Assessing Health-Related Quality of Life in Patients With Diabetic Foot Disease: Why Is It Important and How Can We Improve? The 2017 Roger E. Pecoraro Award Lecture

Dane K. Wukich and Katherine M. Raspovic

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Patient-reported outcomes (PROs) have become an important subject in the area of diabetes-related foot complications. Self-reported health-related quality of life (HRQOL) surveys can provide a generic measure of overall health (global) and can be disease specific (i.e., diabetes) or even region specific (i.e., lower-extremity function). Analysis of PRO measures utilizing validated instruments allows health care providers to determine whether medical and surgical treatments are providing patients with the highest level of outcome possible and are actually improving HRQOL. The 36-item Short Form (SF-36), EuroQol five-dimension questionnaire (EQ-5D-5L), and Foot and Ankle Ability Measure (FAAM) are examples of commonly used HRQOL surveys. Low HRQOL has been associated with higher rates of hospital admission and mortality in patients with diabetes. Previous studies have demonstrated that patients with diabetes-related foot disease have low self-reported physical quality of life but do not typically report low mental quality of life. The impact of mental quality of life may be underestimated in these patients using the SF-36. In this article, we will discuss several widely used outcome instruments used to measure patient HRQOL and the impact of diabetic foot disease on HRQOL. As health care providers, we must continue to adjust and modify our treatments to achieve the best patient outcomes and associated high quality of life. Assessing PROs will become increasingly important as health care systems transition from a volume-based reimbursement model to a value-based model.

Patient-reported outcomes (PROs) have become an important subject in the area of diabetes-related foot complications. One method of assessing outcomes is the through the use of self-reported health-related quality of life (HRQOL) surveys. These instruments provide a generic measure of overall health (global) and can be disease specific (i.e., diabetes) or even region specific (i.e., lower-extremity function). To date, no metric has demonstrated superiority in assessing the impact of diabetes-related foot complications on HRQOL. Each of these measures have different items of interest, scales, and psychometric properties. A recent systematic review identified 20 different diabetes-specific HRQOL instruments, and the authors indicated that combining generic with disease-specific measures may improve specificity (1,2). Analysis of PRO measures utilizing validated instruments allows health care providers to determine

Department of Orthopaedic Surgery, University of Texas Southwestern Medical Center, Dallas, TX

Corresponding authors: Dane K. Wukich, dane.wukich@utsouthwestern.edu, and Katherine M. Raspovic, katherine.raspovic@utsouthwestern.edu.

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whether medical and surgical treatments are providing patients with the highest level of outcome possible and are actually improving HRQOL.

HRQOL has been studied across a broad spectrum of populations and medical conditions such as cardiovascular disease, renal disease, neurological disorders, and diabetes. Diabetes has been shown independently to negatively impact HRQOL (3,4). Neuropathy and peripheral artery disease predispose vulnerable patients to developing diabetic foot disease (DFD), which may include diabetic foot ulcers (DFUs), Charcot neuroarthropathy (CN), and foot infections. In addition to the huge economic burden associated with the care of DFD, patients are at risk for substantial morbidity and mortality. The 5-year mortality rate among patients with newly diagnosed DFU is ~40%, and patients with DFUs are nearly 2.5 times more likely to die than patients with diabetes without DFUs (5). The risk of mortality in patients with CN has been shown to be unexpectedly high as well. Compared with the normal population, patients with CN or DFUs have a reduced life expectancy of 14 years (6). CN, DFU, infection, and ischemia often coexist in patients with DFD, increasing the risk of hospitalization and the need for amputation (7). Outcomes have been reported on a consecutive series of 102 patients who underwent transtibial amputation (7). At a mean follow-up of 109 weeks, contralateral foot problems developed in 34% of patients, and 10% of patients ultimately required a contralateral transtibial amputation. Of 102 patients, 30 (29.4%) died, and the odds of mortality in patients with end-stage renal disease (ESRD) was 3.8 times higher than that for patients without ESRD.

