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ORIGINAL ARTICLE

Alcohol consumption or cigarette smoking and cardiovascular disease risk in youth with type 1 diabetes

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Abstract

Aim To assess the association between alcohol consumption and/or cigarette smoking with other unhealthy behaviors and clinical cardiovascular risk factors in youth with type 1 diabetes.

Methods Two hundred and twenty-eight youth with type 1 diabetes (age 13–19 years) were consecutively enrolled in three Regional Pediatric Diabetes Centers in Italy. Demographic, anthropometric, lifestyle (adherence to the Mediterranean diet pattern and sports participation) and laboratory parameters were compared among youth reporting isolated or combined alcohol consumption and/or cigarette smoking.

Results Ten percent of the youth reported alcohol consumption, 10% cigarette smoking and 6% both alcohol and cigarette use; 74% did not report alcohol or cigarette use. Compared to non-drinker non-smoker youth, smokers showed significantly higher percentages of each of the behavioral and clinical cardiovascular risk factors. Drinkers showed a significantly higher proportion of abdominal adiposity, dyslipidemia and poor adherence to the Mediterranean diet. Alcohol consumption was independently associated with both dyslipidemia and high glycosylated hemoglobin.

Conclusions Our findings emphasize the need to increase the awareness of youth with T1D about the negative impact of alcohol drinking on cardiovascular risk, since the effects of alcohol might be underestimated with respect to the well-known detrimental effects of smoking. Clustering of unhealthy lifestyle should be discouraged in type 1 diabetes youth in order to promote cardiovascular protection.

Keywords Alcohol use · Cardiovascular risk · Glycosylated hemoglobin · Smoking · Type 1 diabetes · Youth

Introduction

People with type 1 diabetes (T1D) are at elevated risk of mortality and cardiovascular disease (CVD) [1]. A recent register-based cohort study in Sweden has underlined that age at onset of T1D appears to be an important determinant of survival and all cardiovascular outcomes [2]. Furthermore, puberty is a crucial time of life; in particular, the pubertal years with diabetes have a stronger impact on vascular complications compared to prepubertal or postpubertal periods [3].

Regarding the management of pediatric diabetes, the use of technologies to support self-care has greatly improved the clinical outcome [4]. For instance, automated bolus calculators or insulin-delivering pumps offer lifestyle flexibility and the potential of improving the quality of life.

However, adolescence is a critical period in the development of unhealthy habits, which are maintained later in

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life. Several studies reported that youth with T1D have the same or even increased risk of unhealthy behaviors when compared to non-diabetic peers [5]. Therefore, along with innovative tools, the educational focus should be maintained on discouraging the unhealthy lifestyle behaviors, which may in turn increase the CVD risk factors [6, 7].

Besides unbalanced nutrition and physical inactivity [8–10], adolescents with T1D may initiate alcohol consumption and/or cigarette smoking as a result of transitional conflicts that usually characterize this developmental age. Unfavorable lifestyle factors are likely to cluster in the same individual and are deemed to increase the CVD risk [9].

Few studies have assessed the impact of alcohol consumption and/or cigarette smoking on the CVD risk in youth with T1D and the association with other unfavorable behaviors. Therefore, the aim of this cross-sectional study was to assess the association between alcohol consumption and/or cigarette smoking with other unhealthy behaviors and clinical CVD risk factors in youth with T1D.

Methods

Subjects

Participants were recruited from three Regional Centers for the care of pediatric diabetes in Italy (Verona, Bologna and Napoli), as previously described [11]. Inclusion criteria were: age 13–19 years; Caucasian ethnicity and diagnosis of T1D > 2 years after the onset. Exclusion criteria were: presence of other diseases, except euthyroid Hashimoto's thyroiditis; micro- and macrovascular complications; switch from multi daily insulin to continuous subcutaneous insulin infusion or vice versa within the last 6 months. Two hundred and forty-two patients were consecutively enrolled during their scheduled visits over a 12-month period (November 1, 2014–October 31, 2015), but only 228 had complete data set for the variables of interest. The study was approved by the Ethics Committees of participating centers, in accordance with the ethical standards laid down in an appropriate version of the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all parents and all patients prior to their inclusion in the study. The clinical parameters of each patient were anonymously registered in a database using an alphanumeric and progressive identification code. Data about demographics, medical history and parents' education level (divided in five groups, from 1 = elementary to 5 = university education or higher) were collected from the patients' medical record, while clinical and laboratory parameters, and information about lifestyle habits were collected on the day of the visit.

