Role and Determinants of Adherence to Off-loading in Diabetic Foot Ulcer Healing: A Prospective Investigation

Diabetes Care 2016;39:1371–1377 | DOI: 10.2337/dc15-2373

Ryan T. Crews,[1] Biing-Jiun Shen,[2] Laura Campbell,[3] Peter J. Lamont,[4] Andrew J.M. Boulton,[4] Mark Peyrot,[5] Robert S. Kirsner,[6] and Loretta Vileikyte[4]

CLIN CARE/EDUCATION/NUTRITION/PSYCHOSOCIAL

OBJECTIVE

Studies indicate that off-loading adherence is low in patients with diabetic foot ulcers (DFUs), which may subsequently delay healing. However, there is little empirical evidence for this relationship or the factors that influence adherence.

RESEARCH DESIGN AND METHODS

This prospective, multicenter, international study of 79 (46 from the U.K. and 33 the U.S.) persons with type 2 diabetes and plantar DFUs assessed the association between off-loading adherence and DFU healing over a 6-week period. Additionally, potential demographic, disease, and psychological determinants of adherence were examined. DFUs were off-loaded with a removable device (77% a removable cast walker). Off-loading adherence was assessed objectively by activity monitors. Patient-reported measures included Hospital Anxiety and Depression Scale (HADS), Neuropathy and Foot Ulcer Quality of Life (NeuroQoL) instrument, and Revised Illness Perception Questionnaire (IPQ-R).

RESULTS

Off-loading adherence was monitored for 35 ± 10 days, and devices were used during 59 ± 22% of subjects' activity. In multivariate analyses, smaller baseline DFU size, U.K. study site, and better off-loading adherence predicted smaller DFU size at 6 weeks ($P < 0.05$). Better off-loading adherence was, in turn, predicted by larger and more severe baseline DFUs, more severe neuropathy, and NeuroQoL foot pain ($P < 0.05$). In contrast, greater NeuroQoL postural instability predicted worse off-loading adherence ($P < 0.001$). HADS and IPQ-R measures were not significantly associated with off-loading adherence.

CONCLUSIONS

Off-loading adherence is associated with the amount of DFU healing that occurs, while postural instability is a powerful predictor of nonadherence. Clinicians should take this neuropathic symptom into consideration when selecting an off-loading device, as off-loading–induced postural instability may further contribute to nonadherence.

In 2010, approximately 73,000 nontraumatic lower-limb amputations were performed on people with diabetes in the U.S, accounting for more than 60% of all nontraumatic lower-limb amputations (1). Although this is a decrease in comparison with the peak of 87,000 amputations performed in 2001, it is predicted that

[1]Center for Lower Extremity Ambulatory Research at the Dr. William M. Scholl College of Podiatric Medicine, Rosalind Franklin University, Chicago, IL
[2]Division of Psychology, Nanyang Technological University, Singapore
[3]The Healing Foundation Centre, Faculty of Life Sciences, University of Manchester, Manchester, U.K.
[4]Department of Medicine, University of Manchester, Manchester, U.K.
[5]Loyola University, Baltimore, MD
[6]Department of Dermatology and Cutaneous Surgery, University of Miami, Miami, FL
Corresponding author: Ryan T. Crews, ryan.crews@rosalindfranklin.edu.

Received 2 November 2015 and accepted 9 May 2016.
This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc15-2373/-/DC1.

amputation rates could be further reduced by 45–85% through comprehensive foot care programs that include treatment of diabetic foot complications (2). The primary foot problem to precede amputation is the occurrence of a diabetic foot ulcer (DFU) (3). A DFU is partly a consequence of the physical stress imparted on the foot during weight-bearing activity (4), and pressure relief under the weight-bearing areas, or "off-loading," is key to healing plantar DFUs (4).