Studies focusing on the impact of DFD on HRQOL have shown a negative impact on patient HRQOL (8–18). Despite the high mortality rates, patients with established DFD fear major amputation more than death (19). In the following sections, we will discuss several widely used outcome instruments used to measure patient HRQOL, as well as the impact of DFD on HRQOL. Measuring PROs can provide valuable information on the effectiveness of a treatment or surgical intervention. Our improved understanding of how a patient's disease process negatively impacts their quality of life may help us to provide better care for these patients. A better understanding of self-reported HRQOL may also help us to identify gaps in patient knowledge and ultimately guide us in providing more impactful patient education that can ultimately help decrease the development of the devastating complications of diabetes.

HRQOL IN PATIENTS WITH DFD: HOW WE CAN MEASURE IT?

SF-36 and SF-12

The Medical Outcomes Study (MOS) 36-item Short Form (SF-36) and 12-item Short Form (SF-12) are the most commonly utilized instruments in assessing DFD and provide information on overall physical and mental quality of life. The SF-36 provides a physical component summary (PCS) score as well as a mental component summary (MCS) score, which are derived from eight different subscales, whereas the SF-12 reports only PCS and MCS scores without reporting the eight subscale scores. The PCS and MCS are standardized so that a score of 50 represents the normative score for the general population, and a higher score is indicative of better HRQOL (20). The SF-12 consists of 12 questions abstracted from the SF-36 and is therefore less of a burden for patients to complete compared with the SF-36. Excellent correlation has been found between PCS and MCS scores calculated from the SF-36 and SF-12 in patients with DFD (21). The SF-36 has shown good correlation with wound-specific outcome instruments, such as the Diabetic Foot Ulcer Scale and the Cardiff Wound Impact Schedule (CWIS) (22).

Five-Level EuroQol Version

The five-level EuroQol version (EQ-5D-5L) was introduced by the EuroQol Group in 2009 to improve the instrument's sensitivity and to reduce ceiling effects, as compared to the EQ-5D-3L (23). It consists of two components, a descriptive system and a visual analogue scale. The EQ-5D-5L has been shown to be equivalent to the SF-36 in assessing HRQOL in patients with diabetes (24) and has been used in several pivotal studies in patients with DFD (22,25).

Foot and Ankle Ability Measure

The Foot and Ankle Ability Measure (FAAM) is an example of a region-specific instrument that was designed to specifically evaluate self-reported lower-extremity function (26). The FAAM provides an activities of daily living (ADL) subscale score (21 questions) and a sports subscale score (8 questions). The ADL and sports subscales of the FAAM are strongly related to the SF-36 physical function subscale and PCS score. It is a validated measure of the physical function of patients across a broad spectrum of lower-extremity musculoskeletal pathologies. A higher score for each represents better function, and the FAAM has been found to responsive in assessing lower-extremity function in patients with DFD (27).

DFD-Specific Instruments

The Neuro-QoL (Quality of Life in Neurological Disorders) is a disease-specific instrument that has been validated for assessing the impact of peripheral neuropathy and foot ulceration and quality of life in patients with diabetes. When compared with the SF-12, the Neuro-QoL has been found to be superior in assessing the severity of neuropathic symptoms and in its impact on HRQOL (28). Similarly, the Diabetic Foot Ulcer Scale, based on 58 questions, is valid and reliable in assessing HRQOL in patients with foot ulcers (29).

THE IMPACT OF DFD ON HRQOL

DFD has been shown to negatively impact HRQOL in numerous studies. A systematic review by Hogg et al. (11) analyzed studies using PRO measures to assess HRQOL in patients with DFD. Fifty-three studies from 1995 to 2010 were reviewed. The SF-36 was most the commonly used generic instrument and was used in 27/53 (51%) of the studies. Three studies utilized the SF-12. Other generic (Sickness Impact Profile [30] and Nottingham Health Profile [31]) and disease-specific (American Orthopaedic Foot & Ankle Society Diabetic Foot Questionnaire [9], Diabetes-39 [D-39] [32], CWIS [33], and the Neuro-QoL [28]) instruments were used. This review demonstrated that multiple PRO measures can be successfully used to evaluate HRQOL in patients with DFD and that no one "gold standard" or ideal instrument exists. Although different PRO measures were used by the 53 studies in this systematic review, all reported reduced HRQOL in patients with DFD (11). Many studies of DFUs using the SF-36 have demonstrated low PCS scores but relatively high MCS scores. PCS scores ranging from 29.0 to 35.0 and MCS scores ranging from 44.8 to 48.6 have been reported (8,10,12,13,18) (Fig. 1). Similarly,

