large-scale prevalence of different lower extremity stress fractures among a wide patient population sample of varying ages and BMIs. These findings can help clinicians identify active populations at greater risk for stress fracture injuries.

Keywords: stress fracture; bone stress injury; female athlete; epidemiology

Stress fractures are one of the most common overuse injuries[19] and can occur in the ribs, spine, and most bones of the extremities.[25] Stress fractures develop as a result of strain caused by micro-trauma due to repetitive action or stress on bone. This can be a disabling condition for active individuals and athletes, and studies have shown that the weight bearing bones of the lower extremities incur stress fractures most often.[16,18,25,32] Stress fracture injuries are commonly caused by bone stress injuries (BSIs), described in Warden et al[38] as the inability of bone to withstand repetitive loading, resulting in structural fatigue and pain. BSI often occurs at first as a stress reaction due to strenuous activity (long-distance running, for

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example), which can then progress to a stress fracture and, without treatment, a complete bone fracture. In athletic populations, the incidence of stress fractures can vary depending on the specific activity and sport.[8] According to Brudvig et al,[8] body type and training activity can be used to characterize stress fractures.[8] For example, the tibia is the most common site of injury for runners, while military recruits most often reported stress fractures in the foot.[19] Duckman et al[12] also stated that stress fractures are frequently seen in the tibia and metatarsals in distance runners, while data are not conclusive on whether one is more common than the other.[12] These injuries often result in time lost from sport, medical disqualification, or early end to sport season, and are important to recognize and treat early.[10]

Several previous studies demonstrated that young adult female long-distance runners are at higher risk for stress fracture–type injuries, specifically female collegiate runners.[30,39] Additionally, military recruits are at increased risk of developing stress fractures, with women typically have a higher incidence of injury than men.[19] Women are at increased risk of developing stress fractures in sport due to a series of clinical manifestations that was previously known as the female athlete triad: menstrual irregularity, disordered eating, and osteopenia.[34] These clinical entities are now recognized as extremes of a spectrum of disordered fueling in sport, which is now referred to as relative energy deficiency in sport (RED-S).[29] In the United States, an estimated 13% of female athletes experience stress fractures, with lower extremity fractures representing 80% to 95% of all stress fractures.[1] According to Javed et al,[17] disordered eating is particularly prevalent in women experiencing these extreme clinical entities, but concern for and the presence of any of these disordered behaviors within the spectrum of RED-S should prompt further investigation. Teneforde et al[35] found that athletes with known oligomenorrhea/amenorrhea status was an important predictor for BSI. Field et al[13] reported that certain women have unique risk factors for stress fracture including older age at menarche, a maternal family history of osteoporosis, and hours per week participating in sports or physical activity. Similar to female athletes, studies have found that male athletes with low bone mineral density were at increased risk for trabecular BSI.[36]

For older adults, stress fractures are more likely the result of insufficiency due to normal stressors on aged or impaired bone and have been found to be common in postmenopausal osteoporotic women.[11,31] Breer et al[7] found that stress fractures of the lower limb were common among elderly men and women, who also had significantly lower lumbar and femoral bone mineral density compared with other age groups, as well as vitamin D insufficiency. Law et al[23] also reported that elderly postmenopausal women who are smokers are at increased risk for hip stress fractures. Modifiable risk factors, such as smoking and low physical activity, may predispose elderly populations to stress fracture injuries.

While the risk factors of age and gender are discussed in the literature, previous studies have not examined the large-scale prevalence of different anatomic groups of lower extremity stress fractures among a wide sample of patients of different age groups. Therefore, the purpose of this study was to compare the age distribution of lower extremity stress fractures between women and men after adjusting for potential confounders. The study further aimed to analyze the anatomic distribution of lower extremity stress fractures between the 2 cohorts. We hypothesized that older female patients would have significantly higher rates of lower extremity stress fractures than male patients.

