Original article

Quality of Life Assessment in Type 2 Diabetes Patients With Cardiovascular and/or Diabetic Complications

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Abstract

Introduction: Type 2 diabetes mellitus is a chronic disease that is causing enormous economic and social costs. It is characterized by many microvascular and macrovascular complications, such as heart attack, stroke, retinopathy, nephropathy, neuropathy, etc. Such complications can cause severe limitations and decrease the quality of life. The objective of this study was to assess the effect of type 2 diabetes mellitus on the quality of life using the EQ-5D-5L questionnaire, taking into account cardiovascular complications (heart attack, hospitalization due to angina pectoris, stroke, hospitalization due to heart insufficiency, transient ischemic attack, coronary revascularisation), complications of diabetes (microalbuminuria, renal failure, retinopathy, and neuropathy), and demographic characteristics (age, gender, body mass index, height, and weight).
Materials and Methods: This cross-sectional study included 484 participants with type 2 diabetes mellitus. Quality of life was estimated by the EuroQol instrument EQ-5D-5L and visual analogue scale (VAS). The following complications related to type 2 diabetes were taken into account: heart attack, hospitalization due to angina pectoris, stroke, hospitalization due to heart insufficiency, transient ischemic attack, coronary revascularization, microalbuminuria, renal insufficiency, retinopathy, and neuropathy.
Results: The mean value of the EQ index was 0.895, with the value of -0.59 as the lowest, and 1.0 as the highest quality of life of the study patients. Multivariate linear regression model showed that heart attack, hospitalization due to unstable angina pectoris, retinopathy, and neuropathy significantly decreased the quality of life of the study participants ($p<0.05$). Spearman's correlation showed that there was a significant correlation between age, height, duration of type 2 diabetes, body mass index, and the EQ index ($p<0.001$).
Conclusion: The results suggest that type 2 diabetes complications, such as heart attack, neuropathy, retinopathy, and hospitalization due to unstable angina pectoris significantly decrease the quality of life of type 2 diabetes mellitus patients (T2DM).

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Introduction

There are two types of methods that can be used for measuring health utilities: direct and indirect. So far, several direct methods have been developed, such as: 1) standard gamble: reflects the assessment of an individual's preference or valuation of their current QoL by quantifying tolerance to risk toward an ultimate bad outcome as a gamble for achieving a perfect state of health (1); 2) time trade-off: individuals are asked to choose between living in their current impaired health state for 10 years or living for a shorter period with perfect health (2); and 3) visual analogue scale: introspective scaling with a rating scale from 0 to 100, where a patient has to choose one number on this scale that correctly reflects his/her quality of life (3). On the other hand, there are many indirect methods which have already been validated, and they can be generic (e.g. the EQ-5D questionnaire) or specific for certain diseases (e.g. FACT-G). Indirect methods do not give immediate values for health utilities; rather, an algorithm must be developed for a transformation of answers to utility values (3).

T2DM is recognized as one of the most common diseases worldwide, which affects every country and different groups of people, regardless of the demographic and socio-economic status (4). Microvascular and macrovascular complications are almost inevitable during the course of the disease. The most common microvascular complications are diabetic nephropathy, neuropathy, and retinopathy, while the most common macrovascular complications are peripheral vascular disease, myocardial infarction, stroke, and congestive heart failure (5). Quality of life assessment in patients with T2DM is important for the development of progressive simulation models used for a long-term assessment of the cost and effectiveness of interventions for the treatment of type 2 diabetes and prevention of accompanying complications. Assessing the utility is the main prerequisite for determining the QALY and it is very important to include participants with a full spectrum of characteristics and health complications (retinopathy, neuropathy, nephropathy, etc.) (6). Zhang et al. conducted a study in the United States of America (USA) on 7327 participants with T2DM. The average EQ index (utility) in this study was 0.80. They concluded that participants without complications of type 2 diabetes, cardiovascular risk factors, and other comorbidities, who were not obese and who had an average income of over USD 40,000, had a better average EQ index, reaching 0.92 (7). Arifin et al. also concluded that T2DM patients with macro/microvascular complications have a lower QoL (0.77-0.79) than those without such complications (0.80). Also, if they have more than two complications, their QoL is even lower (0.74) (8). Pham et al. showed on 214 T2DM patients that those with diabetic retinopathy have a lower QoL (0.92) compared to those who have diabetic heart disease (0.94) or nephropathy (0.93) (9). A study in Japan showed that T2DM patients with more serious microvascular complications have a lower QoL compared to those who have one or no complications. Patients with proliferative retinopathy had a QoL of 0.85, while those with pre-proliferative retinopathy had a better quality of life (0.93). Also, those suffering from stage four nephropathy had a QoL of 0.78, while the QoL of those suffering from stage one nephropathy was as high as as 0.93 (10). There are also other studies showing that patients with complications of type 2 diabetes not only live shorter, but their quality of life is also lower (11,12). However, there is a paucity of studies using the EQ-5D-5L questionnaire for a quality of life assessment in T2DM patients, and their quality estimates vary within a broad range from 0.74 to 0.92 (13-17). EQ-5D-5L questionnaire is a relatively new preference-based instrument with lower ceiling effects and a better sensitivity compared to the EQ-5D-3L. Those two questionnaires are most commonly used in clinical and outcomes research (18).