Anthropometry

Height, weight and waist circumference (WC) were measured by the same investigator in each center following standard procedures. Height was measured to the nearest 0.1 cm with a wall-mounted stadiometer, while weight was determined to the nearest 0.1 kg on a medical scale. WC was measured with the child in a standing position with a flexible tape taken midway between the tenth rib and the iliac crest [12]. The body mass index (BMI) (weight [kg]/height [m^2]) was calculated and transformed into standard deviation scores (SDS), based upon the established Italian BMI normative curves [13]. Overweight and obesity were defined according to BMI > 75th and > 95th Italian percentiles [14]. The waist-to-height ratio (W/Ht) was calculated (WC in centimeters divided by height in centimeters). W/Ht > 0.5 was considered as index of central adiposity [15].

Lifestyle variables

Information about lifestyle habits (adherence to the Mediterranean diet pattern, sports participation, alcohol consumption and cigarette smoking) was collected by a pediatrician of the diabetologic team, in a private setting. The adherence to the Mediterranean diet pattern was assessed by interview through the KIDMED questionnaire [16]. Poor adherence was defined by a score ≤ 3.

Sports participation in the last 12 months was assessed as an index of leisure time physical activity.

Alcohol consumption and cigarette smoking behaviors were assessed by asking questions about the participant's alcohol consumption or tobacco smoking status, regardless of the frequency and dose. Responses were dichotomized into drinker/non-drinker or smoker/non-smoker.

Biochemical assays

Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides (Tg) were measured in each center by using standard methods. The long-term metabolic control was assessed by calculating the mean of four determinations of glycosylated hemoglobin during the previous year ($HbA1c_{mean}$) for each patient; all the HbA1c values were measured by high-performance liquid chromatography and standardized to the DCCT normal range (4.0–6.0%, 20–42 mmol/mol). The Tg-to-HDL-C ratio (Tg/HDL-C) was calculated; a value ≥ 2.0 has been proven able to identify children with insulin resistance, a worst cardiometabolic risk profile or early signs of organ damage [17].

The centers belong to the Italian National Health System and are certified according to international Standards ISO 9000 (www.iso9000.it/), undergoing semi-annual quality controls and inter-laboratory comparisons.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 24.0. (Armonk, NY: IBM Corp). Given the skewed distribution of age, duration, HbA1c, parental scholar indices, these variables were analyzed after log transformation, but they were expressed as untransformed values to allow presentation in text and tables. Continuous data were expressed as mean ± standard deviation (SD), while categorical data were presented as absolute frequencies and percent values. Unpaired *t* tests were used to compare scores between groups (i.e., males vs. females), while one-way ANOVA was used to compare groups stratified according to alcohol use and/or cigarette smoking status. Chi-squared test was used to compare proportions.

Logistic regression analysis was run to estimate the odds ratio (OR) of having high Tg/HDL-C (≥ 2.0) or high $HbA1c_{mean}$ (> 8.5%, > 69 mmol/mol) in youth reporting alcohol consumption and/or cigarette smoking with respect to youth reporting neither behaviors, adjusted for confounding factors. A two-sided *p* value of ≤ 0.05 was considered statistically significant.

Results

The sample characteristics by gender are shown in Table 1. Forty-eight youth (21.1%) were in treatment with continuous subcutaneous insulin infusion (CSII), 180 (78.9%) in multiple daily injections (MDI). Females showed significantly higher values of BMI-SDS, CSII treatment, W/Ht, total cholesterol and HDL-C levels than males.

Youth were then stratified according to the alcohol consumption and/or cigarette smoking status. Twenty-three youth (10.1%) reported alcohol consumption, 23 (10.1%) cigarette smoking, 14 (6.1%) both and 168 (73.7%) did not report alcohol or cigarette use.

The four categories were compared for demographic, parental educational level, clinical and CVD risk factors (Table 2). Youth who denied any alcohol consumption or cigarette smoking were younger and exhibited lower BMI-SDS, W/Ht, $HbA1c_{mean}$ and Tg/HDL-C ratio than the other groups. No difference was found regarding gender, disease duration, insulin dose and parental educational level.