Off-loading devices reduce pressure at the site of a wound by redistributing loading forces across the plantar surface of the foot and in some cases the leg as well, thereby preventing isolated pockets of excessive force at DFU sites. As indicated by a recent systematic review, nonremovable, pressure-relieving casts are the most effective for healing plantar DFU (5). While a total contact cast (TCC) is generally considered the gold standard in DFU off-loading (6), a removable cast walker (RCW) is far more commonly used (6,7). Wu et al. (6) have shown that only 1.7% of U.S. foot clinics use the TCC as the standard for DFU off-loading. Among the reasons for the practitioner's limited use of the TCC are the skill and time required to apply these and the prohibition of wound dressings or negative pressure therapies that require routine access to the wound (8). Although RCW off-loading capacity has been shown to be as good if not better than TCC (9,10), its use is associated with poorer outcomes (10,11). It is generally believed that the discrepancy in outcomes is due to poor adherence to RCWs. The intended irremovable cast design of a TCC ensures continuous adherence, whereas a RCW by definition allows patients to determine their level of adherence. As demonstrated by a randomized controlled study, wrapping RCWs with casting tape in order to make an "instant TCC" resulted in healing results equivalent to those obtained with a traditional TCC (12).

Although clinical opinion speaks to the importance of adherence to off-loading in DFU healing, research conducted to date either examined the role of off-loading adherence in DFU prevention (13) or, when assessing off-loading in DFU healing, focused on total adherence, as assumed with TCC rather than varying levels of adherence, as determined by patients using removable devices (11,12). The only study that examined adherence to RCW in patients with active DFU found it to be low (14); however, no attempt was made to link off-loading adherence to DFU healing in this report. Thus, although previous studies have indicated that off-loading adherence is low and likely results in delayed healing, no empirical evidence to date has demonstrated an association between varying levels of off-loading adherence and DFU healing. The main objective of this investigation was, therefore, using a validated adherence monitoring method (15), to assess the association between off-loading adherence and the amount of DFU healing that occurs during a 6-week treatment period. It was hypothesized that higher levels of off-loading adherence would be associated with smaller end-of-study DFU size.

The second set of hypotheses examined in this investigation pertained to the potential physical and psychological determinants of off-loading adherence. The loss of protective pain sensation due to diabetic neuropathy (DN) may not only be a major risk factor in the development of foot ulcers (16) but also contribute to DFU chronicity, as the lack of pain in patients with active DFUs could contribute to a lack of motivation to adhere to prescribed DFU off-loading devices. Postural instability—another clinical manifestation of DN—is a common disorder, with 23% of DN patients reporting balance problems as present either most of the time or all the time (17). DN is a severely debilitating condition, compromising patients' mobility and functioning (18), and may too negatively impact off-loading adherence by further compromising the mobility of those with neuropathic postural instability.

With regard to psychological determinants of off-loading adherence, DFU patients exhibit high levels of ulcer-specific emotional distress (19,20), which combine with patient beliefs about DFU in guiding adherence to preventive foot self-care (21). Furthermore, depression, a well-established determinant of nonadherence to diabetes self-care behaviors (22), was found to predict incident first DFU (23). Several studies have indicated that depressive symptoms are associated with delayed DFU healing (24,25), although adherence to off-loading was not assessed in these reports. Taken together, we therefore hypothesized that physical (DN and its clinical manifestations) and psychological (patient cognitive and emotional responses to foot ulceration and depression) factors would shape off-loading adherence.

RESEARCH DESIGN AND METHODS

Subjects

Data from 79 patients participating in a prospective, multicenter, international study that examined the role of psychological stress in DFU healing were used. The current report focuses on the behavioral arm of this multifaceted investigation and examines the role and determinants of adherence to off-loading and DFU healing. Eligible patients were recruited from four outpatient clinics in the U.K. (N = 46) and three in the U.S. (N = 33). Permission to conduct this study was granted by institutional review boards at all participating sites. The inclusion criteria comprised type 2 diabetes, 18–80 years of age, and presence of a DFU (defined as a full skin thickness breakdown) at a pressure-bearing area of the foot requiring off-loading. DFUs were required to be classified as 1A up to 2D according to the University of Texas (UT) classification system (16), i.e., neuropathic or neuroischemic DFU without osteomyelitis and severe ischemia (ankle brachial pressure index [ABPI] $\geq$0.5 and at least one palpable pulse per foot). Exclusion criteria consisted of pregnancy or premenopausal status (females), chronic renal impairment (creatinine of $>$250 μmol/L and/or serum albumin of $<$30 mmol/L), autoimmune diseases affecting the adrenal gland (e.g., Cushing disease), present use of anti-inflammatory therapy (e.g., steroids), history of major amputation (any lower-limb amputation proximal to the midfoot), and active tobacco use (as measured by the piCO smokerlyzer [26], Bedfont Scientific Ltd., Harrietsham, U.K.).