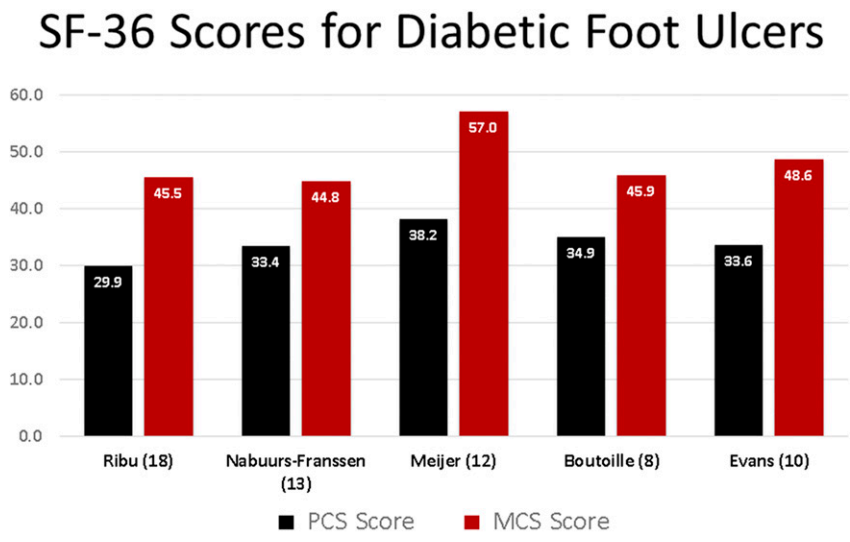

Figure 1—Comparison of the SF-36 PCS score and MCS score of previous studies of HRQOL and DFU.

in patients with CN, PCS scores range from 27.7 to 43.6 and MCS scores range from 43.4 to 48.1 (9,14,17,34,35) (Fig. 2).

A study compared a group of patients with diabetes with CN (N = 50) and a control group of patients with diabetes without foot complaints (N = 56) (17). These two groups were similar with regard to age and sex; however, the CN group had significantly more patients with type 1 diabetes and patients who were more likely to use insulin than the control group. Patients with CN had significantly lower PCS scores than the control group (33 vs. 46, $P < 0.001$); however, the MCS scores were not significantly different (48 vs. 49, P = 0.64). Lower-extremity function was assessed with the FAAM, and patients with CN reported ADL scores that were two standard deviations lower than the control group.

Raspovic et al. (15) examined the effect of ulcer presence on HRQOL in patients with CN. This study of midfoot CN compared 22 patients with ulcers to 35 patients without ulcers. The two groups were similar with regard to age, sex, duration of diabetes, and insulin use. SF-36 scores revealed no significant differences between the two groups. Patients with CN without an ulcer had a PCS score of 30.8 compared with 32.3 in patients with CN and an ulcer

