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Determinants of Health-Related Quality of Life in Patients with Diabetic Foot Ulcers: A Systematic Review and Meta-Analysis

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Abstract

Successful healing of DFUs often requires long periods of treatment with additional limitations in patients' daily activities. This burden in the life of patients adversely affects Health-Related Quality of Life (HRQoL). An understanding of the determinants of DFU patients' HRQoL may help health professionals in clinical decision making, specifying risk groups and allowing the prediction of the HRQoL. The aim of this review was to ascertain the health-related quality of life determining factors of patients with diabetic foot ulcers. A literature review in the PubMed and Scopus databases was conducted in relation to the clinical and sociodemographic determinants of DFU patients' HRQoL. The extraction and evaluation of the studies was carried out, according to preset criteria. Thirty-three publications were detected eight of which met the inclusion criteria. The majority of the included studies were of analytical, retrospective, case-control research design. By the statistical analysis, it was found that positive impact on HRQoL have the use of non-pharmacological interventions for the management of diabetes (Wald Chi- Square=21,61, p<0,001) and the lack of family obligations (X2=24,96, p<0,001), while negative effect have the duration of ulcer from 1 week to 3 months (X2=354,46, p<0,001), the unemployed status (X2=560,68 p<0,001) and the presence of cardiovascular complications (X2=83,35, p<0,001). Since HRQoL is an important health outcome measure, health professionals could emphasize more on the prompt treatment of diabetic ulcers, the prevention and treatment of cardiovascular complications as well as on the promotion of employment among DFU patients and the utilization of non-pharmacological interventions for managing diabetes.

Keywords: Quality of life; Diabetes; Measurement; Foot ulcers

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Introduction

Fifteen to twenty-five percent of persons with diabetes mellitus, sometime in their lifetime, will develop foot ulcers particularly susceptible to infections (diabetic foot ulcers, DFUs). An infection in the feet can rapidly be spread causing severe tissue damages which can lead to the need of amputation [1-3].

Successful healing of DFUs often requires long periods of treatment with additional limitations in patients' daily activities. This burden in the life of patients adversely affects Health-Related Quality of Life (HRQoL) [4-8].

The HRQoL concept was developed to meet the need of measuring the subjective perception of a person's health. The World Health Organization (WHO), in 1948, influenced by the opinions of Sigerist [9,10], defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [9,11]. This evolvement had emerged the

need of measuring the physical, mental and social well-being, concepts which are related to the subjective perception of the individual and are beyond, and many times superior, than the measuring ability of the biomedical indicators. For fulfilling the above need the concept of Health-Related Quality of Life was developed [12].

An understanding of the determinants of DFU patients' HRQoL may help health professionals in clinical decision making, specifying risk groups and allowing the prediction of the HRQoL.

Aim

The aim of this review was to ascertain the health-related quality of life determining factors of patients with diabetic foot ulcers.

Method

Search strategy

This review was conducted by searching in the electronic databases PubMed, and Scopus, for the period 2000 to March 2014.

The literature search was carried out using the following string of terms: "quality of life" AND "foot" AND "ulcers". As a search criterion for the articles identification, the title of the publications was set.

Eligibility criteria

The selection of the studies conducted by two reviewers working independently. (AK, TK). Initially, the articles which yielded through the literature search, were evaluated, the duplicated records were removed and the related to the purpose of the review primary studies were chosen. Afterwards, at the second phase of the selection process, a review of the full text of the publications was taken place **(Figure 1)**.

To include a study in the review, the following criteria were set:

- Articles written in English language.
- *Reference population:* Persons with Type 1 or Type 2 DM, with or without diabetic foot ulcers, regardless of age.
- *Outcome:* The health-related quality of life measured by a reliable and valid scale.
- *Determinants:* Factors concerning the health-related quality of life.
- *Statistical analysis:* Articles with multivariate analysis.
- Publications which are not measurement instrument development studies (scales/questionnaires) and
- Articles published in peer reviewed journals.