Procedures

After obtainment of informed consent, baseline blood tests were taken. After 15 min of relaxation, patients completed the psychological measures. This was followed by DFU treatment using a standardized foot ulcer management protocol that included regular, sharp surgical wound debridement, dressings, and off-loading of ulcers on weight-bearing areas. Locally infected ulcers were treated as per standard protocols (27). The default off-loading modality was an RCW; however, study podiatrists were allowed to use other removable modalities if they deemed it necessary (Table 1).

Assessment of Adherence to Off-loading

Upon enrollment into the study all subjects were provided with an off-loading device for their DFU, with the majority of subjects receiving an RCW (61 of 79 subjects). They were instructed to wear the off-loading device during all weight-bearing activity. Adherence to off-loading was assessed using a validated dual activity monitor method (15). Specifically, a concealed activity monitor (Lifecorder Plus, Suzuken) was attached to the off-loading device, and subjects were instructed to wear a second activity monitor at the hip. Activity data were uploaded by a study podiatrist to a centralized server via internet at the end of the study. After uploading, the time-stamped hip activity data were coded for compliancy using the time-synchronized off-loading device activity data. The activity for each 2-min epoch was coded as adherent if the recorded off-loading device activity was greater than one-half of the recorded hip activity. Subjects returned to the clinic weekly for DFU assessment and treatment by a study podiatrist. Adherence to off-loading and DFU healing were monitored for 6 weeks or until DFU healing if it occurred before the final study visit. A healed DFU was defined as complete epithelialization without drainage, as determined by a study podiatrist.

Assessment of DFU Healing

Digital DFU photographs with scale bars were taken at each study visit. Wound size was determined from digital photographs to measure planimetric wound area using Image Pro Plus software (Media Cybernetics, Rockville, MD). The outcome measure was DFU area at 6 weeks (controlling for the initial wound size).

Other demographic and disease variables assessed at baseline were study site (U.K./U.S.), age, sex, wound severity (UT classification system), neuropathy severity as measured by the Neuropathy Disability Score (NDS) (28), the ABPI, glycated hemoglobin (HbA_{1c}), hemoglobin, creatinine, and albumin.

Table 1—Baseline characteristics of study participants

	N (%)	Minimum	Maximum	Mean	SD
Study site	U.K. 46 (58%), U.S. 33 (42%)				
Age (years)	79	35	79	56.5	9.6
Sex	Male 66 (84%), female 13 (16%)				
Ethnicity	White 39 (49%), black 13 (17%), Asian 6 (8%)				
Diabetes duration (years)	79	0.2	35.0	14.1	8.2
HbA_{1c}, % (mmol/L)	79	4.4 (25)	15.3 (144)	8.9 (74)	2.2 (24)
Hemoglobin (g/dL)	79	8.0	17.3	12.6	1.8
Creatinine (μmol/L)	79	54.0	236	112	44.3
Albumin (g/L)	78	27.0	48.0	40.4	4.4
ABPI	67	0.72	1.88	1.20	0.27
NDS	79	3.0	10.0	7.4	2.2
UT wound classification	1A, 57 (72%); 1B, 9 (11%); 2A, 12 (15%); 2B, 1 (1%)				
Baseline wound size (mm^2)	79	10	1,724	230	288
End-of-study wound size (mm^2)	79	0.00	929	106	155
Off-loading modality	RCW 61 (77%), sandal 13 (16.5%), other 5 (16.5%)				
Monitoring period for off-loading adherence (days)	79	6	50	35	10
Average duration of physical activity per day (h)	79	0.4	17.1	6.7	3.8
Proportion of activity for which off-loading device worn	79	0.00	0.95	0.59	0.22
HADS: depression	79	0.0	21.0	6.0	4.4
NeuroQoL: foot pain	76	1.0	4.7	2.2	0.86
NeuroQoL: loss of feeling	77	1.0	5.0	3.1	1.3
NeuroQoL: postural instability	78	1.0	5.0	2.5	1.3
NeuroQoL: ADL limitations	63	1.0	5.0	3.1	1.3
NeuroQoL: interpersonal/emotional burden	72	1.0	5.0	3.1	1.3
IPQ-R: consequences	77	1.7	5.0	3.7	0.7
IPQ-R: personal control	78	2.0	5.0	3.9	0.59
IPQ-R: treatment control	77	2.2	5.0	4.0	0.6
IPQ-R: coherence	77	1.0	4.4	2.6	0.9
IPQ-R: timeline	75	1.3	5.0	3.1	1.0
IPQ-R: emotions	74	1.0	5.0	3.3	1.0

ADL, activities of daily living.

