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ORIGINAL ARTICLE

Diabetes treatment-related quality of life is associated with levels of self-care activities in insulin injection among Japanese patients with type 2 diabetes: Diabetes Distress and Care Registry at Tenri (DDCRT 8)

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Abstract
Aims We investigated the association between diabetes treatment-related quality of life (QOL) and levels of self-care activities in insulin injection among Japanese patients with type 2 diabetes.
Methods Data from 1394 patients with type 2 diabetes on insulin therapy were obtained from a diabetes registry in Japan. We used the Diabetes Therapy-Related QOL (DTR-QOL) questionnaire and relative risk regression analysis to assess the independent association of high levels of self-care activities in insulin injection and DTR-QOL scores while adjusting for possible confounders.
Results The mean age, BMI and HbA1c level were 65.8 years, 24.8 kg/m^2 and 62 mmol/mol (7.8 %), respectively. The frequency of insulin injection omission was associated with DTR-QOL scores. In the multivariable-adjusted model, the relative risks for high levels of self-care activities in insulin injection was 1.15 (95 % confidence interval, 1.05–1.26) in the highest quintile compared with those in the lowest quintile of DTR-QOL scores. Subgroup analysis confirmed this association in patients <65 years.
Conclusions DTR-QOL was associated with self-reported levels of self-care activities in insulin injection, particularly among Japanese patients <65 years with type 2 diabetes. DTR-QOL might be a useful tool to identify patients who consequently omit insulin. For patients with low DTR-QOL score, healthcare providers should discuss their treatment-related problems to prevent insulin injection omission.

Keywords Insulin · Self-care activities · Omission · Quality of life

Managed by Antonio Secchi.

For the Diabetes Distress and Care Registry at Tenri Study Group.

Diabetes Distress and Care Registry at Tenri Study Group are listed in the Appendix.

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Introduction

Because the progressive impairment of insulin secretion is characteristic of type 2 diabetes [1], guidelines issued by the American Diabetes Association and National Institute for Health and Clinical Excellence (NICE) state that insulin is the most effective glucose-lowering agent and insulin therapy is a key component of effective diabetes management over the course of the disease [2–4].

In a clinical setting, insulin therapy may not achieve optimal outcomes [5]. The Japan Diabetes Clinical Data Management Study, a multicenter study of diabetes in Japan, showed that the average HbA1c level of patients receiving insulin was 66 mmol/mol (8.0 %) and only 20.9 % of these achieved a HbA1c level of <55.9 mmol/mol (7.0 %) [6]. Health-related quality of life (HRQOL) is one of the important factors that should influence glycemic control in the insulin-treated patients with diabetes [7]. Diabetes itself leads to worse HRQOL in patients with acute coronary syndrome treated with coronary angioplasty

[8]. Recently, several studies investigated what factors had an impact on HRQOL in patients with type 1 and type 2 diabetes. Younger age (<40 years) at type 2 diabetes diagnosis was significantly associated with a poor diabetes-related QOL: specific life domains such as freedom to eat and drink [9]. Onset of type 1 diabetes during the first 5 years of life may result in better QOL and less fatalism in the long term as these patients are presumed to have no memory of disease onset, which could reduce trauma and facilitate adaptation to managing life with diabetes. [10]. Continuous subcutaneous insulin infusion (CSII) confers significant advantages in terms of HRQOL with improvements in treatment satisfaction, perceived clinical efficacy and reduction in treatment interference with daily activities [11]. The continuous glucose monitoring on CSII resulted in better metabolic control without imposing an additional burden on the patient [12]. Inadequate adherence to insulin injections is associated with higher HbA1c levels [13, 14]. Therefore, it is important that physicians pay close attention to HRQOL and problems that interfere with adherence to insulin injection and solve these problems with the patient to achieve good glycemic control.

Although there were several questionnaires developed to assess patient perceptions of insulin therapy that could affect insulin adherence [13, 15–20], few of these studies assessed the association between the factors that could affect insulin adherence and levels of self-care activities in insulin injection in other than Western countries. A recent study found that insulin injection-related problems such as interference with daily activities, injection pain and embarrassment were independent risk factors for insulin omission [21]. However, the study did not quantify the patient perceptions associated with the treatment-related problems.

