Impaired postural control in diabetes-a predictor of falls?

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ORIGINAL ARTICLE

Impaired postural control in diabetes—a predictor of falls?

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Abstract

Summary New evidence points toward that impaired postural control judged by center of pressure measures during quiet stance is a predictor of falls in people with type 1 and type 2 diabetes—even in occurrence of well-known risk factors for falls.

Introduction/aim People with type 1 diabetes (T1D) and type 2 diabetes (T2D) are at risk of falling, but the association with impaired postural control is unclear. Therefore, the aim was to investigate postural control by measuring the center of pressure (CoP) during quiet standing and to estimate the prevalence ratio (PR) of falls and the fear of falling among people with diabetes compared to controls.

Methods In a cross-sectional study, participants with T1D ($n=111$) and T2D ($n=106$) and controls without diabetes ($n=328$) were included. Study procedures consisted of handgrip strength (HGS), vibration perception threshold (VPT), orthostatism, visual acuity, and postural control during quiet stance measured by CoP^{Area} (degree of body sway) and $CoP^{Velocity}$ (speed of the body sway) with "eyes open," "eyes closed" in combination with executive function tasks. A history of previous falls and fear of falling was collected by a questionnaire. CoP^{Area} and $CoP^{Velocity}$ measurements were analyzed by using a multiple linear regression model. The PR of falls and the fear of falling were estimated by a Poisson regression model. Age, sex, BMI, previous falls, alcohol use, drug, HGS, VPT, orthostatism, episodes of hypoglycemia, and visual acuity were covariates in multiple adjusted analyses.

Results Significantly larger mean CoP^{Area} measures were observed for participants with T1D ($p=0.022$) and T2D (0.002), whereas mean $CoP^{Velocity}$ measures were only increased in participants with T2D ($p=0.027$) vs. controls. Additionally, T1D and T2D participants had higher PRs for falls ($p=0.044$, $p=0.014$) and fear of falling ($p=0.006$, $p<0.001$) in the crude analyses, but the PRs reduced significantly when adjusted for mean CoP^{Area} and mean $CoP^{Velocity}$, respectively. Furthermore, multiple adjusted PRs were significantly higher than crude the analyses.

Conclusion Impaired postural control during quiet stance was seen in T1D and T2D compared with controls even in the occurrence of well-known risk factors. and correlated well with a higher prevalence of falls.

Keywords Type 1 diabetes · Type 2 diabetes · Postural control · Center of pressure · Falls

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Introduction

Falls are defined as an event resulting in a person coming to rest inadvertently on the ground (WHO) and associated with an increased risk of morbidity and mortality [1, 2]. Falls are the most frequent cause of injuries in most Western countries, and the most common fall-associated injury is a fracture [3–5]. A fall also increases the fear of falling, which is associated with immobility and a reduced quality of life [6]. The consequences of one fall and the fear of falling are associated with an increased risk of more falls that further increase the risk of fatal accidents and fractures [7–10].

People with type 1 diabetes (T1D) and type 2 diabetes (T2D) have an increased risk of falls, including falls that require hospital treatment [11, 12]. In general, the elderly are more prone to a fall, but other causes like mental health issues, physical decay, visual defects, neurological disputes, and cardiovascular and environmental factors dispose to falls at all ages [13]. In addition, the pathogenesis behind a fall is often multifactorial but is often a result of impaired postural control [14]. Postural control is the ability to continuously maintain, achieve, or restore balance during any posture or activity [15]. It is a complex and autonomic chain of events and feedback mechanisms initiated by the external stimulus of the sensory, visual, proprioceptive, or vestibular system. These stimuli are processed in the brainstem and the cerebellum to make neural commands to the blood pressure and heart rate and motor outputs like the vestibular-ocular reflex and motor impulses to control the eyes and to make postural adjustments [15, 16]. Hence, this system is highly vulnerable for impairments at any part of the chain. With high validity and reliability, impaired postural control is quantified by center of pressure (CoP) measurements like CoP^{Area} and $CoP^{Velocity}$ during quiet bipedal stance [17]. In general, the CoP^{Area} represents the area of the 95% confidence ellipse of the center of pressure displacement and is a measurement of the body sway. $CoP^{Velocity}$ represents the total distance traveled by the center of pressure over time and is a measurement of the speed of the sway. A larger CoP^{Area} and increased $CoP^{Velocity}$ are associated with a decreased ability (impaired postural control) to maintain balance and avoid falls. On the contrary, a decrease in the CoP^{Area} and $CoP^{Velocity}$ represents an increased ability to maintain an upright stance and maintain balance (improved postural control) [18]. The CoP can be measured during several conditions and graded in difficulty by adding a visual and cognitive task.

Clinicians have used the CoP^{Area} and $CoP^{Velocity}$ to assess changes in postural control [19–23]. However, sparse data exists regarding people with diabetes and the association with CoP measures, although people with diabetic neuropathy have been shown to perform worse in a variety of CoP measurements during quiet stance [24]. In addition, it is unclear to which extent other risk factors affect CoP during quiet stance like muscle strength, blood pressure, general mobility, BMI, diabetic complications, drugs, alcohol, and blood glucose levels. Hence, CoP measures during quiet stance could be a surrogate marker for the risk of falls.

Therefore, the primary aim was to estimate the postural control by using CoP measures during quiet standing as a surrogate marker of the risk of falls in people with T1D and T2D compared to people without diabetes and to explore risk factors associated with impaired postural control. A second aim was to compare the prevalence ratios of falls and fear of falling among people with and without diabetes stratified by risk factors.

Materials and methods

Source of data

The trial was conducted at Aalborg University Hospital at Steno Diabetes Center North Denmark, collaborating with Aalborg University. To maintain a high study quality, the coefficient of variance (CV) (standard deviation over the mean) was calculated for each study procedure to validate the methods [22–25]. CV percentages below 10% were considered a high standard and as excellent procedures [26]. All data was collected by Research Electronic Data Capture (REDCap).

Study population

This was a cross-sectional single-center study and consisted of participants with T1D ($n = 111$) and T2D ($n = 106$) and control persons without diabetes ($n = 328$). The participants were enrolled from April 1, 2019, until June 30, 2021, and recruited by social media, flyers, and at the outpatient clinics. The participants were freely and openly recruited by social media and flyers at the local hospitals without direct contact and preference to disease status. Each participant met for 1 day of testing, and no participant dropouts were registered during the study day, and more than 95% of the study procedures were completed.

Inclusion

The participants with T1D and T2D were included between 20 and 90 years of age and had more than 1 year of diabetes duration. Control persons were included between 20 and

90 years of age and not diagnosed with diabetes. T1D and T2D were defined by a previous HbA1c above 48 mmol/mol (6.5%). Post hoc analyses of control persons showed HbA1c values < 48 mmol/mol.

Exclusion

The participants were excluded if they had the following conditions (applicable for both T1D and T2D, and control persons): maturity-onset diabetes of the young, decreased liver function (alanine amino-transaminase (ALAT) > 250 µ/L), kidney dysfunction (estimated glomerular filtration rate (eGFR) < 15 mmol/L/1, 73 m^2), were pregnant or breast-feeding, had active malignancy or terminal illness, current or previous alcohol or drug abuse (within 1 year prior to inclusion), were not able to understand Danish written or verbally, terms according to investigators' judgment that made the participants unsuitable to participate, including a lack of understanding or reduced physical ability, and participated in other clinical studies or a current weekly exercise routine more than 10 h per week.

The study protocols

Questionnaire

An extensive questionnaire was handed out to each participant and completed on a tablet under standardized conditions. The questionnaire was provided by the SYSDIET study and included lifestyle variables, medical history, falls, and the fear of falling. Lifestyle variables included smoking status, alcohol consumption, and activity level [27, 28]. Physical and mental health status was determined by the EQ-5D-3L questionnaire - a tool to measure the self-rated perception of general mobility, personal care, pain, and mental status [29]. In addition, it assesses the current state of health rated by the participant on a 100-point scale (0 corresponding to the worst health condition possible and 100 corresponding to the best possible). The medical history included information regarding diabetes duration, diabetic complications, and episodes of hypoglycemia (within 1 year). Fall-associated drugs included SSRI, benzodiazepines (anxiolytics and sedatives), and opioids. Polypharmacy was defined as the intake of more than four types of drug per day. Dispensing of drugs was included at least 3 months before the trial to ensure a current redeemed prescription. Falls and the fear of falling were reported according to the National Clinical Guidelines for fall prevention and included all falls within 1 year [30]. A fall was defined (WHO definition) as an event, which resulted in a person coming to rest inadvertently on the ground or floor or other lower levels [31]. Fear of falling was defined as "not at all" (0), "to some degree" (1), " to a less degree" (2), "to a high degree" (3), or " to a very high degree" (4).

