

Article

# Impact on the Quality of Life and Physiological Parameters in Patients with Diabetes Mellitus

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**Featured Application:** The perception of the quality of life of the patient with diabetic foot depends on the physiological parameters present as well as on other factors such as gender.

**Abstract:** The co-existence of complications and diabetes mellitus is related to a worsening in quality of life compared to not presenting comorbidities. This study aimed to investigate whether there is a different impact on quality of life according to gender and to establish the physiological parameters that these patients have in relation to diabetes-related complications. The sampling was continuous non-probabilistic, involving legal age patients with diabetes mellitus. All of the participants were administered the generic SF-36 quality of life questionnaire. The presence of peripheral artery disease was considered from an ankle brachial index <0.9 and grade II to grade IV of the Leriche–Fontaine classification. Nerve dysfunction was detected from a neurotensimeter test, and the presence of diabetic foot was detected from a dermal examination and co-existence with arteriopathy and/or neuropathy. Men presented significantly better quality of life values on the mental health, emotional role and health transition scales. Despite this, in the presence of complications such as vasculopathy, neuropathy or diabetic foot, the perception of well-being changes, showing that men and women face the disease in different ways. Despite the fact that the physical parameters of diabetic patients are similar according to the complications that they present, the adult women in our environment have lower levels of quality of life than men in most cases. This may be related not only to pathophysiological differences but also to sociocultural factors.

**Keywords:** diabetes mellitus; peripheral arterial disease; peripheral neuropathy; diabetic foot; health-related quality of life (HRQL); gender



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## 1. Introduction

Diabetes mellitus (hereafter, DM) is considered the most prevalent metabolic disorder, according to the latest WHO report. In 2019, an estimated 463 million people had DM. This is estimated to increase to 578 million by 2030 and to 700 million by 2045 [1].

Both type 1 and type 2 DM are associated with complications that, together with the chronic nature of this disease, have a high impact on the quality of life (hereafter, HRQL) of those affected. The increase in life expectancy creates the need to adapt therapeutic strategies aimed at both the control of the pathophysiology and its impact on the patient's well-being [2].

People with DM and a low HRQL have poorer adherence to treatment [3,4] and are more likely to have crises in their disease and develop complications [5,6], which increases the cost of medical care [7] and in turn further impairs quality of life [8].

Thus, the development of studies such as the one presented here are based on that of investigations that cover those dimensions of HRQL that are impaired by the disease,

taking into consideration that, in each subject or group, DM will influence them to different degrees, regardless of the altered physiological values.

Different aspects related to diabetic foot syndrome, such as physical alterations, psychological complaints or socioeconomic difficulties, can affect the quality of life of these patients [9]. The study of the physical parameters that determine the complications of diabetics does not guarantee that, when faced with the same alteration, the impact will be similar for the quality of life in men and women. Gender has been shown to be one of the most important factors associated with lower quality of life in patients with a diabetic foot ulcer [10,11].

This cross-sectional study analysed differences in the impact on HRQL of men and women with DM in the presence of peripheral arteriopathy, peripheral neuropathy and dermal lesions. To analyse the level of quality of life, the generic questionnaire SF-36 [12] was used as a first approximation before using more specific questionnaires for DM and to study DM from a gender perspective.

## 2. Materials and Methods

The present observational cross-sectional study complies with the precepts of the Helsinki Declaration and current legislation. The study was carried out in the Podiatry Clinical Area of the University of Seville (Spain) and was approved by the Bioethics Committee of the Virgen Macarena and Virgen del Rocío University Hospitals of Seville (Spain) (Code: 0227-N-17).

### 2.1. Participants

The sampling was continuous non-probabilistic, including those participants with DM (according to WHO criteria; fasting plasma glucose  $\geq 126$  mg/dL; or 2 h plasma glucose  $\geq 200$  mg/dL during an oral glucose tolerance test; or A1C  $\geq 6.5\%$ ; or in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose  $\geq 200$  mg/dL) [13] of legal age who agreed to participate voluntarily, with prior informed consent. The randomisation was not possible due to the small number of patients who attend this service, since the Podiatry Clinic Area of the University of Seville (Spain) is a non-public health service. It excluded those who had previously participated in a study with the SF-36 questionnaire and those with a low level of understanding of Spanish or who presented cognitive alterations, differential syndromes or disorientation that prevented them from understanding the test questions.