The objective of the present study was to explore the association between patient perceptions of insulin therapy quantified by diabetes therapy-related quality of life (DTR-QOL) and levels of self-care activities in insulin injection in patients with type 2 diabetes using a large-scale single-center registry in Japan. We further hypothesized that DTR-QOL scores associated with levels of self-care activities in insulin injection affected mainly younger patients because older patients appeared to adhere better to daily self-care regimens.

Subject, materials and methods

Patients

Patient data were derived from the second-year survey using a diabetes registry maintained by the Tenri Hospital, a regional tertiary-care teaching hospital in Tenri, Nara, Japan. The details of this registry have been published elsewhere [22, 23]. In brief, the present study included patients with diabetes who were recruited from the registry and visited the outpatient clinic of our hospital from October 2009 to December 2011. The second-year survey was performed from January to December 2011. We excluded patients with pre-diabetes diagnosed by an oral glucose tolerance test, gestational diabetes, type 1 diabetes, diabetes induced by the use of steroids or other endocrinological diseases and finally used the data of patients diagnosed with type 2 diabetes. The Ethics Committee of Tenri Hospital approved this study. Informed consent was obtained from the patients prior to the start of study.

Data collection

Trained clinical research coordinators collected patient demographics from medical charts, which included age, gender, body weight, duration of diabetes, past medical history (micro- and macro-vascular complications) and treatment modalities. On the day of questionnaire distribution, HbA1c values were assessed and expressed as National Glycohemoglobin Standardization Program equivalent values [24]. The presence of depressive symptoms at the time of participation in this study was made using the Patient Health Questionnaire-9 as a screening tool [25]. Influence of diabetes treatment on patient QOL was measured by the DTR-QOL questionnaire [26] with 29 items, rated using a 7-point Likert scale (1: strongly agree to 7: strongly disagree), constituting four domain structures (‘burden on social activities and daily activities,’ ‘anxiety and dissatisfaction with treatment,’ ‘hypoglycemia’ and ‘satisfaction with treatment’). The score of each item was reversed so that 7 represented the highest QOL score. The total score was converted to 0–100 (best-case response 100; worst case response 0). High DTR-QOL score means good QOL for their diabetes treatment. Physical exercise was measured using a short version of the International Physical Activity Questionnaire (IPAQ), a self-reported instrument, which asks for an estimate of total weekly physical activity (walking/vigorous and moderate-intensity activity) during the previous week. The total Metabolic Equivalent of Task (MET) score was calculated by weighting the minutes reported for each activity per week using a MET energy expenditure estimate that was assigned to each category (low, moderate and high), following the IPAQ scoring criteria [27].

Outcome variables

We assessed levels of self-care activities in insulin injection to scheduled insulin regimen using the response to the following questionnaire: ‘Do you have insulin shots as

scheduled?' (response options: 1 = always, 2 = largely, 3 = more than half of the time, 4 = not always and 5 = no). Those who responded 'always' were defined as high levels of self-care activities in insulin injection.

Statistical analysis

Data from patients with type 2 diabetes who were under any type of insulin regimen were included in the current analysis. Continuous variables are reported as the mean and SD or interquartile ranges, where indicated. Differences between groups were evaluated by the trend test. Relative risk regression analyses were used to estimate the relative risks (95 % CI) for high levels of self-care activities in insulin injection in comparison with a reference category of the lowest quartile of DTR-QOL scores. Three statistical models were used; the first was a crude model and the second was adjusted for age and gender (model 1) and the third was adjusted for variables in model 1 plus BMI, duration of diabetes, daily insulin injection frequency, the presence of depressive symptoms and HbA1c levels (model 2). We selected these covariates, because these were considered to be associated with levels of self-care activities in insulin injection.

