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ORIGINAL ARTICLE

Microvascular diabetes complications in a specialist young adult diabetes service

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Abstract

Background and aims The provision of medical care to young adults with type 1 diabetes mellitus is challenging. The aim of this study was to determine the rates of microvascular complications and their progression among patients with type 1 diabetes mellitus attending a specialist young adult diabetes service in Ireland.

Methods A retrospective review of 62 (male 56.5%) patients with type 1 diabetes mellitus attending the young adult diabetes service at our institution was undertaken. Data was recorded across two time points, clinic registration and at 5 years following initial contact.

Results The mean ± SD age at first attendance was 17.4 ± 2.0 years. Mean ± SD duration of diabetes was 6.3 ± 3.9 years with most patients treated using multiple daily insulin injections (75.8%). diabetic retinopathy rate at first attendance was 17.7% and after 5 years was 37.1% ($p = 0.003$). The majority of cases were background retinopathy. The prevalence of diabetic kidney disease was 6.4% and this remained unchanged at follow-up. Mean ± SD HbA_{1c} improved from 76.1 ± 22.4 mmol/mol (9.1 ± 4.2%) to 69.1 ± 14.9 mmol/mol (8.5 ± 3.5%), $p = 0.044$. Duration of diabetes was the only clinical variable associated with retinopathy risk at 5 years on multiple regression analysis ($p = 0.037$).

Conclusions Diabetic retinopathy is prevalent in young adults with type 1 diabetes attending specialist secondary care diabetes services. Duration of diabetes was the strongest determinant of retinopathy risk.

Keywords Complications · Nephropathy · Retinopathy · Type 1 diabetes

Background and aims

The incidence rates of type 1 diabetes mellitus peak in early childhood and adolescence [1, 2]. Although overall incidence rates in European populations have increased, this is not reflected across all reporting countries [3, 4]. It is well recognised that the management of diabetes care during the transition from paediatric to adult care is challenging and remains so during the period of emerging adulthood [5]. During this developmental stage, young individuals with diabetes are particularly vulnerable [6]. Individuals with type 1 diabetes mellitus under the age of 40 years are at increased risk of mortality when compared to their non-diabetic counterparts [7]. Most concerning is the observation that acute diabetes-related complications have been identified as a leading contributor to mortality [7]. Consequently, much of the clinical focus in caring for this cohort is targeted towards a reduction in the rates of acute diabetes-related complications specifically diabetic ketoacidosis and hypoglycaemia. However, as patients with type 1 diabetes mellitus grow older, the mortality rate from acute complications declines and the impact of chronic microvascular and macrovascular complications becomes apparent [7, 8], thus prompting consideration of how we approach these risks in a young adult population. Rates of diabetes-related micro vascular complications during this period are poorly described, so too is the impact of dedicated interventions to manage these patients during emerging adulthood. The primary objective of this study was to determine the prevalence of microvascular complications and progression within a cohort of young adults with type 1 diabetes mellitus attending a specialist young adult diabetes clinical service.

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Methods

The young adult diabetes service is a multidisciplinary clinic that specialises in the care of two distinct patient cohorts, adolescents transitioning from paediatric services with diabetes mellitus and young adults diagnosed with diabetes before the age of 25 years. The service provides clinical reviews with a consultant diabetologist supported by a multidisciplinary team that includes diabetes nurse specialists, dieticians and podiatry. The service also provides a nurse managed telephone service for registered patients to avail of between scheduled clinic visits. All patients had a diagnosis of type 1 diabetes mellitus (history of ketosis and/or autoantibody positivity and/or biochemical evidence of insulin deficiency) and were registered to the young adult diabetes service at our institution. For the purposes of this study, participants were required to have attended the service for a minimum of 5 years. Clinical, anthropometric and biochemical information was collected retrospectively from hospital charts and institutional electronic medical records across two time points, the date of registration to the clinic (February 2000 to December 2010) and a follow-up appointment 5 years after clinic registration. Individuals whose care was transferred to other institutions or failed to attend the clinic for a minimum of 5 years were excluded. Ethical approval was obtained from the Mater Misericordiae University Hospital research ethics committee. Statistical analysis was undertaken using IBM® SPSS® Statistics (Version 20). Data is presented as mean ± SD unless otherwise specified. A paired *t* test was used for parametric data. Multiple logistic regression analysis was undertaken in correlative analyses. The statistical significance threshold was set at a p value of < 0.05.