Self-report Psychological Measures

1. Neuropathy and DFU-related impact on patient physical and psychosocial functioning was evaluated with the Neuropathy and Foot Ulcer Quality of Life (NeuroQoL) scale (19). Three scales assessed the frequency of neuropathic symptoms: a) pain and/or paresthesia (Cronbach α = 0.84), b) symptoms of reduced feeling in the feet (α = 0.83), and c) postural instability (α = 0.96). Restrictions in activities of daily living were examined with a three-item scale asking, "In the past 4 weeks how often have your foot problems interfered with your ability to perform your paid work, tasks around the house, and to take part in leisure activities?" (α = 0.75). An 11-item interpersonal-emotional burden scale asked respondents to rate how much they agree/disagree with statements such as, "people treat them differently from other people; they feel frustrated/embarrassed; they feel more emotionally and physically dependent on their loved ones as a result of their foot problems" (α = 0.93). Responses were rated on a 5-point scale (1 = never; 5 = all the time), with higher scores indicating more impairment.
2. Patient cognitive and emotional responses to foot ulceration were examined using the Revised Illness Perception Questionnaire (IPQ-R) (29). This instrument was adapted to DFU by replacing the generic "illness" with a foot ulcer, referring to it as "an open sore on my foot." The participants were asked to indicate on a 5-point Likert response scale how much they agreed or disagreed with a series of statements (scale ranging from 1 = strongly disagree to 5 = strongly agree). Five cognitive scales evaluated the following: a) beliefs regarding the expected effects of ulceration (consequences, α = 0.64), b) perceived chronicity of ulceration (timeline) (α = 0.81), c) expectations regarding one's personal ability to manage the ulcer (personal control) (α = 0.48), d) beliefs regarding the effectiveness of treatment to manage the ulcer (treatment control) (α = 0.65), and e) perceived understanding of ulceration (coherence) (α = 0.80). Emotional response scale assessed the emotional impact of ulceration (α = 0.84).
3. Depressive symptoms were assessed with a 7-item subscale from the Hospital Anxiety and Depression Scale (HADS), measuring the absence of both positive affect and pleasure from everyday tasks (30). Items are scored so that a higher score indicates greater severity of symptoms. Sample items for example, include, "I feel as if I am slowed down" or "I can laugh and see the funny side of things": nearly all the time = 3, very often = 2, sometimes = 1, or not at all = 0 (Cronbach α = 0.83). A systematic review identified a cutoff score of 8 of 21 as indicative of anxiety or depression (31).

Statistical Analysis

Subjects (n = 79) were included in the analyses reported here if they had valid data for baseline and 6-week DFU wound size, as well as for off-loading adherence. For fulfillment of the normality assumption, DFU size was log (baseline) and square root (6-week) transformed (30).

All analyses used hierarchical stepwise multiple regression with mean substitution for missing values. For healing (prediction of wound size at final follow-up visit), baseline DFU size was forced into the model, along with site (U.K./U.S.) and off-loading adherence. All other measures were allowed to enter the model to determine whether there were any significant confounders that resulted in effect modification. For off-loading adherence, baseline neuropathy severity (NDS), DFU severity (UT classification), and wound size were forced into the model; then, variables were allowed to enter the model in two sequential blocks: *1*) demographic factors (age, sex, country) and *2*) patient-reported factors (NeuroQoL, IPQ-R, and HADS).

Statistical analyses were conducted using SPSS statistical software V.21 (IBM, Chicago, IL). A P value of 0.05 (two-tailed) was chosen as the criterion for statistical significance.