Next, we evaluated the association between the DTR-QOL quartiles and high levels of self-care activities in insulin injection when stratified by age (<65 and ≥65 years) using a multivariable-adjusted relative risk regression model. Furthermore, we evaluated the relative risks for high levels of self-care activities in insulin injection among the quartiles of DTR-QOL subdomain scores with the lowest quartile as a reference ('burden on social activities and daily activities,' 'anxiety and dissatisfaction with treatment,' 'hypoglycemia' and 'satisfaction with treatment') stratified by age (<65 and ≥65 years).

All probability (p)-values were two sided and those <0.05 were considered statistically significant. All analyses were performed using Stata/SE statistical software version 12.0 (Stata Corporation, College Station, TX, USA).

Results

Patient characteristics

Of all the 4330 eligible patients with diabetes [mean age (SD), 65.6 (12.1); 40.5 % female: 4.6 % with type 1 diabetes; 92.3 % with type 2 diabetes], 4191 provided consent to participate in the study, of whom 3717 were confirmed with type 2 diabetes and 1402 were treated with insulin during the study period. All of them used pen-type insulin injections. We further excluded eight patients who failed to complete the DTR-QOL questionnaire. The remaining 1394 patients met the inclusion criteria.

Table 1 shows characteristics of the patients according to levels of self-care activities in insulin injection. Overall, the mean age of the eligible patients was 65.8 years, with a mean BMI of 24.8 kg/m^2 and a mean number of daily insulin injections of 2.4. One thousand and seventy-six patients (77.2 % of the total) reported they always injected their prescribed insulin and 20.7 ($n = 288$), 1.8 ($n = 25$) and 0.4 % ($n = 5$) largely, more than half of time and not always injected their prescribed insulin, respectively. None of them reported they never injected prescribed insulin. Older patients ($p < 0.001$), those who had a longer duration of diabetes ($p < 0.001$), those with lower HbA1c levels ($p < 0.001$), higher DTR-QOL scores ($p < 0.001$) and those with cardiovascular diseases ($p = 0.003$) were less likely to omit insulin injections, whereas those who took more injections ($p = 0.003$), current smokers ($p < 0.001$) and those with depressive symptoms ($p = 0.029$) were more likely to omit insulin injections.

The relative risks for the association between high levels of self-care activities in insulin injection and DTR-QOL quartiles are shown in Table 2. In the crude model, the relative risk for high levels of self-care activities in insulin injection was 1.37 (95 % CI, 1.26–1.49) in the highest DTR-QOL quartile group compared with that of the reference category of the lowest DTR-QOL quartile. We observed a statistically significant linear trend across all DTR-QOL categories ($p < 0.001$). This association was observed after adjusting for other possible confounders, including age and gender (model 1; $p < 0.001$), and the variables in model 1 plus BMI, duration of diabetes, daily insulin injection frequency, the presence of depressive symptoms and HbA1c level (model 2; $p = 0.002$).

Results of multivariable-adjusted relative risk regression analysis stratified by age are shown in Table 3. In patients <65 years of age, the relative risks of those in the 2nd, 3rd and 4th quartile for high levels of self-care activities in insulin injection compared with that of those in the 1st quartile of DTR-QOL scores were 1.27 (95 % CI, 1.07–1.51), 1.32 (95 % CI, 1.11–1.58) and 1.35 (95 % CI, 1.12–1.63), respectively, and we observed a significant trend across all categories ($p = 0.001$). However, we did not observe significant associations among the patients aged ≥65 years after adjusting for multi-variables.

Next, we evaluated the association between high levels of self-care activities in insulin injection and the DTR-QOL subdomain scores stratified by age. As shown in Table 4, higher scores on the 'hypoglycemia' domain of DTR-QOL were significantly associated with high levels of self-care activities in insulin injection in both age categories. However, we observed significant associations between high levels of self-care activities in insulin injection

Table 1 Patient characteristics according to levels of self-care activities in insulin injection