Diabetic kidney disease was defined as the presence of albuminuria and/or a fall in glomerular filtration rate < 60 mL/min/1.73m^2. Urinary albumin creatinine ratios (ACR) were measured on two occasions 3 months apart to confirm the presence of microalbuminuria, > 3.5 mg/mmol in females and > 2.5 mg/mmol in males [9]. Retinal photography was used to assess the presence of diabetic retinopathy. The severity was graded in accordance with NSC-UK retinopathy classification according to the following scale R1 = background retinopathy, R2 = pre-profliferative retinopathy and R3 = proliferative retinopathy [10].

Results

Baseline characteristics (Table 1)

Sixty-two patients (56.5% male) met the eligibility criteria for inclusion in the study. This included individuals diagnosed with type 1 diabetes mellitus in childhood or adolescence that had transitioned from paediatric diabetes services to adult diabetes care and those diagnosed for the first time in early adulthood (17–25 years of age). Mean ± SD age at diagnosis was 11.5 ± 4.5 years with mean duration of diabetes of 6.3 ± 3.9 years. The mean ± SD age of first attendance to the service was 17.4 ± 2 years. The mean ± SD rate of clinic attendances within this cohort was 86.2 ± 14.5% of scheduled appointments during the 5-year period of follow-up equating to a mean number of 10.1 ± 2.9 appointments.

Table 1 Baseline characteristics ($n = 62$)

Sex (% male)	62 (56.5)
Age at diagnosis (years)	11.1 ± 4.5
Age at first attendance (years)	17.4 ± 2
Duration of diabetes (years)	6.3 ± 3.9
Appointments attended	10.1 ± 2.9
Percentage Attendance Rate	86.2 ± 14.5

Data presented as mean ± SD

Anthropometric and biochemical characteristics (Table 2)

Over the 5-year attendance to the service, a significant increase in mean ± SD body mass index (BMI) was observed within the study group, 23.2 ± 4.2 Kg/m^2 at baseline compared to 25.7 ± 4.0 Kg/m^2 at follow-up ($p = < 0.0001$). Mean ± SD BMI significantly increased across both sexes with males increasing from 23.0 ± 4.0 to 26.3 ± 4.0 kg/m^2 ($p = < 0.0001$) and females 23.6 ± 4.5 kg/m^2 compared to 25.0 ± 3.9 kg/m^2 ($p = 0.02$) at follow-up. Systolic blood pressure was significantly higher at follow-up (119.7 ± 10.4 vs 112.6 ± 11.5 mmHg at clinic registration, $p = 0.001$), so too was diastolic blood pressure. There were no significant changes in lipid profile observed within this cohort. Improvements in glycaemic control were recorded with a decline in mean ± SD

Table 2 Anthropometric and biochemical parameters

	Baseline	*n*	5 years	*n*	*P* value
BMI (kg/m^2)	23.2 ± 4.2	57	25.7 ± 4.0	58	< 0.0001
Male	23.0 ± 4.0	32	26.3 ± 4.0	33	< 0.0001
Female	23.6 ± 4.5	25	25.0 ± 3.9	25	0.02
Systolic BP (mmHg)	112.6 ± 11.5	60	119.7 ± 10.4	62	< 0.001
Diastolic BP (mmHg)	66.5 ± 8.5	60	70.9 ± 9.3	62	0.005
Total cholesterol (mmol/L)	4.3 ± 1.0	59	4.5 ± 0.9	56	ns
LDL (mmol/L)	2.5 ± 0.7	58	2.6 ± 0.8	56	ns
Triglyceride (mmol/L)	1.1 ± 0.8	59	1.0 ± 0.8	56	ns
HDL (mmol/L)	1.4 ± 0.5	58	1.5 ± 0.3	56	ns
$HbA1_c$ (mmol/mol)	76.1 ± 22.4	62	69.1 ± 14.9	62	0.044
$HbA1_c$ (%)	9.1 ± 4.2	62	8.5 ± 3.5	62	

Data presented as mean ± SD

HbA_1c from 76.1 ± 22.4 mmol/mol (9.1 ± 4.2%) to 69.1 ± 14.9 mmol/mol (8.5 ± 3.5%), $p = 0.044$.