METHODS

Patient information was queried from PearlDiver (PearlDiver Inc), a commercially available administrative claims database, using International Classification of Diseases, Ninth Revision and Tenth Revision (ICD-9/ICD-10). The study utilized the Humana dataset, which has 15 million patient records from 2007 to 2018, including patients that are commercially insured, privately insured, or who purchased Medicare Advantage plans through Humana Health Insurance. Inpatient and outpatient diagnoses were included. This study is institutional review board exempt, because PearlDiver contains deidentified data and is compliant with the Health Insurance Portability and Accountability Act.

A retrospective cohort design was used to compare male and female patients who had stress fractures. Stress fractures were further classified by ICD-10 diagnosis codes to the tibia, hip, metatarsals, and feet, corresponding to the tibial shaft, proximal femur, phalanges, and other foot bones, respectively. Patient groups were identified using ICD codes because the codes include temporal data detailing a patient's hospital course. Exclusion criteria included patients with a pathologic fracture, nonorthopaedic fractures including skull, mandible, facial, and nasal bone fractures, vertebral column fractures, and rib fractures. ICD-10 codes that define the patient groups are located in the Appendix (available in the online version of this article).

Each patient cohort was queried for demographic information, including age, sex, body mass index (BMI), length of stay, 90-day readmission rate, Charlson comorbidity index (CCI), and incidences of several comorbidities. Specific comorbidities queried from the database included a history of diabetes, hypertension, chronic kidney disease (CKD), congestive heart failure (CHF), rheumatoid arthritis (RA), tobacco use, liver disease, immunocompromised status, other cardiac disease, pneumonia, acute renal failure, respiratory failure, and osteoporosis. In this case, "immunocompromised status" refers to a patient who received an immunologic agent or antineoplastic drug 1 year before their index procedure. "Other cardiac disease" applied to patients who had any prior diagnosis of coronary heart disease or ischemic heart disease.

Data analysis was performed using R statistical software (R Project for Statistical Computing), integrated within the PearlDiver software. An α level less than 0.05 was considered

Table 1. Comparison of clinical and demographic characteristics of male and female patients diagnosed with a stress fracture

Demographic Variable	Male (n = 10,702)	Male, %	Female (n = 30,555)	Female, %	*P*
Age, y					
<14	983	9.2	1281	4.2	<0.001
15-19	1243	11.6	2159	7.1	<0.001
20-24	428	4.0	1058	3.5	0.01
25-29	341	3.2	1023	3.4	0.44
30-39	965	9.0	2971	9.7	0.03
40-49	1441	13.5	4303	14.1	0.12
50-59	1930	18.0	6323	20.7	<0.001
>60	3475	32.5	11,898	38.9	<0.001
	Male (n = 2734)	Male, %	Female (n = 9594)	Female, %	*P*
Body mass index, kg/m^2					
<30	1010	36.9	3562	37.1	0.88
30-34.9	711	26.0	2194	22.9	<0.001
35-39.9	500	18.3	1710	17.8	0.6
≥40	513	18.8	2128	22.2	<0.001
Readmission	414	32.6	857	67.4	<0.001

statistically significant. Categorical variables, including demographic and clinical characteristics, were compared using chi-square analysis, and Welch's *t* test was used to compare continuous variables such as CCI and age. Multivariate logistic regression adjusting for patient age, CCI, and BMI was used to calculate odds ratios (ORs), with corresponding 95% confidence intervals (CIs) for the rates of both local and systemic complications between men and women with stress fractures.

RESULTS

In total, 42,631 stress fractures were identified in the PearlDiver database between 2007 and 2018. Of these, 1374 did not meet the inclusion criteria and were excluded, for a final total of 41,257. Most patients in our sample were older than 60 years (15,373 of 41,257; 37.3%) and had a BMI <30 kg/m^2 (2641 of 12,328; 37.1%). More women (n = 30,555; 70.1%) than men (n = 10,702; 25.9%) presented with stress fractures. A greater number of women (4498 of 41,257; 10.9%) than men (2654 of 41,257; 6.4%) presented with stress fractures between the age of 14 and 24 years. A significantly greater proportion of women over 60 years of age presented with stress fractures compared with men over 60 years of age (age >60 years: 38.9% vs 32.5%, women vs men, $P < 0.001$) (Table 1).

