


RESEARCH: COMPLICATIONS

Falls in individuals with type 2 diabetes; a cross-sectional study on the impact of motor dysfunction, postural instability and diabetic polyneuropathy

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Abstract

Aim: To estimate the incidence of falls in individuals with type 2 diabetes compared to healthy controls and to describe the characteristics of fallers with type 2 diabetes in relation to motor dysfunction, postural instability and diabetic polyneuropathy (DPN).

Methods: This is a cross-sectional study of individuals with type 2 diabetes with DPN ($n = 54$), without DPN ($n = 38$) and healthy controls ($n = 39$). Falls were recorded within the preceding year. DPN was defined by clinical scores and nerve conduction studies. Motor function was assessed by a 6-min walk test (6 MWT), five-time sit-to-stand test (FTSST) and isokinetic dynamometry at the non-dominant ankle and knee. An instability index (ST) was measured using static posturography. Univariate and bivariate descriptive statistics were used for group comparisons.

Results: Compared with healthy controls, individuals with diabetes had a higher incidence of falls 36%, ($n = 33$) versus 15%, ($n = 6$), $p = 0.02$. There were no differences in falls when comparing individuals with and without DPN. Fallers had an impaired 6 MWT versus non-fallers (450 ± 153 m vs. 523 ± 97 m respectively), a slower FTSST (11.9 ± 4.2 s vs. 10.3 ± 2.9 s respectively) and a higher ST (53 ± 29 vs. 41 ± 17 respectively), $p < 0.02$ for all.

Conclusion: Individuals with type 2 diabetes reported a higher number of falls within the preceding year compared to healthy controls, irrespective of the presence of DPN. The main factors associated with falls were increased postural instability, lower walking capacity and slower sit-to-stand movements. The 6 MWT, FTSST and posturography should be considered in future screening programs in identification of individuals at risk for falls.

KEYWORDS

diabetic polyneuropathy, falls, motor dysfunction, postural instability, type 2 diabetes

What are the new findings?

- The main characteristics of fallers with diabetes are increased postural instability, lower walking capacity and slower sit to stand movements, whereas diabetic polyneuropathy and measures of muscle strength did not differ between fallers and non-fallers.

What are the clinical implications of the study?

- Physical tests including the 6-minute walk test, five-time sit-to-stand test and posturography may be included in a future screening program to identify individuals with diabetes at risk for falls.

What is already known about this subject?

- Multiple factors have been identified to increase the risk of falling in diabetes, however, early identification of individuals at risk of falls with diabetes can be challenging.

1 | INTRODUCTION

Falls are a major cause of morbidity and the second leading cause of injury fatalities worldwide.¹ Individuals with diabetes are at increased risk of falling,² and this risk may be even higher when diabetic polyneuropathy (DPN) is present.³ In individuals with type 2 diabetes, falling affects independence in daily life negatively and causes a greater fear of falling compared to healthy individuals.⁴ Studies assessing falling in type 2 diabetes^{2,5-7} have been limited by not including validated, quantitative methods with multifactorial assessments of risk factors for falling⁸ or have not allowed evaluation of the impact of DPN and diabetes per se. Therefore, the parameters needed to identify individuals with type 2 diabetes at risk of falling remain unestablished.

DPN affects up to 50% of individuals with type 2 diabetes.⁹ In DPN, the primary complaints are pain and loss of sensation with a distal to proximal symmetrical pattern.⁹ In later stages, large nerve fibre dysfunction contributes to impaired balance, poor coordination and unstable gait, while motor neuropathy may lead to muscle wasting of the lower limbs,¹⁰ further contributing to postural instability.

Postural balance is highly dependent on muscle strength and motor function.¹¹ Fast compensatory muscle contractions are required to avoid falls during unexpected perturbations of movements or positions.¹² These reactions are highly challenged in individuals with DPN due to reduced postural stability.⁸ Moreover, motor dysfunction in individuals with diabetes can affect activities of daily living negatively, including walking speed and stride length compared to those without diabetes.