Answer to the questionnaire	Total $n = 1394$	Always $n = 1076$	Largely $n = 288$	More than half of time $n = 25$	Not always $n = 5$	p value
Age (years)	65.8 (11.8)	67.7 (10.3)	60.8 (13.3)	46.8 (15.7)	46 (10.6)	<0.001
Female (%)	41.3	42.4	37.2	40.0	60.0	0.280
BMI (kg/m^2)	24.8 (4.2)	24.7 (4.1)	25.0 (4.5)	27.7 (6.8)	22.6 (6.3)	0.160
Duration (years)	18.5 (10.5)	19.2 (10.7)	16.7 (9.9)	12.1 (7.4)	12.8 (9.4)	<0.001
HbA1c (%)	7.8 (1.3)	7.7 (1.2)	8.1 (1.5)	9.3 (1.7)	8.5 (2.3)	<0.001
HbA1c (mmol/mol)	61.6 (14.2)	60.2 (13.1)	65.2 (16.2)	78.3 (18.8)	69.1 (24.7)	
Daily insulin injection frequency	2.4 (0.9)	2.3 (0.9)	2.6 (0.9)	2.4 (1.0)	2.6 (1.1)	<0.001
Prescribed insulin units per day	31.1 (18.7)	30.8 (18.9)	32.1 (17.8)	33.2 (17.9)	19.3 (8.1)	0.218
DTR-QOL score (IQR)	68.0 (54.0–83.3)	70.3 (56.9–85.6)	60.6 (17.8)	57.6 (18.2)	56.6 (23.1)	<0.0001
Non drinker (%)	71.6	72.5	70.0	52.0	60.0	0.057
Exercise (IPAQ category) (%)						0.679
Low	44.3	43.6	47.2	40.0	40.0	
Moderate	27.1	28.0	23.3	28.0	60.0	
High	28.6	28.4	29.5	32.0	0.0	
Nephropathy (%)	27.4	27.7	27.1	16.0	40.0	0.567
Diabetic retinopathy (%)	67.3	66.5	69.9	68.0	80.0	0.101
Past history of cancer (%)	9.7	10.3	8.0	4.0	0.0	0.093
Past history of cardio vascular disease (%)	16.9	18.3	13.5	0.0	0.0	0.003
Smoking (%)						<0.001
Never	45.0	47.4	37.5	32.0	20.0	
Past	36.6	36.9	37.2	20.0	20.0	
Current	18.5	15.7	25.4	48.0	60.0	
Non depression	94.2	94.7	87.5	80.0	5.8	0.029

Nephropathy; urine albumin/creatinine ratio >300 mg/dl or/and eGFR < 30 ml/min/1.73 m^2

Table 2 Correlation between levels of self-care activities in insulin injection and DTR-QOL score

	DTR-QOL score				
	1st quartile $n = 361$	2nd quartile $n = 345$	3rd quartile $n = 343$	4th quartile $n = 345$	p for trend
Range	6.9–54.0	54.6–69.5	70.1–83.3	83.9–100	
Relative risks for never insulin injection omission (crude)	Reference	1.15 (1.04–1.27)	1.25 (1.15–1.37)	1.37 (1.26–1.49)	<0.001
Relative risk for never insulin injection omission (model 1)	Reference	1.12 (1.02–1.23)	1.17 (1.07–1.28)	1.24 (1.14–1.34)	<0.001
Relative risk for never insulin injection omission (model 2)	Reference	1.09 (0.98–1.20)	1.11 (1.01–1.22)	1.15 (1.05–1.26)	0.002

RR relative risk

Model 1 adjusted for age and gender

Model 2 adjusted for the variables in model 1, BMI, duration of diabetes, depression symptoms, HbA1c and daily insulin injection frequency

and other domains, such as 'burden on social activities and daily activities,' 'anxiety and dissatisfaction with treatment' and 'satisfaction with treatment' only in the younger age category.

Discussion

To the best of our knowledge, this is the first cross-sectional study to focus on the association between the

Table 3 Correlation between levels of self-care activities in insulin injection and DTR-QOL score quartile stratified by age