Assessment of biochemistry

Blood samples were taken and handled by the research laboratory technologists and analyzed within the same day at the Clinical Biochemical Department at Aalborg University. Venous blood samples were drawn for each participant. The blood samples were collected as serum, EDTA-plasma, and in hemolytic-free Li-heparin tubes, protected from light and cooled to 2–8 °C. Biochemistry included was HbA1c, creatinine, eGFR, calcium-ion, and ALAT. This laboratory is subject to rigorous quality testing according to international standards, and a CV of 0.53% was shown for HbA1c.

BMI

Body weight was calculated to the nearest 0.1 kg using a column scale (Seca GmbH & Co., Hamburg, Germany) with the participants dressed in a light gown and no shoes. Height was measured to the nearest 0.5 cm using a stadiometer (Seca GmbH & Co., Hamburg, Germany). BMI was calculated as the person's weight in kilograms over their height in meters squared.

The cardiovascular risk was assessed by ECG and orthostatic blood pressure measurement [32, 33]. A regular 12-lead ECG placement was conducted, and the findings were summarized descriptively and quantitatively. This included incidences of abnormal T-inversion, leftward axis, bradycardia, atrial fibrillation, and QTc measures. This yielded a CV for the combination of atrial fibrillation, T-inversion, and leftward axis of 4.5% and a CV of 1.7% for QTc. Orthostatic blood pressure was performed by three consecutive blood pressure measurements. The first was in a lying down position after 5 min of rest and then, a second one after 1 min and a third one after 3 min in a standing position. A positive test was defined as fainting, a decrease in systolic or diastolic blood pressure more than 20 or 10 mmHg, respectively, or an increase of at least 30 beats in the heart rate. Orthostatic symptoms were reported and included dizziness, remoteness, visual disturbances, malaise, or fainting. CV for resting systolic blood pressure was 3.5%.

Vibration perception threshold was assessed by VPT (Biothesiometry, Bio-medical Instrument Co. Newbury, OH 44,065, USA) [34, 35]. The test was performed by slowly graduating the power (amplitude) until the participant registered the vibration on the proximal part of the first toe on each foot. The power was then turned down until the vibration was undetectable and registered. The test was repeated two times for analysis. CV was 2.3%.

Muscle strength and general mobility were assessed by HGS measured using a hydraulic dynamometer (SAEHAN Corporation, Gyeongnam, South Korea) [36, 37]. All the participants were standing and had their arm in an extended position during testing. HGS was defined as the maximal

grip strength achieved by verbally encouraging the participants. Each hand was used, and the best of two trials was registered. CV was 4.8%. General mobility was assessed by the Timed Up and Go (TUG) test [38]. The participant started from a sitting position in a chair (seat height approximately 43–47 cm). All the participants were asked to perform the test barefooted, and running was not allowed. The test was performed one time for analysis. CV was 5.4%.

Visual acuity (VA) was estimated for each eye by a TOPCON Auto Kerato-Refractometer KR-800S [39, 40]. The test was without glasses, and the device automatically made an objective refraction and corrected the lens to the most optimal optic. Then, visual acuity was assessed by a subjective refraction measurement that included the participant reading letters or numbers. CV was 7.8%.

Assessment of postural control

The participants were tested during quiet bipedal barefoot stance on a force platform (Plux Biosignals S.A, Arruda dos Vinhos, Portugal) during six different conditions, including visual and executive function each of 30 s on a firm surface [41–43]. The following conditions were performed: eyes opened (EO), eyes closed (EC), eyes opened counting forward (EOF), eyes closed counting forward (ECF), eyes opened subtracting backwards with seven (EOB), and eyes closed subtracting backwards with seven (ECB). A total of 12 tests were performed as six tests were performed in a serial sequence and repeated after a 5-min break. The sequence of tests and numbers for subtracting were randomized. The number of correct subtractions was noted and summarized.

The vertical forces were extracted from the force platform (a sampling rate at 1 kHz, Open Signals v. 1.2.8). The first and last 2.5 s were excluded after low pass filtering digitally (10 Hz Butterworth, 2nd order and zero lag). CoP^{Area} and $CoP^{Velocity}$ measurements were calculated using the vertical forces in the 30-s analysis window for each condition. The size of the postural sway and the speed of the sway were quantified with the variables 95% prediction ellipse CoP^{Area} and resultant mean $CoP^{Velocity}$ [44]. The mean of two similar conditions for each of the six conditions was used for analysis. CVs were 2.5% for CoP^{Area} and 3.5% for $CoP^{Velocity}$, respectively.

Statistics

Baseline characteristics were described as percentage of participants or mean with a standard deviation (SD) if normally distributed. The distribution of continuous variables was examined by histograms, q-q plots, and box plots. For normally distributed unpaired data, a *t*-test was performed for intergroup comparisons. The data were transformed with natural logarithm if the assumption for normality was violated and rechecked. If still not normally distributed, the Mann–Whitney *U* test was used to assess the difference between the two groups. Differences in categorical data were analyzed using a chi-square or Fisher's exact test (when at least one cell in the contingency table had cell count < 5).

We built a simple multiple linear (for continuous data) or logistic regression (for categorical data) model with each clinical, biochemistry, and different CoP including a mean score measurement as dependent variables, and diagnosis (T1D vs. control or T2D vs. controls) sex and age as independent variables. Data was presented with a resultant *p*-value for intergroup comparising. Then, a multivariate linear regression model was built with each CoP parameter and a mean score as dependent variables, and diagnosis (T1D vs. controls or T2D vs. controls), increasing age, sex (man vs. woman), fallers vs. non-fallers, fall-associated drug (yes vs. no), polypharmacy (yes vs. no), orthostatism (yes vs. no), increasing BMI, increasing alcohol units, increasing HGS, increasing TUG, increasing VPT, and increasing visual acuity as independent variables. The models yielded beta-coefficients, 95% CI, and *p*-values after assessing Pearson's correlation coefficient between potential independent variables. Each parameter was checked to see if it followed a normal distribution, and the residual plot for each linear regression model was inspected.

Then, a Poisson regression model with robust variance was used to estimate the prevalence ratios (PR) for several falls and for fear of falling in the participants with T1D and T2D vs. controls [45]. Dependent variables (falls and degree of fear of falling) were counts that followed a Poisson distribution, with a mean equal to variance assessed by fitted residual plots. The models were assembled crude and then adjusted for sex, age, and BMI and by mean CoP^{Area} and mean $CoP^{Velocity}$. Finally, the models were also adjusted for alcohol, fall-associated drug, polypharmacy, HGS, TUG, VPT, orthostatism, severe hypoglycemia, and visual acuity.

A dedicated MATLAB script (MathWorks, R 2021a, Natick, MA, USA) was used for all post-processing of CoP data. Statistical analyses were conducted in STATA version 17.0 (StataCorp, College Station, TX, USA), and a two-sided p-value < 0.05 was accepted as significant.

Results

General characteristics of the study population

The participants with T1D were younger than controls, but no differences in age was observed between T2D and controls (T1D vs. controls, $p < 0.001$, T2D vs. controls, $p = 0.072$). Sex distribution was unevenly balanced as fewer women were included with T1D and T2D compared with

controls (T1D vs. controls, $p=0.002$, T2D vs. controls, $p=0.005$). The proportion of diabetic complications was lowest in the participants with T1D compared to T2D (T1D vs. T2D, $p<0.001$). EQ-5D-3L revealed an impaired self-rated quality of life, including conditions as mobility, personal care, usual activities, pain, depression, and anxiety among the participants with T1D and T2D compared to controls (T1D vs. controls, $p<0.001$ (for each condition), T2D vs. controls, $p<0.001$ (for each condition)). More falls were reported in T1D and T2D compared to controls (T1D vs. controls, $p<0.001$, T2D vs. controls, $p<0.001$). In addition, the participants with T1D and T2D reported a higher level of fear of falling than controls (T1D vs. controls, $p<0.001$, T2D vs. controls, $p<0.001$) (Table 1).