The aim of this study was to assess the effect of type 2 diabetes mellitus on the quality of life using the EQ-5D-5L questionnaire, taking into account cardiovascular complications (heart attack, hospitalization due to angina pectoris, stroke, hospitalization due to heart insufficiency, transient ischemic attack, and coronary

revascularisation), complications of diabetes (microalbuminuria, renal insufficiency, retinopathy, and neuropathy) and demographic characteristics (age, gender, body mass index, height, weight, smoking status, duration of diabetes, and education level).

Materials and Methods

Study population

This was a cross-sectional study, approved by the Ethics Committee of the Public Institution Health Center of Sarajevo Canton, which included 509 patients from Bosnia and Herzegovina. Between December 2019 and June 2020, 361 patients in total were interviewed in person, while 148 patients were interviewed online. Interviews in person were conducted at several health centers in Sarajevo, such as the Vrazova, Omer Maslić, and Kumrovec Health Center, (urban areas) and Ilijaš Health Centre (rural areas). After reviewing the answers, 484 participants were eligible for the final analysis, while 25 were excluded due to incompleteness. Criteria for inclusion in the study were: diagnosis of T2DM in the patient file, age >18 years, and signed informed consent for participation in the study. Criteria for non-inclusion or exclusion from the study were: persons under the age of 18, not signing the informed consent, pregnancy and/or a diagnosis of a major psychiatric disorder in the patient file.

Questionnaire

In order to collect the patient information, a tripartite questionnaire was used, assessing the demographic/socio-economic characteristics (age, gender, height, weight, education level, duration of type 2 diabetes, and smoking status), quality of life by the EQ-5D-5L questionnaire and by the visual analogue scale (VAS), and cardiovascular and diabetic complications.

The following events were taken into account, reflecting the complications of type 2 diabetes: heart attack, hospitalization because of unstable angina pectoris, stroke, hospitalization because of heart failure, transient ischemic attack, repeated coronary revascularization, microalbuminuria, renal insufficiency, neuropathy, and retinopathy.

EQ-5D-5L questionnaire

The EQ-5D-5L is a generic (19-23) questionnaire validated for the assessment of the quality of life of individuals with various health conditions. It assesses five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is ranked at five levels: no problems – 1, slight problems – 2, moderate problems – 3, severe problems – 4, and extreme problems – 5. After filling in the questionnaire, depending on the patients' answers, the five dimensions are combined in a five-digit number that describes the patient's health state. The five-digit code is further converted to an EQ index using an automatic calculator (24) and the results from our study were checked using the guidelines from a validation study conducted in Poland (25). Since there was no local set of values that had been validated, Poland was selected due to its cultural similarity with Bosnia and Herzegovina. The EQ index ranged between -0.59 (the lowest QoL) and 1 (the highest QoL). The EQ-VAS scale was used together with the EQ-5D-5L questionnaire (26).

A validated Croatian version of EQ-5D-5L was used in our study, since the official language of Bosnia and Herzegovina is the Bosnian/Croatian/Serbian (BHS) language. A laptop/desktop version of the questionnaire was obtained from EuroQol.

Statistical analysis

The results were described by frequencies and proportions for categorical values, and by the arithmetic mean and standard deviation for continuous values (or by the median with interquartile range, if the data were not normally distributed). Normality of data distribution was tested by the Shapiro Wilk and Kolmogorov-Smirnov tests. Nonparametric tests, such as the Mann-Whitney U test, the Kruskal-Wallis test, and non-parametric ANOVA, were used for comparison of the study groups. Impact of health complications, demographic

characteristics, and health state were assessed by a multivariate linear regression model after confirming that the following assumptions were satisfied: linear relationship, independence, homoscedasticity and normality (27). Results with $\alpha \leq 0.05$ or within the 95% confidence interval were considered statistically significant. SPSS for Windows (version 21.0, SPSS Inc, Chicago, Illinois, USA) and Microsoft Excel (version 11.0, Microsoft Corporation, Redmond, WA, USA) were used for statistical analysis.