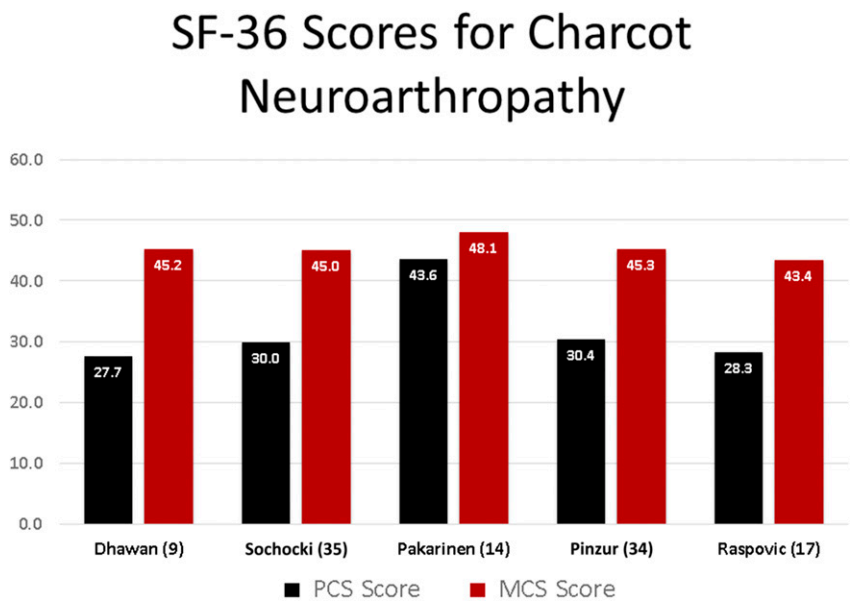

Figure 2—Comparison of the SF-36 PCS and MCS scores of previous studies of HRQOL and CN.

(P = 0.56). The MCS score was 48.4 in patients with CN without ulcer and 50.6 in patients with a concurrent ulcer (P = 0.52). Consistent with previous studies, PCS scores were low in both groups but MCS scores remained high. There was no significant difference in lower-extremity function between the two groups when measuring FAAM scores. This study concluded that the presence of a concurrent ulcer in midfoot CN does not appear to further negatively impact HRQOL when compared with midfoot CN without ulceration.

A recent study evaluated the impact of ESRD on HRQOL in patients with established DFD (36). The study group included 30 patients with ESRD on dialysis who had diabetes-related foot complications such as CN and DFU. A two-to-one match based on age and sex was utilized to select a control group of 60 patients with diabetes who had DFD (CN, DFU) but no ESRD. Patients with ESRD reported significantly reduced PCS scores (26.2 vs. 31.5, $P < 0.05$) but not MCS scores (49.7 vs. 49.2, P = 0.47) compared with patients not on dialysis. The results of the FAAM showed no significant difference in ADL (P = 0.14) and sports (P = 0.79) subscale scores between the two groups. Lower PCS scores were significantly associated with the ultimate need for amputation (P = 0.01). Although not statistically significant, lower PCS scores trended toward higher rates of mortality (P = 0.07). MCS scores had no significant association with mortality or amputation. A similar finding was observed in patients with diabetes on hemodialysis who did not have DFD. Hayashino et al. (37) measured HRQOL using the SF-36 and reported that low physical quality of life was predictive of mortality while mental quality of life was not.

Low HRQOL has been shown to predict amputation and mortality in patients with DFUs. Siersma et al. (25) prospectively studied 1,015 patients with new DFUs as a part of the European Study Group on Diabetes and the Lower Extremity (Eurodiale). The multicenter study included 14 centers in 10 different countries, and HRQOL was measured with the EQ-5D-5L. Reduced HRQOL as manifested by lower EQ-5D-5L scores was significantly associated with higher rates of mortality and major amputation. The physical domains of the EQ-5D-5L significantly associated with major amputation were mobility, usual activities, and self-care; the physical domains significantly associated

with mortality were pain/discomfort, usual activities, and self-care. Although HRQOL was independently associated with major amputation and mortality, HRQOL was not associated with ulcer healing (25).

Other studies have reported that healing of DFUs is associated with significantly higher mental quality of life compared with that of patients who did not heal. A prospective study of the role of hyperbaric oxygen treatment found that patients with healed DFUs had higher MCS scores, social function, and role limitation due to physical and emotional health than patients who did not heal (38). A more recent study by the Eurodiale group demonstrated that healing of DFUs was associated with improved HRQOL; however, nonhealing was not associated with a deterioration in HRQOL (39). Patients with unhealed DFUs report more physical limitations and higher pain than patients with minor amputations (8).