### 2.2. Clinical Tests

#### 2.2.1. Questionnaires

To measure the level of quality of life, we used the Spanish version [14] of the generic SF-36 questionnaire [15], which includes eight fundamental dimensions: physical function, physical role, bodily pain, general health, mental health, emotional role, social function and vitality. This is compiled with a so-called physical component (the first four dimensions) and an emotional component (the second four dimensions). To the above, we added one more dimension of study: health change.

All of the dimensions are individually weighted from 0 to 100, where 0 is the worst possible health status and 100 is the best [16,17].

All questionnaires were administered by the same researcher (I.C.P.-T.).

#### 2.2.2. Peripheral Arterial Disease Assessment

Peripheral arterial disease, understood as an obstructive arteriosclerotic complication with signs and symptoms of complete or partial interruption of peripheral blood flow [18], was considered in the presence of a compatible ankle brachial index (ABI) according to the International Working Group on the Diabetic Foot (IWGDF) ( $<0.9$ )—this method has been validated and is used in the clinical setting [19–21]—and a grade II to grade IV of the Leriche–Fontaine classification of arterial symptomatology was used [22].

The index was calculated by dividing the highest blood pressure at the level of the foot by the brachial blood pressure, which resulted in a higher figure [23]. Blood pressure measurement was performed with a Spead-Doppler-Systeme 8 Mhz emission frequency Doppler and a manual progressive pressure cuff, placed 3–4 cm above the brachial crease and 4–5 cm above the intermalleolar line at the ankle [19,22], bilaterally and simultaneously. Data obtained from the posterior tibial and pedal artery system were also recorded.

### 2.2.3. Nerve Dysfunction Assessment

To consider distal nerve dysfunction, altered vibratory sensitivity [18] was detected using an electrical neurotensimeter test (86,040 Ultrabio-tensimeter<sup>®</sup>)—this method has been validated [24].

The device consists of a rheostat to modulate the generated vibration amplitude with a voltage between 0 and 50 volts. It was applied at the same point as the Rydel-Seiffer graded tuning fork (64/128 Hz)—interphalangeal joint of the first toe—and, if the patient did not perceive the vibration, the test was repeated at a more proximal point (medial metatarsophalangeal joint, tibial malleolus or peroneal malleolus) [21].

The head was applied, and the rheostat was rotated gently until the patient indicated that he/she felt the vibration (reference value). Then, without losing the scanning point, the vibration was progressively reduced until the patient indicated when he/she did not feel the vibration, and finally, the vibration was increased again until the patient reported that he/she felt it again [21]. This was the reliable value, which should normally coincide with the initial value (baseline value). A positive re-test was considered when the patient did not detect values higher than 25 volts [18] at any of the scan points.

A sensitivity examination was completed with Semmes–Weinstein monofilament tests, 10 g/cm<sup>2</sup> of pressure, to find out if they maintained a dermal protective threshold. For the assessment of pain sensitivity, the Neuropen device (a pinprick of 40 g/cm<sup>2</sup>) was employed, and, for sudomotor dysfunction, an indicator plaster (Neuropad<sup>®</sup>) was used.

For the determination of diabetic foot, the IWGDF criteria were used, which consider a foot with infection, ulceration or tissue destruction (including minimal damage to the dermis and part of the epidermis) to be associated with neuropathy and/or vasculopathy [18].

### 2.2.4. Other Physiological Assessments

In addition, other physiological tests were carried out to ascertain the general health status of the participants. To determine the degree of oxygen saturation, values were recorded with a distal pulse oximeter placed on the index finger of the right hand (BeurerPO 40 model<sup>®</sup>).

To detect distal and podiatric lesions, the dermal temperature was taken on the soles of both feet with the Digital Feet Thermo Scale<sup>®</sup> system. Lastly, loaded dorsoplantar radiographs of both feet were taken to detect arterial calcifications.

The presence of diabetic foot was established from a dermal examination and co-existence with arteriopathy and/or neuropathy.

These assessments were performed entirely by the same authors (M.R.-B. and M.d.C.V.-B.).