Results

The final analysis included 484 participants (28.7% men and 71.3% women). Mean duration of T2DM was 8.18 ± 7.08 years and the majority of participants were taking only oral antidiabetic drugs (55.8%) or oral drugs in combination with subcutaneous medication (41.7%). Other demographic characteristics of the study participants are shown in Table 1. More detailed results are shown in Supplement 1.

Table 1. Main demographic/socioeconomic characteristics of study participants (n=484).

Characteristic	Minimum	Maximum	Mean	Median	Std. deviation
Age (years)	20	92	52.68	53	12.11
Body weight (kg)	47	186	89.00	88	18.27
Height (m)	1.45	2.00	1.70	1.69	0.08
Duration of type 2 diabetes (years)	0.02	40	8.18	6.00	7.08
Body Mass Index (BMI) (kg/m²)	18.36	55.54	30.70	30.12	5.68

Characteristic	n (%)
Men	139 (28.7)
Women	345 (71.3)
Education level	
Primary school	17 (3.5)
High school education	275 (56.8)
Associate degree	61 (12.6)
Bachelor's degree	124 (25.6)
Master's/doctor's degree	7 (1.4)
Smoking status	
Yes, active smoker	188 (38.8)
No, never smoked	153 (31.6)
No, stopped smoking	143 (29.5)
Type of therapy	
Oral	270 (55.8)
Oral + subcutaneous	202 (41.7)
Subcutaneous	12 (2.5)

The majority of participants did not have problems with mobility (61%), but 1% of them had extreme problems. Also, most of them did not have problems with self-care (79.5%) and usual activities (62.8%). On the other hand, a high percentage of participants had slight or moderate problems with pain/discomfort and anxiety/depression. More details about the participants' answers are shown in Table 2..

Table 2. Distribution of the EUROQOL 5D-5L answers given by study participants (n=484) according to five dimensions of this questionnaire

	No problems	Slight problems	Moderate problems	Severe problems	Extreme problems
Mobility	295 (61%)	76 (15.7%)	85 (17.6%)	23 (4.8%)	5 (1%)
Self-care	385 (79.5%)	45 (9.3%)	42 (8.7%)	8 (1.7%)	4 (0.8%)
Usual activities	304 (62.8%)	86 (17.8%)	73 (15.1%)	15 (3.1%)	6 (1.2%)
Pain/discomfort	214 (44.2%)	141 (29.1%)	100 (20.7%)	25 (5.2%)	4 (0.8%)
Anxiety/depression	201 (41.5%)	137 (28.3%)	109 (22.5%)	31 (6.4%)	6 (1.2%)

Using the EQ-VAS scale, the participants indicated how they felt at the moment of the interview. The minimum value was 5 and maximum was 100, with 70.40 (SD 20.49) points as the average value. The lowest EQ index was -0.59 and the highest one was 1.0, with 0.895 (SD 0.183) on average (Table 3).

Table 3. Scores on EQ VAS scale and EQ index of study participants (n=484)

	Minimum	Maximum	Mean	Median	Std. deviation	Kolmogorov-Smirnov
EQ VAS scale	5	100	70.40	75	20.49	p = 0.000
EQ INDEX	-0.59	1.00	0.895	0.952	0.183	p = 0.000

Most of the participants did not have any cardiovascular/diabetic complications (46.90%) or had just one (23.97%). The most common complications were neuropathy (31.4%) and retinopathy (28.9%), while microalbuminuria (2.7%) and stroke (3.1%) were the rarest. The most common events occurring due to cardiovascular complications were hospitalization due to unstable angina pectoris (8.3%) or heart attack (8.1%). Renal failure was reported in 9.1% of the cases. More details can be seen in Supplements 2 and 3.

Spearman's correlation showed that there was a significant correlation between age, height, duration of type 2 diabetes and BMI ($p<0.001$) with the EQ index. There was a negative correlation between BMI, age and duration of type 2 diabetes and the EQ index (Table 4).

Table 4. Correlation between demographic characteristics and EQ index of study participants (n=484)

	Spearman's correlation coefficient	p*
Height	0.223	0.000
Body weight	0.019	0.675
BMI	-0.106	0.000
Age	-0.254	0.000
Duration of type 2 diabetes	-0.228	0.000

We analysed whether gender (Mann-Whitney U test) and level of education/smoking status (Kruskal-Wallis test) influenced the EQ index values. The results showed a significant influence of gender (U=19526.500, p=0.001) and level of education (Kruskal-Wallis H 9.949,

p=0.041) on the EQ index. Smoking status did not affect the quality of life (Kruskal-Wallis H 1.082, p=0.582).

