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To cite this article: Kerstin Gutefeldt, Christina A. Hedman, Ingrid S. M. Thyberg, Margareta Bachrach-Lindström, Hans J. Arnqvist & Anna Spångeus (2020): Low health-related quality of life is strongly linked to upper extremity impairments in type 1 diabetes with a long duration, *Disability and Rehabilitation*, DOI: [10.1080/09638288.2019.1705924](https://doi.org/10.1080/09638288.2019.1705924)

To link to this article: <https://doi.org/10.1080/09638288.2019.1705924>



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Published online: 06 Jan 2020.



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Low health-related quality of life is strongly linked to upper extremity impairments in type 1 diabetes with a long duration

Kerstin Gutefeldt^a , Christina A. Hedman^a, Ingrid S. M. Thyberg^b, Margareta Bachrach-Lindström^c, Hans J. Arnqvist^d and Anna Spångeus^e

^aDepartment of Endocrinology and Department of Medical and Health Sciences, Linköping University, Linköping, Sweden; ^bDepartment of Rheumatology and Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden; ^cDepartment of Medical and Health Sciences, Division of Nursing Sciences, Linköping University, Linköping, Sweden; ^dDepartment of Endocrinology and Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden; ^eDepartment of Medical and Health Sciences and Department of Acute Internal Medicine and Geriatrics, Linköping University, Linköping, Sweden

ABSTRACT

Purpose: To compare health-related quality of life (HRQOL) in type 1 diabetes and non-diabetic controls and possible links to upper extremity impairments (UEIs). Prevalence of sick-leave and causes were investigated.

Materials and methods: This Swedish population-based case-control study included type 1 diabetes patients <67 years old and with a diabetes duration ≥ 20 years. Participants completed a postal questionnaire including Short Form 36, and questions regarding UEIs, and sick-leave.

Results: In total, 773 patients, aged 50 ± 10 years (diabetes duration 35 ± 10 years), and 708 non-diabetic controls, aged 54 ± 9 years, completed the study. Patients reported significantly lower HRQOL compared with controls. The difference was greatest for general health, vitality, and bodily pain. Patients with shoulder or hand but not finger impairments scored significantly lower than asymptomatic patients. The prevalence of sick leave was higher in patients vs. controls (23% vs. 9%, $p < 0.001$), and nearly half cited impairments from back, muscles, or joints as the main reason.

Conclusions: Health-related quality of life is lower in type 1 diabetes than controls and in patients with shoulder and hand impairments than in asymptomatic. Musculoskeletal impairments (back/muscle/joints) have impact on work ability. Identification of UEIs is important for initiating preventative-, therapeutic-, and rehabilitative interventions.

ARTICLE HISTORY

Received 30 July 2019
Revised 12 December 2019
Accepted 13 December 2019

KEYWORDS

Quality of life; type 1 diabetes; upper extremity impairments; work ability; disability

► IMPLICATIONS FOR REHABILITATION

- Upper extremity impairments (UEIs) that are common in type 1 diabetes, and associated with reduced health-related quality of life, should preferably be screened for on a regular basis along with other known diabetes complications.
- Early identification of UEIs is important to improve health by initiating preventive as well as therapeutic multi-professional rehabilitative interventions.
- Sick leave is higher in type 1 diabetes than in controls. Musculoskeletal impairments, including the back, muscles, and joints, are a common cause for sick leave warranting further studies.

Introduction

Musculoskeletal complications are common in diabetes and may cause disabilities affecting physical function, mental health, and health-related quality of life (HRQOL) [1–6], and yet they are hardly mentioned in current guidelines or diabetes registers [7,8]. A recent study concluded that the most common cause for disability in diabetes is in fact mental and musculoskeletal symptoms [9].

Most previous comparative reports of HRQOL in relation to musculoskeletal impairments in patients with diabetes and the general population lack a distinction between type 1 and type 2 diabetes [4,5]. To the best of our knowledge, there is only one previous study which has addressed the relationship between HRQOL and upper extremity impairments (UEIs) exclusively in type 1 diabetes [10].