Diabetes-related parameters

The participants with T1D had worse glycemic control with a mean HbA1c of 63.8 mmol/mol compared to 54.7 mmol/mol in T2D ($p<0.001$) (Table 2). Twice as long diabetes duration was registered in the participants with T1D compared to T2D ($p<0.001$), although the proportion of diabetic complications was lowest in the participants with T1D compared to T2D ($p<0.001$) (Table 1). Neuropathy and heart disease were the two predominant diabetic complications. Approximately, a third of the T2 diabetic participants used insulin regularly. The prevalence of episodes with hypoglycemia was more pronounced in T1D than T2D (Table 1).

Clinical tests and biochemical assessment

A significantly higher HGS was seen in the participants with T1D vs. controls in the crude analysis, but the effect leveled when adjusted for age, sex, and BMI. Opposite results were seen for the T2 diabetic participants as the adjusted analyses showed a significantly lower HGS compared to controls ($p=0.016$). The TUG test revealed a significantly slower walking speed among both T1D and T2D compared with controls adjusted for sex, age, and BMI (T1D vs. controls, $p<0.001$, T2D vs. controls, $p=0.032$). In addition, the participants with diabetes had significantly higher VPT measures in the adjusted analysis (T1D vs. controls, $p=0.008$, T2 vs. controls $p=0.001$).

Adjusted for sex, age, and BMI, the participants with T1D had a significantly higher resting systolic blood pressure ($p=0.001$), but both T1D and T2D had a higher heart frequency ($p<0.001$) than controls. In addition, significantly more cases of verified orthostatism were observed in T1D compared with controls ($p=0.049$). ECG analysis showed significantly higher QTc values for the participants with T2D ($p=0.001$). Visual acuity was significantly lower for the right eye in T1D ($p=0.038$) compared with controls. No significant differences were observed in eGFR or ALAT levels between the groups, and they were within the normal range (Table 2).

Center of pressure—Area and Velocity measures

All variables were compared crude, adjusted for age, sex, and BMI (including mean CoP^{Area} and mean $CoP^{Velocity}$ to elucidate the effect of the postural control parameters) and in a multivariate linear regression model (adjusted for sex, age, BMI, alcohol consumption, fall-associated drug, polypharmacy, HGS, TUG, VPT, orthostatism, and visual acuity).

Type 1 diabetes

The participants with T1D had significantly larger sex, age, and BMI-adjusted CoP^{Area} displacements for EOF ($p=0.029$), EOB ($p=0.029$), ECB ($p=0.023$), and mean CoP ($p=0.027$) than controls (Table 3). In addition, type 1 diabetics had significantly fewer correct executive function tasks than controls (EOB true, $p=0.002$; ECB true, $p=0.001$) (Table 3). In the multivariate regression analyses, larger mean CoP^{Area} ($p=0.022$) displacements were observed, including EOF ($p=0.042$), EOB ($p=0.029$), and ECB ($p=0.023$) compared with controls (Table 4).

Type 2 diabetes

The participants with T2D had significantly larger mean CoP^{Area} displacements and increased mean $CoP^{Velocity}$ speed during quiet stance compared with controls for each condition (EO, EOF, EOB, EC, ECF, and ECB, $p<0.001$) (Table 3). These results were recurring in the multivariate regression analyses for mean CoP^{Area} ($p=0.002$) displacement regarding EO ($p=0.006$), EOF ($p=0.005$), EOB ($p=0.042$), EC ($p=0.042$), ECF ($p=0.015$), and ECB ($p=0.027$). Mean $CoP^{Velocity}$ ($p=0.027$) included EO ($p=0.047$), EOF ($p=0.003$), and ECB (0.034) compared with controls (Table 4).

Other associations

Other significant associations were seen in the multivariate regression analyses as larger CoP^{Area} displacement (EO, $p=0.006$; EOB, $p=0.002$; and ECB, $p=0.021$) and increased $CoP^{Velocity}$ speed (EO, $p=0.019$) were seen in fallers vs. non-fallers. A visual representation of the difference between a faller vs. a non-faller is shown in Fig. 1. In general, a stronger association was seen as the different conditions raised in difficulty, e.g., deprived vision (EC) and executive function tasks (EOB and ECB). In addition, several risk factors affected the CoP^{Area} displacement negatively, such as increasing age, increasing

Table 1 General person characteristics

Variables	People with T1D ($n=111$)	People with T2D ($n=106$)	Controls ($n=328$)
Age, years (SD)	52.9 (15.3)*	62.1 (10.1)	57.7 (15.8)
Sex			
Women, % (n)	57.7 (63)*	47.2 (50)*	62.8 (206)
Men, % (n)	43.3 (48)	52.8 (56)	37.2 (122)
BMI, kg/m^2 (SD)	26.1 (5)	29.2 (4)	27.4 (15)
Diabetes duration, years (SD)	26.44 (14.2)	11.4 (9.3)	-
Diabetic complications			
Retinopathy, % (n)	8.1 (9)	5.6 (6)	-
Nephropathy, % (n)	0.0 (0)	3.7 (4)	-
Heart disease, % (n)	6.3 (7) *	13.2 (14)*	-
Neuropathy, % (n)	9.1 (10)*	13.2 (14)*	-
Foot ulcers, % (n)	0.0 (0)	0.9 (1)	-
More than one complication, % (n)	14.4 (16)	23.5 (25)	-
Total, % (n)	23.3 (26)*	36.8 (39)*	-
Smoking, alcohol, and physical activity			
Smoking, % (n)	24.1 (26)*	8.1 (8)	7.4 (24)
Alcohol units/month (SD)	18.4 (22.7)	16.6 (21.1)	23.9 (24.0)*
Physical active[1], % (n)	50.4 (56)*	48.4 (51)*	67.4 (221)
EQ-5D-3L			
Movement problems, % (n)	17.8 (16)*	18.8 (17)*	9.4 (30)
Personal care problems, % (n)	2.2 (1)	3.8 (4)	0.3 (1)
Usual activity problems, % (n)	18.9 (17)*	23.8 (22)*	10.2 (32)
Pain problems, % (n)	71.1 (64)*	58.7 (56)	54.4 (148)
Anxiety and depression problems, % (n)	15.6 (14)*	11.5 (10)*	8.3 (28)
VAS 1–100 (SD)	74.8 (78.2)*	74.5 (72.8)*	83.5 (81.3)
Falls			
1 or more falls within the last year, % (n)	16.2 (18)*	18.8 (20)*	10.9 (36)
1 fall within the last year, % (n)	4.5 (5)	4.7 (5)	5.8 (19)
2 falls within the last year, % (n)	7.2 (8)*	4.7 (5)	3.6 (12)
3 ≥ falls within the last year, % (n)	4.5 (5)*	9.4 (10)*	1.5 (5)
Fear of falling			
Fear of falling, % (n)	30.2 (32)*	33.9 (36)*	15.0 (49)
To some degree, % (n)	14.1 (16)*	18.6 (18)*	6.8 (21)
To a less degree, % (n)	9.9 (11)	8.4 (9)	7.8 (24)
To a high degree, % (n)	3.6 (4)	6.6 (7)	0.3 (1)
To a very high degree, % (n)	0.9 (1)	0.9 (1)	0.9 (3)

Table 1 (continued)