Multivariate linear regression was used to determine the effects of study variables on the quality of life. The EQ index was appointed as a dependent variable, and gender, age, level of education, weight, height, BMI, duration of type 2 diabetes, and cardiovascular/diabetic complications were used as independent variables in the analysis. Results showed that four complications – neuropathy, heart attack, stroke, and hospitalization because of unstable angina pectoris – had the greatest impact on the quality of life. These four dependent variables explained 49.3% of model variance (R=0.493, F=34.550, p=4.98*10-25) (Table 5).

Table 5. Effects of certain diabetic complications on the QoL of study participants (n=484): results of multivariate linear regression

Model	B	Sig.	95% confidence interval for B	
			Lower bound	Upper bound
Neuropathy	0.675	0.000	0.610	0.739
Neuropathy	0.115	0.000	0.079	0.150
Heart attack	0.178	0.000	0.119	0.237
Neuropathy	0.103	0.000	0.069	0.138
Heart attack	0.174	0.000	0.117	0.230
Stroke	0.263	0.000	0.176	0.350
Neuropathy	0.097	0.000	0.062	0.944
Heart attack	0.142	0.000	0.080	0.807
Stroke	0.249	0.000	0.162	0.970
Unstable angina	0.081	0.017	0.147	0.776

Discussion

This cross-sectional study conducted in Bosnia and Herzegovina investigated the association between type 2 diabetes, its complications and the QoL using the EQ-5D-5L questionnaire. EQ-5D-5L is an easy-to-understand and validated generic questionnaire for a QoL assessment (28). BMI, age, and duration of T2DM showed a negative correlation with the QoL, meaning that older patients, with a higher BMI and longer duration of illness had a lower QoL. The results also showed that most of the participants did not have problems with mobility or self-care, but they had problems with pain/discomfort and anxiety/depression, which is similar to previous studies. Regarding T2DM patients, Luk et al. reported that more patients had problems with pain/discomfort (24.8%) and anxiety/depression (20.3%) than with other dimensions of the EQ-5D-5L questionnaire (29). In several other studies, it has been shown that pain/discomfort was the most affected domain in patients (30-32). Such results may be due to the fact that the most common T2DM complication was neuropathy, which may cause pain/discomfort. Also, T2DM can change mood and lower self-esteem, leading to anxiety and depression (33). A study by Parik and Patel showed that anxiety and depression have a stronger impact on younger T2DM patients (34). A CODE-2 study on 1,371 T2DM participants showed that anxiety and depression were increased at a younger age and

then decreased with age (35). Auslli et al. suggested that patients with T2DM should be advised carefully about the importance of foot care and exercise. They concluded that physical exercise is a very important determinant of positive clinical outcomes of T2DM and it is associated with better HbA1C levels, a lower BMI, fewer diabetic complications and a higher QoL (36).

Our results also showed that the QoL is dependent on gender, age, and education level, where females, older participants and those with a lower level of education had a lower QoL. Smoking status and weight did not have a significant impact on the QoL. A study in Korea showed that age is an important factor of the QoL of patients with T2DM and that younger participants had a better QoL, most likely because they had T2DM for a shorter period of time and fewer health-related complications (37). Stojanović et al. also showed that lower level of education was highly related to lower QoL. Possible mechanisms include insufficient access to healthcare services, unhealthy habits, poor mental health, and higher frequency of complications (38). A study in Denmark, involving 2419 patients with T2DM, showed that poor socioeconomic status, age, female gender, presence of comorbidity, poor glycemic control and lower level of education were associated with depressive episodes and lower QoL of T2DM participants (39). There have been many other studies showing that these factors are strong determinants of the QoL (37-50).

Most of the participants did not have any diabetic complications (46.90%). Among those who had some of the complications, the most common were neuropathy (31.4%) and retinopathy (28.9%), while microalbuminuria and stroke were the rarest. Data from the American Diabetes Association shows that 75-80% of adults with diagnosed DM will ultimately die from cardiovascular disease due to chronic macrovascular complications (41). Microvascular and macrovascular complications of T2DM put a great burden on every healthcare system, even in developed countries like the USA. However, this is not the only problem. Many studies have shown that patients with T2DM who have one or more diabetic complications also have a significantly lower QoL compared to those who do not have T2DM-related complications (42-46).

In our study, the values of the VAS scale varied from 5 to 100, with 70.40 as the average value. After converting the scores to the EQ index, the lowest value was -0.59 and the highest was 1.0., with 0.895 as the average value. According to Mlitt et al., a negative index is possible when researchers use the EQ-5D-5L questionnaire (40). It suggests that the health state of these participants is deemed to be worse than death. The VAS scale score can vary between different group of participants. A Norwegian study of T2DM patients showed a mean EQ index of 0.85 (51), while an Iranian study reported an even lower average value (0.70) (52).

