Pedal Bone Density, Strength, Orientation, and Plantar Loads Preceding Incipient Metatarsal Fracture After Charcot Neuroarthropathy: 2 Case Reports

Charcot neuroarthropathy (CN) is a progressive, inflammation-mediated destruction of bones and joints leading to fracture, subluxation, and dislocation, which in turn result in progressive foot deformities that increase the risk of plantar ulceration. Diabetes mellitus and peripheral neuropathy are the most common precursors of CN. The etiology of CN remains incompletely understood, but is likely due to a combination of repetitive, unperceived trauma during weight-bearing activities, focal bone loss, and pedal joint malalignment. Bone injury and subtle articular damage characteristic of incipient CN are difficult to visualize with planar radiographs. As a result, CN typically progresses until more serious, clinically obvious events occur.

Previously published cross-sectional studies provide evidence for the importance of bone loss, foot deformity, and elevated biomechanical loading in the development and progression of CN. Individuals with acute CN have lower calcaneal areal bone mineral density (aBMD), estimated using quantitative ultrasound, than matched subjects with diabetes mellitus and peripheral neuropathy but without CN. Moreover, the clinical manifestation of CN may depend on aBMD, as pedal fractures predominate in individuals with osteopenia (as measured by dual-energy X-ray absorptiometry at the hip), whereas pedal subluxations and dislocations are more pronounced in individuals with osteoporosis.

**CASE DESCRIPTION:** Two women, aged 45 and 54 years at the onset of an acute, nonfracture Charcot neuroarthropathy event, received regular physical therapy with wound care and total-contact casting. Both enrolled in a larger research study that included plantar pressure assessment and quantitative computed tomography at enrollment and 3, 6, and 12 months later. The women sustained mid-diaphyseal fifth metatarsal fracture 10 to 11 months after enrollment. Quantitative computed tomography image-analysis techniques were used to measure vBMD; bone geometric indices reflecting strength in compression, bending, and cortical buckling; and 3-D bone-to-bone orientation angles reflecting foot deformity.

**OUTCOMES:** Fifth metatarsal mid-diaphyseal vBMD decreased during offloading treatment from 0 to 3 months, then increased to above baseline levels by 6 months. All geometric strength indices improved from baseline through 6 months. Plantar loading in the lateral midfoot increased preceding fracture, concomitant with alterations in bone orientation angles, which suggest progressive development of metatarsus adductus and equinovarus foot deformity.

**DISCUSSION:** Fractures may occur when bone strength decreases or when biomechanical loading increases. Incipient fracture was preceded by increased loading in the lateral midfoot but not by reductions in vBMD or geometric strength indices, suggesting that loading played a greater role in fracture. Moreover, the progression of foot deformities may be causally linked to the increased plantar loading.

**LEVEL OF EVIDENCE:** Prognosis, level 4. 

**KEY WORDS:** diabetes, foot, fracture, plantar ulcers

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common in those with normal or high aBMD. Recent advances in quantitative computed tomography (QCT) image processing and image analysis allow direct quantitative measurement of volumetric bone mineral density (vBMD) in foot bones. Commean et al developed a semi-automated bone segmentation technique to compute bone volumes and vBMD for the 7 tarsals and 5 metatarsals with high precision. Still, the importance of vBMD as a prospective risk factor for incipient fracture is unclear. At other anatomical sites, bone geometric strength indices have been more highly correlated to fracture risk than has aBMD or vBMD alone. A recent ex vivo validation study performed using cadaver metatarsals found that mid-diaphyseal indices of bending strength (minimum moment of inertia [$I_{min}$] and section modulus [$S_{min}$]) and cortical integrity (average thickness ($t_{avg}$) and buckling ratio [BR]) were more highly correlated than vBMD to metatarsal breaking loads. Ultimate force was directly related to $I_{min}$, $S_{min}$, and $t_{avg}$ and inversely related to BR (where BR is the periosteal radius divided by $t_{avg}$).