Of the total stress fractures identified (n = 41,257), 26,970 (65.4%) were organized into stress fracture type based on ICD-10 diagnosis codes, including stress fractures of the foot (n = 17,604; 65.3%), tibia (n = 6302; 23.4%), hip (n = 2410; 8.9%), and metatarsals (n = 654; 2.4%). Significantly more women (n = 20,397; 75.6%) than men (n = 6573; 24.4%) ($P < 0.001$) presented with hip, tibia, foot, and metatarsal stress fractures. A greater proportion of women had foot stress fractures (67.7% vs 57.7%, women vs men, $P < 0.001$), while a greater proportion of men had metatarsals (3.0% vs 2.3%; $P < 0.001$), hip (3.0% vs 2.3%; $P = 0.002$), and tibia stress fractures (29.0% vs 21.6%; $P < 0.001$) (Table 2).

A greater proportion of boys younger than 14 years had metatarsal stress fractures compared with girls (29 of 193 vs 14 of 461, 15.0% vs 3.0%; men vs women, $P < 0.001$), and a greater proportion of women over the age of 60 years had metatarsal stress fractures compared with men (48 of 193 vs 178 of 461, 24.9% vs 38.6%, men vs women, $P < 0.001$). Men who presented with metatarsal stress fractures were significantly younger than women with metatarsal stress fractures (43.6 years vs 51.7 years, $P < 0.001$) (Table 3). The majority of women who presented with metatarsal stress fractures had a BMI <30 kg/m^2 (49 of 153; 32.0%).

Table 2. Stress fractures by anatomic distribution in male and female patients

Overall	Male (n = 10,702)	Male, %	Female (n = 30,555)	Female, %	*P*
Hip	680	6.4	1730	5.7	<0.001
Tibia	1907	17.8	4395	14.4	<0.001
Foot	3793	35.4	13,811	45.2	<0.001
Metatarsal	193	1.8	461	1.5	0.002
Other	4129	38.6	10,158	33.2	<0.001

Table 3. Age of men and women who presented with hip, tibia, foot, and metatarsal stress fractures

	Men	Women	*P*
Hip			
Age, y, mean ± SD	64.43 ± 17.43	63.56 ± 17.92	0.27
Tibia			
Age, y, mean ± SD	39.54 ± 21.37	44.68 ± 21.60	<0.001
Foot			
Age, y, mean ± SD	46.35 ± 19.61	49.82 ± 17.46	<0.001
Metatarsal			
Age, y, mean ± SD	43.72 ± 21.26	51.70 ± 17.76	<0.001

A greater proportion of boys younger than 14 years had foot stress fractures compared with girls (3271 of 3793 vs 487 of 13811, 86.2% vs 3.5%, men vs women, $P < 0.001$), and a greater proportion of women over the age of 60 years had foot stress fractures compared with men (1137 of 3793 vs 4608 of 13811, 30.0% vs 33.4%, men vs women, $P < 0.001$). Men with foot stress fractures were significantly younger than women with foot stress fractures (46.4 years vs 49.8 years, $P < 0.001$) (Table 3). The majority of male (314 of 1083, 29.0%) and female (1485 of 4456, 33.3%) patients with foot stress fractures had a BMI <30 kg/m^2.

A greater proportion of men over the age of 60 years had hip stress fractures compared with women (497 of 680 vs 1203 of 1730, 73.1% vs 69.5%, men vs women, $P < 0.001$). Men and women with hip stress fractures were older (64.43 years vs 63.56 years) than men and women with tibia, foot, and metatarsal stress fractures, although this difference was not statistically significant ($P = 0.27$) (Table 3). The majority of male (110 of 191, 57.59%) and female (303 of 520, 58.27%) patients with hip stress fractures had a BMI <30 kg/m^2.