RESULTS

Between January 2008 and December 2012, 118 subjects were enrolled into the broader parent study that examined the role of psychological stress in DFU healing. However, 31 of those subjects were lacking adherence data. Both device failure and failure by personnel to appropriately upload data contributed to missing adherence data. Patient characteristics for the 79 subjects with adherence data are presented in Table 1. The 31 subjects lacking adherence data did not differ from those included in the study in terms of baseline wound size, wound severity (UT Classification), HbA_{1c}, albumin, ABPI, duration of diabetes, or sex. They were, however, significantly older (61 $\pm$ 11 vs. 57 $\pm$ 10 years, $P < 0.05$). Subjects were predominantly white men in their mid-50s, with poor glycemic control; however, hemoglobin, creatinine, and albumin were within the normal range. Study participants had severe neuropathy and no evidence of peripheral arterial disease. They presented with predominantly superficial, noninfected ulcers as defined by the UT wound classification system.

With respect to ulcer-specific cognitive and emotional scores (IPQ-R and NeuroQoL), study participants were moderately distressed as a result of having DFUs, held rather high perceived DFU controllability beliefs, both personal and professional, and reported potentially serious DFU consequences. They were, however, somewhat uncertain with respect to the nature and chronicity of DFUs. The mean HADS depression score was below the range of clinically significant depression.

At 6-week follow-up, there was a substantial reduction in DFU size (from 230 $\pm$ 288 mm^2 to 106 $\pm$ 155 mm^2, $P < 0.001$) and 19 (24%) subjects achieved complete wound closure. The average duration of adherence monitoring was 35 $\pm$ 10 days. The mean is less than the study design of 42 days for two reasons. Patients whose wound healed prior to 6 weeks of monitoring had their final follow-up visit conducted at the clinic visit in which their wound was determined to be healed, and off-loading adherence was discontinued at that time. In addition, there was either hardware or user errors in the collection of adherence for some subjects (N = 27) that resulted in a reduced adherence-monitoring period (mean 24 $\pm$ 11 days). Subjects were actively moving 6.7 $\pm$ 3.8 h per day and adherently wore their off-loading device during 59 $\pm$ 22% of this physical activity.

In multivariate analyses, smaller baseline DFU size, U.K. site, and better off-loading adherence significantly predicted smaller DFU size at 6 weeks (Table 2). No other measures met the criterion to enter the regression model.

Table 2—Final multivariate regression model predicting wound size at final follow-up visit

	Unstandardized coefficients		Standardized coefficients: β	Significance
	β	SE		
Constant	−11.92	2.38		0.000
Baseline wound size	4.42	0.47	0.72	0.000
Site (U.S.)	2.93	1.01	0.22	0.005
Proportion of activity for which off-loading device worn	−4.89	2.31	−0.16	0.038

Healing outcome scored such that smaller values correspond to a decrease in wound size, so that a negative association represents a decrease in wound size.

A multivariate model examining determinants of off-loading adherence (Table 3) found that larger and more severe (UT classification) baseline DFUs, more severe neuropathy, and greater NeuroQoL foot pain significantly predicted better off-loading adherence ($P < 0.05$), while more severe NeuroQoL postural instability significantly predicted worse off-loading adherence ($P < 0.05$). Other measures were not significantly associated with off-loading adherence.

CONCLUSIONS

The results of this prospective study provide evidence for a relationship between objectively measured varying levels of off-loading adherence and the amount of DFU healing that occurred during a 6-week period. To date, this work represents the largest sample size in a series of studies investigating the association of DFU healing with off-loading adherence and is the first to explore determinants of off-loading adherence in patients with active DFU. We demonstrated that better off-loading adherence predicted a greater amount of DFU healing at 6-week follow-up and identified neuropathic postural instability as the key barrier to off-loading adherence in active DFU patients.

Even though this was the first study to objectively report on the association between off-loading adherence and DFU healing, several studies have shown that the efficacy of footwear for preventing DFUs is dependent on patient adherence level (13,32). In investigating the potential of a plantar pressure–optimized custom orthosis to prevent recurrent DFUs, Bus et al. (32) found via objective adherence monitoring that a reduction in incidence of recurrence was only evident when focusing on patients who wore their devices for ≥80% of steps taken per day.