Medical therapy (Table 3)

At first attendance, the majority (75.8%) of patients were utilising multiple daily injections (MDI) of insulin while 17.7% were prescribed continuous subcutaneous insulin infusion (CSII) therapy. Three individuals (4.8%) were using premixed insulin preparations and a single patient was prescribed metformin but was subsequently commenced on insulin therapy as the clinical diagnosis was revised to type 1 diabetes mellitus. Overall rates of MDI usage did not change within this group. However, more patients were using CSII at follow-up (22.6%). None of the cohort were prescribed anti-hypertensive agents at the time of first contact with the service. After 5 years, the rates of anti-hypertensive usage had increased to 12.8%; all agents prescribed were angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs). One patient (1.6%) was taking lipid-lowering therapy at the time of registration to the young adult diabetes service and at follow-up 9.6% of the cohort were prescribed lipid-lowering therapy. Lipid-lowering therapies were predominantly Statin agents. Finally, the rate of hormonal contraception usage was 18.5% among females at the outset, which increased to 33.3% during the period of follow-up.

Microvascular complications (Table 4)

The baseline prevalence of diabetic retinopathy (DR) within the study group was 17.7% while maculopathy rates were much lower at 1.6%. The majority of retinopathy was non-proliferative, 10 (16.1%) patients had grade R1 disease and one having grade R3 retinopathy. Rates of retinopathy increased significantly within the group over the 5-year period to 37.1%, $p = 0.0026$. There was a fourfold increase in the rate maculopathy (6.5%) after 5 years of follow-up. Multiple logistic regression analysis was undertaken to determine clinical variables that may be associated with the presence of retinopathy after 5 years' clinical intervention. Duration of diabetes was the strongest predictor of development of retinopathy at 5 years ($p = 0.037$) while no relationship was observed for age at transition, sex, BMI, attendance rates, insulin therapy, glycaemic control, blood pressure and lipid profile. None of these variables were associated with retinopathy risk at baseline. The overall prevalence of diabetic kidney disease (DKD) was low within the study group. At the outset, four individuals (6.5%) were recorded as having evidence of microalbuminuria; overall rates remained unchanged at follow-up. Of the individuals with DKD at 5 years, 50% had microalbuminuria with the remaining half recorded as having overt proteinuria. Despite the increased use of ACEi and ARB's at follow-up, only two of the patients with DKD at follow-up were prescribed agents blocking the renin-angiotensin-aldosterone pathway.

Table 3 Medical therapy

	Baseline	5 years	
	%(*n*)	%(*n*)	*P* value
MDI[a]	75.8 (47)	75.8 (47)	ns
CSII[b]	17.7 (11)	22.6 (14)	ns
Pre-mixed	4.8 (3)	1.6 (1)	ns
Other	1.6 (1)	0 (0)	ns
Lipid lowering agents	1.6 (1)	9.7 (6)	ns
Antihypertensive agents	0 (0)	12.9 (8)	0.006
Hormonal contraception (females $n = 27$)	18.5 (5)	33.3 (9)	ns

[a] *MDI* multiple daily injections

[b] *CSII* continuous subcutaneous insulin infusion

Table 4 Microvascular complications

	Baseline	5 years	
	%(*n*)	%(*n*)	*P* value
Retinopathy	17.7 (11)	37.1 (23)	0.026
R1	16.1 (10)	35.5 (22)	
R2	0 (0)	0 (0)	
R3	1.6 (1)	1.6 (1)	
Maculopathy	1.6 (1)	6.5 (4)	ns
DKD	6.5 (4)	6.5 (4)	ns

Discussion

The primary outcome of this study was to determine the rates of microvascular complications among individuals with type 1 diabetes mellitus during the period of emerging adulthood and to evaluate the impact of 5 years specialised clinical intervention on the rates. Within our cohort, the background prevalence of diabetic retinopathy was 17.7% at first presentation to the Young Adult Diabetes Clinic. There is limited published data specifically pertaining to microvascular complications within this group and particularly progression over time. Our findings are in agreement with a previous study of demographically similar patients, where the prevalence of retinopathy within a group of adults with a diabetes diagnosis less than 7 years was 31.1%; the majority of disease was pre-proliferative [11]. However, the rate of retinopathy we report is in conflict with recently published rates within an Israeli population of young adults specifically transitioning from paediatric care with a comparable duration of diabetes [12]. The possible reasons for the increased retinopathy rates within our cohort include glycaemic control which was lower within the Israeli study; authors quoted a mean HbA_1c of 67.2 mmol/

mol (8.3%) compared to 76.1 mmol/mol (9.1%) within our group. In addition, more of the patients in that study were utilising CSII therapy (62%) and the study participants transitioned between 2010 and 2014, which was later than our patients, as such the group were more likely to have been treated with insulin analogues and CSII during the early years of their diagnosis. We may be observing the influence of diabetes treatment advances on microvascular outcomes.