QCT has been used increasingly to measure foot morphology in neuropathy. QCT can overcome inherent limitations of radiography, such as obscured views and out-of-plane rotations. Hammer-toe deformity of the first 3 rays has been shown to predict high peak plantar pressures under the metatarsal heads, though these studies utilized planar reconstructions of QCT images. New techniques take full advantage of the ability of QCT to measure joint angles and quantify structural morphology in all 3 anatomical planes, including the frontal plane, but, to our knowledge, no QCT study has measured 3-D foot bone and joint orientations in individuals with diabetes mellitus, peripheral neuropathy, or CN.

Elevated plantar pressure has been linked to neuropathic foot ulcers retrospectively and prospectively and has been identified as a factor contributing to prolonged healing time and higher risk of reulceration. Fixed foot deformities resulting from CN play a role in many neuropathic ulcers, but even in the absence of ulceration, CN is associated with elevated peak plantar pressure. To our knowledge, no previous research has assessed plantar loads over time following an acute CN event, or assessed the relationship between plantar loads and incipient fracture risk.

As part of a prospective study of individuals with acute CN, we assessed plantar pressure and acquired QCT scans at enrollment and 3, 6, and 12 months later. Image analysis techniques were used to measure vBMD, bone geometric strength indices, and 3-D bone-to-bone orientation angles. Two of the volunteers incidentally experienced mid-diaphyseal fractures of the fifth metatarsal (Met5) between 6 and 12 months after study enrollment. These serial data collections allowed a unique prospective assessment of changes in bone strength, foot deformity, and applied loads, leading to eventual metatarsal fracture.

**CASE DESCRIPTION**

**Volunteer A** was a 45-year-old woman who was diagnosed with type 1 diabetes mellitus at age 21. She was diagnosed with peripheral neuropathy at age 38, based on clinical evidence of impaired sensation to pressure, vibration, and light touch, and reported regular tingling and numbness in her feet. She had palpable pulses bilaterally in the dorsal pedal and posterior tibial regions. At the time of enrollment, she had plantar-flexed first rays and prominent first metatarsal heads bilaterally, and a bunion on the right Met5 head. Because she had sustained CN-related fractures of her left foot 1 year prior to the present study, her left foot could not be used as a comparison. She had prior history of plantar ulceration at the right Met5 and right great-toe sulcus, and was receiving offloading and wound care treatments to heal a plantar ulcer at the base of the left Met5 when a diagnosis was made of an acute CN event located at the right first cuneiform, with possible secondary CN in the proximal region of the right Met5.

Volunteer B was a 54-year-old woman with no prior diagnosis of diabetes mellitus. However, based on her glycosylated hemoglobin value of 5.8%, she would have been identified as prediabetic using updated criteria by the American Diabetes Association criteria; furthermore, she was diagnosed with type 2 diabetes after the 12-month follow-up, based on results of an oral glucose tolerance test. Following a fracture of her right cuboid at age 50, she was diagnosed with idiopathic peripheral neuropathy, based on clinical evidence of bilateral impaired sensation to pressure, vibration, and light touch. She reported painful neuropathy bilaterally in the digits and forefoot region, had

**TABLE 1**

**Baseline Demographic Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Volunteer A</th>
<th>Volunteer B</th>
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</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>45</td>
<td>54</td>
</tr>
<tr>
<td>Height, cm</td>
<td>1676</td>
<td>175.3</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>101.8</td>
<td>83.7</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>36.2</td>
<td>272</td>
</tr>
<tr>
<td>Diabetes status</td>
<td>Type 1</td>
<td>None</td>
</tr>
<tr>
<td>Diabetes duration, y</td>
<td>24</td>
<td>NA</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>8.1</td>
<td>5.8</td>
</tr>
<tr>
<td>Peripheral neuropathy, y</td>
<td>7 (secondary to DM)</td>
<td>4 (idiopathic)</td>
</tr>
</tbody>
</table>

Abbreviations: DM, diabetes mellitus; HbA1c, percentage of glycosylated hemoglobin; NA, not applicable.
palpable pulses bilaterally in the dorsal pedal and posterior tibial regions, and had no history of plantar ulceration. She had a complete hysterectomy at age 37, and had received estrogen replacement therapy from age 37 to age 50. Volunteer B was diagnosed with an acute CN event located at the junction of the right cuboid and the base of the right Met5. Detailed demographic characteristics are provided in Table 1.