## 2.3. Statistical Analysis

The analysis of the data was carried out using the statistical software IBM SPSS Statistics 22<sup>®</sup> (IBM, Armonk, NY, USA). The descriptive data provided the mean values and the standard deviations and the absolute frequencies and percentages depending on whether the variables were continuous or categorical. For continuous variables, Shapiro–Wilk normality tests were conducted to determine the most appropriate test to use. Data showed an abnormal distribution, so non-parametric tests were carried out (Mann–Whitney U test). Physical parameters with dichotomous or categorical responses were analysed using the chi-square test.

The variables “Presence of peripheral neuropathy” and “Presence of peripheral arteriopathy” were coded so that the subject either had (in the presence of a positive diagnostic

test result) or did not have (in the presence of a negative test result) the complication [25]. The SF-36 questionnaires were processed in their specific programme [26] and incorporated into the data matrix, with the principal investigator being blinded.

*p* values lower than 0.05 were considered significant.

### 3. Results

Based on non-probabilistic convenience sampling, 50 participants (70% men and 30% women) were recruited; foot problems are more prevalent in adult men with long-standing DM [27,28]. The mean age was homogeneous in both gender groups ( $65 \pm 0.03$  years) as was the proportion of type 1 and type 2 diabetics ( $\chi^2 = 0.000$ ). Eighty-eight percent of the total had type 2 DM with a mean duration of 16.5 (11.85) years. This distribution is practically the same according to gender.

To study the presence of weight disorders in the sample, in a valid sample of  $n = 46$ , the mean BMI was 29 (P25: 25.2–P75: 33.7).

The study variables corresponding to the complementary physical parameters are summarised in Table 1.

**Table 1.** Descriptive values and comparison of physical parameters according to gender.

Variables N = Valid Sample	Men	Women	Significance *
Calcification presence on RX. Right foot. N = 46	n = 18 58.1%	n = 3 20%	$p = 0.016$
Calcification presence on RX. Left foot. N = 46	n = 19 61.3%	n = 3 20%	$p = 0.009$
Sensory neuropathy. Right foot. Semmes–Weinstein monofilament tests. N = 50	n = 6 17.1%	n = 2 13.3%	$p = 0.345$
Sensory neuropathy. Left foot. Semmes–Weinstein monofilament tests. N = 50	n = 8 22.9%	n = 2 13.3%	$p = 0.243$
Pain sensitivity disorder. Right foot. (Neuropen) N = 46	n = 5 16.1%	n = 2 13.3%	$p = 0.589$
Pain sensitivity disorder. Left foot. (Neuropen) N = 46	n = 5 16.1%	n = 2 13.3%	$p = 0.589$
Sudomotor dysfunction. Right foot. (Neuropad) N = 42	n = 11 39.3%	n = 2 14.3%	$p = 0.246$
Sudomotor dysfunction. Left foot. (Neuropad) N = 42	n = 11 39.3%	n = 2 14.3%	$p = 0.246$
Altered vibratory sensitivity. Right foot. (Rydel–Seiffer graded tuning fork) N = 42	n = 13 41.9%	n = 3 20%	$p = 0.128$
Altered vibratory sensitivity. Left foot. (Rydel–Seiffer graded tuning fork) N = 42	n = 14 45.2%	n = 3 20%	$p = 0.090$
More than 2 °C in skin temperature difference. (Digital Feet Thermo Scale system) N = 44	n = 1 3.3%	n = 0 0%	$p = 0.682$
Oxygen saturation level less than 95%. (Distal pulse oximeter) N = 47	n = 4 12.5%	n = 4 26.8%	$p = 0.196$

\* Chi-square test. Statistical study of contrast between variables of physical parameters according to gender differentiation, for  $p$  value  $\alpha = 0.05$ .

All of the tests were performed bilaterally, with the exception of the oxygen saturation level. As expected, in the case of the measurements corresponding to the sensitivity tests, the results were similar in both feet.

In addition, the subjects studied accumulated complications, with a lower percentage in the female group than in the male group (Table 2).

