Factors influencing the diabetes-specific health-related quality of life in children and adolescents with type 1 diabetes mellitus
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Abstract
This study aimed to investigate the association of the anthropometric, clinical variables and maximal oxygen uptake (VO2max) with diabetes-specific health-related quality of life (HRQoL) in youths with type 1 diabetes mellitus (T1DM) and to find the predictors of HRQoL and blood glucose control. A total of 239 youths with diabetes (124 boys and 115 girls) were recruited from diabetes-based summer camps. HRQoL assessment was carried out with the Pediatric Quality of Life Inventory™ 3.0 Diabetes Module (Information Resources Centre, Mapi Research Trust, France); VO2max was evaluated by conducting the 20-m shuttle run test. Higher VO2max and the insulin pump therapy were significant predictors of the HRQoL in the multiple regression analysis; other clinical and anthropometric variables had no effect. The better blood glucose control was explained only by the higher VO2max. The good cardiorespiratory fitness (expressed by VO2max) has clinical and QoL benefits for paediatric patients with T1DM.

Keywords: adolescents, children, diabetes-specific health-related quality of life, maximal oxygen uptake, type 1 diabetes mellitus

Introduction
Type 1 diabetes mellitus (T1DM) is an autoimmune chronic disease that tends to occur in childhood, adolescents or early adulthood, but it may have its clinical onset at any age. It needs lifelong diabetes treatment and care to avoid or delay short-term and long-term complications. Children with proper treatment and care can live productive lives, just like their healthy peers. However, diabetes has an impact on many aspects of life. It is important to understand how the disease and the clinical conditions influence patients’ health-related quality of life (HRQoL).

Generic measures evaluate and compare health status in patients with different diseases and provide valuable information for comparing outcomes between sick and healthy populations. Generic questionnaires are not sensitive to detect small but clinically significant changes in HRQoL (Chassany et al., 2002). The diabetes-specific measures are more suitable for assessing the physical well-being, the health status of the patients as associated with diabetes management,
including medical regimen adherence, blood glucose control and risk of long-term complications of diabetes (Cameron et al., 2007; Guttman-Bauman et al., 1998). There is little evidence that the QoL measures are routinely used in clinical practice, but for health-care professionals a key goal in diabetes management is to help patients improve their QoL (Clarke and Eiser, 2004).

The Pediatric Quality of Life Inventory 3.0 Diabetes Module (PedsQL™ 3.0 DM) was developed for measuring diabetes-specific HRQoL for youths with T1DM. This module is a multidimensional instrument that assessed a broad age range of 2–18 years (Varni et al., 2003). While the original validation of the PedsQL DM included only subscale scores, findings of Nansel et al. (2008) gave evidence for using the total score of the module for assessing diabetes-specific HRQoL. Generally, parents of children with chronic diseases underestimate their children’s QoL (Eiser and Morse, 2001). Paediatric patients aged 5–18 years can reliably and validly self-report their HRQoL when an age-appropriate measurement instrument is utilized (Varni et al., 2007). In our study, we focused on disease-specific child self-report in order to examine the factors that influence the HRQoL in children and adolescents with T1DM.

Cardiorespiratory fitness reflects the functions of the circulatory and respiratory systems providing adequate oxygen supply to the muscles during prolonged exercise. The maximal oxygen uptake (expressed by VO2max) is widely accepted as the single best measure of cardiorespiratory fitness (Hyde and Gengenbach, 2007: 845). VO2max is defined as the highest rate of oxygen delivery and extraction that can be achieved at a maximal level of exertion, and it is measured mostly in millilitres of oxygen per kilogram of body weight per minute (ml/kg/minute). There is some evidence that cardiorespiratory fitness is reduced in youths with T1DM compared with healthy peers (Huttunen et al., 1984; Maggio et al., 2010; Williams et al., 2011).

This study aimed to evaluate how diabetes-related clinical variables, anthropometric and cardiorespiratory fitness parameters were associated with self-rated diabetes-specific HRQoL in children and adolescents with T1DM. Furthermore, the study aimed to find the predictors of diabetes-specific HRQoL and blood glucose control.