Both women were treated with total-contact casting (TCC) that was changed weekly until the acute CN event had subsided. Before the plaster and fiberglass wrapping of the TCC were applied, the involved foot was cleaned, dried, and covered in a seamless antimicrobial stocking, with an additional layer of low-density foam padding to cover the toes. Volunteer A wore a TCC for a total of 94 days, and Volunteer B for 179 days. Upon agreeing to participate in the research study of CN, both volunteers gave written informed consent in accordance with the guidelines put forth by the Institutional Review Board and the Human Research Protection Office at Washington University in St Louis.

**QCT Scans**

QCT scans were taken at the Center for Clinical Imaging Research at the Washington University School of Medicine, using a SOMATOM Definition computed tomography scanner (Siemens AG, Erlangen, Germany) with the following acquisition parameters: current-time product, 220 mA·s; peak kilovoltage, 120 kVp; pitch, 1; rotation time, 0.33 seconds; matrix, 512 × 512. Positioning was standardized across scans, with the ankle in a neutral position, as shown in Figure 1. Raw data were reconstructed at 0.6-mm slice reconstruction intervals using a B70F kernel to create QCT images with in-plane resolution of 0.4 to 0.55 mm. In brief, a custom density-based filtering plug-in (ImageJ Version 1.46h; National Institutes of Health, Bethesda, MD) was used to distinguish bone tissue from surrounding soft tissue. Then, Analyze Version 10.0 (AnalyzeDirect, Inc, Overland Park, KS) and a custom graph-cut software tool were used to segment bones from each other at their articulating surfaces. The end result of segmentation is a series of bone object maps, as shown in Figure 2, which are then used to assess bone geometric strength indices or bone-to-bone orientation angles.

**Bone Segmentation Processing**

The bone segmentation process has been described in detail elsewhere. In brief, the segmented bone object maps were overlaid on the raw grayscale voxel data, and the resulting Met5 voxel data sets were transformed along each bone’s longitudinal axis using the BoneJ plug-in (Version 1.2.4) in ImageJ. Realigned voxel data were interpolated to isotropic voxels (0.5-mm dimension) using a cubic spline function in Analyze, then exported to custom Excel (Microsoft Corporation, Redmond, WA) macros for computation of regional vBMD and cross-sectional $I_{avg}$, $S_{max}$, and $t_{max}$, and BR in the central 3 mm of the mid-diaphysis. Although there are not yet normative data or test-retest least-significant change values for these bone geometric strength variables, we have reported their high correlations to ex vivo ultimate bending loads using identical image-analysis methods in cadaver samples.

Average Hounsfield unit values for each bone were then converted to equivalent vBMD (mg/cm$^2$) using scan-specific hydroxyapatite calibration phantoms. Previous work by our group has shown high test-retest measurement precision for vBMD, with a least-significant change of 10 mg/cm$^2$ for Met5 and a coefficient of variation of 1.9%.

Full methods for bone geometric strength processing are provided elsewhere. In brief, the segmented bone object maps were overlaid on the raw grayscale voxel data, and the resulting Met5 voxel data sets were transformed along each bone’s longitudinal axis using the BoneJ plug-in (Version 1.2.4) in ImageJ. Realigned voxel data were interpolated to isotropic voxels (0.5-mm dimension) using a cubic spline function in Analyze, then exported to custom Excel (Microsoft Corporation, Redmond, WA) macros for computation of regional vBMD and cross-sectional $I_{avg}$, $S_{max}$, and $t_{max}$, and BR in the central 3 mm of the mid-diaphysis. Although there are not yet normative data or test-retest least-significant change values for these bone geometric strength variables, we have reported their high correlations to ex vivo ultimate bending loads using identical image-analysis methods in cadaver samples.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
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<tr>
<td>Age at onset of CN (years)</td>
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<tr>
<td>Age at last scan (years)</td>
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<tr>
<td>Ethnicity</td>
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<tr>
<td>Gender</td>
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</tbody>
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**FIGURE 1.** Standard positioning of the lower extremity in a quantitative computed tomography scanner.