The aim of the study was to estimate the incidence of falls in individuals with type 2 diabetes compared to

healthy controls and describe characteristics of fallers and the impact of motor dysfunction, postural instability and DPN. We hypothesized that individuals with type 2 diabetes fall more frequently than healthy individuals and that individuals with type 2 diabetes experiencing falls are more likely to have DPN, motor dysfunction and postural instability.

2 | RESEARCH DESIGN AND METHODS

This was a cross-sectional study comparing individuals with type 2 diabetes with and without DPN and healthy controls, conducted at Aarhus University Hospital in Denmark between June 2017 and November 2018. This study was part of baseline evaluations in a randomized controlled trial investigating the effects of training in individuals with diabetes, which was approved by the Central Denmark Region Committees on Health Research Ethics (approval no.: 1-10-72-282-16) and registered with the Danish Data Protection Agency (approval no.: 1-16-02-5639-16).

Individuals with type 2 diabetes were recruited from Departments of Neurology and Department of Endocrinology and Internal Medicine at Aarhus University Hospital and from the Diabetes Type 2 Cohort (DD2), described elsewhere¹³ (<https://dd2.nu/>). Individuals living in proximity to Aarhus University Hospital were invited to participate. All individuals provided written informed consent, prior to inclusion.

Inclusion criteria were: Age 18–80 years and a diagnosis of type 2 diabetes based on the 1999 WHO criteria.¹⁴ Exclusion criteria were: History of transplantation, stroke or ischaemic heart disease, other causes of polyneuropathy, amputation or severe deformity of the lower extremities, musculoskeletal disease, peripheral vascular disease (including abnormal pedal pulses, cool skin and abnormal skin colour), blindness, other neurological or endocrine diseases and symptomatic osteoarthritis.

Age-matched healthy volunteers with normal glucose tolerance, normal blood pressure and normal lipid profiles were recruited by local advertising. Figure S1 presents the flow chart of inclusion.

2.1 | DPN assessment

The presence of DPN was graded according to guidelines by the Toronto Diabetic Neuropathy Expert Group.¹⁵ Individuals were assigned to the DPN groups if meeting the following criteria of confirmed polyneuropathy: the presence of an abnormality in nerve conduction studies (NCS) of at least two nerves combined with a symptom and/or sign of DPN based on the validated Toronto Clinical Neuropathy Score (TCNS).¹⁶

Symptoms and signs of DPN were described by two additional validated clinical scales: The Michigan Neuropathy screening instrument (MNSI)¹⁷ and the Utah Early Neuropathy.

Distal latency, conduction velocity, compound muscle action potential and sensory nerve action potential amplitudes were measured in the right median, peroneal, tibial and bilateral sural nerves with standard surface electrodes. Examination conditions of temperature, segment length and electrode type were applied according to standardized guidelines and Z-scores were calculated based on values from laboratory controls.¹⁸ DPN was confirmed by abnormal findings in at least two separate nerves, of which one was the sural nerve in accordance with current guidelines.¹⁹

2.2 | Clinical assessment

All individuals were screened by a physician and a thorough medical history was obtained. Data were collected on alcohol consumption, smoking habits and weekly exercise habits; moreover, weight, height and waist circumference were measured. Blood pressure was measured twice with 5-minute intervals in a supine position and subsequently a third time after standing for 3 min. Orthostatic hypotension was defined as a drop in systolic BP ≥ 20 mm Hg or diastolic BP ≥ 10 mm Hg from supine to standing position for 3 min. Visual acuity was assessed by the Snellen's test. Blindness was defined as central visual acuity of 20/200 or less. Decreased and normal vision were defined as 20/50–20/70 and 20/20–20/40 respectively. Blood samples were collected and analysed for HbA_{1c}, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, creatine kinase, plasma glucose, serum-creatinine and estimated glomerular filtration rate (eGFR).