A multivariate linear regression model based on our data showed that factors such as neuropathy, heart attack, stroke, and hospitalization due to angina pectoris are strong predictors of the QoL, which is a finding congruent with the results of previous studies analysing patients with diabetes type 2. A univariate and multivariate regression analysis by Stojanović et al. also showed that angina pectoris, heart failure, diabetic retinopathy, and diabetic nephropathy are factors that impact the QoL of T2DM patients the most (38). A study in China, which was conducted on 1,275 patients with T1DM, showed that the presence of any of the four major diabetic complications (heart disease, stroke, end-stage renal disease, sight-threatening diabetic retinopathy) have a significant impact on the QoL (48). The United Kingdom Prospective Diabetes Study showed that utilities are significantly reduced in T2DM patients who have serious complications, like end-stage renal disease, blindness, stroke or heart attack (50). There is a plethora of other studies showing that T2DM patients with complications have a decreased QoL compared to T2DM patients without such complications (12,49,51,53,54).

Our study has certain limitations. Firstly, the EQ-5D-5L questionnaire was not previously validated in Bosnia and Herzegovina. Therefore,

the transformation of raw scores to the EQ index had to be based on the results from another population that is as similar as possible to the Bosnian population in terms of culture (the Polish population), which still creates a certain potential for bias. Secondly, the sample used in the study was not ideally balanced in regard to frequency and severity of type 2 diabetes complications, which could have led to an overestimate of the EQ scores.

Conclusions

Our study gave an overview of average EQ index values in the population of diabetes type 2 patients from Bosnia and Herzegovina, and showed a prevailing influence of diabetic complications on the quality of life, which could be used for further pharmacoeconomic analyses. Demographic characteristics, such as the BMI, age and duration of T2DM were negatively correlated with the QoL, meaning that patients with a higher BMI, who are older and have suffered from the illness for a longer period of time, had a lower QoL. Neuropathy, heart attack, stroke, and hospitalization due to unstable angina had the greatest impact on the QoL in T2DM patients.

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References

1. Slaughter KB, Meyer EG, Bambhroliya AB, Meeks JR, Ahmed W, Bowry R, Behrouz R, Mir O, Begley C, Tyson JE, Miller C, Warach S, Grotta JC, McCullough LD, Savitz SI, S Vahidy FS. Direct assessment of health utilities using the standard gamble among patients with primary intracerebral hemorrhage. Circ Cardiovasc Qual Outcomes. 2019; 12(9):e005606.

2. Jervaeus A, Fritzell K, Lundh-Hagelin C, Vogelsang von AC. Does the time trade-off method reflect health-related quality of life? A mixed-methods analysis of preference measures 10 years after aneurysmal subarachnoid hemorrhage. World Neurosurg. 2019; 126:11-20.

3. Brauer CA, Rosen AB, Greenberg D, Neumann PJ. Trends in the measurement of health utilities in published cost-utility analyses. Value Health. 2006; 9(4): 213-18.

4. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of Diabetes 2017. J Diabetes Res. 2018; 11:3086167.

5. Doumas M, Imprialos K, Stavropoulos K, Athyros VG. Pharmacological management of type 2 diabetes complications. Curr Vasc Pharmacol. 2020; 18(2):101-103.

6. Kiadaliri AA, Gerdtham UG, Eliasson B, Gudbjornsdottir S, Svensson AM, Carlsson KS. Health utilities of type 2 diabetes-related complications: a cross-sectional study in Sweden. Int J Environ Res Public Health. 2014; 11(5):4939-52.

7. Zhang P, Brown MB, Bilik D, Ackermann RT, Li R, Herman W. Health utility scores for people with type 2 diabetes in U.S. managed care health plans. Diabetes Care. 2012; 35:2250-6.

8. Arifin B, Idrus LR, Asselt van ADI, Purba FD, Perwitasari DA Thobari JA, Cao Q, Krabbe PFM, Postma MJ. Health-related quality of life in Indonesian type 2 diabetes mellitus outpatients measured with the Bahasa version of EQ-5D. Qual Life Res. 2019; 28(5):1179-1190.

9. Pham TB, Nguyen TT, Truong HT, Trinh CH, Du HNT, Ngo TT, Nguyen LH. Effects of diabetic complications on health-related quality of life impairment in Vietnamese patients with type 2 diabetes. J Diabetes Res. 2020; 23:4360804.

10. Ishii H, Takamura H, Nishioka Y, Langer J, Watanabe M, Kim HR et al. Quality of Life and Utility Values for Cost-effectiveness Modeling in Japanese Patients with Type 2 Diabetes. Diabetes Ther. 2020; 11(12):2931-2943.

11. Grandy S, Fox KM. Change in health status (EQ-5D) over 5 years among individuals with and without type 2 diabetes mellitus in the SHIELD

longitudinal study. Health Qual Life Outcomes. 2012; 10:99.