**FIGURE 2.** Bone segmentation processing. (A) Photograph of an individual with acute Charcot, (B) quantitative computed tomography image, (C) filtered quantitative computed tomography image to remove soft tissue, (D) segmented, filled bone object maps for tarsals and metatarsals.

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Bone-to-Bone Orientations
Segmented bone object maps for all 12 tarsal and metatarsal bones were imported into an in-house software tool that allows placement of user-defined anatomic landmarks on volume-rendered surface meshes. These landmarks were chosen to produce clinically relevant 3-D coordinate axes for each bone, with $x$ directed laterally, $y$ directed axially (primarily anterior), and $z$ directed vertically. Bone-to-bone orientations were computed using $x$-$y$-$z$ Cardan rotation sequences, corresponding, respectively, to sagittal ($\alpha$), frontal ($\beta$), and transverse ($\gamma$) angles. As the QCT scans did not include an external frame of reference, individual bone angles were expressed with respect to the calcaneus. Additionally, a number of other bone-to-bone angles were considered as relevant indices of deformity in the CN foot: orientation of the navicular with respect to the talus, the first metatarsal with respect to the talus, and the Met5 with respect to the cuboid.

Plantar Loading Assessment
Plantar pressure data were not recorded at enrollment due to the inflammation and injury risk associated with acute CN, but were recorded at 3, 6, and 12 months postenrollment. Barefoot walking trials were collected using a 2-step method using an EMED-ST P2 pressure platform (novel GmbH, Munich, Germany) with a spatial resolution of 2 sensors per cm$^2$ and a sampling frequency of 50 Hz. Each walking trial yielded a plantar pressure map that was divided into 5 regions using Percent Mask software (novel GmbH).

OUTCOMES

vBMD and Geometric Strength Indices

For both women, whole-bone vBMD of Met5 decreased during the offloading TCC period from baseline to 3 months (losing 4% and 8% of baseline vBMD, respectively), as shown in Table 2. Both women’s whole-bone vBMD improved between the 3-month and 6-month follow-up measurements (+1% and ~3% compared to baseline vBMD, respectively), then decreased after Met5 fracture to 16% and 23% below baseline, respectively, at the 12-month follow-up measurement. Fracture occurred at roughly 10.5 months after baseline testing for volunteer A and 11 months after baseline for volunteer B, meaning that the 12-month follow-up testing took place roughly 6 and 4 weeks, respectively, after fracture. Mid-diaphyseal vBMD showed a similar trend, decreasing slightly below
baseline values after TCC offloading, rebounding to slightly above baseline values by the 6-month scan, then falling to roughly a quarter below baseline after the fracture event.

Mid-diaphyseal resistance to bending loads ($I_{\text{min}}$ and $S_{\text{min}}$) changed differently over time in the 2 volunteers. In volunteer A, $I_{\text{min}}$ and $S_{\text{min}}$ increased progressively from baseline through 6 months, whereas volunteer B exhibited minor reductions at 3 months that rebounded to slightly above baseline values by 6 months. At 12 months, both volunteers showed large losses in bending strength following fracture and another prolonged period of offloading. Mid-diaphyseal $t_{\text{avg}}$ increased from baseline to 6 months in both volunteers by 8% to 9%; this thickening of cortical shell was also reflected in the 6% to 10% reduction of BR.

**Plantar Loading**

While barefoot plantar pressure was not measured at baseline, the measurements at 3 months and 6 months postenrollment showed elevated peak pressure and maximum force in the lateral midfoot (representing the lateral metatarsals) compared to normative data. TABLE 3 provides data for plantar loading and FIGURE 3 for peak plantar pressure maps. Volunteer A showed greater load increases, with a rough doubling of peak plantar pressure values between 3 and 6 months and an approximately 60% increase in maximum force, with further load increases at 12 months following fracture. Volunteer B began with higher peak plantar pressure and maximum force in the lateral midfoot than volunteer A and experienced smaller increases at the 6-month and 12-month follow-ups.