Variables	People with T1D ($n=111$)	People with T2D ($n=106$)	Controls ($n=328$)
Drug			
Drug, different types per day (SD)	2.9 (2.4)*	3.9 (3.4)*	1.1 (1.5)
Drug ≥ 4 different types/day, % (n)	32.4 (39)*	58.5 (62)*	9.1 (30)
Fall-associated[2], % (n)	21.6 (24)*	18.9 (20)*	7.9 (26)
Mild painkillers[3], % (n)	19.8 (22)*	20.8 (22)*	8.8 (29)
Strong painkillers[4], % (n)	2.3 (3)	1.9 (2)	2.3 (7)
Antihypertensive drugs, % (n)	41.2 (46)*	53.8 (57)*	17.1 (56)
Antidiabetic drugs (not insulin), % (n)	0.0 (0)	67.9 (72)	-
Insulin use, % (n)	100 (111)	32.2 (34)	-
Hypoglycemia			
Awareness[a], % (n)	91.8 (102)*	56.6 (60)	-
Mild episodes[b], weekly, % (n)	48.6 (54)*	2.8 (3)	-
Mild episodes[b], monthly, % (n)	31.5 (35)*	7.5 (8)	-
Severe episode[c], weekly, % (n)	4.5 (5)	0.0 (0)	-
Severe episodes[c], monthly, % (n)	4.5 (5)	1.8 (2)	-

Data is presented as mean values with standard deviation (SD) or percentages (%)

[1]Physical activity in spare time more than twice and 30 min/week. [2]Fall-associated includes SSRI, benzodiazepines (anxiolytics and sedatives), and opioids. [3]Mild painkillers include paracetamol, nonsteroids anti-inflammatory drug. [4]Strong painkillers include gabapentin, pregabalin, and amitriptyline, not opioids

[a]Awareness of symptoms of a blood glucose below 3.0 mmol/L. [b]Capable of acting on a blood glucose below 3.5 mmol/l. [c]Not able to act on a blood glucose below 3.5 mmol/l

*Indicates a significant difference between groups (T1D vs. controls, T2D vs. controls or T1D vs. T2D when no data on control persons is present). Crude analyses by *t*-test or the Mann–Whitney *U* test were performed for intergroup comparisons. Differences in categorical data were analyzed using a chi-square or Fisher's exact test

T1D, type 1 diabetes; *T2D*, type 2 diabetes; *SD*, standard deviation; *EQ-5D-3L*, European quality of life dimension with three levels; *VAS*, visual analog scale

Table 2 Clinical measurements and biochemistry

Variables	People with T1D ($n=111$)	People with T2D ($n=106$)	Controls ($n=328$)	T1D vs. controls p-value	T1D vs. controls #p-value	T2D vs. controls p-value	T2D vs. controls #p-value
Muscle strength and general mobility							
Handgrip strength kg (SD)	37.5 (11.6)	36.2 (11.7)	36.8 (11.6)	**0.021**	0.089	0.836	**0.016**
TUG sec (SD)	8.41 (3.1)	9.0 (2.5)	8.0 (1.9)	0.148	**< 0.001**	**0.017**	**0.032**
Neuropathy							
VPT (SD)	15 (9.1)	20.4 (14.3)	14 (9.2)	0.270	**0.008**	**0.026**	**0.001**
Blood pressure							
Systolic BP mmHg (SD)	139.7 (17.7)	138.7 (16.1)	136.5 (19.7)	0.084	**0.001**	0.197	0.239
Diastolic BP mmHg (SD)	82.2 (9.2)	85.6 (9.7)	85.1 (11.2)	**0.019**	0.132	0.463	0.536
Heart frequency beats/min (SD)	68.4 (12.8)	72.2 (13.2)	63.9 (10.8)	**< 0.000**	**< 0.000**	**< 0.000**	**< 0.000**
Orthostatism verified, % (n)	19.8 (22)	16.0 (17)	12.8 (42)	0.080	**0.049**	0.399	0.482
Orthostatic symptoms, % (n)	11.7 (13)	10.4 (11)	6.7 (22)	0.070	0.128	0.173	0.221
ECG							
Abnormal t-inversion, % (n)	3.3 (4)	9.4 (10)	6.2 (17)	0.443	0.334	0.110	0.544
Bradycardia, % (n)	8.1 (9)	4.7 (5)	7.3 (24)	0.766	0.433	0.125	0.444
AFLI, % (n)	0.9 (1)	2.8 (3)	0.9 (3)	0.965	0.922	0.833	0.833
QTc (SD)	411 (21.55)	423 (29.5)	409 (23.8)	0.205	0.082	**< 0.000**	**< 0.000**
Visual acuity							
Right eye (SD)	0.95 (0.24)	0.94 (0.23)	1.0 (0.12)	**0.038**	**0.003**	**0.020**	0.310
Left eye (SD)	1.0 (0.23)	0.94 (0.25)	1.0 (0.13)	0.588	0.099	**0.009**	0.227
Biochemistry							
HbA1c, mmml/mol (SD)	63.8 (12.2)	54.7 (14.1)	35.2 (3.3)	-	-	-	-
eGFR ml/min (SD)	84.5 (10.1)	81.6 (9.5)	85.3 (12.2)	0.654	0.822	0.231	0.811
ALAT U/l (SD)	23.1 (31.1)	27.8 (20.5)	23.9 (12.2)	0.555	0.111	0.066	0.051

Data is presented as mean values with standard deviation (SD) or as percentage with numbers (n)

p: unadjusted t-test for two samples, chi-square or Mann–Whitney U test as appropriate for intercomparison between two groups

#p: adjustment for age, sex, and BMI by multiple linear regression (continuous data) or logistic regression (categorical data). p-values in bold indicate a significant value

T1D, type 1 diabetes; *T2D*, type 2 diabetes; *SD*, standard deviation; *VPT*, vibratory perception thresholds; *AFLI*, atrial fibrillation; *QTc*, corrected QT interval

BMI, fall-associated drug use, and polypharmacy (all significantly increased). A significantly smaller CoP^{Area} displacement indicated a better balance and was observed in women and persons with high HGS. Lastly, a significantly increased $CoP^{Velocity}$ speed was seen in aging and at increased VPT, whereas women, a higher HGS, and a higher visual acuity decreased the $CoP^{Velocity}$ speed (Table 4).

Falls and fear of falling

The crude analyses showed significantly higher PRs of falls and fear of falling amongst type T1 and T2 diabetic participants compared with controls (Falls: T1D vs. controls, p = 0.044; T2D vs. controls, p = 0.014. Fear of falling: T1D vs. controls, p = 0.006; T2D vs. controls, p < 0.001). However, adjusted for mean CoP^{Area} or mean $CoP^{Velocity}$, respectively, the PRs decreased for both outcomes. Although, in the multible adjusted analyses, the PRs were even higher in T1D and T2D than controls (Falls: T1D vs. controls, $p = 0.026$; T2D vs. controls, $p < 0.001$. Fear of falling: T1D vs. controls, p = 0.021; T2D vs. controls, p=0.032) (Table 5).

Discussion

This is the first larger-scale study to assess postural control and fall prevalence in a group of participants with longstanding T1D and T2D compared with controls stratified by several potential and well-known risk factors for falling.

In general, we found imparied postural control parameters judged by a larger mean CoP^{Area} displacement and

increased mean $CoP^{Velocity}$ and a higher PR of self-reported falls and fear of falling among participants with T1D and T2D compared to controls, although, the effect was highest in the participants with T2D. In addition, we identified a solid correlation between these measures as fallers vs. non-fallers had impaird postural control and decreased PRs for falls were seen when mean CoP measures were added to the analyses. This was a proof of concept as the findings of a higher PR of self-reported falls correlated with CoP measures in a cohort including diabetes participants [12]. Finally, several risk factors were identified that were associated with impaired postural control during quiet stance like increased age, higher BMI, fall-related drug, polypharmacy, decreased HGS, higher degree of VPT, reduced visual acuity, and visual deprivation.