Unfortunately, a substantial number of patients with DFD ultimately require either minor or major amputations due to soft tissue and bone loss from infection and ischemia or to deformity that causes the lower extremity to no longer be biomechanically stable or functional. Measurement of HRQOL has been used to evaluate function and outcomes in patients after amputation. Evans et al. (40) reported that patients who underwent a minor amputation (preservation of the ankle) had a significantly higher 2-year survival rate (80%) compared with patients who underwent transtibial amputation (48%). They were unable to demonstrate any significant difference in the rate of ambulation between those who had a minor (64%) or major (64%) amputation. A recent study evaluated HRQOL in 41 patients with diabetes-related foot complications who underwent transtibial amputation (41). After a minimum of 1 year of follow-up, all eight subscales of the SF-36 significantly improved when compared with the preoperative SF-36 subscale scores ($P < 0.05$ for each of the eight subscales). The average PCS score improved from 26.2 preoperatively to 36.6 postoperatively ($P = 0.001$), and the average MCS score improved from 43.7 preoperatively to 56.1 postoperatively ($P = 0.001$). The FAAM results demonstrated a significant improvement in lower-extremity function after amputation, with ADL subscale scores increasing from 35.7% to 58.3% ($P = 0.001$) and sports subscale scores increasing from 3.1 to 12.5% ($P = 0.01$). The ability of the patient to ambulate after transtibial amputation was significantly associated with improvement in the postoperative PCS score ($P < 0.05$). Seventy-five percent of patients reported improvement in HRQOL, whereas 25% reported worsening. Other studies have indicated that major amputation, in selected patients, can result in improved patient outcomes (8,42). In other words, rather than continued efforts to salvage a foot that is biomechanically nonfunctional, patients may function better with a below-knee amputation and a well-fitting prosthesis. The ability to ambulate with a prosthesis after transtibial amputation is associated with higher quality of life and reduced mortality (7,41). Using a Cox proportional hazards model, the mortality rate was reduced by 62% in patients with diabetes who ambulated after transtibial amputation compared with those who did not ambulate (7). Patients who ambulated after transtibial amputation were six times more likely to demonstrate improvement in quality of life compared with those who did not ambulate (41). Increased energy expenditure is required to ambulate with a prosthesis, and consequently, those who ambulate have better baseline cardiovascular health than those who do not ambulate. The act of walking with a prosthesis promotes cardiovascular fitness as a form of exercise to maintain cardiac health. Those who do not ambulate after amputation remain deconditioned and are prone to deterioration of cardiovascular fitness, potentially contributing to higher rates of mortality.

Other studies have compared patients with active DFUs to those who have undergone below-knee amputation. Boutoille et al. (8) found that patients who had undergone transtibial amputation had similar SF-36 scores as patients with active DFUs, with the exception that patients with DFUs reported higher bodily pain scores. The authors hypothesized that pain in the DFU group may have been due to persistent ischemia. Consistent with the positive correlation observed between ambulation after amputation and HRQOL, Carrington et al. (42) found that ambulatory patients after transtibial amputation had a better psychological status than patients with active DFUs. Minor amputations did not adversely impact HRQOL in patients with DFUs. Compared with patients with active DFUs, patients who had undergone minor amputations had higher physical function and less pain (8). Another study of DFUs demonstrated that improvement in the anxiety/depression score on the EQ-5D-5L instrument was significantly higher in patients who healed by minor amputation compared with patients who healed with conservative methods. The authors stated that oftentimes amputation is perceived as a "failure"; however, the results of their study demonstrated that minor amputation is a viable treatment option (22). Overall, the above findings suggest that amputations not be viewed as a failure and that, in select patients (generally patients with better underlying cardiovascular status), amputation can improve self-reported HRQOL when it results in an improvement of physical function.