The results of our study supported the hypothesized role of DN-related symptoms as determinants of adherence to off-loading. Specifically, NeuroQoL-assessed postural instability emerged as a symptom strongly associated with poorer off-loading adherence. Goodworth et al. (33) noted that even in healthy populations, standing balance, functional reach, and gait all suffer detriments when a walking boot is worn. Considering the neuropathy-related changes that accompany diabetes, it is likely that the biomechanical challenges observed by Goodworth et al. are even greater in DFU patients treated with off-loading devices.

Unfortunately, balance deficits may be overlooked by clinicians, as patients often do not report balance concerns during medical consultations because of the perception that these are an indicator of diminishing self-resources—a sign of premature aging rather than illness-related disability (19). In view of these findings, clinicians should actively inquire about postural instability in patients presenting with active DFU and take neuropathic unsteadiness into consideration when choosing an off-loading device. Moreover, off-loading devices used for DFU healing are generally much heavier than the shoes designed to prevent ulcers. A recent study found that reducing the height of an RCW can reduce the weight while still providing similar off-loading capacity (34). In addition to the sheer weight of off-loading devices, their design features such as rocker bottom soles and forced fixation of the ankle joint substantially alter the gait and stability of DFU patients (35). While at present there appears to be a tradeoff between off-loading capacity and degraded balance concerning off-loading device design, future designs should try to optimize off-loading while limiting the impairment of balance.

The other predictors of off-loading adherence were physical (more severe neuropathy, larger and more severe DFU) and more severe perceived foot pain. Patients with these characteristics adhered more consistently with off-loading, presumably because they were more motivated by the greater diagnosed and experienced severity of their medical condition. Clinicians should be mindful of the tendency of patients with less severe wounds to be less adherent with their off-loading regimens. Based upon the results of this study, the reduced adherence will limit healing. Delayed healing in turn will result in greater opportunity for infections or other complications to develop.

Somewhat unexpectedly, there were no significant associations of adherence to off-loading with ulcer-specific beliefs and emotional responses, as measured by IPQ-R. This challenges the relevance of recent findings by Vedhara et al. (36) regarding the importance of DFU-specific beliefs in predicting foot self-care in those with active foot ulcers. While the foot self-care behaviors included in their report (checking of feet, inspecting inside of shoes, washing feet, soaking feet and drying between toes) may well be helpful in DFU prevention, they have little benefit in those with active DFU, where adherence to off-loading rather than preventive foot care is

Table 3—Final multivariate regression model for predicting off-loading adherence

	Unstandardized coefficients		Standardized coefficients: β	Significance
	β	SE		
NDS	0.024	0.011	0.247	0.025
UT wound classification	0.062	0.030	0.225	0.038
Baseline wound size	0.063	0.021	0.311	0.003
NeuroQoL: postural instability	−0.060	0.018	−0.365	0.001
NeuroQoL: foot pain	0.068	0.031	0.259	0.029

central to the healing of foot ulcers. Perhaps beliefs that are more closely focused on RCW, such as expected efficacy of RCW or convenience of RCW, might be more powerful predictors than patient perceptions of their DFU. A patient's decision to use diabetic footwear for prevention of secondary DFU has previously been shown to be based on the perceived value of the footwear and not on the patient's previous history of foot complications (37,38).

The apparent lack of a significant association between depression and adherence to off-loading, while counterintuitive, is not unique to the study of depression and foot self-care. This finding is consistent with the meta-analytic review of the studies that examined the relationship between depression and a variety of diabetes self-care behaviors (22). The effect of depression on self-care varied across different types of self-care behaviors in this meta-analysis, with the strongest effect size found for missed medical appointments and the smallest effect size found for foot self-care, which was nonsignificant. Studies that have found an association between depression and foot self-care adherence might have had some uncontrolled confounding. Unsteadiness may increase depression (17,39), and, as suggested by this study, unsteadiness decreases off-loading adherence, thereby resulting in a spurious relationship between adherence and depression.

The continuous objective monitoring of adherence for the full duration of the study's protocol was a major advantage of this investigation in contrast to self-reports of adherence. However, the methodology for determining adherence to off-loading used in this study does have some limitations. Ensuring subjects wore the hip monitors during all waking hours was not possible with the activity monitors used. As adherence calculations were based entirely on when the hip monitor recorded activity, any activity that occurred when the hip monitor was not worn could not be coded for adherence. Future studies would benefit from use of a primary monitor that could accurately record when the monitor was worn by relying on identification of respiration or other means such as thermal (32) or skin conductance monitoring that were not commonly available at the initiation of this investigation. Another limitation of our study was that the activity monitors only recorded data on ambulatory activity; no information was available regarding periods of standing. Recent research has shown the amount of time spent standing daily is approximately twice that of ambulation in persons at high risk of DFU (40). Thus off-loading adherence during standing may significantly impact wound healing.