2.3 | Muscle strength

Maximal isokinetic muscle strength was determined using dynamometry (BIODEX System 3, Biodex Medical Systems Inc. Shirley, NY, US). Maximal peak torque was determined for ankle dorsal and plantar flexors as well as knee extensors

and knee flexors of the non-dominant leg using a test protocol as described elsewhere.²⁰ The percentage of expected muscle strength was calculated based on normative values in healthy controls with adjustment for age, gender, weight and height using the following equation. 'Predicted peak torque [Nm] = intercept + $\beta_1 \times$ age + $\beta_2 \times$ height + $\beta_3 \times$ body mass' Prediction interval = Predicted peak torque ± 1.96 SD; β unstandardized regression coefficient, Nm Newton metre; as described elsewhere.²⁰

2.4 | Balance measurements

We used a reliable and validated static posturographic balance system (Tetrax, IA, Israel)²¹ and measured sway during eight sessions of 32 seconds (eyes open/closed, on foam pads and on hard surface, head turned right and left, head up and head down). The platform consists of four independent force plates supporting the heel and forefoot. Individuals were informed to stand on the platform without shoes with their feet aligned on the marked fields on the platform with their arms along their side. Sway was described by a stability index (ST), reflecting the extent of sway over the four force plates. ST ranges from 10 to 1500, a high ST value reflecting poor postural stability. The force platform measures the ground reaction forces generated by a body standing or moving across it to obtain a quantified measurement of the centre of pressure movements of the body. The ST value is calculated as follows: "ST = $t \{ \sum n 1 [(an - na - 1)2 + (bn - bn - 1)2 + (cn - cn - 1)2 + (dn - dn - 1)2] \} 1/2 / W$ ".²² The four plates (a/b/c/d), W = total body weight, t = time (32 s), n = number of signals recorded.

2.5 | Functional capacity and endurance

To determine walking capacity, gait speed and endurance, all individuals underwent a 6-minute walk test²³ (6 MWT). Furthermore, functional mobility and strength in transitional movements were quantified applying a five-time sit to stand test (FTSST).²³

2.6 | Falls

A fall was defined as 'an event that results in a person coming to a rest unintentionally on the ground or another level'.²⁴ A physician ensured that all individuals concurred on the definition of a fall excluding the following causes of falling; cardiogenic syncopal episodes, vasovagal, hypoglycaemia, mechanical or external forces. All individuals reported the frequency of falls over the past year. Fear of falling was assessed by a validated questionnaire consisting

of a 16-item scale (Falls efficacy scale-International [FES-I])²⁵ [range: 16–64]). A cut-off of 28 was used to indicate fear of falling.²⁵

2.7 | Statistical analysis

Statistical analyses were performed using Stata I/C version 14.2. (StataCorp, USA) and the level of significance was set at $p < 0.05$, no adjustment was performed for multiplicity of statistical tests. Descriptive statistics concerning the characteristics of individuals are presented as medians (p25, p75) for non-normal distributed continuous covariates. The Wilcoxon Rank Sum test was applied for comparison of non-normally distributed data, and the t -test was applied for normally distributed data. Data are presented as frequencies and proportions for categorical variables and compared by the chi-square test.

Average muscle strength was calculated as the average sum of the percentage of expected strength for the knee flexors, knee extensors, ankle dorsal and ankle plantar flexor muscles total. The sum of sway was calculated for all eight positions and as the sum of the four neutral (NOST, NCST, POST, PCST) and four head tilt/turn positions (HR, HL, HB, HF). To evaluate associations between muscle strength, TCNS, ST and 6 MWT, Pearson's correlation coefficients were calculated. Data in Table 2 were tested for normality and differences between groups were tested using the two-sample t -test.

3 | RESULTS

In total, 131 individuals completed all evaluations, including individuals with type 2 diabetes and confirmed DPN ($n = 54$), type 2 diabetes individuals without DPN ($n = 38$) and healthy controls ($n = 39$). All individuals included were Caucasian of northern European descent, except for five individuals (Mediterranean [$n = 2$], Middle Eastern [$n = 1$], South West Asian [$n = 1$], South American [$n = 1$]). Clinical and biochemical characteristics are presented in Table 1 and Table S1. Age, renal function, visual acuity, alcohol consumption, educational background and level of physical activity levels were similar between the groups. However, women with DPN had a larger waist circumference compared to women without DPN ($p < 0.05$ for all). Individuals with DPN were more often men (72%), had longer diabetes duration, and were more likely to be treated with insulin and anti-diabetes medications compared with individuals without DPN (Table 1). Only five individuals received sulfonylureas of which four were non-fallers. Characteristics of the NCS and clinical examinations are presented in Table S2.