**Bone and Joint Orientations**

In the sagittal plane, both volunteers showed progressive increases in the relative plantar flexion of the metatarsals with respect to the calcaneus (TABLE 4). Moreover, increases in metatarsal plantar flexion were generally larger in the lateral metatarsals: the first metatarsal plantar flexion increased by 2° to 8°, second metatarsal increased by 3° to 7°, third metatarsal increased by 6° to 11°, fourth metatarsal increased by 10° to 11°, and Met5 increased by 11° to 13°. No obvious trends occurred for the metatarsals in the frontal plane. In the transverse plane, the metatarsals showed greater adduction with respect to the calcaneus from baseline to 6 months. For the other bone-to-bone orientation angles that were assessed, only a greater adduction of the first metatarsal with respect to the talus (13° in volunteer A and 2° in volunteer B) showed consistent alteration preceding the fracture.

**DISCUSSION**

The prospective design of these case reports has allowed a unique opportunity to assess changes in vBMD, bone geometric strength indices, foot deformities, and biomechanical loads preceding incipient mid-diaphyseal load increases.
Fractures of Met5. Specifically, comparing load variables provide indices of the approximate load variable responsible for the observed fractures. Mid-diaphyseal vBMD had reductions in the involved feet of CN participants, and 977 mg/cm\(^2\) in the uninvolved feet, and 954 mg/cm\(^2\) in the uninvolved feet, with diabetes and peripheral neuralgia. Several of the bone variables reported were the highest correlates of ex vivo biomechanical loading to correlates of bone strength allows a determination of the factor of risk for fracture. Our results suggest that in these 2 women, a reduction in fracture load was not the likely causal mechanism for the observed Met5 fractures. Preceding this, mid-diaphyseal vBMD had reduced vBMD, mid-diaphyseal BMD had reduced vBMD. In the involved foot of the CN participants, mid-diaphyseal vBMD averaged 814 mg/cm\(^2\). Full longitudinal results for vBMD and bone geometry are not yet available for the larger prospective study, but the 2 cases presented here can be compared to baseline results. Mid-diaphyseal vBMD has been predicted to increase based on our previous cadaver study. Mid-diaphyseal vBMD was not the likely causal mechanism for the observed Met5 fractures. Preceding this, mid-diaphyseal vBMD had reduced vBMD in the uninvolved foot of the CN participants, mid-diaphyseal vBMD averaged 814 mg/cm\(^2\). Full longitudinal results for vBMD and bone geometry are not yet available for the larger prospective study, but the 2 cases presented here can be compared to baseline results. Mid-diaphyseal vBMD has been predicted to increase based on our previous cadaver study.

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### TABLE 4

<table>
<thead>
<tr>
<th>Met 5 Cuboid</th>
<th>Met 5 Calcaneus</th>
<th>Met 1 Navicular</th>
<th>Met 1 Talus</th>
<th>Met 2 Calcaneus</th>
<th>Met 2 Talus</th>
<th>Met 3 Calculus</th>
<th>Met 3 Talus</th>
<th>Met 4 Talus</th>
<th>Met 5 Metatarsal</th>
<th>Baseline</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
<th>Baseline</th>
<th>3 mo</th>
<th>6 mo</th>
<th>12 mo</th>
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<td>65</td>
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<td>67</td>
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</tbody>
</table>

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**Table Notes:** Positive values are inversion. Positive values are adduction. Positive values are plantar flexion.

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**Abbreviations:** Met1, first metatarsal; Met2, second metatarsal; Met3, third metatarsal; Met4, fourth metatarsal; Met5, fifth metatarsal.
neuropathy but did not have CN. Both volunteer A (642 mg/cm²) and volunteer B (735 mg/cm²) had substantially lower vBMD than even their CN counterparts. For S_{null}, volunteer A had a higher than average value (36.8 mg/mm compared to roughly 32 mg/mm for control volunteers and CN involved feet), whereas volunteer B had one of the lowest baseline values (18.1 mg-mm) in the entire CN cohort. Both volunteers had lower values than those of the CN group average for t_{avg}, though values similar to those of the control group.\(^{16}\) Upon completion of the larger prospective study, we will compare the changes observed in these 2 volunteers to changes in study volunteers who did not sustain a foot fracture.