Impaired work ability (sick leave or disability pension) in adults with diabetes has earlier been reported [11–15]. However, data concerning type 1 diabetes and the relationships between musculoskeletal disorders and work ability are limited [11,12]. Previous comparative reports of work ability in diabetes patients and the general population focus on financial aspects of occupational status rather than possible explanatory factors [16–18]. A Danish population-based study reported 12% higher sick leave per year in patients with type 1 diabetes compared with the general population, and additionally impaired HRQOL in type 1 diabetes patients. The authors did not report the possible role of specific diabetes complications [14]. It is important to appreciate patient experiences and possible disease-related limitations, as perceived HRQOL in patients appears to be one of the most important clinical and research outcomes [19]. Additionally, addressing these

disabilities can facilitate enhanced preventive strategies, rehabilitation, reduce costs, and limit suffering for individuals living with type 1 diabetes.

In the current study, we aimed to compare perceived HRQOL in men and women with type 1 diabetes of long duration with that in matched non-diabetic controls from the general population, and to explore possible relationships between the presence of physical impairments and HRQOL. Furthermore, we aimed to investigate the prevalence of sick leave and possible causes.

Research design and methods

Design and inclusion

This population-based case control study was performed in cooperation with all nine hospitals in the Southeast region of Sweden between the years 2010 and 2013. Using the hospitals' local diabetes register, all patients with type 1 diabetes diagnosed before 35 years of age, and who were not older than 67 years, with a diabetes duration ≥ 20 years, were invited to participate. Invitations were sent by letter with a questionnaire enclosed. When a patient consented to participate corresponding controls were invited. Controls matched for sex and age ± 5 years were obtained from the Swedish population register. Controls were excluded if they reported diabetes or if laboratory tests showed an elevated fasting plasma glucose level ≥ 7 mmol/L.

Questionnaire

The self-administered questionnaire sent to the patients contained several parts. Controls received the same questionnaire except for diabetes-specific questions. The first part of the questionnaire was study-specific and has been described in a previous publication [20]. In brief, this part of the questionnaire contained issues on background characteristics such as weight, height, sex, diabetes duration, presence of diabetes complications such as retinopathy, UELs, occupation, and work incapacity. Reasons for work incapacity were categorized as "problems from back, muscles or joints", "anxiety, stress, depression", "Diabetes or diabetes complications specify", and "Other". UELs were categorized into five groups: (1) shoulder pain and stiffness, (2) tingling and numbness in the fingers and/or wakening in the night because of pain and/or numbness in the hand or fingers, (3) hand stiffness, (4) finger lock

phenomenon, defined as finger/s locking in a flexed position, and (5) flexed finger, defined as the inability to extend one or several fingers. There were also questions regarding previous surgery for carpal tunnel syndrome or trigger finger. The questionnaire did not include any specific questions on impairments from lower extremity or back pain.

The second part of the questionnaire included health assessment questionnaires, which have been published previously [20]. The last part of the questionnaire included the Short Form 36 Health Survey (SF-36). The SF-36 is used to evaluate individual health status in a multi-dimensional fashion. It covers broad aspects of physical, mental, and social well-being as well as a more personal estimate of perceived health [21]. The SF-36 contains an eight-item scale; physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The outcome measure is a score range of 1–100, with higher scores indicating better perceived health. The International Quality of Life Assessment (IQOLA) SF-36 Standard Swedish Version 1.0 was used in this study [22].

Participant characteristics

Altogether, 773 patients with type 1 diabetes and 708 age (± 5 years) – and gender matched non-diabetic controls participated (Table 1). Compared with the patients, the control group included more women (61% vs. 55%, $p < 0.05$) and were older (54 ± 9 vs. 50 ± 10 years, $p < 0.001$). The patients had a mean diabetes duration of 35 ± 10 years (Table 1) and a mean HbA1c level of 65 ± 11 mmol/mol ($8.1\% \pm 1.0\%$).