The distribution of the behavioral and clinical CVD risk factors was compared among groups distributed by alcohol consumption and/or cigarette smoking status; results are shown in Fig. 1. Smokers showed significantly higher percentages of each of the behavioral and clinical CVD risk factors than youth reporting no alcohol or cigarette use. Drinkers showed a significantly higher proportion uniquely of high W/Ht, high Tg/HDL-C ($p < 0.002$) and poor adherence to the Mediterranean diet ($p < 0.05$) than youth who denied any alcohol or cigarette use. Drinkers and smokers differed only in sports participation, with higher frequency of inactivity in the smokers ($p < 0.03$).

The OR of presenting high Tg/HDL-C (≥ 2.0) or poor $HbA1c_{mean}$ (≥ 8.5%, ≥ 69 mmol/mol) in relation to alcohol consumption and/or cigarette smoking versus the reference group (non-drinkers–non-smokers), after adjusting for confounders, is shown in Table 3. Alcohol consumption was independently associated to both high Tg/HDL-C and high $HbA1c_{mean}$.

Table 1 Demographics, clinical and cardiovascular disease risk factors characteristics of youth with T1D stratified by gender

	Males	Females	*p*
Number	123	105	
Age (years)	16.1 ± 1.9	15.8 ± 2.1	0.244
Post-pubertal stage, *n* (%)	74 (60.2)	93 (88.6)	< 0.001
Disease duration (years)	8.2 ± 4.1	8.1 ± 3.9	0.912
Height (cm)	171.7 ± 9.2	161.3 ± 6.0	< 0.001
Weight (kg)	65.8 ± 12.7	59.1 ± 8.8	< 0.001
BMI (kg/m^2)	22.2 ± 3.2	22.7 ± 2.7	0.035
BMI-SDS	0.1 ± 0.9	0.5 ± 0.7	< 0.001
Waist (cm)	75.1 ± 8.5	72.4 ± 7.7	0.009
Waist-to-height ratio	0.44 ± 0.04	0.45 ± 0.05	0.027
CSII/MDI (*n*)	19/104	29/76	0.025
Insulin dose (U/kg/day)	0.86 ± 0.25	0.88 ± 0.27	0.521
Fathers' education level	2.9 ± 1.2	2.6 ± 0.9	0.109
Mothers' education level	2.8 ± 1.1	2.7 ± 0.9	0.520
Adherence to mediterranean diet (score)	6.1 ± 2.3	6.5 ± 2.3	0.146
Sports participation *n* (%)	91 (74.0)	68 (64.8)	0.131
$HbA1c_{mean}$ (%) (mmol)	8.1 ± 0.9	8.0 ± 0.9	0.619
	64.9 ± 10.2	64.1 ± 10.1	0.619
Total cholesterol (mg/dL)	152.5 ± 28.8	171.6 ± 35.3	< 0.001
HDL-cholesterol (mg/dL)	57.2 ± 13.9	62.9 ± 13.9	0.001
Triglycerides (mg/dL)	65.8 ± 32.4	73.1 ± 38.8	0.134
Tg/HDL-C ratio	1.28 ± 0.89	1.28 ± 0.89	0.797

BMI body mass index, *CSII* continuous subcutaneous insulin infusion, *HbA1c* glycosylated hemoglobin, *MDI* multiple daily injection, *SDS* standard deviation score, *Tg/HDL-C* triglycerides/high-density cholesterol

Discussion

The main results of this study indicated that the proportion of alcohol drinkers and/or cigarette smokers in T1D youth in Italy is 26.3%. The absence of alcohol or cigarette use was

Table 2 Demographics, clinical and cardiovascular disease risk factors characteristics of youth with T1D stratified according to alcohol consumption and/or cigarette smoking