11. Al-Shehri AH, Taha AZ, Bahnassy AA, Salah M. Health-related quality of life in type 2 diabetic patients. Ann Saudi Med. 2008; 28:352-60.

13. Takahara M, Katakami N, Shiraiwa T, Abe K, Ayame H, Ishimaru Y, Iwamoto M, Shimizu M, Tomonaga O, Yokoyama H, Matsuoka T-A, Shimomura I. Evaluation of health utility values for diabetic complications, treatment regimens, glycemic control and other subjective symptoms in diabetic patients using the EQ-5D-5L. Acta Diabetol. 2019; 56(3):309-19.

14. Jalkanen K, Aarnio E, Lavikainen P, Jauhonen HM, Enlund H, Martikainen J. Impact of type 2 diabetes treated with non-insulin medication and number of diabetes-coexisting diseases on EQ-5D-5L index scores in the Finnish population. Health Qual of Life Outcomes. 2019; 17(117):1-10.

15. Andayani TM, Endarti D. Health utility scores in patients with type 2 diabetes mellitus in Indonesia. Value Health. 2018; 21(2):40.

16. Mateo DC, Gordillo MAG, Olivares PR, Adsuar JC. Normative values of EQ-5D-5L for diabetes patients from Spain. Nutr Hosp. 2015; 32(4):1595-1602.

17. Pan CW, Sun HP, Zhou HJ, Ma Q, Xu Y, Luo N, Wang P. Valuing health-related quality of life in type 2 diabetes patients in China. Med Decis Making. 2015:1-8.

18. Gandhi M, Ang M, Teo K, Wong CW, Wei YCH, Tan RLY, Janssen MF, Luo N. EQ-5D-5L is More Responsive than EQ-5D-3L to treatment benefit of cataract surgery. Patient. 2019; 12(4): 383-392.

19. Nolan CM, Longworth L, Lord J, Canavan JL, Jones SE, Kon SSC, Man W D-C. The EQ-5D-5L health status questionnaire in COPD: validity, responsiveness and minimum important difference. Thorax. 2016; 71:493-500.

20. Cheung PWH, Wong CKH, Samartzis D, Luk KDK, Lam CLK, Cheung KMC, Cheung JPY. Psychometric validation of the EuroQol 5-dimension 5-level (EQ-5D-5L) in Chinese patients with adolescent idiopathic scoliosis. Scoliosis Spinal Disord. 2016; 11(19):1-12.

21. Golicki D, Niewada M, Buczek J, Karlinska A, Kobayashi A, Janssen MF, Pickard AS. Validity of the EQ-5D-5L in stroke patients. Qual Life Res. 2015 Apr;24(4):845-50. doi: 10.1007/s11136-014-0834-1.

22. Parik PC, Patel VJ. Health-related quality of life of patients with type 2 diabetes mellitus at a tertiary care hospital in India using EQ-5D-5L. Indian J Endocrinol Metab. 2019; 23(4):407-11.

23. Hernandez F, Garin O, Dima AL, Pont A, Pastor MM, Alonso J, Van Ganse E, Laforest L, de Bruin M, Mayoral K, Serra-Sutton V, Ferrer M, ASTRO-LAB Group. EuroQol (EQ-5D-5L) validity in assessing the quality of life in adults with asthma: cross-sectional study. J Med Internet Res. 2019; 21(1):e10178.

24. EQ-5D-5L online analysis. https://fragla.shinyapps.io/shiny-eq5d/. Accessed: 15 June 2020.

25. Golicki D, Jakubczyk M, Graczyk K, Niewada M. Valuation of EQ-5D-5L health states in Poland: the first EQ-VT-based study in Central and Eastern Europe. Pharmacoeconomics. 2019; 37(9):1165-1176.

26. EuroQol Office. EQ-5D-5L: all about. The Netherlands, Rotterdam. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/. Accessed: 20 June 2020.

27. Osborne J, Water E. Four assumptions of multiple regression that researchers should always test. Practical Assessment, Research & Evaluation. 2002; 8(2).

28. Janssen MF, Lubetkin EI, Sekhobo JP, Pickard AS. The use of the EQ-5D preference-based health status measure in adults with Type 2 diabetes mellitus. Diabet Med. 2011; 28:395-413.

29. Luk AOY, Zhang Y, Ko GTC, Brown N, Ozaki R, Tong PCY, Ma RCW, Tsang CC, Cheung Y, Kong APS, Chow CC, Chung H, Lau M, Cheung M, Wong R, Wolthers T, Lyubomirsky G, So W, Chan JCN, On behalf of the Joint Asia Diabetes Evaluation (JADE) Hong Kong Study Group. Health-related quality of life in Chinese patients with type 2 diabetes: an analysis of the joint Asia

diabetes evaluation (JADE) Program. J Diabetes Metab. 2014; 5: 333.