All five impairments were more prevalent in patients compared with controls, including shoulder pain and stiffness 38% vs. 18%, $p < 0.001$, hand paresthesia 48% vs. 28%, $p < 0.001$, hand stiffness 34% vs. 16%, $p < 0.001$, finger locking 31% vs. 12%, $p < 0.001$, and flexed finger 28% vs. 7%, $p < 0.001$. Previous carpal tunnel syndrome surgery was reported by 26% of the patients vs. 6% of controls and previous surgery for trigger finger in 22% vs. 1%, respectively, $p < 0.001$.

The absence of any of the five UELs or previous surgery was reported by 21% of the patients vs. 56% of the controls ($p < 0.001$).

Table 1. Descriptive characteristics of the population with type 1 diabetes in Southeast Sweden from 2010 to 2013 in comparison with the general population.

	Patients All	Controls All	Patients		Controls	
			Female	Male	Female	Male
Questionnaire (n)	773	708	421	352	431	277
Female (%)	55	61*				
Age (years)	50 ± 10	$54 \pm 9^*$	50 ± 10^a	51.0 ± 9.6^b	$53 \pm 10^{a,d}$	$56 \pm 9^{b,d}$
BMI (kg/m ²)	26.3 ± 4.1	26.0 ± 3.9	26.3 ± 4.3^a	26.1 ± 3.9	$25.6 \pm 4.1^{a,d}$	26.6 ± 3.4^d
Diabetes duration (years)	35 ± 10		36 ± 10^c	34 ± 9^c		
SF-36 subscales						
Physical function	80 ± 23	$87 \pm 19^*$	$76 \pm 24^{a,c}$	$85 \pm 20^{b,c}$	$85 \pm 20^{a,d}$	$90 \pm 16^{b,d}$
Role physical	72 ± 38	$82 \pm 34^*$	$68 \pm 39^{a,c}$	$77 \pm 36^{b,c}$	$79 \pm 36^{a,d}$	$86 \pm 30^{b,d}$
Bodily pain	64 ± 27	$74 \pm 25^*$	$59 \pm 26^{a,c}$	$69 \pm 27^{b,c}$	$71 \pm 26^{a,d}$	$78 \pm 24^{b,d}$
General health	59 ± 26	$74 \pm 22^*$	$57 \pm 26^{a,c}$	$62 \pm 25^{b,c}$	$73 \pm 23^{a,d}$	$77 \pm 20^{b,d}$
Vitality	55 ± 26	$67 \pm 24^*$	$51 \pm 26^{a,c}$	$60 \pm 25^{b,c}$	$63 \pm 25^{a,d}$	$72 \pm 21^{b,d}$
Social functioning	82 ± 23	$89 \pm 20^*$	$80 \pm 24^{a,c}$	$85 \pm 22^{b,c}$	$86 \pm 22^{a,d}$	$92 \pm 16^{b,d}$
Role emotional	81 ± 33	$88 \pm 30^*$	79 ± 35^c	$84 \pm 31^{b,c}$	84 ± 34^d	$94 \pm 21^{b,d}$
Mental health	77 ± 18	$81 \pm 18^*$	$75 \pm 18^{a,c}$	$80 \pm 18^{b,c}$	$79 \pm 18^{a,d}$	$84 \pm 16^{b,d}$
Blood samples (n)	603		338	265		

The data are presented as numbers, mean \pm SD values or %. Letters a–d indicate statistical significance ($p < 0.05$) for separate gender analyses. ^aFemale with type 1 diabetes vs. control female; ^bmale with type 1 diabetes vs. control male; ^cfemale with type 1 diabetes vs. male with type 1 diabetes; ^dcontrol female vs. control male.

* $p < 0.05$ for diabetes vs. control.

Drop out analysis

The drop out analysis procedure has been reported in a previous publication [20]. Of all the type 1 diabetes patients invited ($n = 1727$), 773 consented to participate and were included in the study. In total, 721 controls consented to participate ($n = 1995$ invited). Thirteen controls were excluded because of fasting plasma glucose levels of ≥ 7.0 mmol/L, thus leaving 708 controls in the study. The drop-out analysis showed that non-responding patients were significantly younger than the participating patients (46 ± 10 years vs. 50 ± 10 years, $p < 0.001$) and were more often males (i.e., 60% males in dropouts vs. 45% males in participants, $p < 0.001$). No drop-out analysis was performed in the control group.