	DTR-QOL				
	1st quartile	2nd quartile	3rd quartile	4th quartile	*p* for trend
RRs for no insulin injection omission stratified by age					
Gender-adjusted model (age < 65)	Reference	1.33 (1.13–1.57)	1.42 (1.20–1.68)	1.52 (1.29–1.79)	<0.001
Gender-adjusted model (age ≥ 65)	Reference	0.97 (0.87–1.08)	1.04 (0.95–1.14)	1.13 (1.04–1.23)	0.003
Model 1[a]					
Multivariable-adjusted model (age < 65)	Reference	1.27 (1.07–1.51)	1.32 (1.11–1.58)	1.35 (1.12–1.63)	0.001
Multivariable-adjusted model (age ≥ 65)	Reference	0.94 (0.84–1.06)	1.00 (0.90–1.10)	1.07 (0.97–1.17)	0.034

[a] Model 1 adjusted for gender, BMI, duration of diabetes, depression symptoms, HbA1c and daily insulin injection frequency

patient's perception about diabetes treatment quantified by DTR-QOL questionnaire and levels of self-care activities using a large sample of patients with type 2 diabetes. We found for the first time that DTR-QOL scores were significantly associated with self-reported levels of self-care activities in insulin injection, and better diabetes-specific health-related QOL was associated with higher levels of self-care activities in insulin injection among Japanese patients with type 2 diabetes, independent of possible confounders. We also observed that this association varied depending on patient characteristics and may be applicable only to patients aged <65 years. Our results showed that diabetes therapy-related QOL, as quantified by DTR-QOL questionnaire, is an important measure that may probe into levels of self-care activities in insulin injection in Japanese clinical settings. Healthcare providers should pay close attention to the treatment-related QOL of relatively young patients treated with insulin therapy because poor glycemic control may result from insufficient adherence to insulin injection schedules.

Peyrot et al. [21] reported that >25 % of patients in their internet survey of 501 patients with diabetes treated by insulin responded that insulin injections interfered with daily activities and had a major or moderate impact on QOL. Many factors have been suggested to impact on QOL of daily activities, such as age, gender, diabetic complications [28], complexity of treatment regimens [29] and symptoms of depression [30]. Cramer et al. [31] reported that adherence to an insulin regimen varied from 62 to 64 % in patients with type 2 diabetes in developed countries. Therefore, the identification of factors associated with non-adherence to insulin therapy is essential to prevent diabetic complications. Davies et al. [32] reviewed real-world factors affecting adherence to insulin therapy in patients with type 1 or type 2 diabetes and identified the following factors associated with non-adherence: patient-perceived barriers to adherence, type of delivery device and cost of medication. Furthermore, they identified that age and female gender were predictive factors of non-adherence as well as traveling, dislike of injections, embarrassment because of injections, challenging social conditions and stress or emotional problems were patient-perceived barriers to adherence. They also identified that changing to insulin administration by a pen device instead of a vial or syringe and an insurance scheme, in which a co-payment system reduced the cost of medication, would improve adherence to insulin injection. Ishii et al. [7] reported that the improvement in patient convenience obtained by switching from regular insulin to insulin lispro provided better adherence with insulin injection timing and improved QOL, as measured by the diabetes therapy-related QOL questionnaire. The timing of insulin injections appears to be a primary factor associated with better adherence to insulin injection. However, the previous studies did not quantify what factors affected patient QOL associated with insulin injection adherence. In our cross-sectional study, we also found that self-reported levels of self-care activities in insulin injection was higher in older patients with a longer duration of diabetes and lower HbA1c levels.

In this study, we used DTR-QOL to measure health-related QOL. There are various tools that are frequently used to measure health-related QOL, such as the diabetes-specific Diabetes QOL (DQOL) questionnaire [33], Audit of Diabetes-Dependent QOL (ADDQoL) [34], Short-Form 36 (SF-36) [35], EuroQoL 5-Dimension (EQ-5D) [36] and Diabetes Treatment Satisfaction Questionnaire (DTSQ) [37]. Because SF-36 and EQ-5D are generic instruments that are non-specific to diabetes, neither enhances our understanding of the impact of adherence to insulin injection. DQOL and ADDQoL are diabetes-specific instruments that are likely to be responsive to subgroup differences [34]. It is crucial to validate QOL questionnaires to ensure that the obtained data are meaningful. However, the Japanese version of ADDQoL has not yet been validated. Recently, Sato et al. [38] evaluated the validity and reliability of the Japanese version of DQOL. However, they did not demonstrate the validity of the questionnaire for use with Japanese patients with type 2 diabetes, particularly in domains associated with patient stress, although the reliability