While vBMD and geometric strength indices did not decrease preceding fracture, as might be expected, applied load began high and rose further in the lateral midfoot in both women. Peak plantar pressure at baseline was 203 and 355 kPa for the 2 women, which far exceeds the upper limit of the 99% confidence interval (120 kPa) for control subjects from a previous analysis.\(^{16}\) Increased plantar loading is frequently observed in individuals with diabetes and peripheral neuropathy as a result of loss of protective sensation, impaired proprioception, and inadequate muscle strength (particularly the foot intrinsics). Limitations of this study include the lack of serial measurements of sensory capacity and foot muscle strength. Loss of muscle strength may be especially relevant following the prolonged offloading period in TCCs. A loss of muscle strength during TCC offloading may contribute to altered bone-to-bone orientation angles and plantar loading.

A possible explanation for the observed results is that the increased values of vBMD and geometric strength indices—especially in volunteer A—reflect a response to increased loading, or even a hypertrophic response to bone injury. Of course, causality cannot be determined from the concomitant increases in plantar loading and indices of bone strength, nor can the likely role of weak bones\(^{20}\) on neuropathic fracture be refuted by these data. Rather, we report only that the increases observed in vBMD and geometric strength indices do not support the hypothesis that CN-related reductions in bone strength indices are a necessary precursor to metatarsal fracture. Furthermore, the findings reported here suggest that altered bone-to-bone orientation angles may help explain the link between acute CN and increased biomechanical loading. Increased plantar flexion and adduction of the metatarsals, particularly the lateral metatarsals, are consistent with the progression of a varus hindfoot with metatarsus adductus deformity. Hindfoot varus\(^{32}\) and metatarsus adductus\(^{32-41}\) have been previously implicated in lateral metatarsal fractures.

One variable that may increase fracture risk is the patient’s activity level. We cannot rule out the role of load-bearing volume in the observed fractures, though neither volunteer reported an increase in walking or other load-bearing activity preceding incipient fracture. Future studies may utilize activity monitoring to help assess the role of activity in neuropathic fracture. Additionally, we recognize that our measures of barefoot plantar loading present an incomplete description of biomechanical loads that may influence fracture. It would be most physiologically relevant to use plantar pressure data in conjunction with motion-capture data and QCT-derived measures of bone strength to compute bending stresses applied to the metatarsals throughout a range of weight-bearing activities. Nonetheless, we consider peak pressure and maximum force to be adequate proxy measures of biomechanical loading within the metatarsals.

**CONCLUSION**

We assessed 2 individuals with CN before and after mid-diaphyseal fracture of Met5, using plantar pressure measurement and novel QCT techniques to quantify bone strength and 3-D bone-to-bone orientation angles. Many of the techniques used in these case reports are currently limited to research applications, but our results are nonetheless relevant to physical therapy clinical practice. Clinicians are advised to consider individuals with diabetes, peripheral neuropathy, and especially those with CN as at risk for pedal fracture. Those treating individuals with CN are advised to monitor plantar loading if possible (recommended for any patients with diabetic neuropathy at risk of ulceration), as our results suggest that abnormal plantar loading may increase risk for metatarsal fracture as well as soft tissue injury. Plantar loads were high at enrollment and increased before incipient metatarsal fracture, which lends support to the possible causal role of biomechanical loading in metatarsal fractures. In these 2 individuals, vBMD and geometric strength indices increased mildly to moderately preceding fracture, which does not completely explain the possible link between weakening bone material properties and incident fractures. Finally, our results suggest that the progression of metatarsus adductus and equinovarus foot deformities that have been previously associated with lateral metatarsal fractures may lead to increased metatarsal loading.

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**REFERENCES**

3. Armstrong DG, Lavery LA, Bushman TR. Peak foot pressures influence the healing time of diabetic foot ulcers treated with total contact casts. J Re-