30. Cardoso AF, Cruz R, Queiros P, Santiago L, Ribeiro CF, Ferriera PL. Assessment of health-related quality of life using the EQ-5D-3L in individuals with type 2 diabetes mellitus. J Diabetes Metab Disord Control. 2016;3(2):33-40. DOI: 10.15406/jdmdc.2016.03.00064

31. Shim YT, Lee J, Toh MP, Tang WE, Ko Y. Health-related quality of life and glycaemic control in patients with type 2 diabetes mellitus in Singapore. Diabet Med. 2012; 29: e241-248.

32. Ekwunife OI, Ezenduka CC; Uzoma BE. Evaluation the sensitivity of EQ-5D in a sample of patients with type 2 diabetes mellitus in two tertiary health care facilities in Nigeria. BMC Res Notes. 2016; 9: 24-28.

33. Avila CC, Lima MG, Barros de MBA. Influence of Diabetes complications and limitations on health-related quality of life: a study in a southeastern Brazilian city. Qual Life Res. 2019; 29(2):473-482.

34. Parik PC, Patel VJ. Health-related quality of life in patients with type 2 diabetes mellitus at a tertiary care hospital in India using EQ-5D-5L. Indian J Endocrinol Metab. 2019; 23(4):407-11.

35. Redekop WK, Koopmnaschap MA, Stolk RP, Rutten GE, Wolffenbuttel BH, Niessen LW. Health-related quality of life and treatment satisfaction in Dutch patients with type 2 diabetes. Diabetes Care. 2002; 25:458-63.

36. Ausili D, Bulgheroni M, Ballatore P, Specchia C, Ajdini A, Bezze S, Di Mauro S, Genovese S. Self-care, quality of life and clinical outcomes of type 2 diabetes patients: an observational cross-sectional study. Acta Diabetol. 2017; 54(11):1001-1008.

37. Lee WJ, Song KH, Noh JH, Choi YJ, Jo MW. Health-related quality of life using the EuroQol 5D questionnaire in Korean patients with type 2 diabetes. J Korean Med Sci. 2012; 27(3):255-60.

38. Stojanović M, Cvetanović G, Anđelković-Apostolović M, Stojanović D, Rančić N. Impact of socio-demographic characteristics and long-term complications on quality of life in patients with diabetes mellitus. Cent Eur J Public Health. 2018; 26(2):104-110.

39. Joensen LE, Almdal TP, Willaing I. Type I diabetes and living without a partner: psychological and social aspects, self-management behaviour, and glycaemic control. Diabetes Res Clin Pract. 2013; 101(3):278-85.

40. Mlitt WDK, McCahon RA, Ravenscroft A, Hodgkinson V, Evley R, Hardman JG. Responsiveness of the EQ-5D Health-Related Quality-of-Life Instrument in Assessing Low Back Pain. Value Health. 2013; 16(1):124-132.

41. American Diabetes Association. Peripheral arterial disease in people with diabetes. Diabetes Care. 2003; 26(12):3333-41.

42. Alinia C, Mohammadi SF, Lashay A, Rashidian A. Impact of Diabetic Retinopathy on Health-related Quality of Life in Iranian Diabetics. Iran J Public Health. 2017; 46(1):55-65.

43. Ghanchi F and Diabetic Retinopathy Guidelines Working Group. The Royal College of Ophthalmologists' clinical guidelines for diabetic retinopathy: a summary. Eye (Lond.). 2013; 27(2):285-287.

44. Ratanasukon M, Tongsomboon J, Bhurayanontachai P, Jirarattanasopa P. The Impact of Vision Impairment (IVI) Questionnaire; Validation of the Thai-Version and Implementation on Vision-Related Quality of Life in Thai Rural Community. PloS One. 2016; 11(5): e0155509.

45. Sharma S, Oliver-Fernandez A, Liu W, Buchholz P, Walt J. The impact of diabetic retinopathy on health-related quality of life. Curr Opin Ophtalmol. 2005; 16(3):155-159.

46. Trento M, Durando O, Lavecchia S, Charrier L, Cavallo F, Angelo Costa M, Hernández C, Simó R, Porta M, EUROCONDOR trial investigators. Vision related quality of life in patients with type 2 diabetes in the EUROCONDOR trial. Endocrine. 2017; 57(1):83-88.

47. Georgia L, Ploubidis M, Foteli S, Kontou IP, Nikolaou C, Tentolouris N. Quality of life in subjects with type 2 diabetes mellitus with

diabetic retinopathy: a case-control study. Diabetes Metab Syndr. 2019; 13(2):947-952.