Laboratory measures

Patients and controls were asked to provide a blood sample at their local hospital and the results have been published previously [20,23]. Blood sampling was performed through venipuncture after an overnight fast. All blood samples were analyzed through routine measurements at the Department of Clinical Chemistry, Linköping University Hospital. The laboratory is accredited by the Swedish Board for Accreditation and Conformity Assessment. Plasma glucose was analyzed using an Advia 1200 instrument (Siemens Healthcare Diagnostics, Munich, Germany).

HbA1c was analyzed using a TOSOH G7 automated hemoglobin analyzer (Tosoh Bioscience, Tokyo, Japan). Controls were also asked to provide a blood sample in the same manner as the patients, although HbA1c analysis was not performed.

Statistical analysis

Mean and standard deviation are reported for continuous variables. Student's t -test was performed when comparing two groups and analysis of variance (ANOVA) using a Bonferroni post hoc test if there were three or more groups. A possible association between UELs and HRQOL was assessed using the generic SF-36 measures with a multiple linear regression model. In this model, the eight dimensions of SF-36 were set as dependent variables and reported UELs as independent variables. The model was adjusted for age, gender, diabetes duration, HbA1c, and retinopathy. When investigating a possible association between sick-leave and reported impairments, a χ^2 -test was used. All statistical

tests were performed using a 5% significance level. Statistics were calculated using SPSS 23.0 for Windows software (IBM Statistics, Armonk, NY).

Ethics

Informed signed consent was obtained from all the participants. The Research Ethics Committee of the Faculty of Health Sciences, Linköping University, approved of the study (M245-09:2010-03-17).

Results

Overall HRQOL in patients and controls

Type 1 diabetes patients reported significantly lower HRQOL in all eight subscales of the SF-36 compared with controls (Table 1). The greatest difference was observed for general health (59 ± 26 vs. 74 ± 22 , $p < 0.001$) and for vitality (55 ± 26 vs. 67 ± 24 , $p < 0.001$). The smallest difference was observed for mental health (77 ± 18 vs. 81 ± 16 , $p < 0.001$).

When stratifying HRQOL by gender, female participants reported significantly lower HRQOL than males in both the patient and control group. The greatest discrepancy in the diabetes group was observed for bodily pain (59 ± 26 in women vs. 69 ± 27 in men, $p = 0.001$). In the control group, the greatest difference was in perceived role emotional (84 ± 34 in women vs. 94 ± 21 in men, $p < 0.001$).

When analyzing genders separately, males and females with type 1 diabetes scored lower for HRQOL in every subscale, than male and female controls, respectively. An exception was observed for role emotional where the difference was not quite significant ($p = 0.062$) in female patients (79 ± 35) vs. female controls (84 ± 34). The most prominent differences for both genders were observed for general health where patients had considerably lower HRQOL than controls (female: 57 ± 26 vs. 73 ± 23 , $p < 0.001$ and male: 62 ± 25 vs. 77 ± 20 , $p < 0.001$, respectively).

UEIs and HRQOL

The presence of UELs was significantly related to lower HRQOL in patients with type 1 diabetes (Figure 1). The absence of any impairment was associated with an HRQOL level consistent with that of non-diabetic controls. As shown in Figure 1, all dimensions of HRQOL decreased with multiple coexisting UELs. The physical