**Table 2.** Presence of diabetic complications included in the study, segmented according to gender.

		Wounds	Neuropathy	Fontaine (Between II and IV)
Women (15)	N (positive) *	3 (15)	3 (15)	4 (15)
	Percentage	20.0%	20.0%	26.7
Men (35)	N (positive) *	16 (35)	15 (30)	4 (33)
	Percentage	45.7%	42.9%	11.4%

\* N (positive): A wound at least, deficient NTS, symptomatic Fontaine (>2).

As a starting point, it was considered appropriate to test whether it was possible to infer differences between genders for the different dimensions of the SF-36 questionnaire. The non-parametric Mann–Whitney U test was used to study whether significant differences exist. For the “emotional role”, “mental health” and “health change” dimensions, men have better HRQL (Table 3).

**Table 3.** SF-36 questionnaire for HRQL dimension descriptive analysis and comparisons.

Variables	Women Mean (SD)	Men Mean (SD)	Significance ( <i>p</i> )
Total health	54.2 ± (17.5)	63.77 ± (20.21)	0.073
Physical function	66.33 ± (21.25)	65.14 ± (26.91)	0.966
Physical role	60 ± (44.12)	60 ± (39.85)	0.938
Bodily pain	54.67 ± (26.72)	59.2 ± (30.75)	0.595
General health	52 ± (13.47)	62 ± (20.41)	0.094
Vitality	57.33 ± (22.67)	58.71 ± (27.02)	0.164
Social function	65.47 ± (28.57)	75.91 ± (27.28)	0.200
Emotional role	37.67 ± (4.55)	69.43 ± (42.32)	0.028
Mental health	56.27 ± (17.60)	72.83 ± (21.32)	0.003
Health change	41.67 ± (15.43)	54.46 ± (18.66)	0.028

\* Mann–Whitney U test. Statistical study of contrast between HRQL variables according to gender differentiation, for *p* value  $\alpha = 0.05$ .

In general, the male group showed better results in the questionnaire despite having a higher rate of complications derived from DM. To explore this point further, it was decided to study HRQL in the presence of different complications: “presence of peripheral artery disease”, “presence of neuropathy” and “presence of wounds”.

A differentiated analysis was carried out, considering the dichotomy of presence or non-presence as an independent variable. Because most of the dimensions of the SF-36 questionnaire score were reduced in the presence of these complications ( $p < 0.05$ ), the analysis continued. The summarised results are presented in Table 4.

**Table 4.** SF-36 questionnaire for HRQL dimension descriptive analysis in wound, neuropathy and peripheral arteriopathy presence and differences according to gender.

		Wound		Neuropathy		Peripheral Arteriopathy			
		Yes	No	Yes	No	Yes	No		
T	M	66.13	61.79	M	58.67	67.80	M	43.00	67.10
	W	49.33	55.42	W	39.00	58.00	W	40.00	59.36
	<i>p</i>	0.465		<i>p</i>	0.246		<i>p</i>	0.136	
PF	M	65.00	65.26	M	58.67	67.67	M	31.25	69.31
	W	56.67	68.75	W	46.67	71.25	W	43.75	74.55
	<i>p</i>	0.733		<i>p</i>	0.094		<i>p</i>	0.672	
PR	M	60.94	59.21	M	55.00	66.67	M	50.00	62.07
	W	41.67	64.58	W	58.33	72.92	W	18.75	75.00
	<i>p</i>	0.729		<i>p</i>	0.091		<i>p</i>	0.408	
BP	M	61.63	57.16	M	54.60	61.07	M	36.50	62.62
	W	42.00	57.83	W	45.33	57.00	W	47.00	57.45
	<i>p</i>	0.968		<i>p</i>	0.402		<i>p</i>	0.348	
GH	M	67.50	57.37	M	59.33	64.00	M	37.50	65.52
	W	48.33	52.92	W	48.33	52.92	W	42.50	55.45
	<i>p</i>	0.121		<i>p</i>	0.852		<i>p</i>	0.048	
V	M	63.44	54.74	M	50.67	63.67	M	26.25	63.10
	W	66.67	55.00	W	53.33	58.33	W	66.25	54.09
	<i>p</i>	0.316		<i>p</i>	0.231		<i>p</i>	0.030	
SF	M	76.88	75.11	M	70.07	82.80	M	45.25	82.03
	W	49.00	69.59	W	49.67	69.42	W	56.00	68.91
	<i>p</i>	0.839		<i>p</i>	0.376		<i>p</i>	0.126	
ER	M	77.00	63.05	M	59.93	79.93	M	66.50	72.34
	W	44.33	36.00	W	51.00	44.33	W	16.50	45.36
	<i>p</i>	0.149		<i>p</i>	0.343		<i>p</i>	0.290	
MH	M	70.75	74.58	M	72.60	75.20	M	54.00	76.86
	W	62.67	54.67	W	57.33	56.00	W	47.00	59.64
	<i>p</i>	0.826		<i>p</i>	0.403		<i>p</i>	0.012	
HC	M	56.25	52.95	M	52.07	51.67	M	43.75	53.66
	W	33.33	43.75	W	33.33	43.75	W	25.00	47.73
	<i>p</i>	0.469		<i>p</i>	0.471		<i>p</i>	0.410	

