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Health-related quality of life in diabetic patients with diabetic retinopathy

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Abstract

Introduction: *Diabetic retinopathy (DR) is a major cause of blindness, so the impact on health related quality of life (HRQL) is fundamental to assess the complete burden of this pathology. The present study has the aim of: a) assessing HRQL in diabetic patients with diabetic retinopathy through the administration of the SF-12 questionnaire; b)evaluating what is the impact of the associated treatments on the HRQL.*
Methods: *The study was an observational study carried out using a cross-sectional design in 2017.The patients were recruited in the cities of Rome and Palermo in outpatients ambulatories of Diabetology and Ophthalmology. The SF-12 questionnaire was administered to calculate two main indicators of HRQL, i.e., Physical composite score (PCS) and Mental composite score (MCS).*
Results: *137 diabetic patients entered the study, 65% males, 65.7% married or cohabitant. The educational level was generally low (37.2% with elementary school. The vast majority were patients with type 2 diabetes mellitus, with a median duration of the pathology of ten years. 27.7% of the diabetic patients had a retinopathy. Those patients with Diabetic macular edema (DME) (38) were treated with Dexamethasone implant (39.5%), Ranibizumab (28.9%), Aflibercept(7.9%), laser (15.8%). Concerning the MCS and PCS, respectively, the highest scores are present among males ($p = 0.009$ and $p = 0.007$) and highly educated patients ($p = 0.025$ and $p = 0.023$). No association was found between retinopathy and HRQL scores, both for MCS ($p = 0.759$) and PCS ($p = 0.120$), even if the highest scores are for patients without retinopathy (43.4 for MCS and 42.1 for PCS). Limiting the analysis to patients with DME only, MCS score was found higher in patients treated with Laser and Dexamethasone implant, and lower for patients treated with Aflibercepy. However, only patients treated with Dexamethasone implant these results are statistically significant (Beta= 6.685; $p = 0.039$).*
Conclusion: *This study confirmed that lowest HRQL scores are among patients with retinopathy. Moreover, diabetic patients as a whole showed lowest HRQL scores if compared to the general Italian population. Our results shows the longer the diabetes the best the HRQL for the MCS score and the worst the PCS scores. Finally, patients with DR treated for retinopathy had highest MCS score if treated with laser and Dexamethasone implant, but only for Dexamethasone implant the results are statistically significant., while no association was found between type of treatment for retinopathy and PCS scores.*

Keywords: *Health related quality of life, diabetes, diabetic retinopathy.*

Introduction

Diabetic retinopathy (DR) is a major cause of blindness, so the impact on health related quality of life (HRQL) is fundamental to assess the complete burden of this pathology.

The impact of diabetic retinopathy on HRQL has been assessed by several studies. A review conducted by Sharma and coll. demonstrated both a qualitative and a quantitative reduction in HRQL in persons with diabetic retinopathy [1].

Diabetic's QoL becomes worse when complications start to develop or comorbidities coexist. Dominant amongst complications, in HRQoL lowering, but not related to risk factors (genetic, the weight of birth, or others) is coronary arterial disease followed by renal failure, blindness, and the combination of micro- and macro-vascular complications and in some studies by sexual dysfunction [2].

Generally speaking, the longer the diabetes the worse the HRQL [3]. Moreover, the presence of any of the four major diabetic complications, i.e cardiovascular disease, stroke, end-stage renal disease (ESRD) and sight-threatening diabetic retinopathy (STDR), is usually associated with lower HRQoL [4].

Quality of life was significantly lower in diabetics with DR when compared with those without DR with maximum effect seen on general health, general vision and mental health. Quality of life decreased as the duration of retinopathy and severity of retinopathy increased [5].

Trento et al. demonstrated that diabetic retinopathy and vision loss modify the way people perceive their own ability to function autonomously [6].

There is evidence that visual acuity and the vision related quality of life of the patients with diabetic retinopathy improved significantly after cataract surgery [7].

Moreover, there is evidence that in general, HRQL has been improved following interventions for Diabetic Retinopathy [8].

Since the scientific literature in Italy on this issue is scarce, the present study has the aim of :

a) assessing HRQL in diabetic patients with diabetic retinopathy through the administration of the SF-12 questionnaire;
b) evaluating what is the impact of the associated treatments on the HRQL.

Materials and Methods

Setting and populations

The study was an observational study carried out using a cross-sectional design in 2017.

The patients were recruited in the cities of Rome and Palermo in outpatients ambulatories of Diabetology and Ophthalmology.

Diabetic patients with and without retinopathy entered the study.

The sample populations were comprised of three different groups:

a) Diabetic patients with retinopathy before the starting of any treatment for the ocular disease;
b) Diabetic patients with retinopathy after the starting of any treatment for the ocular disease;
c) Diabetic patients without retinopathy.

The questionnaire

To all participants, the following data were collected:

- Socio-demographic data (age, gender, civil status, educational level);
- Clinical data (type of diabetes, years of disease, presence of retinopathy, type of treatment for the diabetic retinopathy);
- Measurement of the HRQL, using the Italian version of the SF-12 questionnaire.