Table 4 Correlation between levels of self-care activities in insulin injection and DTR-QOL subdomain quartile stratified by age category

	1st quartile	2nd quartile	3rd quartile	4th quartile	*p* for trend
Age < 65 ($n = 596$)					
Burden on social activities and daily activities (mean, IQR)	45.6 (42.3–53.8)	69.3 (64.1–74.4)	88.5 (84.6–92.3)	98.9 (97.4–100)	
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.29 (1.10–1.53)	1.40 (1.19–1.64)	1.45 (1.21–1.73)	<0.001
Multivariable-adjusted model	Reference	1.21 (1.02–1.44)	1.28 (1.08–1.51)	1.30 (1.08–1.56)	0.002
Anxiety and dissatisfaction with treatment (mean, IQR)	30.3 (22.9–39.6)	51.7 (47.9–56.3)	69.2 (62.5–75.0)	91.7 (87.5–97.9)	
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.22 (1.04–1.43)	1.37 (1.17–1.61)	1.39 (1.18–1.65)	<0.001
Multivariable-adjusted model	Reference	1.15 (0.97–1.35)	1.23 (1.04–1.46)	1.21 (1.01–1.46)	0.017
Satisfaction with treatment (mean, IQR)	28.5 (20.8–37.5)	49.7 (50.0–50.0)	65.3 (58.3–70.8)	89.7 (83.3–100)	
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.18 (1.02–1.38)	1.21 (1.02–1.43)	1.41 (1.20–1.65)	<0.001
Multivariable-adjusted model	Reference	1.14 (0.98–1.33)	1.11 (0.94–1.31	1.22 (1.02–1.44)	0.026
Hypoglycemia (mean, IQR)	35.7 (29.2–50.0)	65.7 (58.3–75.0)	93.7 (87.5–100)		
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.14 (0.96–1.35)	1.27 (1.11–1.46)		<0.001
Multivariable-adjusted model	Reference	1.12 (0.94–1.33)	1.23 (1.07–1.42)		0.004
Age ≥ 65 ($n = 798$)					
Burden on social activities and daily activities (mean, IQR)	47.1 (42.3–53.8)	70.9 (60.3–75.6)	88.7 (84.6–92.3)	99.1 (98.7–100)	
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.02 (0.92–1.13)	1.08 (0.99–1.18)	1.12 (1.03–1.23)	0.003
Multivariable-adjusted model	Reference	0.98 (0.88–1.09)	1.03 (0.94–1.14)	1.07 (0.98–1.18)	0.055
Anxiety and dissatisfaction with treatment (mean, IQR)	29.6 (25.0–37.5)	52.4 (50.0–56.25)	71.4 (64.6–77.1)	93.8 (87.5–100)	
RRs for full insulin adherence					
Gender-adjusted model	Reference	0.98 (0.88–1.09)	1.06 (0.97–1.16)	1.12 (1.03–1.21)	0.001
Multivariable-adjusted model	Reference	0.96 (0.86–1.07)	1.01 (0.92–1.11)	1.05 (0.97–1.14)	0.155
Satisfaction with treatment (mean, IQR)	28.4 (20.8–37.5)	49.9 (50.0–50.0)	67.5 (62.5–75.0)	92.7 (87.5–100)	
RRs for full insulin adherence					
Gender-adjusted model	reference	1.00 (0.91–1.10)	1.05 (0.97–1.14)	1.06 (0.97–1.15)	0.099
Multivariable-adjusted model	reference	0.99 (0.90–1.09)	1.02 (0.94–1.11)	1.02 (0.93–1.11)	0.402
Hypoglycemia (mean, IQR)	32.5 (20.8–50.0)	65.9 (62.5–75.0)	95.4 (87.5–100)		
RRs for full insulin adherence					
Gender-adjusted model	Reference	1.05 (0.96–1.16)	1.12 (1.04–1.21)		0.002
Multivariable-adjusted model	Reference	1.05 (0.95–1.16)	1.09 (1.01–1.18)		0.032