A greater proportion of boys younger than 14 years had tibia stress fractures compared with girls (207 of 1907, 278 of 4396, 10.9% vs 6.3%, men vs women, $P < 0.001$), and a greater proportion of women over the age of 60 years had tibia stress fractures compared with men (418 of 1907, 1362 of 4396, 21.9% vs 31.0%, $P < 0.001$). The majority of men (159 of 391, 40.7%) and women (456 of 1169, 39.01%) with tibia stress fractures had a BMI <30 kg/m^2.

Men had a higher burden of comorbidities compared with women (CCI: 0.873 vs. 0.765; men vs women; $P < 0.001$) (Table 4). Men with stress fractures had significantly higher rates of comorbidities, including diabetes ($P < 0.001$), CKD ($P < 0.001$), CHF ($P = 0.003$), tobacco use ($P < 0.001$), liver disease ($P < 0.001$), cardiac issues ($P < 0.001$), acute renal failure ($P < 0.001$), and respiratory failure ($P = 0.017$). Women with stress fractures had significantly higher rates of RA ($P = 0.007$), immunocompromised status ($P < 0.001$), and osteoporosis ($P < 0.001$) (Table 5).

DISCUSSION

This study demonstrates that overall, women have a significantly higher rate of stress fractures than men. The majority of stress

Table 4. Age, LOS, and CCI of male and female patients with a stress fracture

Demographic Variable	Male (n = 10,702)	Female (n = 30,555)	*P*
Age, y, mean ± SD	46.0 ± 21.7	50.9 ± 19.6	<0.001
LOS, d, mean ± SD	5.0 ± 4.6	4.5 ± 3.8	0.28
CCI, mean ± SD	0.87 ± 1.9	0.77 ± 1.6	<0.001

CCI, Charlson comorbidity index; LOS, length of stay.

Table 5. Specific comorbidities of male and female patients diagnosed with a stress fracture

Specific Comorbidity	Male (n = 10,702)	Male, %	Female (n = 30,555)	Female, %	*P*
Diabetes	2481	23.2	6673	21.8	<0.001
Hypertension	4303	40.2	12,322	40.3	0.83
Chronic kidney disease	834	7.8	1795	5.9	<0.001
Congestive heart failure	526	4.9	1293	4.2	0.003
Rheumatoid arthritis	170	1.6	1203	3.9	0.007
Tobacco use	1578	14.7	3889	12.7	<0.001
Liver disease	720	6.7	1884	6.2	0.04
Immunocompromised	173	1.6	927	3.0	<0.001
Cardiac issues	1393	13.0	3128	10.2	<0.001
Pneumonia	815	7.6	2189	7.2	0.12
Acute renal failure	597	5.6	1193	3.9	<0.001
Respiratory failure	310	2.9	755	2.5	0.02
Osteoporosis	303	2.8	3280	10.7	<0.001

fractures in this sample occurred in nonobese, older adults. Women had higher numbers of stress fractures in every group, including metatarsal stress fractures, navicular/foot stress fractures, hip stress fractures, and tibia stress fractures. Metatarsal and tibia stress fractures were the most common, a finding that is supported by previous studies.[15-17] A greater proportion of women compared with men had foot stress fractures, and a greater proportion of younger male patients (age <14 years) had metatarsal, hip, and tibia stress fractures compared to younger female patients. Additionally, a greater proportion of older male patients (age >60 years) had hip stress fractures compared with female patients.

In accordance with previous research, our study demonstrated that patients with low BMI (<30 kg/m^2) were more likely to present with stress fractures.[3,14] In 2018, Knapik et al[21] found that a lower BMI was associated with a higher risk of stress fractures in US Army Basic Combat Training for both men and women. Low BMI could increase susceptibility to stress fracture, as it may result in overuse of the surrounding soft tissue or it may indicate an insufficient amount of bone or fat density in patients with low BMI making them more susceptible to stress induced injuries.