In conclusion, there is an independent relationship between the level of adherence to off-loading devices and the amount of DFU healing that occurs. Neuropathic postural instability was found to be the strongest barrier to off-loading adherence. Future studies aiming to improve adherence to off-loading should consider ways to improve patient education regarding the importance of adherence as well as seek to better understand the relationship between patients' balance and off-loading adherence.

Funding. The project was supported by National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases grant R01-DK-071066.

Duality of Interest. R.T.C. serves as a consultant to Ossur Americas, a manufacturer of off-loading devices. No other potential conflicts of interest relevant to this article were reported.

R.T.C. had no contact with Ossur Americas in regard to the conduct of this study.

Author Contributions. R.T.C. researched and conducted off-loading adherence analyses and wrote the manuscript. B.-J.S. and M.P. conducted statistical data analysis and reviewed the manuscript. L.C. conducted wound healing data analysis. P.J.L. collected clinical/adherence data. A.J.M.B. reviewed the manuscript. R.S.K. researched data and reviewed and edited the manuscript. L.V. researched clinical/psychology data, conducted data analyses, and wrote the manuscript. R.T.C. and L.V. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Prior Presentation. Parts of this study were presented in abstract form at the 71st Scientific Sessions of the American Diabetes Association, San Diego, CA, 24–28 June 2011.

References

1. Centers for Disease Control and Prevention. *National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States*. Atlanta, GA, Centers for Disease Control and Prevention, 2014
2. Centers for Disease Control and Prevention. Fast facts on diabetes: national diabetes fact sheet, 2011 [Internet], 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. Available from http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed 15 September 2015
3. Boulton AJ, Vileikyte L. The diabetic foot: the scope of the problem. J Fam Pract 2000;49 (Suppl.):S3–S8
4. Brand PW. The diabetic foot. In *Diabetes Mellitus, Theory and Practice*. 3rd ed. Ellenberg M, Rifkin H, Eds. New York, Medical Examination Publishing, 1983, p. 803–828
5. Lewis J, Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. Cochrane Database Syst Rev 2013;1:CD002302
6. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? Diabetes Care 2008;31:2118–2119
7. Raspovic A, Landorf KB. A survey of offloading practices for diabetes-related plantar neuropathic foot ulcers. J Foot Ankle Res 2014;7:35
8. Wu SC, Crews RT, Armstrong DG. The pivotal role of offloading in the management of neuropathic foot ulceration. Curr Diab Rep 2005;5:423–429
9. Lavery LA, Vela SA, Lavery DC, Quebedeaux TL. Reducing dynamic foot pressures in high-risk diabetic subjects with foot ulcerations. A comparison of treatments. Diabetes Care 1996;19: 818–821
10. Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. Clin Biomech (Bristol, Avon) 2011;26(6):649–654
11. Armstrong DG, Nguyen HC, Lavery LA, van Schie CH, Boulton AJ, Harkless LB. Off-loading the diabetic foot wound: a randomized clinical trial. Diabetes Care 2001;24:1019–1022
12. Katz IA, Harlan A, Miranda-Palma B, et al. A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers. Diabetes Care 2005;28:555–559
13. Waaijman R, de Haart M, Arts ML, et al. Risk factors for plantar foot ulcer recurrence in neuropathic diabetic patients. Diabetes Care 2014; 37:1697–1705
14. Armstrong DG, Lavery LA, Kimbriel HR, Nixon BP, Boulton AJ. Activity patterns of patients with diabetic foot ulceration: patients with active ulceration may not adhere to a standard pressure off-loading regimen. Diabetes Care 2003;26:2595–2597
15. Crews RT, Armstrong DG, Boulton AJ. A method for assessing off-loading compliance. J Am Podiatr Med Assoc 2009;99:100–103
16. Boulton AJ, Kirsner RS, Vileikyte L. Clinical practice. Neuropathic diabetic foot ulcers. N Engl J Med 2004;351:48–55
17. Vileikyte L, Leventhal H, Gonzalez JS, et al. Diabetic peripheral neuropathy and depressive symptoms: the association revisited. Diabetes Care 2005;28:2378–2383
18. Vileikyte L, Gonzalez JS. Recognition and management of psychosocial issues in diabetic neuropathy. Handb Clin Neurol 2014;126:195–209
19. Vileikyte L, Peyrot M, Bundy C, et al. The development and validation of a neuropathy-and foot ulcer-specific quality of life instrument. Diabetes Care 2003;26:2549–2555