One common observation reported in various studies using the SF-36 is that DFD did not negatively affect mental quality of life, with the exception of patients hospitalized with moderate and severe diabetic foot infections. A recent study evaluated 47 patients hospitalized with moderate and severe diabetic foot infections compared with a control group of 47 patients with diabetes and no foot complaints who were not hospitalized (16). No significant differences were found between the groups in regard to type of diabetes (1 vs. 2), age, or sex. Patients hospitalized with infections had a mean PCS score of (28.3 ± 9.5), which was significantly lower compared with the control group (46.3 ± 8.7; $P < 0.001$). Patients with diabetic foot infections had a mean MCS score of 43.4 ± 14.8, which was also significantly lower than that of the control group (49.6 ± 11.5; $P = 0.025$). The mean FAAM ADL and sports subscale scores were also significantly reduced in the infection group (37.0 ± 24.7 and 12.6 ± 17.6) compared with the control group (81.6 ± 18.9; $P < 0.0001$ and 63.0 ± 30.0; $P < 0.0001$). In a comprehensive study of mental health issues in patients with diabetic foot complications, Hoban et al. (43) evaluated 96 patients with the Hospital Anxiety and Depression Scale, SF-36, McGill Pain Questionnaire, Suicidal Behaviors Questionnaire, Alcohol Use Disorder IdentificationTest, and Diabetes Symptom Checklist-2. The study group included 47 patients with a diagnosis of DFU, CN, osteomyelitis, or cellulitis, and

the control group comprised 49 patients with diabetes without foot problems. The patients with DFD had significantly increased symptoms of diabetes, depression, pain, suicide, and lower physical quality of life when compared with patients without foot complaints. Despite six of eight SF-36 subscales being significantly worse in patients with foot complications, the mental health, role emotional, and MCS scores were not significantly different between the two groups. A unique aspect of this study was that the caregivers of the patients were evaluated regarding their quality of life. Caregivers self-reported SF-36 PCS and MCS scores that were similar to the general population; however, they were found to have increased caregiver burden manifested by depression and anxiety.

Multiple theories have been proposed regarding the lack of decrease in MCS scores in patients with DFD. Vileikyte (44) noted that this may be counterintuitive, as neuropathic foot ulcers result in reduction in mobility and ADL. Although these patients present with peripheral neuropathy, they may not experience significant pain. Consequently, it may be inaccurate to assume that foot ulcers and CN do not cause emotional distress due to the absence of pain. As suggested by Vileikyte (44), the SF-36 is a generic measure of HRQOL and may not adequately capture lower-extremity–related emotional distress in patients with DFD. Consistent with this theory, Hoban et al. (43) opined that the SF-36 may not differentiate depression or other emotional distress in patients with DFD compared with other outcome measures. While generic PRO measures (i.e., SF-12, SF-36) are helpful, they are limited by their inability to detect outcomes that are disease specific such as diabetes-related distress. Outcome instruments such as NeuroQol may be more useful to study certain groups and their response to treatment, particularly with regard to distress related to neuropathy (42). Postural instability and pain, as measured from the NeuroQol, are significantly associated with noncompliance with off-loading regimens in patients with diabetes with foot ulcers (45). Identifying emotional distress in patients with diabetes with neuropathy is important because depression is associated with development of an index foot ulcer (46). In addition, the presence of neuropathy in patients with diabetes is independently associated with depression (47). Given the fact that virtually every patient with DFD has neuropathy, it remains surprising that these patients do not manifest impaired mental quality of life using the SF-36 and SF-12 as health measures. Given the inability of the SF-36 and SF-12 to identify emotional distress in patients with DFD, disease-specific measures that assess diabetes distress and depression should be considered in future investigations of HRQOL (48).

Another alternative theory to account for the high SF-36 MCS scores may be the concept of the "hedonic treadmill." This psychological theory is based on the premise that patients adapt to their situation and environment in an effort to maintain a stable base of function and quality of life (49). For example, the emotional distress caused by a major illness such as a DFU or CN may be minimized by this adaptive process. These chronic illnesses potentially result in a transient reduction in mental quality of life; however, habitual adaption causes the mental distress to fade into the background. This concept may be illustrated by the findings of the Eurodiale group, who reported that nonhealing of DFUs was not associated with a deterioration in HRQOL.

The SF-36 may be overestimating mental health when subscale scores are calculated using the traditional "orthogonal method" (50). The orthogonal method of calculating PCS and MCS scores was based on the assumption that physical and mental health did not correlate. Negative coefficients have been used in the scoring, and consequently, low scores on the physical subgroups of the SF-36 (physical functioning, role physical, and bodily pain) artificially raise the MCS (51). A similar finding was observed in patients with multiple sclerosis (52). Although physical quality of life was markedly reduced in these patients, mental quality of life was only slightly reduced in comparison with the general population. Other investigators have proposed using an oblique method of scoring, which assumes that mental and physical health are correlated (50–53). Based on our experience, we believe that diabetes-related foot disease impacts mental HRQOL in a negative manner and that further research is warranted. Alternative HRQOL tools such as Patient-Reported Outcomes Measurement Information System (PROMIS) merit further study on the impact of DFD on mental health.