Method

Patients

Participants in the age range 8–18 were recruited from diabetes-based summer camps. The participants included 124 boys (aged 13.64 ±2.73) and 115 girls (aged 13.09 ±3.01). The mean diabetes duration was 5.64 ±2.41 years in boys and 6.06 ±2.99 years in girls. The mean glycated haemoglobin (HbA1c) was 8.45 ±1.57% in boys and 8.96 ±1.50% in girls. Inclusion criteria were having been diagnosed with T1DM for at least two years and being aged 8–18 years. Exclusion criteria were physical problems that made it difficult for the patient to carry out the shuttle run test (due to musculoskeletal, cardiac and respiratory disorders). The camps were supported by foundations, so participation was made possible for everyone regardless of the financial background of the families. Table 1 presents the sample characteristics.

Parents and their children were informed about the purpose and methods of the research verbally and in written form. Written consent was obtained from the parents and verbal assent from youths younger than 18 years before the completion of study measurement.

This research study was approved by the Borsod–Abau’j–Zemple’n County Regional Scientific and Research Ethics Committee.

Measurements

HRQoL measurement. The PedsQL 3.0 DM was developed by Varni et al. (2003). The questionnaire takes 5–10 minutes to complete. The 28-item scale encompasses five subscales:
diabetes symptoms (11 items), treatment barriers (four items), treatment adherence (seven items), worry (three items) and communication (three items). The instructions ask how much of a problem each item has been during the past one month. A 5-point Likert-type scale is used (0 = never a problem, 1 = almost never a problem, 2 = sometimes a problem, 3 = often a problem and 4 = almost always a problem). Items are reverse scored and linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0), so the higher scores indicate better HRQoL. The PedsQL 3.0 DM has been validated for Hungarian usage (Lukačs et al., 2012).

Cardiorespiratory fitness. Cardiorespiratory fitness was measured by conducting the widely used 20-m shuttle run test. The participants ran back and forth between two lines 20 m apart, while the running speed was dictated by compact disk audio beeps. Initial speed was 8.5 km/hour and increased by 0.5 km/hour every minute. The participants were instructed to keep pace with the signal as long as possible. The test was considered complete when the runner could not reach the line consecutively twice with the beep or stop voluntarily. The VO₂max was predicted from the last stage using Le’ger’s regression equation (Le’ger et al., 1988). The validity of the 20-m shuttle run test to predict VO₂max has been established previously (Léger and Lambert, 1982; Liu et al., 1992; Ramsbottom et al., 1988). If the blood glucose measured before the test was out of the target range (5–10 mmol/l), a new appointment was given to perform the test on a second occasion.

Body mass index and blood glucose control. Height and weight were measured for calculating body mass index (BMI; kg/m²) and BMI z score (adjusted for child age and sex). z score (or SD score) was calculated according to the formula (Xi – Mx)/SD, where Xi is the actual measurement, Mx is the mean value for that age and sex and SD is the standard deviation corresponding to that age and sex (National Institute of Child Health, 2012). The latest insulin dose and HbA₁c values for the blood glucose control were extracted from medical records of the participants during the study. The HbA₁c test is the most accepted measure of glycemic control and diagnostic test for diabetes (American Diabetes Association, 2003).

Intensive insulin therapy. The results of the Diabetes Control and Complications Trial (1993) showed the benefits of intensive insulin therapy for achieving tight blood glucose control and reducing the risk of micro- and macrovascular complications. Multiple daily injection (MDI) treatment is the most widely used method of insulin administration. This method involves intermediate or longacting insulin once or twice a day as a basal dose and rapid-acting insulin at each meal time, and patients need to administer at least three or more injections a day. A technological alternative to this method of insulin delivery is the continuous subcutaneous insulin infusion (CSII, or insulin pump therapy). The insulin pump is a programmable medical device that offers the most physiologic way of insulin delivery and the amount of insulin delivered can be changed by the user.