Impaired postural control—a possible predictor of falls

The participants with T1D had significantly larger CoP^{Area} measurements during different executive function tasks and a significantly reduced subtraction capability compared with control, but no changes in CoP measures were observed during the less-demanding condition. This may imply a link between executive dysfunction and impaired postural control in T1D. Previously, people with T1D have been associated with executive dysfunction, e.g., reduced subtraction capability while handling difficult tasks [46]. Hence, executive dysfunction in participants with T1D is a potential risk of impairments in postural control systems. However, in consideration of type-1 errors, future studies should aim for causality. The participants with T2D had larger CoP^{Area} and increased $CoP^{Velocity}$, which increased additionally during visual deprivation and during executive function tasks compared to controls. Moreover, compared with controls, no difference was seen in subtraction capability. The larger CoP^{Area} and increased $CoP^{Velocity}$ indicated a greater body sway and higher speed of the sway during quiet stance in T2D. This was despite extensive adjustments for known risk factors that impair postural control. In addition, the participants with self-reported previous falls also had impaired postural control during quiet stance compared to non-fallers, and the PRs of self-reported falls were higher among the participants with T1D and T2D than controls. Furthermore, when adjusted for mean CoP measures, the prevalence of falls decreased, which additionally indicated a strong correlation between a sufficient postural control apparatus and the ability to avoid a fall as seen in previous findings [11, 12]. This is novel information as no other studies previously have combined the prevalence of falls and measurements for postural control to identify the potential prevalence of falls in people with T1D and T2D. Therefore, it is reasonable to suggest that people with diabetes who suffer from falls are associated with impaired postural control. This method could be suitable for identifying particularly vulnerable people with diabetes and possible predict their risk of falls. Consequently, this may decrease the likelihood of fall-associated injuries like fractures and contribute to at lower proportion of hip fractures among people with diabetes [47].

Fear of falling—the driver of falls and quality of life

We also showed that the participants with T1D and T2D reported more fear of falling than the controls, as previously seen in the literature [6]. The fear of falling is likely associated with a history of falls and impaired postural control leading to a vicious circle of additional falls and fear of falling. Furthermore, falls are associated with immobility and reduced quality of life. This was supported by the self-rated data reported in the quality of life (EQ-5D-3L) questionnaire. This showed that the people with T1D and T2D reported a decrease in physical activity, had more problems with movement, and experienced more pain and depression compared with controls. Other studies have used this specific questionnaire to estimate health status in diabetes and found that a general decrease in these health parameters indicates a higher severity of disease-associated symptoms [48]. In addition, the general physical mobility parameters were also decreased in both T1D and T2D and corresponded well to the reported quality of life. Therefore, the combination of self-reported quality of life measures and the information of fear of falling in diabetes could be useful in identifying the potential risk of falls in people with T1D and T2D. Several studies have already shown marked effect from different kinds of an exercise intervention on people with diabetes to reduce the risk for falling and decrease the degree of fear of falling by improving the postural control [49, 50]. This underlines the importance of detecting impaired postural control at early stages to reduce the risk of falls by early exercise intervention.

Risk factors for postural control and falls

Aging was associated with impaired postural control measured by CoP during quiet stance as shown in several other studies [11, 51, 52]. The aging process is multifactorial and includes changes that often involve the nervous and musculoskeletal system and cardiovascular system. These changes were confirmed by HGS, TUG, VPN, orthostatism, and ECG and confirmed by self-reported outcomes from the participants, which could explain the modest increase in CoP measures.

Female participants were associated with improved postural control measures compared with men measured by CoP during quiet stance, which improved even more while visually deprived and during executive function tasks. A

Table 3 Center of pressure (CoP) measurements of participants with T1D and T2D and controls without diabetes

Balance, CoP (SD)	People with T1D ($n=111$)	People with T2D ($n=106$)	Controls ($n=328$)	T1D vs. controls p-value	T1D vs. controls #p-value	T2D vs. controls p-value	T2D vs. controls #p-value
Area (cm^2)							
Eyes open	2.76 (5.0)	3.43 (4.1)	1.93 (1.7)	**0.004**	0.251	**< 0.001**	**< 0.001**
Eyes open forward	3.32 (5.0)	4.77 (5.9)	3.07 (4.5)	0.447	**0.042**	**< 0.001**	**< 0.001**
Eyes open backward	4.73 (6.0)	6.36 (6.8)	4.55 (6.0)	0.714	**0.029**	**< 0.001**	**< 0.001**
Eyes closed	3.23 (3.5)	5.88 (7.4)	3.41 (4.2)	0.982	0.707	**< 0.001**	**< 0.001**
Eyes closed forward	3.26 (2.8)	5.79 (6.3)	3.43 (4.5)	0.575	0.341	**< 0.001**	**< 0.001**
Eyes closed backward	4.46 (3.7)	6.54 (6.9)	4.33 (5.1)	0.511	**0.023**	**< 0.001**	**< 0.001**
CoP mean	3.65 (3.1)	5.65 (5.1)	2.93 (1.9)	0.300	**0.027**	**< 0.001**	**< 0.001**
Velocity (cm/s)							
Eyes open	1.10 (0.6)	1.28 (0.9)	1.02 (0.4)	0.174	0.083	**< 0.001**	**0.004**
Eyes open forward	1.35 (0.8)	1.69 (0.9)	1.37 (0.8)	0.770	0.119	**< 0.001**	**0.001**
Eyes open backward	1.63 (1.0)	2.04 (1.12)	1.68 (1.0)	0.986	0.350	**< 0.001**	**0.016**
Eyes closed	1.50 (0.8)	2.18 (1.6)	1.57 (1.0)	0.844	0.910	**< 0.001**	**< 0.001**
Eyes closed forward	1.72 (1.1)	2.36 (1.6)	1.81 (1.3)	0.746	0.765	**< 0.001**	**0.002**
Eyes closed backward	1.84 (1.2)	2.56 (1.7)	1.93 (1.3)	0.284	0.549	**< 0.001**	**0.001**
CoP mean	1.53 (0.8)	2.0 (1.2)	1.45 (0.6)	0.891	0.199	**< 0.001**	**< 0.001**
Calculation (SD)							
Eyes open backwards, true	8.0 (8.6)	9.6 (9.1)	9.6 (8.4)	**0.001**	**0.002**	0.958	0.443
Eyes closed backwards, true	8.2 (9.5)	9.5 (10.1)	9.5 (7.9)	**0.004**	**0.001**	0.931	0.455

Data is presented as mean values and standard deviations (SD)

"Forward" refers to counting forward in a slow pace from zero (an easy executive task); "Backwards" refers to continuously subtracting with seven from a random start number (a difficult executive task); "Calculation true" refers to the number of true calculations

p: unadjusted *t*-test for two samples, chi-square or Mann–Whitney *U* test as appropriate

#*p*: adjustment for age, sex, and BMI by multiple linear regression. *p*-values in bold indicate a significant value

T1D, type 1 diabetes; *T2D*, type 2 diabetes; *SD*, standard deviation; *CoP*, center of pressure

Velocity (cm/s), area (cm^2), and calculation (SD)

meta-analysis on younger people observed a small positive effect for CoP measures during quiet stance in younger women but not for dynamic testing compared to younger men [53]. Another study on postural control found no difference between men and women during quiet stance but showed that men had better CoP measures during dynamic testing compared to women [54]. Fat distribution could be an important factor during quiet stance as women have more fat padding on the hips (increasing stability), whereas men have increased abdominal fat (decreasing stability). In addition, challenging conditions increase the demand of biomechanical competences and higher muscle mass and function, which could explain that women have a higher prevalence of falls despite more favorable CoP measurements during quiet stance but not during dynamic testing.

A higher BMI only impaired postural control slightly during quiet stance measured by CoP. Contradictive studies exist, as one study found that especially obesity increased CoP measurements in post-menopausal women [19]. Another study showed that external loading resulted in a lower CoP^{Area} displacement in older age groups and suggested a stabilizing effect during quiet standing [55]. Hence, an increased BMI could have a stabilizing effect during quiet stance on body sway but a destabilizing effect in motion. Only a larger CoP^{Area} was observed for increasing BMI values. Though, new studies should include body composition measurements to elucidate the impact of BMI on postural control during quiet stance, and fall risk as abdominal fat could offer less stability (larger CoP^{Area}), whereas hip padding could offer more stability (smaller CoP^{Area}). A higher BMI is associated with inactivity and more participants with T1D and T2D reported problems with physical activity and movement compared to controls. Physical inactivity could also be due to higher amounts of self-reported pain among people with diabetes as higher amounts of painkillers were reported.