Multivariable-adjusted model adjusted for gender, BMI, duration of diabetes, depression symptoms, HbA1c and daily insulin injection frequency

IQR Inter quartile range

of the questionnaire was confirmed. DTSQ is widely used to measure therapy-related issues. While there are no universally accepted specific definitions of QOL, there is a general consensus that QOL is multidimensional and includes physical, psychological and social aspects, which are subjective, meaning that each individual perceives

aspects of their personal lives differently [39]. Although DTSQ is widely used as a diabetes-specific questionnaire in clinical trials, it measures only treatment satisfaction, which is a relatively limited portion of QOL. The DTR-QOL questionnaire consists of the following four domains: 'burden on social activities and daily activities,' 'anxiety and dissatisfaction with treatment,' 'hypoglycemia' and 'satisfaction with treatment.' The reliability and validity of the DTR-QOL questionnaire used in this study were psychometrically evaluated using survey results obtained from 284 Japanese patients with diabetes [26]. The validity of the instrument was considered verified because DTR-QOL score was moderately correlated with that of DTSQ and the Japanese version of SF-8.

In this study, we demonstrated a positive association between health-related QOL, as measured by DTR-QOL, and levels of self-care activities in insulin injection applicable only to patients aged <65 years. We previously reported an association between self-reported high adherence to a daily insulin regimen and good glycemic control, which was also true only in the same population of relatively younger patients with type 2 diabetes on insulin therapy [14]. To explain the significant association among adherence to insulin, QOL and glycemic control observed in a limited age group shown in this study, we found that in actual clinical settings, we often experience employed patients who do not achieve good glycemic control because insulin injections were intrusive to daily activities, whereas retired patients rarely made this complaint. We observed that the subdomain of DTR-QOL 'burden on social activities and daily activities' was associated with levels of self-care activities in insulin injection in the patients aged <65 years but not for those aged >65 years. Our results suggest that parameters such as 'burden on social activities and daily activities,' 'anxiety and dissatisfaction with treatment' and 'satisfaction with treatment' are more applicable to the working-age population. Therefore, to increase patient adherence to a prescribed insulin regimen, we should increase communication with patients to discuss their problems and perception related to insulin regimen and how these problems influence their social and daily activities, particularly for patients <65 years.

The present study has several important limitations. First, there was no objective measure of insulin use, and the evaluation of levels of self-care activities in insulin injection using a simple straightforward questionnaire in this study may lead to misclassification of the patients who omit their scheduled insulin injections intentionally or accidentally. In addition, we did not evaluate the ability of self-titration of insulin dosage in each patient. Because patient-lead insulin titration allows for more frequent insulin dose titration, which can lead to better glycemic control and lifestyle flexibility than physician-lead insulin titration [40], insulin titration method might be associated with adherence to insulin injection and HRQOL. Secondly, adherence to medication schedules may be affected by the Japanese universal health insurance system because large part of medication cost are covered and the patient does not need to pay the total expense. However, we did not address medication cost as a possible confounder in this study; therefore, cost cannot be excluded as a cofounder in the relationship between adherence and glycemic control. Finally, this study was conducted in a Japanese diabetes-specialty center, and we limited the patients to those who could visit our outpatient clinic though the strong point was the large sample of patients with type 2 diabetes treated by insulin. Because our study focused on a Japanese population, our results may not be generalized to other ethnic populations.

In conclusion, the results of this large cross-sectional sample of patients with type 2 diabetes from a diabetes registry in Japan revealed that levels of self-care activities in insulin injection were associated with DTR-QOL scores. However, this association may be applicable only to patients with diabetes aged <65 years. Healthcare provider should discuss the problems and perception about insulin treatment with patients to prevent insulin injection omission. This may lead to improved insulin adherence and consequent good glycemic control.

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Conflict of interest None declared for all authors.

Ethical standard This study was approved by the Institutional Ethics Committee of Tenri Hospital.

Human and Animal Rights disclosure All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent disclosure Informed consent was obtained from all patients for being included in the study.

Appendix

Members of the Diabetes Distress and Care Registry at Tenri Study Group:

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