20. Vileikyte L, Gonzalez JS, Leventhal H, et al. Patient Interpretation of Neuropathy (PIN) questionnaire: an instrument for assessment of cognitive and emotional factors associated with foot self-care. Diabetes Care 2006;29: 2617–2624
21. Vileikyte L. Psychosocial and behavioral aspects of diabetic foot lesions. Curr Diab Rep 2008;8:119–125
22. Gonzalez JS, Peyrot M, McCarl LA, et al. Depression and diabetes treatment nonadherence: a meta-analysis. Diabetes Care 2008;31: 2398–2403
23. Gonzalez JS, Vileikyte L, Ulbrecht JS, et al. Depression predicts first but not recurrent diabetic foot ulcers. Diabetologia 2010;53:2241–2248
24. Monami M, Longo R, Desideri CM, Masotti G, Marchionni N, Mannucci E. The diabetic person beyond a foot ulcer: healing, recurrence, and depressive symptoms. J Am Podiatr Med Assoc 2008;98:130–136
25. Vedhara K, Miles JN, Wetherell MA, et al. Coping style and depression influence the healing of diabetic foot ulcers: observational and mechanistic evidence. Diabetologia 2010;53: 1590–1598
26. Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vesey C, Saloojee Y. Comparison of tests used to distinguish smokers from nonsmokers. Am J Public Health 1987;77:1435–1438
27. Brownrigg JR, Apelqvist J, Bakker K, Schaper NC, Hinchliffe RJ. Evidence-based management of PAD & the diabetic foot. Eur J Vasc Endovasc Surg 2013;45:673–681
28. Young MJ, Boulton AJ, MacLeod AF, Williams DR, Sonksen PH. A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. Diabetologia 1993;36:150–154
29. Moss-Morris R, Weinman J, Petrie KJ, Horne R, Cameron LD, Buick D. The Revised Illness Perception Questionnaire (IPQ-R). Psychol Health 2002;17:1–16
30. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–370
31. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002;52:69–77
32. Bus SA, Waaijman R, Arts M, et al. Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. Diabetes Care 2013;36:4109–4116
33. Goodworth AD, Kunsman M, DePietro V, LaPenta G, Miles K, Murphy J. Characterization of how a walking boot affects balance. J Prosthet Orthot 2014;26:6
34. Crews RT, Sayeed F, Najafi B. Impact of strut height on offloading capacity of removable cast walkers. Clin Biomech (Bristol, Avon) 2012;27: 725–730
35. van Deursen R. Footwear for the neuropathic patient: offloading and stability. Diabetes Metab Res Rev 2008;24(Suppl. 1):S96–S100
36. Vedhara K, Dawe K, Wetherell MA, et al. Illness beliefs predict self-care behaviours in patients with diabetic foot ulcers: a prospective study. Diabetes Res Clin Pract 2014;106:67–72
37. Macfarlane DJ, Jensen JL. Factors in diabetic footwear compliance. J Am Podiatr Med Assoc 2003;93:485–491
38. Arts ML, de Haart M, Bus SA, Bakker JP, Hacking HG, Nollet F. Perceived usability and use of custom-made footwear in diabetic patients at high risk for foot ulceration. J Rehabil Med 2014;46:357–362
39. Vileikyte L, Peyrot M, Gonzalez JS, et al. Predictors of depressive symptoms in persons with diabetic peripheral neuropathy: a longitudinal study. Diabetologia 2009;52:1265–1273
40. Najafi B, Crews RT, Wrobel JS. Importance of time spent standing for those at risk of diabetic foot ulceration. Diabetes Care 2010;33: 2448–2450