Table 4 A heat map of center of pressure (CoP) measurements presented by multivariate regression models

CoP	T1D vs. Controls	T2D vs. control	Fallers vs. non-fallers	Age (years)	Woman vs. man	BMI (kg/m^2)	Alcohol (units)	Fall-associated drug	Polypharmacy	HGS (kg)	TUG (sec)	VPT	Orthostatism	Visual acuity
Area (cm^2)														
EO	0.407 ± 0.354 (p=0.251)	1.118 ± 0.400 **(p=0.006)**	1.873 ± 0.672 **(p=0.006)**	0.001 ± 0.013 (p=0.916)	-1.054 ± 0.432 **(p=0.014)**	0.042 ± 0.029 (p=0.141)	-0.002 ± 0.003 (p=0.698)	1.349 ± 0.400 **(p=0.001)**	0.973 ± 0.324 **(p=0.005)**	-0.068 ± 0.032 **(p=0.046)**	-0.049 ± 0.079 (p=0.534)	0.025 ± 0.015 (p=0.100)	0.197 ± 0.523 (p=0.704)	-0.938 ± 0.734 (p=0.200)
EOF	0.833 ± 0.365 **(p=0.042)**	1.254 ± 0.518 **(p=0.005)**	0.638 ± 0.509 (p=0.212)	0.004 ± 0.017 **(p=0.022)**	-0.108 ± 0.558 **(p=0.050)**	0.056 ± 0.355 (p=0.129)	-0.005 ± 0.532 (p=0.492)	1.015 ± 0.423 **(p=0.036)**	0.582 ± 0.442 (p=0.187)	-0.065 ± 0.025 **(p=0.010)**	-0.179 ± 0.101 (p=0.079)	0.012 ± 0.025 (p=0.521)	-0.458 ± 0.666 (p=0.472)	-1.234 ± 0.963 (p=0.203)
EOB	1.411 ± 0.502 **(p=0.029)**	1.386 ± 0.607 **(p=0.042)**	3.050 ± 0.902 **(p=0.002)**	0.074 ± 0.030 **(p=0.016)**	-1.543 ± 0.973 (p=0.330)	0.119 ± 0.066 (p=0.072)	-0.014 ± 0.014 (p=0.283)	1.652 ± 0.721 **(p=0.042)**	0.337 ± 0.744 (p=0.663)	-0.065 ± 0.173 (p=0.421)	-0.144 ± 0.176 (p=0.293)	0.037 ± 0.045 (p=0.293)	-0.871 ± 1.192 (p=0.456)	-1.653 ± 1.684 (p=0.697)
EC	0.191 ± 0.501 (p=0.707)	1.183 ± 0.360 **(p=0.009)**	0.045 ± 0.455 (p=0.633)	0.015 ± 0.019 (p=0.425)	-1.941 ± 0.591 **(p=0.000)**	0.079 ± 0.032 **(p=0.042)**	-0.012 ± 0.008 (p=0.156)	2.234 ± 0.579 **(p=0.000)**	0.982 ± 0.477 **(p=0.040)**	0.240 ± 0.677 (p=0.311)	0.045 ± 0.455 (p=0.633)	0.005 ± 0.021 (p=0.792)	0.901 ± 0.721 (p=0.225)	-
ECF	0.591 ± 0.551 (p=0.341)	1.322 ± 0.523 **(p=0.015)**	0.444 ± 0.663 (p=0.565)	0.039 ± 0.020 (p=0.069)	-1.732 ± 0.663 **(p=0.010)**	0.045 ± 0.046 (p=0.344)	-0.008 ± 0.009 (p=0.367)	1.572 ± 0.643 **(p=0.003)**	0.683 ± 0.542 (p=0.203)	-0.058 ± 0.022 **(p=0.038)**	-0.032 ± 0.123 (p=0.765)	0.029 ± 0.025 (p=0.543)	1.053 ± 0.843 (p=0.204)	-
ECB	1.463 ± 0.642 **(p=0.023)**	1.663 ± 0.711 **(p=0.027)**	1.422 ± 0.543 **(p=0.021)**	0.045 ± 0.023 (p=0.051)	-2.152 ± 0.764 **(p=0.005)**	0.0123 ± 0.052 **(p=0.021)**	-0.002 ± 0.002 (p=0.532)	1.969 ± 0.731 **(p=0.031)**	0.543 ± 0.611 (p=0.377)	-0.089 ± 0.034 **(p=0.014)**	-0.032 ± 0.143 (p=0.819)	0.037 ± 0.038 (p=0.182)	-0.368 ± 0.933 (p=0.698)	-
Mean	0.780 ± 0.460 **(p=0.022)**	1.591 ± 0.512 **(p=0.002)**	1.34 ± 0.512 **(p=0.010)**	0.032 ± 0.012 (p=0.052)	-1.623 ± 0.548 **(p=0.003)**	0.062 ± 0.037 (p=0.068)	-0.004 ± 0.001 (p=0.386)	1.623 ± 0.519 **(p=0.003)**	0.511 ± 0.455 (p=0.608)	-0.072 ± 0.023 (p=0.017)	-0.024 ± 0.011 (p=0.821)	0.033 ± 0.021 (p=0.123)	0.234 ± 0.026 (p=0.608)	-
Velocity (cm/sec)														
EO	0.083 ± 0.062 (p=0.181)	0.141 ± 0.078 **(p=0.047)**	0.201 ± 0.087 **(p=0.019)**	0.003 ± 0.078 (p=0.187)	-0.205 ± 0.076 **(p=0.008)**	0.005 ± 0.005 (p=0.278)	0.001 ± 0.001 (p=0.536)	0.083 ± 0.072 (p=0.255)	0.017 ± 0.063 (p=0.773)	-0.004 ± 0.003 (p=0.192)	0.009 ± 0.138 (p=0.481)	0.007 ± 0.001 **(p=0.007)**	-0.009 ± 0.023 (p=0.832)	-0.292 ± 0.223 **(p=0.026)**
EOF	0.134 ± 0.085 (p=0.119)	0.250 ± 0.057 **(p=0.003)**	-0.03 ± 0.094 (p=0.723)	0.009 ± 0.003 **(p=0.006)**	-0.276 ± 0.104 **(p=0.008)**	0.008 ± 0.007 (p=0.252)	0.000 ± 0.007 (p=0.972)	0.120 ± 0.099 (p=0.226)	0.045 ± 0.083 (p=0.585)	-0.017 ± 0.004 **(p=0.035)**	-0.011 ± 0.019 (p=0.554)	0.006 ± 0.002 **(p=0.033)**	-0.043 ± 0.124 (p=0.760)	-0.479 ± 0.177 **(p=0.008)**
EOB	0.114 ± 0.123 (p=0.350)	0.111 ± 0.139 (p=0.427)	0.194 ± 0.143 (p=0.176)	0.013 ± 0.004 **(p=0.005)**	-0.201 ± 0.154 (p=0.181)	0.012 ± 0.012 (p=0.210)	-0.001 ± 0.002 (p=0.358)	0.081 ± 0.148 (p=0.568)	0.165 ± 0.119 (p=0.167)	-0.006 ± 0.006 (p=0.353)	-0.004 ± 0.027 (p=0.884)	0.015 ± 0.005 **(p=0.010)**	-0.182 ± 0.188 (p=0.300)	-0.658 ± 0.258 **(p=0.011)**
EC	0.016 ± 0.145 (p=0.910)	0.274 ± 0.160 (p=0.088)	0.180 ± 0.166 (p=0.085)	0.005 ± 0.005 (p=0.458)	-0.433 ± 0.172 **(p=0.012)**	0.018 ± 0.011 (p=0.121)	0.000 ± 0.002 (p=0.913)	0.100 ± 0.169 (p=0.556)	0.022 ± 0.141 (p=0.888)	-0.005 ± 0.008 (p=0.468)	0.054 ± 0.031 (p=0.085)	0.021 ± 0.006 **(p=0.002)**	0.062 ± 0.209 (p=0.766)	-
ECF	0.052 ± 0.176 (p=0.765)	0.245 ± 0.200 (p=0.221)	0.00 ± 0.000 (p=0.996)	0.008 ± 0.006 (p=0.170)	-0.456 ± 0.212 **(p=0.034)**	0.008 ± 0.012 (p=0.561)	-0.007 ± 0.002 (p=0.897)	0.092 ± 0.293 (p=0.656)	0.069 ± 0.177 (p=0.688)	-0.016 ± 0.007 **(p=0.046)**	0.023 ± 0.039 (p=0.551)	0.023 ± 0.007 **(p=0.003)**	-0.113 ± 0.265 (p=0.671)	-
ECB	0.103 ± 0.167 (p=0.549)	0.373 ± 0.19 **(p=0.034)**	0.098 ± 0.196 (p=0.616)	0.012 ± 0.005 **(p=0.032)**	-0.527 ± 0.201 **(p=0.010)**	0.017 ± 0.013 (p=0.206)	-0.000 ± 0.001 (p=0.372)	0.078 ± 0.195 (p=0.690)	0.083 ± 0.163 (p=0.608)	-0.018 ± 0.008 **(p=0.044)**	0.051 ± 0.038 (p=0.174)	0.022 ± 0.007 **(p=0.002)**	-0.339 ± 0.257 (p=0.178)	-
Mean	0.105 ± 0.115 (p=0.365)	0.276 ± 0.121 **(p=0.027)**		0.001 ± 0.001 (p=0.136)	-0.309 ± 0.145 (p=0.032)	0.012 ± 0.145 (p=303)	-0.000 ± 0.001 (p=0.622)	0.089 ± 0.111 (p=0.501)	0.061 ± 0.113 (p=0.321=	-0.007 ± 0.006 (p=0.263)	0.032 ± 0.027 (p=.229)	0.015 ± 0.005 **(p=0.004)**	-0.061 ± 0.117 (p=0.545)	-