	Non-drinkers–non-smokers	Drinkers	Smokers	Drinkers and smokers	*p*
Number	168	23	23	14	
Gender, M/F	85/83	15/8	13/10	10/4	0.293
Age, years	15.5 ± 1.9***	17.7 ± 1.5	16.9 ± 1.6	17.0 ± 1.9	0.000
Post-pubertal stage, *n* (%)	114 (67.9)	21 (91.3)	19 (82.6)	13 (92.9)	0.018
Disease duration, years	7.9 ± 4.0	8.9 ± 4.7	9.0 ± 3.5	7.6 ± 3.3	0.488
BMI, kg/m^2	21.8 ± 2.5***	24.1 ± 3.6	23.8 ± 3.3	24.9 ± 3.7	0.000
BMI-SDS	0.1 ± 0.8**	0.6 ± 0.8	0.6 ± 0.9	0.8 ± 0.9	0.000
Waist, cm	72.3 ± 6.9**	79.7 ± 11.0	76.1 ± 10.5	79.1 ± 6.9	0.000
Waist-to-height ratio	0.44 ± 0.04*	0.46 ± 0.06	0.46 ± 0.06	0.47 ± 0.03	0.004
CSII/MDI, *n*	37/131	4/19	6/17	1/13	0.520
Insulin dose, U/kg/day	0.9 ± 0.3	0.8 ± 0.2	0.9 ± 0.2	0.8 ± 0.4	0.467
Fathers' education level, years	2.7 ± 1.1	3.2 ± 1.4	2.6 ± 0.9	3.0 ± 0.9	0.186
Mothers' education level, years	2.8 ± 1.0	3.0 ± 1.0	2.4 ± 0.6	2.6 ± 1.0	0.281
Adherence to mediterranean diet (score)	6.6 ± 2.2°	5.6 ± 2.3	4.8 ± 2.3	5.7 ± 2.2	0.004
HbA1c $_{mean}$, % mmol	7.9 ± 0.9° 63.3 ± 9.7°	8.4 ± 1.1 67.9 ± 12.0	8.5 ± 0.9 69.0 ± 9.6	8.2 ± 0.9 66.5 ± 10.3	0.017
Total cholesterol, mg/dL	159.2 ± 30.5	172.4 ± 50.8	160.3 ± 33.8	170.4 ± 28.1	0.486
HDL-cholesterol, mg/dL	61.9 ± 13.9°	55.6 ± 13.9	51.4 ± 12.7	55.0 ± 12.8	0.001
Triglycerides, mg/dL	63.9 ± 30.8**	90.2 ± 47.7	75.2 ± 39.9	86.9 ± 43.3	0.010
Tg/HDL-C ratio	1.1 ± 0.7***	1.9 ± 1.4	1.6 ± 1.1	1.7 ± 0.9	0.001

BMI body mass index, *CSII* continuous subcutaneous insulin infusion, *HbA1c* glycosylated hemoglobin, *MDI* multiple daily injection, *SDS* standard deviation score, *Tg/HDL-C* triglycerides/high-density cholesterol

***$p < 0.05$ non-drinkers–non-smokers vs each other groups; **$p < 0.05$ non-drinkers–non-smokers versus drinkers or versus drinkers and smokers; *$p < 0.05$ non-drinkers–non-smokers vs drinkers; °$p < 0.05$ non-drinkers–non-smokers versus smokers

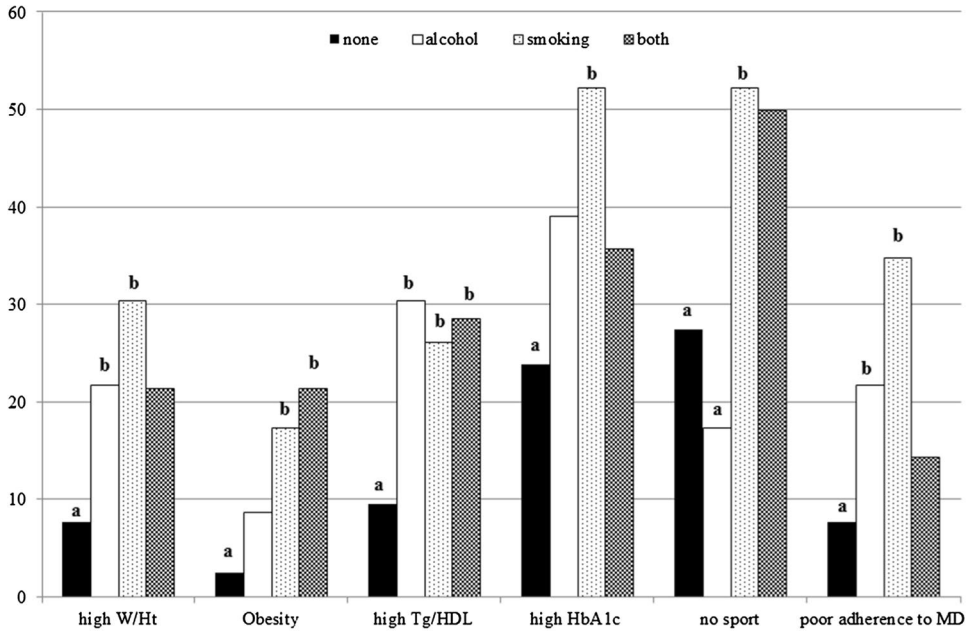

Fig. 1 Frequency of cardiovascular risk factors in youth with T1D stratified according to alcohol consumption and/or cigarette smoking. W/Ht, waist-to-height ratio; Tg/HDL, triglycerides-to-high-density lipoprotein cholesterol ratio; HbA1c, glycosylated hemoglobin A1c; MD, Mediterranean Diet. Different letters (a, b) indicate statically significant differences ($p < 0.05$) among groups stratified according to alcohol consumption and/or cigarette smoking for each cardiovascular risk factor