Diabetes registries have been able to provide the statistical power needed to explore the relationship between diabetic eye disease and clinical parameters. A German registry collating data on over 8500 patients with type 1 diabetes illustrated that male sex, smoking, increasing HbA_1c and longer duration of diabetes all correlated to retinopathy risk [13]. Another European registry study addressed the same question but specifically reported on adolescents and young adults. The authors showed that similar variables increased the odds ratio of microvascular complications in this demographic with the exception of male sex [14]. Although informative from an epidemiological view point these studies do not report on specific interventions for young adults with diabetes. Within our dedicated clinical service, we report a significant rise in retinopathy rates to 37.7% over 5 years. Although the rate of new retinopathy in this cohort is of concern it is important to consider these findings in the context of diabetic retinopathy severity. All new cases were R1 grade retinopathy (background retinopathy). In addition, we observed three new cases of maculopathy within this group. We sought to explore the clinical variables that may contribute to the increased rates of retinopathy in our study group. Despite significant increases in systolic and diastolic blood pressure and the sub-optimal glycaemic control, the only variable associated with developing retinopathy over the 5-year period was the duration of diabetes, a non-modifiable risk. Although we demonstrated a relationship between duration of diabetes and retinopathy in our study, the contribution of suboptimal glycaemic control should not be disregarded. Had the cohort been larger, HbA_1c may have influenced retinopathy risk within this group, further highlighting the need for larger scale prospective studies in this population. We acknowledge the contribution to retinopathy risk seen from smoking in both registry studies. Although we were unable to accurately report smoking status within our study group, it represents another important modifiable factor in the development of DR.

The Diabetes Control and Complications Trial (DCCT) identified the challenges in attempting to achieve intensive glycaemic targets among adolescents. Throughout the course of the DCCT, adolescents who progressed through emerging adulthood in the intensive insulin therapy group had significantly higher mean HbA_{1c} compared to those entering the study as adults [15]. During the Epidemiology of Diabetes Interventions and Complications (EDIC) follow-up phase of the study, those who entered the DCCT as adolescents had a faster rate of retinopathy progression compared to those entering the study as adults, this was attributable the differences in HbA_{1c} during the intervention trial. Guidance from the American Diabetes Association on the management of adolescents and young adults is reflective of the DCCT and EDIC findings, recommending a target HbA_1c of 58 mmol/mol (7.5%) across all paediatric age groups where safely possible, targeting a HbA1c of less than 53 mmol/mol (7%) among adults who are free of hypoglycaemia [16, 17]. Despite 5 years of specialised intervention, glycaemic control within our cohort of young adults failed to meet these targets with a mean HbA_{1c} of 69.1 mmol/mol (8.5%). This highlights the challenges experienced by many centers in optimising glycaemic control within this group despite advancements in insulin and its delivery systems [11].

Rates of diabetic kidney disease were low within this cohort of patients at 6.4% and comparable to reports in similar cohorts [18, 19]. None of the study group experienced a decline in renal function based on eGFR, although this is not unexpected given that rates of overt nephropathy are low in diabetes patients with a mean duration of diabetes similar to our cohort [20]. A limitation of studying the cohort at two time points is that new cases of microalbuminuria arising during the follow-up period may not have been captured where microalbuminuria may have been ameliorated by the initiation of Renin Angiotensin Aldosterone system blockade therapy. As we have demonstrated, 12.8% of this population was prescribed either ACEi or ARBs over the 5-year follow-up, conceivably masking a higher underlying prevalence of DKD.