Data is presented as beta-coefficients, standard error of the mean and *p*-values (in brackets) derived from multivariate linear regression models

Fall-associated drugs included SSRI, benzodiazepines (anxiolytics and sedatives), and opioids. Orthostatic blood pressure was positive either with symptoms or a sufficient drop in blood pressure. Polypharmacy was defined as the intake of more than 4 types of drugs per day

p-values in bold indicate a significant value. *p*-value ≤ 0.05 > 0.01: shady gray. *p*-value ≤ 0.01: light gray. *p*-value > 0.05: dark gray

T1D, type 1 diabetes; *T2D*, type 2 diabetes; *SD*, standard deviation; *CoP*, center of pressure; *BMI*, body mass index; HGS, handgrip strength; *TUG*, timed up and GO; *VPT*, vibratory perception thresholds; *EO*, eyes open; *EOF*, eyes open forward; *EOB*, eyes open backward; *EC*, eyes closed; *ECF*, eyes closed forward; *ECB*, eyes closed backward. Mean: calculated as a mean of the six conditions

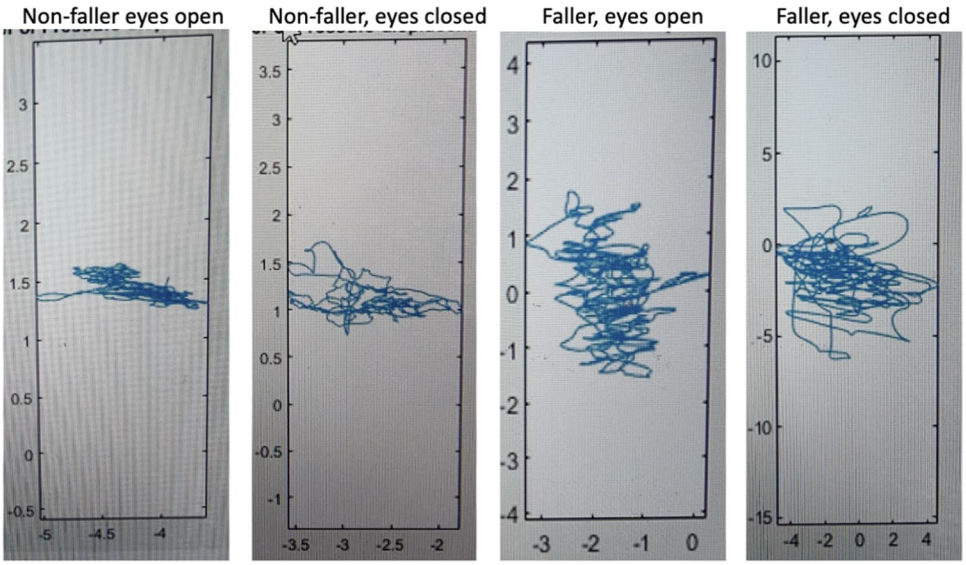

Fig. 1 Visualization of a real-life example of the center of pressure (CoP)^{Area} measures during quiet stance in a person with no previous falls (non-fallers) vs. a person with previous falls (fallers), including two conditions (eyes open and eyes closed). The CoP^{Area} represents the areas of the 95% confidence ellipse of the CoP displacement and is a measurement of the body sway. A larger body sway is seen in the person with previous falls in both conditions compared with the non-faller

Alcohol use is normally associated with impaired postural control but was not in this study. Chronic alcohol use over the recommended limit was an exclusion criterion, and the average self-reported alcohol use was twice as low as the average use in the Danish population [56]. However, self-reported alcohol use is in general inaccurate, which probably explains that no direct effect was seen regarding CoP measures, although derived effects from a previous alcohol abuse were not elucidated.

The use of fall-associated drugs impaired postural control during quiet stance in several conditions as CoP^{Area} measurements increased additionally during visual deprivation

Table 5 Prevalence rates of several falls and fear of falling in participants with T1D, T2D compared to controls without diabetes

	T1D vs. controls		T2D vs. controls	
	PR (CI95%)	*p*-value	PR (CI 95%)	*p*-value
Falling				
Unadjusted	1.16 (1.01–1.26)	**0.044**	1.42 (1.07–1.89)	**0.014**
Adjustment: age, sex, and BMI	1.09 (0.81–1.43)	0.562	1.32 (1.02–1.88)	**0.002**
Adjustment: age, sex, BMI, and mean CoP^{Area}	0.95 (0.68–1.34)	0.881	1.19 (0.79–1.80)	0.387
Adjustment: age, sex, BMI, and mean $CoP^{Velocity}$	1.01 (0.72–1.42)	0.932	1.28 (0.86–1.99)	0.211
Mult. adjusted*	1.54 (1.14–2.02)	**0.026**	1.93 (1.35–2.73)	**< 0.001**
Fear of falling				
Unadjusted	1.77 (1.18–2.67)	**0.006**	2.28 (1.54–3.34)	**< 0.001**
Adjustment: age, sex, and BMI	2.25 (1.57–3.73)	**< 0.001**	2.03 (1.33–3.10)	**0.001**
Adjustment: age, sex, BMI, and mean CoP^{Area}	1.33 (1.14–2.33)	**0.001**	1.41 (1.19–2.44)	**0.002**
Adjustment: age, sex, BMI, and mean $CoP^{Velocity}$	1.52 (1.15–3.01)	**0.001**	1.42 (1.11–2.52)	**0.002**
Mult. adjusted*	2.01 (1.10–3.65)	**0.021**	2.09 (1.06–4.02)	**0.032**

A Poisson regression model was used to estimate crude and adjusted prevalence rates (PR) for several falls, fear of falling, and the association between these two in participants with T1D and T2D compared with controls

*Mult. Adjustment for sex, age, BMI, alcohol, fall-associated drugs (SSRIs, benzodiazepine, and opioids), number of drugs per day, handgrip strength, timed up and GO test, vibration perception threshold, presence of orthostatism, hypoglycemia, and visual acuity

T1D, type 1 diabetes; *T2D*, type 2 diabetes; *SD*, standard deviation; *CoP*, center of pressure; *BMI*, body mass index; *CI*, confidence interval

and executive function tasks. Fall-associated drugs included SSRIs, opioids, and anxiolytics, which are commonly used among people with diabetes, and the self-reported amounts of these drugs were higher in both T1D and T2D compared to controls. Spares knowledge exists on postural control and the association with different types of drugs and their reported side effects. The treatment with SSRIs has been associated with a 1.4- to sixfold increased risk of falls [57–59]. The excessive use of SSRIs could be an expression of depression in people with diabetes as more anxiety and depression were reported among participants with diabetes and partly explain the decreased executive function during postural control testing seen in the participants with T1D. The self-reported use of opioids was higher among the participants with diabetes, and the use of opioids 1 month before a fall has been associated with a greater risk of suffering a fall-related hip fracture [OR 4.49 (95% CI: 2.72–7.42)] [60]. Opioids and anxiolytics may dispose to an impaired postural control due to the occurrence of drowsiness, muscle weakness, and vertigo and thereby increase the risk of falls. Antidiabetic drugs and insulin use should not directly impair postural control, only in case of hypoglycemia, which was not the cases during testing. Self-reported cases of hypoglycemia awareness and cases of hypoglycemia were high but expected in both diabetes groups. Hypoglycemia is a well-known factor of falls and fractures and was also included in the adjusted model of falls and fear of falling [61]. Twice as many participants with diabetes reported a use of more than four drugs per day than controls. Polypharmacy is associated with falls and impaired postural control, which is consistent with the findings of this study as impaired postural control during quiet stance was seen in the presence of polypharmacy vs. non-polypharmacy [62]. The awareness of certain harmful drug on the senso-motoric system in different combinations should be considered carefully in the management of people with diabetes.