Statistical analyses

Data were analysed using SPSS 19.0 statistical analysis software (SPSS Inc, on IBM Company, 1989, 2010). Data are presented as mean + SD. The effect of indicator variables (gender and method of intensive therapy) on the HRQoL was analyzed with F test. Correlation between the HRQoL and the different parameters was evaluated with the Pearson’s coefficients. Multiple regression analysis with stepwise method was used to explore the effect of age, gender, duration of diabetes, insulin dosage, method of intensive therapy, VO₂max,BMI z score and HbA₁c on self-reported diabetes-specific HRQoL.
Results

Gender significantly influenced the HRQoL. The boys had better perception of HRQoL than girls (boys (n = 124): 72.76 ±13.04 vs girls (n = 115): 69.03 ±11.18; p = 0.019). The method of intensive insulin therapy also significantly influenced the HRQoL. Patients treated with CSII (or insulin pump therapy) had significantly higher HRQoL score than patients on MDIs (CSII (n = 104): 73.12 ±11.66 vs MDIs (n = 135): 69.31 ±12.56; p = 0.017). We found significant correlation between the diabetes-specific HRQoL and VO2max (r = 0.435; p < 0.001) and HbA1c (r = 0.185; p = 0.004). In the multiple regression analysis, the VO2max (p < 0.000) and the method of the intensive insulin therapy (p = 0.054) were significant independent predictors of the self-rated diabetes-specific HRQoL (Table 2). The blood glucose control, gender, age, insulin dosage, BMI z score and the duration of diabetes as independent variables were not significant in the model. When HbA1c was used as the dependent variable in the regression analysis, VO2max proved to be the single significant predictor of the blood glucose control (B = -0.093, SE(B) = 0.016, b = -0.353, t = -5.813, p < 0.001), explaining 12.5% of the variance. Increase in the VO2max associated with decrease in the HbA1c in tendency nature (Figure 1).

Discussion

In this study, we examined the factors that could affect the diabetes-specific HRQoL in children and adolescents. There are several studies in the literature assessing the HRQoL of youths with T1DM, but we found no studies that evaluated in parallel the effect of the diabetes-related clinical, anthropometric parameters and the cardiorespiratory fitness on diabetes-specific QoL in younger ages.

A number of studies suggest that males have better QoL perception than females, not only in chronic diseases (Mrus et al., 2005; Riedinger et al., 2001; Wijnhoven et al., 2003), but also in the healthy paediatric population as well (Bisegger et al., 2005; Michel et al., 2009). In our patient population, we also observed gender differences in HRQoL without age differences, although this latter often has been shown in other studies. Boys reported better QoL perception than girls, which is congruent with Kalyva et al. (2011) and the SEARCH for Diabetes in Youth Study Group’s findings (Naughton et al., 2008). The diabetes-specific HRQoL questionnaire is sensitive to the blood glucose control, but the relationship between these parameters is rather weak. When we analysed the different parameters in the regression model, we found that higher VO2max and the CSII had an effect on the disease-specific HRQoL. We observed the tendency that diabetic youths with impaired cardiorespiratory fitness had even unfavourable disease-specific HRQoL. The CSII therapy also seemed to be a determinative factor of the HRQoL of young diabetic patients, as was concluded in the SEARCH for Diabetes in Youth Study Group’s examination (Naughton et al., 2008). The main task of diabetes management is to achieve as near normal blood glucose control as possible. Using HbA1c as the dependent variable in the regression model, VO2max was the only predictive parameter for blood glucose control and the other variables had no effect. These findings highlight the importance of appropriate cardiorespiratory fitness, both in improvement of HRQoL and in the care and treatment of diabetes. Our result of VO2max being the only predictive parameter for HbA1c also suggests the importance of aerobic exercise in achieving and maintaining good glycemic control.

There are a few limitations in this study. The findings of this cross-sectional nonrandomized cohort study design may have been caused by selection bias, although the whole childhood population in the summer camps was invited to take part in the study. Cost-effectiveness data to determine superiority of the insulin pump over the MDIs and the socioeconomic status of
the families were not available. The insulin pump is almost fully supported in the paediatric population by the National Health Insurance in Hungary, so the use of an insulin pump device does not depend on the family’s financial situation. Our investigated participants represented one ethnicity. These imperfections may limit the generalizability of the findings. The main strength of our study is that we used the same cohort and large sample size to evaluate diabetes-specific QoL, cardiorespiratory fitness, and clinical and anthropometric variables at the same time, which is rather unique in the literature.