Another feature of this cohort has been the rise in body mass index (BMI) over the duration of follow-up. Large cohort studies of adolescents with type 1 diabetes report obesity prevalence as high as 15% (WHO criteria), with 24% overweight [21]. The implications of weight gain in this cohort are significant and result in insulin resistance, dyslipidemia and hypertension, in addition to the observed deteriorations in glycaemic control [21, 22]. At 5 years' follow up, 46.6% of our cohort were overweight and 12.1% obese. We speculate that the increasing BMI may relate to higher insulin doses perhaps as a consequence of improved compliance with prescribed therapy. Alternatively, it may be due to over insulinisation in individuals who fail to adequately monitor blood glucose readings. The study design did not allow us to capture data relating to insulin dosing over the 5-year period to answer that question. There were, however, no significant changes in the mode of insulin delivery across time points with the majority of patients prescribed MDI therapy. Interestingly, the increases observed in BMI were more marked in males than females. The reason for this is not clear, however, we acknowledge that the increased prevalence of eating disorders particularly in females of this age group deserves consideration [23]. Insulin restriction has been shown to be associated with eating disorders in adolescent females

with type 1 diabetes mellitus [24]. We do not have the prevalence of eating disorders within our cohort.

Conclusions

This study reflects the Irish experience of a focused multidisciplinary intervention in the management of young adults with type 1 diabetes demonstrating a reduction in HbA_{1c} over a 5-year period coupled with significant increases in blood pressure and BMI. Increased retinopathy rates were associated with a longer duration of diabetes. There are many challenges to undertaking research in this cohort and interpreting the results of such studies should be approached with caution. In reporting the outcomes of our study cohort, we have included only those who attended the service. Non-attenders would be an informative control group when considering the impact of any clinical intervention in young adults with diabetes. However, there are many practical implications to studying non-attenders. Future strategies that will better inform our practice should include prospective multicentre studies with robust methodologies addressing novel approaches to improve aspects of diabetes care during the period of emerging adulthood. This study also highlights the importance of regular screening of microvascular complications to ensure early detection and management.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Dahlquist GG, Nystrom L, Patterson CC (2011) Swedish childhood diabetes study G, diabetes incidence in Sweden study G. Incidence of type 1 diabetes in Sweden among individuals aged 0-34 years, 1983-2007: an analysis of time trends. Diabetes Care 34(8):1754–1759
2. Patterson CC, Dahlquist GG, Gyurus E, Green A, Soltesz G (2009) Incidence trends for childhood type 1 diabetes in Europe during 1989-2003 and predicted new cases 2005-20: a multicentre prospective registration study. Lancet (London, England) 373(9680):2027–2033
3. Patterson CC, Gyurus E, Rosenbauer J, Cinek O, Neu A, Schober E et al (2012) Trends in childhood type 1 diabetes incidence in Europe during 1989-2008: evidence of non-uniformity over time in rates of increase. Diabetologia 55(8):2142–2147
4. Roche EF, McKenna AM, Ryder KJ, Brennan AA, O'Regan M, Hoey HM (2016) Is the incidence of type 1 diabetes in children and adolescents stabilising? The first 6 years of a National Register. Eur J Pediatr 175(12):1913–1919
5. Arnett JJ (2000) Emerging adulthood. A theory of development from the late teens through the twenties. Am Psychol 55(5):469–480