Gender differences are important to consider when evaluating male and female patients presenting to orthopaedic clinics with stress fractures. Previous studies have described a higher rate of stress fracture occurrence in young female versus male athletes.[4-6,20,28] Our study demonstrated that stress fractures most commonly occur in women, and more women had stress fractures between the age of 15 and 24 years compared with men, building on previous work describing a higher incidence of stress fractures among teenage and young adult female athletes. Stress fractures among this age group have been found to be associated with the RED-S, where low energy availability, which occurs as a result of disordered eating, can lead to oligomenorrhea and result in neuroendocrine changes and osteopenia.[2,4,33] Nieves et al[27] found that postpubertal adolescent boys have thicker cortical bone, greater bone length, circumference, and strength possibly serving as a protective measure against stress fracture injury. However, in prepubertal boys and girls (age <14 years), differences in cortical bone area and the size of the appendicular skeleton have not been found to be statistically significant.[15] This suggests that our finding that a greater proportion of younger male patients (age <14 years) had metatarsal, hip, and tibia stress fractures is not due to anatomic or hormonal differences, but possibly due to a difference in amount and type of physical activity prepubertal boys and girls are participating in. Further research is necessary to understand sex and anatomic differences in stress fractures in prepubertal groups.

Our study adds to the existing body of literature by describing female and male stress fracture patients across both younger and older age groups. Traditionally, studies examining stress fractures have focused on female athletes younger than 24 years, and female endurance athletes specifically.[6,12,20,22] We demonstrate that stress fractures are extremely prevalent among male and female patients between the ages of 50 and 60 years, with significantly more fractures occurring in women than men ($P < 0.001$). The majority of patients in our sample were over the age of 60 years, and we found that the majority of men and women with hip stress fractures were older than 60 years. Previous studies have found a positive correlation between older age and higher stress fracture risk in military combat training specifically.[8,26] In 2018, Knapik et al[21] found a linear predictive relationship between older age and increasing risk of stress fracture. Older women are at higher risk of developing stress fractures compared with other age groups due to a dramatic decrease in cortical bone mass and bone mineral density with the loss of ovarian estrogens after menopause.[9] While our study found that men had a higher burden of comorbidities, women specifically presented with higher rates of RA ($P = 0.007$) and osteoporosis ($P < 0.001$), which could affect the likelihood of this group to develop stress fractures. In addition, both male and female older adults have age-related decreases in collagen, which affects bone strength. They also have an increase in bone porosity, which can impact bone stiffness, thereby increasing the risk of stress fracture.[37] Lotz et al[24] described that while osteoporosis leads to an increase in the magnitude of peak stress on the femoral neck and intertrochanteric region during walking and movement, it is actually unstable gait patterns and an increased fall risk that predispose geriatric patients to stress fractures rather than the strength of the bone.[27] These injuries present a public health issue as elderly patients are often frail, prone to complications, and rely on public institutions such as hospitals and nursing homes for care. Further research is needed to investigate the prevalence of hip stress fractures, their relation to gait pattern and falls, and their presenting characteristics in this population.

Limitations

There are several limitations to this study. Because of the nature of an administrative claims database, the accuracy of the reported findings is dependent on the accuracy of the codes listed and categorized in the database. In addition, other relevant clinical information such as athletic status, mechanism of injury, adherence to physical therapy, and type of conservative or operative treatment for the stress fracture could not be queried from the database. The administrative database presents a heterogeneous sample with a variety of private, Medicare, and Medicaid patients. However, generalizability of this study to the entire US patient population is limited as a large amount of data are derived from private insurance companies with patient populations based in the Midwest and Southern regions.

CONCLUSION

We examined stress fractures in a commercially available administrative claims database, using ICD-9/ICD-10, over a period of 8 years. Stress fractures most commonly occur in women. The majority of stress fractures occurred in older adults with low BMIs. Metatarsal and tibia stress fractures were the most common, and a greater proportion of women had foot stress fractures, while more younger men (age <14 years) had hip, metatarsal, and tibia stress fractures. Further research is needed to understand the anatomic differences in stress fractures between different age groups and genders. These findings can help clinicians be better informed about what populations are at greater risk for stress fracture injuries and provide evidence for increased screening for stress fractures among young adults.

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