In conclusion, better diabetes-specific HRQoL is associated with male gender, treatment with insulin pump therapy, favourable blood glucose control and better VO2max. Two dominant variables were observed that explained the favourable disease-specific HRQoL, namely, the CSII therapy and the better cardiorespiratory fitness. It is well documented that the major goal of diabetes care is to manage the patients’ condition as much as possible by improving their QoL. Treatment with CSII therapy has some restrictions and not all patients are willing to wear the insulin pump device, but most physical activities are recommended for type 1 diabetics (American Diabetes Association, 2004). Clinicians should encourage their young patients to exercise regularly – especially to do aerobic sport – for their clinical and QoL benefits.

Acknowledgements
We are very grateful to all diabetes patients and their parents for taking part in this research study. We would like to thank to the physicians and assistants of the summer camp for their interest and co-operation.

Funding
This research work was carried out as part of the TAMOP-4.2.1.B-10/2/KONV-2010-0001 project with support by the European Union, co-financed by the European Social Fund. Andrea Luka’cs was granted by the Hungarian Diabetes Association.

References


Table 1. Characteristics of the study participants with type 1 diabetes mellitus by gender (mean ± SD; N = 239).

<table>
<thead>
<tr>
<th></th>
<th>Girls</th>
<th>Boys</th>
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<tbody>
<tr>
<td>Sample size</td>
<td>115</td>
<td>124</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.09 ± 3.01</td>
<td>13.64 ± 2.73</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>6.06 ± 2.99</td>
<td>5.64 ± 2.41</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.96 ± 1.50</td>
<td>8.45 ± 1.57</td>
</tr>
<tr>
<td>VO2max (ml/kg/minute)</td>
<td>38.34 ± 5.13</td>
<td>43.56 ± 5.46</td>
</tr>
<tr>
<td>CSII-MDI therapy ratio</td>
<td>51.64</td>
<td>53.71</td>
</tr>
<tr>
<td>Insulin dose (units/kg/day)</td>
<td>.92 ± .18</td>
<td>.91 ± .22</td>
</tr>
<tr>
<td>BMI z score</td>
<td>.39 ± .82</td>
<td>.35 ± .80</td>
</tr>
<tr>
<td>PedsQL™ 3.0 DM</td>
<td>69.03 ± 11.18</td>
<td>72.76 ± 13.04</td>
</tr>
</tbody>
</table>

PedsQL™ 3.0 DM: Pediatric Quality of Life Inventory 3.0 Diabetes Module; BMI: body mass index; CSII: continuous subcutaneous insulin infusion; MDI: multiple daily injection; VO2max: maximal oxygen uptake; HbA1c: glycated haemoglobin.

Table 2. Summary of multiple regression analysis for self-rated diabetes-specific HRQoL (N = 239).a

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SE(B)</th>
<th>β</th>
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<th>p</th>
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<tbody>
<tr>
<td>Constant</td>
<td>36.303</td>
<td>5.188</td>
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<tr>
<td>VO2max (ml/kg/minute)</td>
<td>.883</td>
<td>.122</td>
<td>.424</td>
<td>7.255</td>
<td>.000</td>
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<tr>
<td>Method of intensive insulin therapy</td>
<td>-2.798</td>
<td>1.446</td>
<td>-.113</td>
<td>-1.935</td>
<td>.054</td>
</tr>
</tbody>
</table>
  CSII = 0, MDIs = 1

CSII: continuous subcutaneous insulin infusion; MDI: multiple daily injections; VO2max: maximal oxygen uptake; HRQoL: health-related quality of life.

Figure 1. Improvement of blood glucose control (HbA1c) depending on maximal oxygen uptake ($N = 239$).
Note: HbA1c: glycated haemoglobin.