6. Peters A, Laffel L, American Diabetes Association Transitions Working G (2011) Diabetes care for emerging adults: recommendations for transition from pediatric to adult diabetes care systems: a position statement of the American Diabetes Association, with representation by the American College of Osteopathic Family Physicians, the American Academy of Pediatrics, the American Association of Clinical Endocrinologists, the American Osteopathic Association, the Centers for Disease Control and Prevention, Children with iabetes, The Endocrine Society, the International Society for Pediatric and Adolescent Diabetes, Juvenile Diabetes Research Foundation International, the National Diabetes Education Program, and the Pediatric Endocrine Society (formerly Lawson Wilkins Pediatric Endocrine Society). Diabetes Care 34(11):2477–2485
7. Livingstone SJ, Looker HC, Hothersall EJ, Wild SH, Lindsay RS, Chalmers J, Cleland S, Leese GP, McKnight J, Morris AD, Pearson DWM, Peden NR, Petrie JR, Philip S, Sattar N, Sullivan F, Colhoun HM (2012) Risk of cardiovascular disease and total mortality in adults with type 1 diabetes: Scottish registry linkage study. PLoS Med 9(10):e1001321
8. Livingstone SJ, Levin D, Looker HC, Lindsay RS, Wild SH, Joss N, Leese G, Leslie P, McCrimmon R, Metcalfe W, McKnight J, Morris AD, Pearson DW, Petrie JR, Philip S, Sattar NA, Traynor JP, Colhoun HM, Scottish Diabetes Research Network epidemiology group, Scottish Renal Registry (2015) Estimated life expectancy in a Scottish cohort with type 1 diabetes, 2008-2010. JAMA 313(1):37–44
9. American Diabetes Association (2017) Microvascular complications and foot care. Diabetes Care 40(Suppl 1):S88–S98
10. Diabetic Retinopathy Guidelines (2012) The Royal College of Ophthalmologists. www.rcophth.ac.uk
11. Johnson B, Elliott J, Scott A, Heller S, Eiser C (2014) Medical and psychological outcomes for young adults with type 1 diabetes: no improvement despite recent advances in diabetes care. Diabet Med 31(2):227–231
12. Levy-Shraga Y, Elisha N, Ben-Ami M, Boyko V, Lerner-Geva L, Ziv T, Konvalina N, Cohen O, Pinhas-Hamiel O (2016) Glycemic control and clinic attendance of emerging adults with type 1 diabetes at a transition care clinic. Acta Diabetol 53(1):27–33
13. Hammes HP, Kerner W, Hofer S, Kordonouri O, Raile K, Holl RW et al (2011) Diabetic retinopathy in type 1 diabetes-a contemporary analysis of 8,784 patients. Diabetologia 54(8):1977–1984
14. Carlsen S, Skrivarhaug T, Thue G, Cooper JG, Goransson L, Lovaas K et al (2016) Glycemic control and complications in patients with type 1 diabetes - a registry-based longitudinal study of adolescents and young adults. Pediatr Diabetes
15. White NH, Sun W, Cleary PA, Tamborlane WV, Danis RP, Hainsworth DP, Davis MD, for the DCCT-EDIC Research Group (2010) Effect of prior intensive therapy in type 1 diabetes on 10-year progression of retinopathy in the DCCT/EDIC: comparison of adults and adolescents. Diabetes 59(5):1244–1253
16. American Diabetes Association (2017) Children and adolescents. Diabetes Care 40(Suppl 1):S105–S113
17. American Diabetes Association (2017) Glycemic Targets. Diabetes Care 40(Suppl 1):S48–S56
18. Casey R, O'Hara MC, Cunningham A, Wall D, Geoghegan R, Hynes L, McGuire B, Gately M, Bell M, Dinneen SF (2014) Young adult type 1 diabetes care in the West of Ireland: an audit of hospital practice. QJM 107(11):903–908
19. Bryden S, Dunger DB, Mayou RA, Peveler RC, Neil HAW (2003) Poor prognosis of young adults with type 1 diabetes. Diabetes Care 26:1052–1057
20. Nordwall M., Abrahamsson M., Dhir M., Fredrikson M., Ludvigsson J., H.J. A. Impact of HbA1c , followed from onset of

type 1 diabetes, on the development of severe retinopathy and nephropathy: the VISS study (vascular diabetic complications in Southeast Sweden). Diabetes Care 2015;38:308–315

21. DuBose SN, Hermann JM, Tamborlane WV, Beck RW, Dost A, DiMeglio LA et al (2015) Obesity in Youth with Type 1 Diabetes in Germany, Austria, and the United States. J Pediatr 167(3):627–32 e1–4
22. Homma TK, Endo CM, Saruhashi T, Mori AP, Noronha RM, Monte O et al (2015) Dyslipidemia in young patients with type 1 diabetes mellitus. Arch Endocrinol Metab 59(3):215–219
23. Jacobson AM, Hauser ST, Willett JB, Wolfsdorf JI, Dvorak R, Herman L, Groot MD (1997) Psychological adjustment to IDDM: 10-year follow-up of an onset cohort of child and adolescent patients. Diabetes Care 20(5):811–818
24. Wisting L, Bang L, Skrivarhaug T, Dahl-Jorgensen K, Ro O (2015) Adolescents with type 1 diabetes–the impact of gender, age, and health-related functioning on eating disorder psychopathology. PLoS One 10(11):e0141386