The administration of the SF-12 questionnaire allowed us to calculate two main indicators of HRQL, that are:

- Physical composite score (PCS);
- Mental composite score (MCS).

Statistical analysis

The statistical analysis was carried out using the SPSS statistical software, release 23.0. Frequency tables with absolute numbers and percentages were calculated. Differences between groups were tested using the chi^2 test for categorical variables and Mann-Withney and Kruskal-Wallis tests for quantitative variables. A bivariate analysis was carried out for the quantitative variables (age, years of diabetes, PCS and MCS). In this case a Pearson correlation coefficient was calculated.

A linear regression analysis was finally conducted using PCS and MCS scores as dependent variables. The results are shown as beta coefficients. The goodness of fit was assessed using the R^2. The statistical significance was set at $p< 0.05$.

Results

In **table 1** the characteristics of the patients are shown. 137 diabetic patients entered the study, 65% males, 65.7% married or cohabitant. The educational level was generally low (37.2% with elementary school and 20.4% with junior high school). The vast majority were patients with type 2 diabetes mellitus, with a median duration of the pathology of ten years. 27.7% of the diabetic patients had a retinopathy.

The most frequent comorbidities were hypertension (41.6%) and hyperlipidemia (40.1%). Those patients with Diabetic macular edema (DME) (38) were treated with Dexamethasone implant (39.5%), Ranibizumab (28.9%), Aflibercept(7.9%), laser (15.8%), while 21.1% received no treatment. These treatments have been used according to the summary of product characteristics

Table 1 – Characteristics of the diabetic patients

Variable	n (%) or median (range)
Age (Median)	65 (42 - 87)
Gender	
Females	48 (35)
Males	89 (65)
Civil Status	
Married/Cohabitant	90 (65.7)
Divorced	25 (18.2)
Widowed	10 (7.3)
Single	12 (8.8)
Educational Level	
Elementary	51 (37.2)
Junior High School	38 (20.4)
Senior High School	28 (20.4)
University	20 (14.6)
Type Of Diabetes	
Type 1	4 (2.9)
Type 2	133 (97.1)
Years Of Diabetes (Median. Range)	10 (1 – 50)
Retinopathy	
Yes-	38 (27.7)
No	99 (72.3)
Other Pathologies	
Hypertension	57 (41.6)
Hyperlipidemia	55 (40.1)
Obesity	36 (26.3)
Type Of Treatment For Diabetic Macular Edema	
None	8 (21.1)
Laser	6(15.8)
Dexamethasone Implant	15 (39.5)
Ranibizumab	11 (28.9)
Aflibercept	3 (7.9)
Pegaptanib Sodium	0 (0)

In **table 2** the univariate and bivaiate analyses are shown. Concerning the first score, there is an association between MCS and gender as well as educational level. The highest scores are present among males (p = 0.009) and highly educated patients (47.8 for patients with junior high school and 44.7 for patients with a degree, p = 0.025).

The same pattern is shown as far as concerns PCS, with the highest scores among males (p = 0.007) and patients with a university degree (p = 0.023). there is no association between retinopathy and health-related quality of life scores, both for MCS (p = 0.759) and PCS (p = 0.120), even if the highest scores are for patients without retinopathy (43.4 for MCS and 42.1 for PCS).

In relation to the bivariate analysis, no correlation was found between age and years of diabetes with the health-related quality of life scores.

Considering the treatment for retinopathy, no association was found with MCS (p = 0.189) and PCS (p = 0.489). In the first case the highest score for the pharmacological treatment was found for the patients treated with Dexamethasone implant (MCS = 42.8), while for PCS the highest score was for diabetic patients treated with Aflibercept (median = 45.1).

Table 2 – Results of the univariate and bivariate analyses: Dependent variables PCS and MCS