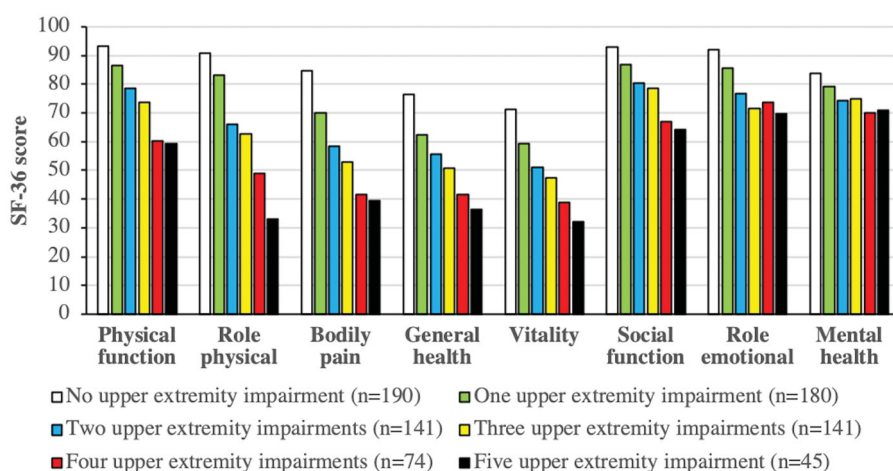


Figure 1. Short Form 36 (SF-36) scores in patients with diabetes in relation to the number of upper extremity impairments, UEL (shoulder pain and stiffness, hand paresthesia, hand stiffness, finger locking, or flexed finger).

subscales of SF-36 (physical function, role physical, and bodily pain), as well as the combined physical and mental subscales (general health and vitality), were the most affected subscales in patients with UEs compared with those without.

In Table 2, a multiple linear regression analysis is presented. The model included all five UEs and adjustments were made for age, gender, diabetes duration, metabolic control (HbA1c), and retinopathy. The presence of shoulder impairment, hand paresthesia, and hand stiffness was independently associated with lower SF-36 scores in all eight subscales, except for hand paresthesia regarding role emotional and shoulder impairment for mental health, which were non-significant. Presence of finger impairments (flexed finger and finger locking) did not seem to have any significant effect on perceived HRQOL. The presence of shoulder impairment reduced role physical and bodily pain scores by 16.4 and 19.4 points, respectively, vs. asymptomatic patients ($p < 0.001$). The corresponding reductions for hand stiffness were: role physical 18.8 points and bodily pain 14.7 points ($p < 0.001$).

Furthermore, metabolic control, as measured using a single HbA1c, was negatively associated with all dimensions except for role emotional and mental health. Older age was associated with lower scores for physical function, bodily pain, and vitality. Female gender was associated with lower scores for physical function and bodily pain. In this model, diabetes duration did not affect perceived HRQOL. Retinopathy was associated with lower scores for physical function, role physical, bodily pain and general health. When age was removed from the model, gender did not influence HRQOL except for physical function where score was reduced with 3.6 points, p value 0.032. In the same model, a longer diabetes duration slightly reduced physical function 0.4 points, p value < 0.001 .

Work incapacity

As shown in Figure 2, the prevalence of sick leave was more than twice as high in patients compared with controls (23% vs. 9%, $p < 0.001$). Almost half of the patients on sick leave cited musculoskeletal disorders, i.e., problems from back, muscles or joints, as a reason (i.e., 11% of all patients and 5% of all controls, $p < 0.001$).

Discussion

As far as we know, we are the first to demonstrate that UEs in a type 1 diabetes cohort are related to lower perceived HRQOL compared with controls, using the well-validated short-form SF-36 [24]. The current study shows that shoulder and hand impairments are related to lower HRQOL outcomes. On the contrary, finger impairments did not appear to have an impact on perceived HRQOL. The coexistence of several impairments seemed to worsen HRQOL, as shown by decreasing HRQOL scores with increasing numbers of reported impairments. The current study shows that type 1 diabetes patients have a higher frequency of sick leave than the general population and that a common reason for impaired work ability is musculoskeletal manifestations.

Patients reported significantly lower HRQOL in all eight subscales of the SF-36 compared with controls. We used the generic, well validated, SF-36 which makes it possible to compare our results to those from other chronic diseases as well as to those from a healthy population, unlike disease-specific HRQOL measurements. When we compared the reported HRQOL in our control group with Swedish SF-36 reference data, we found the results to be consistent overall [24]. The "General health" subscale

Table 2. Multiple linear regression of variables influencing SF-36 in patients with diabetes with eight SF-36 dimensions as dependent variables.