Statistical study of contrast between CV variables according to the presence of vascular symptoms and gender differentiation, for  $\alpha = 0.05$ . M = men; W = women; *p* = significance (Mann–Whitney U test); T = Total health; PF = Physical function; PR = Physical role; BP = Bodily pain; GH = General health; V = Vitality; SF = Social function; ER = Emotional role; MH = Mental health; HC = Health change.

The descriptive comparative analysis and subsequent non-parametric tests showed, in “general health”, “vitality” and “mental health”, more marked low values in the male group for peripheral artery disease. Only the “physical role” dimension had worse results in women.

#### 4. Discussion

The results showed higher values in men in most dimensions of the SF-36 questionnaire, supported by several related studies [29]. However, the physical parameters assessment indicated that there were no significant differences in the values presented according to gender. Among the parameters studied, only the gender of the patient with diabetes had an influence on the presence of arterial calcifications, shown on the X-ray, which were more frequent in men. Although the physical/clinical aspects of women and men with DM were similar, the perception of their quality of life differed.

We found significant differences in the “emotional role”, “mental health” and “health change” dimensions. Low levels in the mental and emotional component and the development of depressive or anxiety disorders were reported by [30]. These findings are



relevant because of [30]. In addition, the presence of emotional disorders is associated with a decrease of up to three times to the adherence to treatment with the consequent development of complications associated with the disease [29], which is a serious concern because polypharmacy and other related comorbidities such as dyslipidaemia are very common in elderly people with type 2 diabetes mellitus [31,32]. According to Aurrecochea et al. [33], it is the physical limitation that triggers the development of emotional imbalance, depression and anxiety. This is more frequent in women than in men.

Sepúlveda et al. [34] explained their outcomes by presenting two arguments: the women in their study group presented a higher risk of comorbidities, and they were overloaded by the combination of housework and labour activities.

Del Core et al. [35], sustained that women would interpret their health status differently due to culturally established roles of genders.

Actually, these arguments are consistent with daily life in many countries, where equal sharing of tasks and housework is not very common. After retirement, women tend to be more active and are more limited than men in the presence of diabetes complications.

It is, therefore, relevant to identify the origin of these differences in order to prevent complications arising from this situation.

In DM, the high prevalence of vascular pathology together with the high rate of complications associated with this phenomenon places diabetic vascular disease, as dyslipidaemia, among the most influential complications concerning well-being [32,36].

These data can be seen in our results, where their presence significantly affects almost all of the components or scales analysed in the SF-36, confirmed in recent studies such as the one carried out by Domínguez et al. [22]. As described by Yeboah et al. [37], we understand that diabetic patients who have asymptomatic arterial disease are unaware of the evolution and sometimes the presence of this condition.

According to our results, when analysing the dimensions of the SF-36, the presence of vascular symptomatology causes significant differences in previously unaffected HRQL scales, such as “vitality”, “general health” and “mental health”. Moreover, it is interesting that, in this case, when we analysed the data by gender differentiation, it was the only time that women had better results than men, in parameters such as “vitality” or “mental health”. This phenomenon is supported by authors such as Kacerovsky et al. [38], who explained it via the relationship of vascular disorders and the development of erectile dysfunction and the impact this had on the perception of vitality among their male study group.