A systematic review by Vickers et al. (54) was performed with the goal of understanding how patients "understand and anticipate the potential negative outcomes of ulceration and amputation." The consistent theme in the articles reviewed was that patients feel "powerless" and that this emotion is further exacerbated by lack of communication or adequate education by their providers. In a similar context, Vileikyte et al. (55) studied the emotional aspects of diabetic neuropathy as it related to foot self-care.

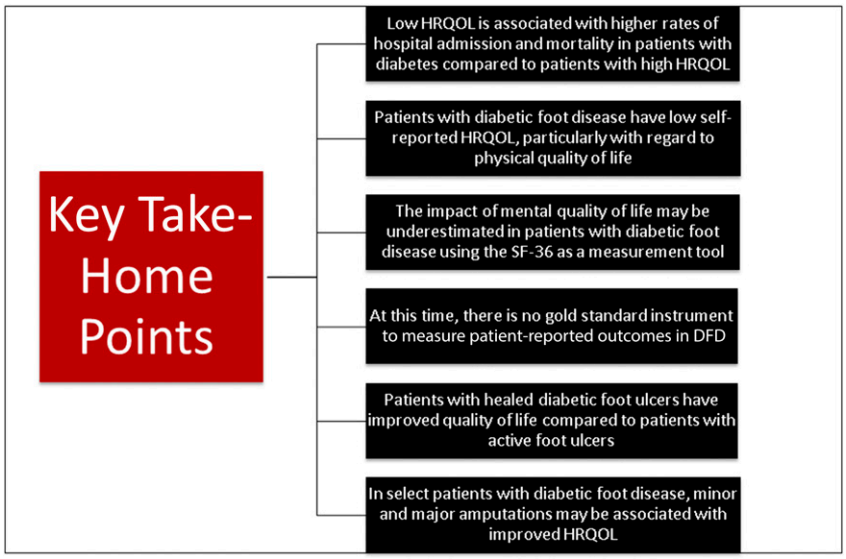

Figure 3—Key summary points on the impact of diabetes and diabetes-related foot complications on HRQOL.

The fear of amputation, perceived lack of compassion, poor communication, and anger directed at health care providers were reported as factors that could negatively influence self-care behaviors. The goal of future studies addressing HRQOL in patients with DFD should be to identify not only the physical impairment but also the impact on mental health and emotional distress.

CONCLUSIONS AND LIMITATIONS

Patients with DFD report low HRQOL, particularly in regard to physical quality of life. No particular instrument is superior in evaluating the impact of DFD on HRQOL. One of the major limitations of assessing HRQOL in patients with DFD is the heterogeneity of the studies. Different outcome instruments such as the SF-36 and EQ-5D-5L may identify subtle disparities in HRQOL. The design of the study (i.e., prospective vs. retrospective, cross-sectional vs. longitudinal) may introduce seemingly conflicting results, such as how healing is associated with improvement in quality of life while lack of healing does not reduce quality of life. Generic instruments such as the SF-36 and SF-12 may underestimate the impact on mental quality of life using the traditional method of scoring. Health care providers should realize that the SF-36 and SF-12 may not capture the impact of diabetes-related distress and that disease-specific instruments in patients with DFD may be beneficial. Measuring HRQOL with generic, diabetes-specific, and region-specific surveys can be burdensome to patients. In the future, health care providers will be expected to demonstrate improvement in PROs as a part of their treatment measures, as the treatment of DFD is costly. Assessing HRQOL provides an opportunity to address specific physical or mental health concerns of patients. Studies have shown that minor amputations do not adversely impact HRQOL when compared with patients with active DFUs. In patients who ultimately require major amputation, the ability to maintain mobility is associated with improved HRQOL and reduced mortality. Key take-home summary points are illustrated in Fig. 3.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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