	Physical function ($R^2=0.308$)		Role physical ($R^2=0.241$)		Bodily pain ($R^2=0.399$)		General health ($R^2=0.288$)		Vitality ($R^2=0.271$)		Social functioning ($R^2=0.184$)		Role emotional ($R^2=0.076$)		Mental health ($R^2=0.09$)	
	B	p Value	B	p Value	B	p Value	B	p Value	B	p Value	B	p Value	B	p Value	B	p Value
Age (years)	-0.5	<0.001	-0.1	0.491	-0.2	0.034	-0.1	0.4	0.3	0.03	-0.1	0.497	0.0	0.855	0.1	0.327
Gender	-4.7	0.005	-1.1	0.719	-4.2	0.025	1.2	0.516	-2.0	0.302	-1.2	0.499	-1.1	0.68	-1.0	0.52
Diabetes duration (years)	-0.1	0.491	-0.1	0.456	0.0	0.985	-0.0	0.822	0.0	0.984	0.0	0.789	0.2	0.222	0.1	0.583
HbA1c (mmol/mol)	-0.2	0.019	-0.3	0.034	-0.2	0.003	-0.3	<0.001	-0.3	0.002	-0.2	0.009	-0.1	0.24	-0.1	0.066
Retinopathy ^a	-4.3	0.016	-8.7	0.006	-4.6	0.02	-7.8	<0.001	-2.7	0.187	-3.1	0.113	-3.0	0.299	-2.8	0.079
Shoulder pain and stiffness ^b	-9.0	<0.001	-16.4	<0.001	-19.4	<0.001	-12.3	<0.001	-11.8	<0.001	-9.4	<0.001	-7.5	0.011	-2.6	0.101
Hand paresthesia ^c	-3.7	0.033	-6.0	0.049	-6.0	0.002	-6.6	0.001	-7.8	<0.001	-5.2	0.006	-4.0	0.164	-4.6	0.003
Hand stiffness ^d	-9.8	<0.001	-18.8	<0.001	-14.7	<0.001	-9.1	<0.001	-12.9	<0.001	-7.1	0.001	-10.3	0.002	-5.0	0.005
Finger locking ^e	-1.6	0.433	-1.7	0.627	-0.4	0.838	-3.9	0.08	-1.5	0.512	-1.7	0.417	3.4	0.301	0.1	0.969
Flexed finger ^f	-3.4	0.101	-3.7	0.312	-1.7	0.475	-2.0	0.401	-1.9	0.435	-2.6	0.25	-3.9	0.258	-0.8	0.677

Model adjusted for age, gender, diabetes duration, and HbA1c. In the analysis, female was set as 0 and male as 1. The absence of a respective upper extremity impairment (shoulder pain and stiffness, hand paresthesia, hand stiffness, finger locking, or flexed finger) was set as 0 and the presence as 1.

Bold values indicate $p < 0.05$.

^aRetinopathy defined as self-reported history of laser treatment to either of the eyes. Presence of five types of UEs (self-reported).

^bShoulder pain and stiffness.

^cHand paresthesia tingling and numbness in fingers and/or waking in the night because of pain and/or numbness in the hand or fingers.

^dHand stiffness.

^eFinger lock phenomenon when bending a finger.

^fFlexed finger defined as inability to extend one or several fingers.

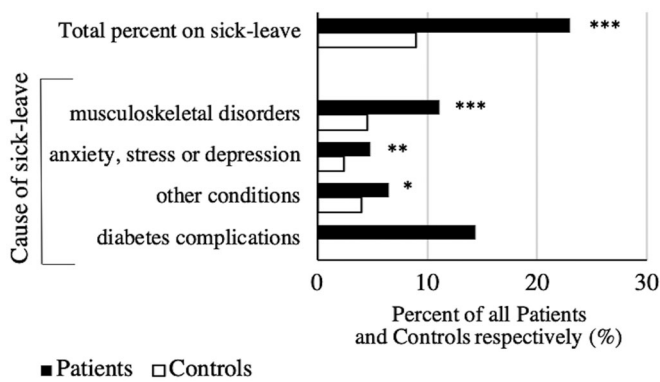


Figure 2. Work incapacity and self-reported cause of this, in patients with diabetes compared with controls. Data are shown as percentage of all patients and controls, respectively. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