Data extraction

The data which retrieved from the studies, included in the review, came along after consensus of the AK and TK reviewers. The name of the study first author (or the names of the study authors in case they were two), measurement instrument, sample size, research design, gender, diabetes type (1 or 2), educational level, working status, care from others, marital status, duration of diabetes, type of treatment (insulin, medications or diet), ulcer size, ulcer duration, ulcer location, infection presence or absence, diabetes chronic complications, other health problems, body mass index (BMI), HbA1c levels, serum creatinine levels, CRP levels, ankle brachial index (ABI), Wagner ulcer classification and HRQoL outcomes were summarized **(Tables 1 and 2)**.

Data analysis

The Wald chi-square test was used to evaluate the contribution of each sociodemographic and clinical variable in the multivariate model. The dependent variable of the linear model was the SF-36 domains mean score.

Results

After the selection process **(Figure 1)** eight studies were included in the review, five of analytical, retrospective, case-control research design and three of cross-sectional.

The studies of Ali Alzahrani and Sehlo [13] from Saudi Arabia, Sanjari et al. [14] and Yekta & Ghasemirad [15] from Iran, Yao et al. [16] from China and Valensi et al. [17] from France were of the analytical, retrospective case-control design while the two

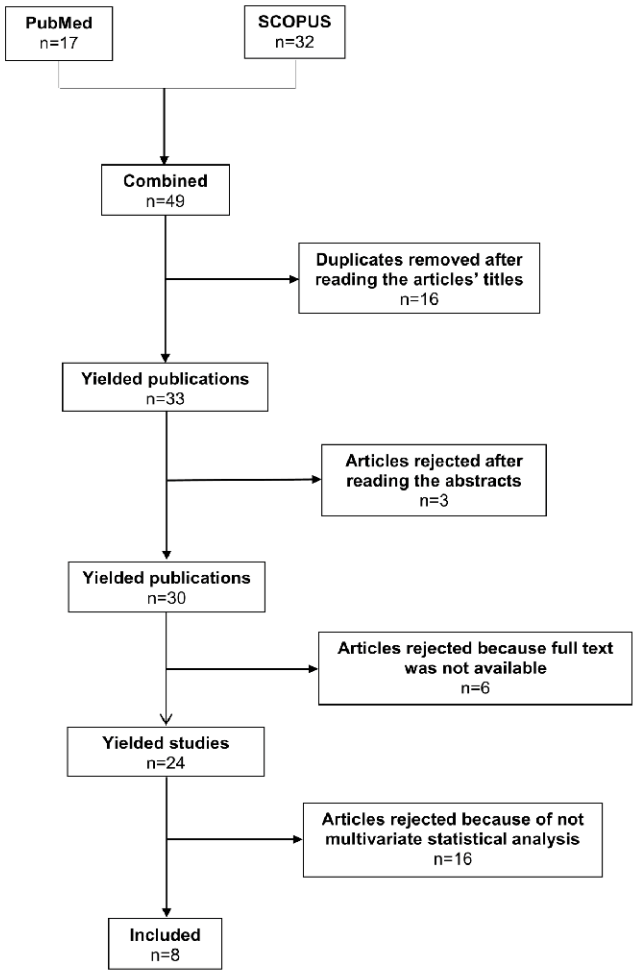

Figure 1 Flow Chart – Review process.

Table 1 Summary of the studies included in the review.

Study	Country	Sample	Research design	Measurement instrument
Ali Alzahrani & Sehlo [13]	Saudi Arabia	60 randomly selected adult persons with DFUs, 60 randomly selected adult people with DM and 60 matched healthy controls	Analytical, retrospective, case-control	SF-36
Ribu et al. [6]	Norway	127 patients with DFUs	Cross-sectional	DFS, SF-36
Ribu et al. [7]	Norway	127 patients with DFUs	Cross-sectional	SF-36
Sanjari et al. [14]	Iran	54 patients with DFUs and 78 persons with DM Type 1 or Type 2	Analytical, retrospective, case-control	SF-36
Siersma et al. [18]	Multicenter	1232 patients with a new foot ulcer	Cross-sectional	Euro-Qol-5D
Yao et al. [16]	China	131 patients with DFUs	Analytical, retrospective, case-control	SF-36
Yekta & Ghasemirad [15]	Iran	90 patients with DFUs and 160 persons with DM Type 2	Analytical, retrospective, case-control	SF-36
Valensi et al. [17]	France	239 patients with DFUs and 116 people with DM	Analytical, retrospective, case-control	DFS, SF-36

Table 2 Descriptive table of patients' characteristics.