Table 3 Odds ratio of presenting high triglycerides-to-high-density cholesterol (≥ 2.0) or poor $HbA1c_{mean}$ (> 8.5%) in relation to alcohol consumption and/or cigarette smoking against the reference group (non-drinker–non-smoker group)

	Non-drinker–non-smokers	Drinkers	Smokers	Drinkers and smokers
Tg/HDL-C ≥ 2.0[a]	1.00	4.633* (1.244–17.255)	1.261 (0.365–4.353)	0.910 (0.198–4.175)
HbA1c ≥ 8.5%[a]	1.00	3.676** (1.333–10.138)	1.768 (0.642–4.870)	0.922 (0.279–3.084)

HbA1c glycosylated hemoglobin, *Tg/HDL-C* triglycerides/high-density cholesterol

*$p = 0.022$; **$p = 0.012$

[a]Adjusted for age, gender, post-pubertal stage, daily insulin dose, BMI-SDS, poor KIDMED score and sports participation

protective from CVD risk. Alcohol drinking independently influenced both the profile of atherogenic dyslipidemia and poor metabolic control.

Since alcohol use and cigarette smoking tend to cluster in the same individuals, we analyzed youth reporting only alcohol or smoking use separately from those reporting both drinking and smoking habits in order to disentangle the effects of each behavior on the CVD risk factors.

Socio-cultural norms consider drinking alcohol socially acceptable, therefore this behavior is widely experienced among adolescents, including the chronically ill youth [18, 19]. The frequency of alcohol use among the Italian adolescents as assessed by the last Health Behaviour in School-aged Children (HBSC) survey in 2014 was 24.1% [18]. Similar to the previous studies [20, 21], self-reported alcohol use in our T1DM population was lower than the general population, accounting for 10% when the only drinkers were considered, while it was 16.2% also considering youth reporting both drinking and smoking. This last proportion is quite similar to the proportion of drinkers in the DPV registry of German and Austrian patients with T1D [21]. As in the case of the general population, boys with T1D had higher risk of alcohol use than girls.

Although fewer adolescents with T1DM drink alcohol than their healthy peers, they are more vulnerable to the alcohol-related harms on health than the general population. Poor education about the effects of alcohol on glycemic control and inappropriate insulin adjustment or carbohydrate intake may increase the risk of hypoglycemia in fasting condition or ketoacidosis [22, 23]. Alcohol use is also a marker for poor adherence to diabetes self-care behaviors [24]. Indeed, we found that the adherence to the Mediterranean diet pattern was lower in youth reporting only alcohol use with respect to their non-drinker, non-smoker peers. Alcohol is a high-calorie beverage, which can contribute to increase weight gain. Moreover, excessive alcohol intake can exacerbate the diabetes-related lipid abnormalities, while it is retained that light-to-moderate alcohol consumption may have a beneficial effect on Tg [22, 25]. Indeed, we found that the BMI-SDS was significantly higher in youth reporting only alcohol use with respect to their non-drinker, non-smoker peers. The proportion of youth with high Tg accounted for 26.1% in the drinkers versus the 4.2% in the non-drinker non-smoker group. Since we assessed the presence of alcohol consumption regardless of the frequency and dose, we could not evaluate the effect of high quantity of alcoholic beverage. However, it should not be disregarded that the effect of alcohol on lipids may be modulated by the type of alcoholic beverage consumed as well as by the genetic polymorphisms and lifestyle factors of the subject. Specifically, we found that self-reported alcohol use was an independent risk factor for atherogenic dyslipidemia and poor metabolic control, after adjusting for demographic, anthropometric and behavioral confounders with respect to the non-drinker, non-smoker youth.