HGS and TUG tests were used to assess muscle strength and general mobility. HGS is a common tool to estimate strength and is highly correlated with general strength and inversely with cardiovascular diseases and all-cause mortality [21]. In this study, HGS was inversely associated with impaired postural control during quiet stance for most CoP measurements, as a decrease in HGS showed larger CoP^{Area} displacement and increased $CoP^{Velocity}$. HGS is a simple and easy tool and was used as a surrogate measure for muscle strength. However, spares evidence exists between arm and lower leg strength and HGS and falls [37, 63]. Yet, reduced muscle strength is an important predictor of falls [64]. Therefore, HGS should probably not be used as a single measurement to estimate fall risk but used in combination with others as the TUG test. The latter showed slower walking speed and corresponded to the self-reported decreased physical activity and movement problems among the participants with T1D and T2D compared with controls.

Neuropathy was assessed by VPT and monofilament. Increasing VPT was slightly associated with impaired postural control during quiet stance for $CoP^{Velocity}$ measurements in all conditions. However, VPT only tests for large fiber neuropathy, and DPN is hard to detect at earlier stages. Approximately, 50% of people with diabetes develop DPN, but in

recent years, newer and more precise techniques have arrived that more thoroughly assess large- and small-fiber neuropathy, including autonomic function [65]. DPN is a strong predictor of falls and fear of falling [24, 66]. Hence, the effect of DPN on CoP measures was probably underestimated in this study like the self-reported prevalence of neuropathy.

The association between the cardiovascular system and postural control was assessed by orthostatic blood pressure and ECG analyses. The effects of orthostatism occur when changing position, which could explain why CoP measures were not affected during testing despite higher incidences of orthostatism in both diabetes groups compared with controls. However, the presence of orthostatic symptoms but not orthostatism has been associated with falls, and, conversely, the use of antihypertensive drugs has been associated with a reduced risk of falls [67, 68]. The self-reported use of antihypertensive drugs was twice as high in the diabetes groups compared to controls. The presence of orthostatism is an important predictor of falls but should not be evaluated by CoP measures during quiet stance. The findings from the ECG analyses were not associated with previous well-known factors of impaired postural control or falls. However, the presence of different types of arrythmias is normally associated with falls, but few cases were shown in this study, although ECG monitoring should be performed in future studies to identify fall-associated arrythmias.

Visual acuity was associated with decreased $CoP^{Velocity}$ measurements. This could indicate that the postural control system needs sufficient visual information to faster stabilize the body sway and that higher visual acuity is needed during executive function tasks. Therefore, people with diabetes who have reduced visual acuity due to, e.g., retinopathy could experience increased $CoP^{Velocity}$ doing challenging tasks. Self-reported retinopathy was approximately 10% (T1D) and 5% (T2D), but none had a visual acuity below 0.3. The International Council of Ophthalmology has stated that moderate vision impairments (VA < 0.3) are associated with potential movement problems, whereas mild vision impairment (VA between 0.8 and 0.3) is not [69]. Only four participants had a visual acuity < 0.5, and small decreases in visual acuity could, however, impair postural control and increase the prevalence of falls as shown in this study.

Limitations

This present study's findings should be interpreted within the context of its strengths and limitations. First, regarding selection bias, the participants with diabetes were mainly recruited from the outpatient clinics and by social media and flyers. However, this probably limited the recruitment to a group of more well-regulated and responsive participants and subsequently underestimated the study findings. Similar conditions were seen in the control group. Second, in questionnaire-based studies, recall bias must be considered. However, the true PR of falls was probably higher, and therefore underestimated the study results as people in general have a hard time remembering a fall. Reporting prior falls is mostly unreliable because individuals often forget their falls, which further increases with age. Hence, the PRs for the elderly were probably more underestimated than for the young as, but presumably the same for all groups. In addition, the use of drug, health status, and diabetic complications were probably underreported but equally between the groups. In addition, the response rate was high as the participants were instructed how to complete the questionnaire and thereby minimizing response bias. Third, the participants with T1D were younger and contained a higher percentage of men compared to the control group. It could also be speculated that this group perhaps was healthier than the general patient with T1D. Fourth, neuropathy was assessed by VPT and modestly associated with impaired postural control during quiet stance for $CoP^{Velocity}$ measurements in all conditions. However, VPT only tests for large-fiber neuropathy, and DN is hard to detect at earlier stages. DN is a strong predictor of falls and fear of falling [24, 66]. Hence, the effect of DN on CoP measures was probably underestimated in this study like the self-reported prevalence of neuropathy. Finally, CVs were calculated for all study procedures including CoP and showed acceptable repeatable measures, which indicated a high level of strength for the study procedures.

Conclusion

In conclusion, we provided new evidence of postural control and fall prevalence in a cohort of relatively healthy participants with T1D and T2D and controls. We demonstrated that the participants with T1D and T2D had impaired postural control during quiet stance, which correlated well with a higher prevalence of falls. In addition, the participants with T1D and T2D experienced more fear of falling than controls and several risk factors for falls were identified. These study findings were in accordance our objective findings and supported by the self-reported data in the quality of life (EQ-5D-3L) questionnaire. However, the cross-sectional study design does not allow for concluding causality, but, nevertheless, these associations only are compelling. Therfore, we suggests that T1D and T2D are crucial determinants of impaired postural control during quietstance regardless of well-known risk factors for falls and associated with a higher PR of falls. In future perspectives, CoP measures during quiet stance could be a helpful tool to predict falls in diabetes. Until then, clinicians should address modifiable

risk factors associated with impaired postural control like drug, BMI, and muscle strength, and by using targeted strategies that enhance postural stability to reduce fall prevalence among people with diabetes.

Author contribution All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version.

Data availability All sensitive data were collected and secured in REDCap under "DIAFALL" in accordance with current legislation. Data was stored anonymized after termination of the project. Physical data achieved doing the study was stored in locked desks with locked doors. Computer equipment was borrowed by the North Jutland Region and was password protected in accordance with current guidelines. The data and study material are not available.

Code availability The code is not available.

Declarations

Ethics approval The methods used have been tested and performed in several studies both in Denmark and abroad, and no long-term side effects have been reported. The risks associated with the project are few, and the tests implied limited risks. The potential benefits in terms of well-being were large and estimated to outweigh the potential risks. The trial was reported to the local ethical committee in the North Jutland Region (N-2019–0004). The trial was conducted in compliance with Harmonized Tripartite Guideline for Good Clinical Practice (ICH GCP) and applicable regulatory requirements and in accordance with the Helsinki Declaration for biomedical research involving test participants [70, 71]. Finally, the project was reported to the North Jutland Research department (ID-number of 2018–174).

Consent to participate Consent for each participant was achieved.

Consent for publication Consent for each participant was achieved.

Conflicts of interest Peter Vestergaard is head of research in the Steno Diabetes Center North Denmark sponsored by the Novo Nordisk Foundation. Joop van den Bergh is involved in research that is sponsored by Amgen, Eli Lilly, and UCB. Morten Hasselstrøm Jensen is a former employee of Novo Nordisk and holds shares in Novo Nordisk. Nicklas H. Rasmussen holds shares in Novo Nordisk. Jakob Dal: unrestricted research grants and lecture fee from Pfizer and IPSEN. The other authors Rogerio Pessoto Hirata and Annika Kvist declare that they have no conflict of interest.

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