In our work, we have not obtained statistically significant results that allow us to accept that there is a direct relationship between the presence of neuropathy and changes in the different levels of well-being. However, studies with a larger sample have established associations between the two variables.

According to Venkataraman et al. [36], it is the only complication in which the impact of the mental component is greater than the physical component, and in more severe conditions, the two will be equalised. This results in a greater impact on all of the scales of the HRQL study. Thus, for example, with the onset of neuropathic pain or loss of proprioceptive sensitivity, there would be a decrease in the physical assessment [39], as we observed in our descriptive study when comparing the groups according to gender.

Despite this, we found no evidence to study possible differences between men and women in relation to peripheral neuropathy, so we cannot cross-check the data obtained.

The lack of such studies may be due to the different proportion of men and women with neuropathy. Men are more frequently affected by this complication. In our sample, half of the male group had neuropathy and only 20% of the female group did.

Diabetic foot is a devastating complication of DM because of its progression to amputation, as well as the emotional consequences for the individual [40].

In our analyses, we have seen a greater impact of the presence of ulcerations on the physical role, especially in women, where a range of up to 62 points was described.

Although we have not obtained statistically significant results, we can support this on the evidence reviewed [41,42].

However, Katherine et al. [43] report that a significant impact of ulcers will not be observed unless the injury is complicated or has resulted in the hospitalisation of the patient.

Although there is very little literature on the possible relationships between diabetic foot and HRQL from a gender perspective, we did find authors who observed, as we do, that the proportion of men with this complication is significantly higher than that of women [44,45].

Descriptively, the SF-36 “physical role” dimension was slightly higher in women, but, in the presence of positive neuropathy, the values in the female group fell substantially. The influence of the ulcer variable on the HRQL dimensions was not representative in this study, but this relationship did vary by gender.

Thus, it is possible to detect that in the “physical role” dimension, women lowered their median from 80 to 20 when they were affected by foot ulcers, while men did not perceive the same tendency, possibly because they had asymptomatic lesions (co-existence with neuropathy).

In addition, the strong interaction that we have detected in the “physical role” dimension by adding the gender variable in the study of diabetic foot and HRQL may serve as an antecedent for further research on this topic. It is curious that men even increase the values in this dimension, a phenomenon that may be justified by the absence of nociception (among them, there is a higher frequency of neuropathy). By not feeling pain, the male group ignores the seriousness of the situation so that the drop in levels of well-being that the female group shows will not be observed.

To improve the quality of life and adherence to treatment in people with diabetes, physical and physiological aspects should be considered. Psychological support could be necessary, especially to older women affected. Moreover, preventive programmes must be implemented according to gender, as emotional imbalance may influence the management and progression of the disease. In addition, if adequate health education is promoted, between 49% and 85% of foot complications can be potentially avoided.

Further studies are needed to focus on this topic.

### *Limitations*

The small sample and the disproportion of genders limit the validity of the study’s scientific outputs, and the impossibility of randomising the sampling condition thus affects the representativeness.

The podiatry service not being incorporated into the public system, while constituting a sociocultural and economic bias due to the accessibility of the patients to the unit, is a limitation in obtaining a larger number of subjects and a more homogeneous sample. Moreover, the Podiatry Clinical Area of the University of Seville is an independent health unit only for the prevention and management of diabetic foot without any connection with general, internal or endocrinology services, so only participants with lower limb problems voluntarily pay the fees.

In addition, in order to obtain the minimum sample size, it was decided not to exclude patients with additional comorbidities to those studied, such as cardiovascular accidents, amputations, obesity and dyslipidaemia, which may act as extraneous variables.

The use of a generic questionnaire such as the SF-36 was considered more appropriate. In order to explore this issue in greater depth, it would be advisable to use specific questionnaires for DM and the use of specific measures to investigate from a gender perspective.

Furthermore, whenever a questionnaire is administered, there are instances of social desirability bias. To control for this, extreme values that were considered contradictory were excluded.

## **5. Conclusions**

Despite the fact that the physical parameters of diabetic patients are similar according to the complications that they present, the adult women in our environment have



lower levels of quality of life than men in most cases. This may be related not only to pathophysiological differences but also to sociocultural factors.

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