48. Jiao F, Wong CKH, Gangwani R, Tan KCB, Tang SCW, Lam CLK. Health-related quality of life and health preference of Chinese patients with diabetes mellitus managed in primary care and secondary care setting: decrements associated with individual complication and number of complications. Health Qual of Life Outcomes. 2017; 15(1):125.

49. Venkataraman K, Wee HL, Leow MKS, Tai ES, Lee J, Lim SC, Tavintharan S, Wong TY, Ma S, Heng D, Thumboo J. Associations between complications and health-related quality of life in individuals with diabetes. Clin Endocrinol (Oxf). 2013; 78(6): 865-873.

50. Clarke P, Gray A, Holman R. Estimating utility values for health states for type 2 diabetic patients using the EQ-5D (UKPDS 62). Med Decis Making. 2002; 22(4): 340-349.

51. Solli O, Stavem K, Kristiansen I. Health-related quality of life in diabetes: The associations of complication with EQ-5D scores. Health Qual Life Outcomes. 2010; 8:18. doi: 10.1186/1477-7525-8-18

52. Javanbakht M, Abolhasani F, Mashayekhi A, Baradaran HR, Jahanhirinoudeh Y. Health related quality of life in patients with type 2 diabetes mellitus in Iran: A national survey. PloS One. 2012; 7: e44526.

53. Khunkaew S, Fernandez R, Sim J. Demographic and clinical predictors of health-related quality of life among people with type 2 diabetes mellitus living in northern Thailand: a cross-sectional study. Health Qual of Life Outcomes. 2019; 17(1):177. doi: 10.1186/s12955-019-1246-2

54. Clarke PM, Hayes AJ, Glasziou PG, Scott R, Simes J, Keech AC. Using the EQ-5D Index Score as a Predictor of Outcomes in Patients With Type 2 Diabetes. Med Care. 2009; 47:61-68.

SUPPLEMENTS

Supplement 1. EQ Index mean values (n=484)

	Number of patients (n=484)	EQ Index: mean (SD)
Gender		
Male	139	0.894 (0.250)
Female	345	0.895 (0.148)
Age (years)		
18-25	7	0.940 (0.838)
26-35	32	0.926 (0.106)
36-45	101	0.934 (0.100)
46-55	151	0.914 (0.134)
56-65	115	0.888 (0.189)
66+	78	0.803 (0.304)
Education level		
Primary school	17	0.810 (0.181)
High school education	275	0.902 (0.165)
Associate degree	61	0.882 (0.234)
Bachelor's degree	124	0.925 (0.126)
Master's/doctor's degree	7	0.798 (0.216)
BMI (kg/m²)		
18-24.99	95	0.884 (0.257)
25-29.99	134	0.880 (0.216)
30-34.99	161	0.920 (0.115)
>35	94	0.885 (0.128)
Duration of diabetes (years)		
0.01-2.99	121	0.945 (0.077)
3.00-5.99	107	0.888 (0.186)
6.00-8.99	67	0.910 (0.121)
9.00-14.99	119	0.904 (0.107)
> 15	70	0.788 (0.349)
Smoking status		
Yes, active smoker	188	0.897 (0.175)
No, never smoked	153	0.890 (0.164)
No, stopped smoking	143	0.889 (0.214)

Supplement 2. Type 2 diabetes - related complications

Complication	n (%)
Heart attack	
Yes	39 (8.1)
No	445 (91.9)
Hospitalization due to unstable angina pectoris	
Yes	40 (8.3)
No	444 (91.7)
Stroke	
Yes	15 (3.1)
No	469 (96.9)
Hospitalization due to heart failure	
Yes	21 (4.3)
No	463 (95.7)
Transient ischemic attack	
Yes	27 (5.6)
No	457 (94.4)
Coronary revascularisation	
Yes	35 (7.2)
No	449 (92.8)
Microalbuminuria	
Yes	13 (2.7)
No	471 (97.3)
Renal insufficiency	
Yes	44 (9.1)
No	440 (90.9)
Retinopathy	
Yes	140 (28.9)
No	344 (71.1)
Neuropathy	
Yes	152 (31.4)
No	332 (68.6)

Supplement 3. Number of complications discovered in the study population

Number of complications	n (%)
Without complications	227 (46.90)
One complication	116 (23.97)
Two complications	75 (15.50)
Three complications	26 (5.37)
Four complications	26 (5.37)
Five complications	9 (1.86)
Six complications	3 (0.62)
Seven complications	1 (0.21)
Eight complications	1 (0.21)

Author contribution.
Mehović S., Janković S., and Zana S. conceived the study design and participated in data collection. Mehović S. and Janković S. led the data analysis and interpretation. All authors approved the final manuscript.