Higher alcohol consumption has been also associated with worse glycemic control and poor diabetes self-care, such as self-monitoring of blood glucose, HbA1c testing and adherence to diabetes medications [24]. We also found that youth reporting only alcohol use had a fourfold risk to have poor HbA1c levels respect to their non-drinker, non-smoker peers; due to the small size, we could not demonstrate a similar association in youth reporting both alcohol and cigarette use. Our data are in agreement with those of Hermann et al. [21], who assessed the patients according to the amount of daily alcohol intake. The authors reported that HbA1c levels were higher in patients with at-risk drinking behavior (females ≥ 12 g alcohol/day; males ≥ 24 g alcohol/day) compared to low-risk drinkers (females 0.1–< 12 g alcohol/day; males 0.1–< 24 g alcohol/day) and abstainers. However, at variance with our study, 70% patients in the at-risk drinking group reported also current cigarette smoking compared to 42% and 15%, respectively, which may have contributed to find such differences between the two groups.

From a health point of view, cigarette smoking is considered far less acceptable than alcohol drinking. The ISPAD Clinical Practice Consensus Guidelines recommend refraining from any use of cigarettes and other tobacco products, and promoting smoking cessation in adolescents, as the most important steps in preventing diabetes complications [26, 27]. Indeed, several studies have shown the adverse effects

of smoking both on macrovascular and microvascular complications of diabetes [28].

According to the 2014 HBSC survey in the Italian adolescents, regular cigarette smoking accounted for 5% at 13 years of age and 20% at 15 years, with no gender differences [29]. Self-reported cigarette smoking in our T1D youth accounted for 10% when the only smokers were considered, while it was 16.2%, considering smokers and drinkers; no gender differences were found. This proportion is comparable to the 17% in T1DM youth documented in the SEARCH for Diabetes in Youth study, which may have contributed to the differences [30].

As established in a recent systematic review and meta-analysis of studies performed in patients with T1D or type 2 diabetes [31], non-smokers generally have lower levels of $HbA1_c$, higher levels of HDL-cholesterol and lower levels of LDL cholesterol, compared to smokers. Cigarette smoking was also associated with higher odds of high TG levels in youth with T1D [31].

We found that T1D youth exposed to cigarette smoking exhibited a higher frequency of all the behavioral and clinical CVD risk factors than the non-drinker, non-smoker youth. Youth with T1D reporting smoking had higher odds of poor Hba1c levels than the non-drinker, non-smoker peers, after adjusting for demographic, anthropometric and behavioral confounders, while no independent association with atherogenic dyslipidemia was demonstrated.

It is interesting to note the lower sports participation found in the smokers' group, compared to the higher participation found in the drinkers' group. As far as we know, no study has examined the association between sports participation and alcohol use in youth with T1D, while Reynolds et al. [30] confirmed that current smokers with T1D were more likely to be physically inactive.

By appraising the literature, we found two reviews which confirmed a positive association between alcohol consumption and sports participation also in non-diabetic adolescents and young adults, while cigarette smoking was inversely related [32, 33]. Considering the inverse association of physical activity with all-cause mortality and incident cardiovascular disease in T1D [34], the presence of both inactivity and smoking in T1D youth is particularly worrisome.

There are some potential limitations in this study that need to be acknowledged. First, the cross-sectional design of the study cannot prove the causal relationship between alcohol or cigarette use and CVD risk factors. Second, we used self-reported health behaviors, and therefore, the results could be biased by socially desirable responses. To avoid bias, lifestyle was investigated in a private setting; moreover, we avoided questions about the quantity and frequency of alcohol use and cigarette smoking. As a result of these limitations, we are likely to have underestimated the associations between alcohol use or cigarette smoking and CVD risk factors. Lastly in sub-group analyses, significant differences of most behavioral and CVD risk factors in the drinker and smoker youth could not be established due to a reduced sample size of this group.

In conclusion, our study highlights that it is necessary to increase the awareness of adolescents with T1D about the negative impact of alcohol drinking on CVD risk, since the effects of alcohol might be underestimated with respect to the well-known detrimental effects of smoking. Smoking seems to be more frequently associated with significant differences of most behavioral and CVD risk factors than alcohol use. In a critical period for the development of vascular complications, clustering of unhealthy lifestyle should be discouraged in T1D youth in order to promote cardiovascular protection.

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Compliance with ethical standards

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

Ethical approval The study has been approved by the Ethics Committees of all participating centers, in accordance with the ethical standards of the institutional and or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all the parents and patients prior to their inclusion in the study.

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