Variables		N	Percentage
Gender	Male	1291	62,9%
	Female	762	37,1%
	Total	2053	100,0%
Educational level	Secondary education	169	8,2%
	Bachelor's degree	61	3,0%
	Missing values	1823	88,8%
	Total	2053	100,0%
Working status	Employed	154	7,5%
	Unemployed	154	7,5%
	Missing values	1745	85,0%
	Total	2053	100,0%
Care from others	Yes	729	35,5%
	Missing values	1324	64,5%
	Total	2053	100,0%
Marital status	Single	122	5,9%
	Married	17	0,8%
	Cohabitation	78	3,8%
	Missing values	1836	89,4%
	Total	2053	100,0%
Diabetes duration	< 5 years	167	8,1%
	5 – 10 years	275	13,4%
	> 10 years	1443	70,3%
	Missing values	168	8,2%
	Total	2053	100,0%
Treatment	Insulin	1244	60,6%
	Medications	190	9,3%
	Diet	4	0,2%
	Total	2053	100,0%
Ulcer size	< 1 cm^2	540	26,3%
	1 – 5 cm^2	665	32,4%
	> 5 cm^2	147	7,2%
	Missing values	701	34,1%
	Total	2053	100,0%
Duration of ulcer	< 1 week	194	9,4%
	1 week – 3 months	787	38,3%
	> 3 months	429	20,9%
	Missing values	643	31,3%
	Total	2053	100,0%

Ulcer location	Forefoot	702	34,2%
	Midfoot	392	19,1%
	Heel	166	8,1%
	Missing values	793	38,6%
	Total	2053	100,0%
Infection	Yes	673	32,8%
	Missing values	1380	67,2%
	Total	2053	100,0%
Diabetes chronic complications	Cardiovascular disease	264	12,9%
	Retinopathy	397	19,3%
	Charcot foot	9	0,4%
	Amputation	103	5,0%
	Missing values	1280	62,3%
	Total	2053	100,0%
Renal insufficiency	Yes	27	1,3%
	Missing values	2026	98,7%
	Total	2053	100,0%
Other health problems	Yes	362	17,6%
	Missing values	1691	82,4%
	Total	2053	100,0%
Body mass index (BMI)	< 25 Kg/m^2	79	3,8%
	25 – 29,9 kg/m^2	349	17,0%
	> 30 kg/m^2	189	9,2%
	Missing values	1436	69,9%
	Total	2053	100,0%
HbA1c	< 48 mmol/mol	7	0,3%
	48 – 58 mmol/mol	89	4,3%
	> 58 mmol/mol	339	16,5%
	Missing values	1618	78,8%
	Total	2053	100,0%
Serum creatinine	Normal	56	2,7%
	High	57	2,8%
	Missing values	1940	94,5%
	Total	2053	100,0%
CRP	< 10 mg/l	68	3,3%
	> 10 mg/l	38	1,9%
	Missing values	1947	94,8%
	Total	2053	100,0%
Ankle Branchial Index (ABI)	< 0,9	58	2,8%
	0,9 – 1,2	59	2,9%
	> 1,2 or unable to be determined	25	1,2%
	Missing values	1911	93,1%
	Total	2053	100,0%
Wagner ulcer classification	Grade 1	127	6,2%
	Grade 2	58	2,8%
	Grade 3	158	7,7%
	Grade 4	31	1,5%
	Missing values	1679	81,8%
	Total	2053	100,0%

studies of Ribu et al. [6,7] and the study of Siersma et al. [18] were of the cross-sectional design **(Table 1)**.