Variable	MCS	p	PCS	P
Age *	0.012	0.894	-0.136	0.116
Gender				
Females	39.0 (18.1 – 62.5)	0.009	37.2 (18.5- 59.3)	0.007
Males	46.2 (13.9 – 61.4)		42.8 (18.1 – 65.2)	
Civil Status				
Married/Cohabitant	41.4 (18-9 – 62.5)		40.0 (18.1 – 65.2)	
Divorced	40.8 (18.1 – 61.4)	0.272	47.1 (25.4 – 58.8)	0.396
Widowed	51.4 (27.6 – 61.2)		45.0 (26 – 53.8)	
Single	46.2 (13.9 – 56.7)		41.2 (20.2 - 57)	
Educational Level				
Elementary	40 (18.1 – 53.8)		39.1 (23 - 57)	
Junior High School	39.3 (13.9 – 61.2)	0.025	39 (18.1 – 65.2)	0.023
Senior High School	47.8 (18.9 – 62.5)		42.4 (25.8 – 55.6)	
University	44.7 (26.1 – 57.9)		49.9 (20.2 -59)	
Type of diabetes				
Type 1	45.5 (26.5 – 54.5)	0.744	42.7 (32.3 50.5)	0.958
Type 2	42.4 (13.9 – 62 .5)		41.1 (18.1 – 65.2)	
Years of diabetes *	0.039	0.658	-0.019	0.825
Retinopathy				
Yes	40.4 (18.1 – 61.4)	0.759	39.4 (18.1 – 55.1)	0.120
No	43.4 (13.9 – 62.5)		42.1 (18.5 – 65.2)	
Other Pathologies				
Hypertension	43.6 (18.9 – 61.4)	0.369	39.9 (18.5 – 57.1)	0.369
Hyperlipidemia	40.3 (18.9 – 61.2)	0.304	38.8 (20.8 – 57.1)	0.098
Obesity	44.4 (19.8 – 57.8)	0.591	45.4 (18.5 – 58.8)	0.366
Type of treatment for diabetic retinopathy				
None	48.9 (35 – 51.9)		34.3 (31.9 – 46.9)	
Laser	51.4 (36.8 – 61.4)	0.189	47.6 (37.6 – 48.3)	0.489
Dexamethasone implant	42.8 (28.7 – 55.8)		38.3 (25.8 – 55.1)	
Ranibizumab	36.7 (19.8 – 56.1)		39 (18.1 – 46.3)	
Aflibercept	36.1 (26.5 – 38.8)		45.1 (34.5 – 46.3)	

*correlation coefficient

In **table 3** the results of the multivariate analyses are shown. As far as concerns MCS, the mental score is significantly influenced by gender (lower score for females: Beta=-3.935; p = 0.047) and educational level (highest score for higher education Beta= 5-165; p = 0.012). On the other hand, in relation to PCS, a similar pattern is shown.

The physical score is influenced by gender (lower score for females: Beta=-4.515; p = 0.047) and educational level (highest score for higher education Beta= 3.964; p = 0.072). In both models, diabetic patients with retinopathy have lower MCS and PCS scores, but these differences are not statistically significant.

Table 3 – Results of the multivariate analyses: Dependent variables PCS and MCS

Variable	MCS Beta	p	PCS Beta	p
Age	0.122	0.255	0.010	0.936
Gender				
Females	-3.935	0.047	-4.515	0.035
Civil status				
Married/cohabitant	-0.593	0.764	-2.305	0.301
Educational Level				
Senior High School/University	5.165	0.012	3.964	0.072
Type Of Diabetes				
Type 2	-2.179	0.686	-2.562	0.673
Years of diabetes (median)	0.033	0.812	0.041	0.793
Retinopathy				
Yes	-1.644	0.537	-3.044	0.305
Other Pathologies				
Hypertension	1.792	0.365	-1.086	0.610
Hyperlipidemia	-2.566	0.189	-2.933	0.164
Obesity	-0.060	0.979	0.712	0.769

Limiting the analysis to patients with retinopathy only (**Table 4**), and taking patients treated with Ranibizumab as a reference, MCS score was found higher in patients treated with Laser and Dexamethasone implant, and lower for patients treated with Aflibercepy. However, only patients treated with Dexamethasone implant these results are statistically significant (Beta= 6.685; p = 0.039).

On the other hand, for the PCS, the physical score is higher in patients treated with Laser, Dexamethasone implant and Aflibercepy, but these differences are not significant.

Table 4 - Results of the multivariate analyses including only patients with retinopathy: Dependent variables PCS and MCS

Variable	MCS Beta*	p	PCS Beta*	p
Type of treatment				
Ranibizumab (reference)				
Laser	11.054	0.059	5.810	0.340
Dexamethasone implant	6.668	0.039	0.613	0.847
Aflibercepy	-4.552	0.439	6.110	0.289

*Linear regression analysis adjusted for age, gender, years of diabetes, educational level, civil status

Discussion

This study took in consideration almost 140 patients with diabetes mellitus, and one fourth of them had a DME. As far as we know, this is the first study conducted in Italy that measured the HRQL in patients with DR.

As seen in previous studies [1,9,10], we found lowest HRQL scores among patients with retinopathy, even if in a non-significant way. The diabetic patients as a whole showed lowest HRQL scores if compared to the general Italian population [11].

Our results are partially in contrast with those of Schanner and coll [3], concerning the correlation between the duration of the diabetes and the HRQL scores. In our sample the longer the diabetes the best the HRQL for the MCS score and the longer the diabetes the worst the PCS scores.

The study also shows that patients with DR treated for retinopathy had highest MCS score if treated with laser and Dexamethasone implant, but only for Dexamethasone implant the results are statistically significant.

No association was found between type of treatment for retinopathy and PCS scores.

The present study suffers from some limitations. First of all this is a cross-sectional study and the association between the variables investigated and HRQL scores was checked only once. Moreover, some of the variables taken into consideration were self-reported by the patients and there was no possibility for checking for completeness and correctness. In future studies, it will be wise to collect data prospectively in order to see differences in time of the HRQL scores in patients with DR, both for all patients and for patients treated with different type of drugs.

In terms of strengths of the study, the sample was drawn from two Italian regions. Moreover, multivariate analyses were performed so that the results were adjusted for possible confounders.

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