represents patient estimates including subjective comparisons with others and expectations for the future and is strongly associated with physical health status [24]. The general health subscale showed the greatest difference, i.e., a 15-point reduction, between the patient and control groups, implying that type 1 diabetes has a significant negative impact on physical function. A comparable study by Nielsen et al. reported a five-point reduction for the corresponding dimension [14]. Vitality represents a measure of energy and tiredness ratings and in addition to social functioning, role emotional and mental health measurements capture mental wellbeing [24]. Mental health also appears to be impaired in type 1 diabetes but in the current study not as prominently as physical components. Therefore, even though some studies suggest that depressive disorders are overrepresented in diabetes [25–27], in the current study, only a small difference between patients and controls was observed for the mental health subscale (four point reduction, $p < 0.001$), suggesting that type 1 diabetes had a stronger impact on the physical aspects of HRQOL than the mental components. Previous comparable studies are ambiguous. Nielsen et al. reported smaller but significant differences in patients with type 1 diabetes vs. controls with negligible differences between physical and mental health [14]. Wee et al. reported lower HRQOL in patients with diabetes in terms of physical dimensions compared with mental dimensions, which is similar to the results of the current study, but did not differentiate between subjects with type 1 diabetes and type 2 diabetes [5].

In a previous study, we reported that 74% of adults with type 1 diabetes vs. 42% of controls experienced UELs [20]. Similarly, a high prevalence of UELs, 66%, was observed in the Diabetes Control and Complications Trial (DCCT) cohort by Larkin et al. [1]. To the best of our knowledge, there is only one previous report on the relationship between HRQOL and UELs in type 1 diabetes exclusively [10]. Similar to that study [10], we found that the presence of shoulder and hand impairments, but not finger impairments, was associated with lower HRQOL in type 1 diabetes. An interesting finding in the current study was that patients with type 1 diabetes without UELs demonstrated a similar HRQOL as non-diabetic subjects, indicating the high impact of UELs on HRQOL. Physical function, role physical, and bodily pain constitute measurements of physical health [24]. In the current study, subscales corresponding to physical health were all lower in the presence of UELs in type 1 diabetes. These results concerning detrimental physical function are in agreement with previous findings [6,28], but we are the first to demonstrate a relationship between HRQOL and UELs in type 1 diabetes and a non-diabetic population. Another study performed by Redmond et al. found

that type 2 diabetes patients scored lower in physical dimensions (physical function -7.2 and role physical -7.3) [6].

In the present study, metabolic control measured through a single HbA1c value was associated with lower perceived HRQOL. Previous reports have been inconclusive and one could speculate that disparate results may indicate a possible relationship between glycemic control and HRQOL, which could be explained by the HRQOL utility used: i.e., generic vs. diabetes-specific measures [29].

An important finding in the current study was the high prevalence of work incapacity in patients (23%) vs. controls (9%). Corresponding general data concerning work incapacity in Sweden in the year 2010 indicated a mean 5.7% prevalence [30]. Earlier studies have mostly addressed the financial aspects of impaired work ability [13,15,16,18]. Additionally, earlier reports often lack direct comparisons with the general population. In agreement with the current findings, Nielsen et al. reported that adults with type 1 diabetes had a higher frequency of sick leave, i.e., 12% more than controls, but did not specify possible associated complications [14]. In the current study, 11% of all patients reported musculoskeletal symptoms as a reason for sick leave vs. 4.5% in the control group. The current study highlights working incapacity in adults with longstanding type 1 diabetes and demonstrates differences in patients with type 1 diabetes compared with the general population. It is important to gain further insights into these issues to allow for prevention and rehabilitation where possible.

UELs in type 1 and type 2 diabetes are specific disorders reported under various headings including “musculoskeletal complications in diabetes”, “cheiroarthropathy”, “rheumatological manifestations in diabetes”, and “hand and shoulder symptoms in diabetes”. They are associated with other diabetes complications such as neuropathy and retinopathy, the latter as shown in this study which may affect HRQOL. To our knowledge, no connection to common conditions such as low neck pain, low back pain, and spinal pain has been reported. According to a recent meta-analysis, these conditions may be more prevalent in diabetes but the results are not entirely concordant [31]. Additionally in a review article by Lebiez-Odrobina and Kay, they concluded that shoulder and hand impairments are more prevalent than other musculoskeletal manifestations of diabetes [2].