By the statistical analysis it was detected that positive impact on DFU patients' HRQoL had the Type 1 DM (Wald Chi-Square=164,69, p<0,001), the lack of family obligations (X^2=24,96, p<0,001), the utilization of non-pharmacological interventions for the management of diabetes (diet) (X^2=21,61, p<0,001), the ulcer size of >5cm^2 (X^2=1758,92, p<0,001), the ulcer location at the forefoot or midfoot (X^2=24,23, p<0,001 and X^2=39,21, p<0,001 respectively), the BMI of 25-29,9kg/m^2 (X^2=215,67, p<0,001) and the high serum creatinine levels (X^2=391,97, p<0,001).

On the other hand, negative influence on DFU patients' HRQoL

Table 3 DFU patients' HRQoL determining factors.

Factors		B	Wald Chi-Square	P value
Type of diabetes	Type 1	9,89	164,69	< 0,001
	Type 2	8,34	169,03	< 0,001
Working status	Employed	-18,64	496,43	< 0,001
	Unemployed	-19,47	560,69	< 0,001
Marital status	Single	2,82	24,97	< 0,001
	Married	1,23	1,49	0,223
	Cohabitation	-1,49	2,41	0,120
Diabetes duration	< 5 years	-1,72	3,38	0,066
	5 – 10 years	-2,91	18,48	< 0,001
	> 10 years	-6,85	158,84	< 0,001
Treatment	Insulin	2,06	27,07	< 0,001
	Medications	5,67	90,76	< 0,001
	Diet	7,47	21,61	< 0,001
Ulcer size	< 1 cm^2	28,27	1029,85	< 0,001
	1 – 5 cm^2	28,89	1249,23	< 0,001
	> 5 cm^2	29,22	1758,92	< 0,001
Duration of ulcer	< 1 week	-10,33	178,44	< 0,001
	1 week – 3 months	-10,59	354,46	< 0,001
	> 3 months	-8,06	203,06	< 0,001
Ulcer location	Forefoot	3,89	24,23	< 0,001
	Midfoot	3,89	39,21	< 0,001
	Heel	2,92	32,37	< 0,001
Diabetes chronic complications	Cardiovascular disease	-4,96	83,35	< 0,001
	Retinopathy	-3,55	114,64	< 0,001
	Charcot foot	-2,85	6,21	0,013
	Amputation	-3,57	31,98	< 0,001
Body mass index (BMI)	< 25 Kg/m^2	6,16	49,75	< 0,001
	25 – 29,9 kg/m^2	9,32	215,67	< 0,001
	> 30 kg/m^2	7,43	135,26	< 0,001
HbA1c	< 48 mmol/mol	-26,69	255,06	< 0,001
	48 – 58 mmol/mol	-26,69	458,71	< 0,001
	> 58 mmol/mol	-27,59	1331,41	< 0,001
Serum creatinine	Normal	44,01	398,94	< 0,001
	High	44,32	391,97	< 0,001

had the unemployment status (X^2=560,69, p<0,001), the duration of diabetes >10 years (X^2=158,84, p<0,001), the duration of ulcer/s from 1 week to 3 months (X^2=354,46, p<0,001), the cardiovascular complications (X^2=83,35, p<0,001), and the HbA1c levels >58 mmol/mol (X^2=1331,41, p<0,001) **(Tables 2 and 3)**.

Discussion

Diabetic foot ulcers, for being successfully managed, need long periods of treatment that bring about restrictions on patients' daily activities and negatively influence the HRQoL. An understanding of the determinants of DFU patients' HRQoL could help health professionals in clinical decision making as well as in screening and in the prediction of quality of life [4].

The most significant finding of this review, was the fact that cardiovascular complications have a negative effect on HRQoL. This finding is in agreement with the study done by De Visser et al. [19] in which the cardiovascular disease had a negative impact on quality of life of people with DM Type 2.

Another weighty finding was the positive effect on HRQoL of the diet as main diabetes treatment. Diet as a non-pharmacological intervention may promote the empowerment of the DFU patients and hence the, subjectively assessed, HRQoL. According to Elvin-Lewis [20] "for a variety of reasons more individuals are nowadays preferring to take personal control over their health, not only in the prevention of diseases but also to treat them". It is worth mentioning that numerous trials has been conducted regarding the effectiveness of herbs and dietary supplements on DM glycemic control but with insufficient evidence to be provided [21].

In regard to working status, it was detected that unemployment status has adverse influence on HRQoL. Employment is a factor of wealth production and therefore a factor of better health services receiving [22,23].

With respect to ulcer size, size >5cm^2 was found to have positive impact on HRQoL. This finding seems a bit peculiar but it could be explained by the fact that the patients with bigger ulcers may receive better therapeutic equipment (casts or appropriate footwear) resulting in better everyday functionality.

With regard to diabetes type, DM Type 1 had positive effect on HRQoL. DFUs usually occurs much later after diagnosis in persons with DM Type 1 [24]. There is a possibility the people's with DM Type 1 total sample of the studies which were included in the systematic review to reflect the aforementioned acknowledgement, and hence, the prevalence of diabetic foot syndrome to be lower than the persons' with DM Type 2 commensurate sample.

In terms of diabetes duration, duration >10 years had negative impact on HRQoL. This detection is consonant to the findings of Sparring et al. study [25] that diabetes duration associated negatively to HRQoL levels such as of Redekop et al. study [26] in which persons with ≥10 years diabetes duration was the subgroup with the lowest quality of life score (for mobility Euroqol 5D subscale, the P value was <0,0001) and of Papadopoulos et al. [27] (Physical Functioning SF-36 subscale, 56,4 score, p=0,049 and Vitality subscale, 47,4 score, p=0,016).

In relation to marital status, single status was found to have affirmative influence on HRQoL. Although in accordance to the literature [27,28] married people mark better scores on quality of life measurement instruments, this could be explained by the case that DFUs affect primarily physical well-being and therefore having family obligations might burden more persons with diabetic ulcers. Additionally, an alternative explanatory hypothesis could be that the concrete detection mirrors relevant sample synthesis. For example, concordantly to the study done by Han et al. [29], single women have higher quality of life values than single men.

By the data analysis, it was detected that ulcer durations from <1 week and 1 week to 3 months affect HRQoL more adversely than duration >3 months. Duration of 1 week to 3 months could be considered to be included in the crisis phase of diabetic foot disease, so, the burden on the individual is greater [30]. Furthermore, in a time period of >3 months, it is likely the ulcers to have been cured largely.

With respect to the ulcer location, site of the sore did not have negative influence on HRQoL. Less positive contribution in the multivariate model had the location of the heel (B=2,92, p<0,001).

Regarding BMI, it was found that BMIs of 25-29,9 kg/m^2 and of >30 kg/m^2 have more positive impact on HRQoL than a BMI of <25 Kg/m^2. This detection is in contrast with the literature [31-33]. However, DFU patients with higher BMI than the normal may be unconcerned with their health issues and this could be reflected on their subjective perception of their well-being. They might have developed a fictitious sense of good well-being.

Concerning HbA1c levels, concentration of >58 mmol/mol had adverse effect on HRQoL. Low HbA1c values are associated with higher mental quality of life scores [34].

With regard to serum creatinine levels, high levels were detected to have affirmative effect on HRQoL. Physical exercise, and hence unrestricted mobility, is positively associated with serum creatinine for both men and women [35]. High creatinine levels might correspond to persons with less foot problems.

Limitations

The two reviewers (AK, TK) did not have direct access to the EMBASE database [36]. Although the review of Burnham [37] claims that Scopus has 100% coverage of EMBASE, recently published studies might was absented.

Conclusions

Since HRQoL is an important health outcome measure, health professionals could emphasize more on the prompt treatment of diabetic ulcers, the prevention and treatment of cardiovascular complications as well as on the promotion of employment among DFU patients and the utilization of non-pharmacological interventions for managing diabetes.

Another modifiable factor which should be taken into account is HbA1c and its regulation through glycemic control.

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