There are several limitations to consider. We performed a cross-sectional study, and therefore no causative conclusions can be made. The rather low response rate (patients 45% and controls 36%) raises questions concerning the validity of the collected data. However, a low response rate is considered a common phenomenon in questionnaire-based surveys [32]. With self-reported data, there is a risk of recollection error and misinterpretation. Nonetheless, self-reported data on sick-leave have been fairly consistent with register collected data [33]. Another limitation with our study is that we cannot distinguish UELs impact on work ability from other musculoskeletal impairments reported in regard to reason for sick-leave. Furthermore, we do not have data on colocalized lower extremity or back impairments which might as well affect HRQOL and thus we were not able to adjust for these variables in the multiple regression model. In addition, it is important to remember that self-reported musculoskeletal symptoms are not equivalent to a formal diagnosis. However, the reported UELs in the current study are consistent with those reported in another large study [1]. The current study includes type 1 diabetes patients with a long duration of diabetes in the South-east of Sweden and one should be cautious when comparing the current results with those from other countries as there are multiple

factors involved when estimating HRQOL. The HRQOL reported by the control group was in line with normative values in Sweden [24]. The strengths of the current study include the population-based design, the large sample size, a patient group consisting exclusively of type 1 diabetes patients and a control group to detect diabetes-specific disparities.

The goal of diabetes care is not only to minimize complications and symptoms of the disease but also to optimize the individual's function [34]. The World Health Organization introduced the International Classification of Functioning Disability and Health (ICF), which includes a terminology and a classification system for disabilities related to disease. The ICF aims to provide a scientific basis for understanding health-related states, and to provide a common language to facilitate communication about these issues between health care workers, researchers, the public and people with disabilities [35]. The current study aimed to highlight UELs which are a common, but underestimated complication of diabetes affecting daily life as well as perceived HRQOL. We suggest clinical monitoring of diabetes patients for UELs, and proactively looking for these symptoms on a regular basis during office visits, as with other diabetes complications. Furthermore, these UELs should be documented in the national diabetes registers. This will facilitate the detection of UELs and low HRQOL. Through earlier detection, multi-professional rehabilitative interventions directed at physical impairments and low HRQOL could contribute to better patient health, less suffering, and reduced costs for society as a complement to regulating metabolic control.

In conclusion, the current results show that patients with type 1 diabetes experience lower HRQOL compared with the general population and that this is more prominent in women than in men. The presence of shoulder or hand impairments are related to lower HRQOL. Type 1 diabetes patients also have a higher frequency of sick leave than the general population and a common cause of impaired work ability is musculoskeletal manifestations.

Based on these findings, we highlight a need to promote early detection of UELs and low HRQOL. A better awareness and initiation of multi-professional rehabilitative interventions might achieve better health, reduced suffering for type 1 diabetes patients and reduced costs for society.

Acknowledgements

The authors are grateful to all patients who participated in our study by answering a questionnaire and donating blood samples. We thank all colleagues in south-east Sweden who assisted with the recruitment of patients.

Prior presentations: Parts of this study were presented in abstract form at the 54th Annual Meeting of the European Association for the Study of Diabetes, Berlin, Germany, 1–5 October 2018.

Disclosure statement

No potential conflicts of interest were reported by the authors.

Author contributions

KG, HA, CH, IT, MBL and AS researched the literature and designed the study, collected and reviewed the data and made the statistical analysis. KG wrote the first draft of the article. All authors approved the final version of the report. AS is the guarantor of this work and as such, had full access to all data in the

study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

This work was supported by the Medical Research Council South-east Sweden (FORSS), The County Council, and Stiftelseförvaltningen of Region Östergötland, Sweden.

ORCID

Kerstin Gutefeldt  <http://orcid.org/0000-0002-4157-660X>

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