3.1 | Individuals with type 2 diabetes versus healthy controls

Individuals with type 2 diabetes had experienced more falls than healthy controls (Table 1). Individuals with diabetes had more fear of falls based on the FES-I (Table 1), a higher postural instability index in neutral and head tilt/turn positions and decreased measures of motor function including the 6 MWT and FTSST (Table 1). In all individuals with diabetes isokinetic muscle strength of all joints was decreased, except for the knee joint which was borderline significantly decreased ($p = 0.041$).

3.2 | Individuals with DPN versus individuals without DPN

As shown in Table 1 there were no differences in the number of falls between those with and without DPN. However, individuals with DPN reported a higher fear of falling and had lower walking capacity compared to individuals without DPN ($p < 0.01$). Those with DPN had lower muscle strength (Table 1) and a higher ST for all eight positions compared to those without DPN (Figures S2a, S2b).

3.3 | Fallers versus non-fallers

Data from individuals with diabetes and with falls ($N = 33$) versus no-falls ($N = 59$) are presented in Figure 1 and Table 2. Fallers had lower walking distance, slower sit-to-stand movements and had more postural instability compared to non-fallers. There were no differences in gender, age, BMI, orthostatic hypotension, muscle strength, prevalence of DPN or neuropathy scores between fallers and non-fallers.

The percentage of expected muscle strength correlated inversely to TCNS (Figure 2a) and the ST for all individuals with diabetes (Figure 2b). Muscle strength was related to the ST for all eight positions (Figure 2c) and to the 6 MWT (Figure 2d). These correlations were found for both fallers and non-fallers, although correlations were stronger among fallers.

4 | DISCUSSION

Our main finding was that individuals with type 2 diabetes reported a higher number of falls within the previous 12 months, compared to healthy controls, irrespective of the presence of DPN. Individuals with type 2 diabetes and one or more falls had lower postural stability and walking speed (6 MWT), and slower transitional movements (FTSST).

TABLE 1 Clinical characteristics, measures of falls, balance and motor functions

	Control Individuals	Individuals with type 2 diabetes				
	Total N = 39	Total N = 92	p-value	With DPN N = 54	Without DPN N = 38	p-value
Age, years	64 (56; 68)	64 (58; 69)	0.396	64 (60; 69)	64 (58; 70)	0.902
Female gender (n, %)	19 (49)	36 (39)	0.309	15 (28)	21 (55)	0.008
DD2 cohort (n, %)	N/A	52 (57)		18 (33)	34 (89)	<0.001
Height (cm)	174 (170; 179)	173 (165; 179)	0.230	177 (169; 180)	169 (165; 175)	<0.001
Weight (kg)	88 (75; 96)	100 (85; 113)	<0.001	108 (93; 116)	94 (76; 103)	<0.001
BMI (kg/m ²)	28.4 (24.6; 30.9)	33.5 (29.2; 37.2)	<0.001	34.7 (30.4; 37.3)	31.3 (27.0; 35.8)	0.069
Waist circumference						
Women (cm)	97 (80; 110)	109 (100; 122)	0.020	116 (106; 126)	105 (96; 118)	0.047
Men (cm)	106 (96; 111)	121 (108; 128)	<0.001	122 (113; 130)	112 (106; 126)	0.060
Diabetes profile						
Diabetes duration (years)	N/A	9 (5; 14)		10 (6; 18)	7 (5; 10)	0.032
HbA1c, (mmol/mol)	36 (34; 39)	52 (47; 63)	<0.001	56 (48; 69)	49 (45; 55)	0.002
HbA1c, %	5.4 (5.3;5.7)	6.9 (6.5;7.9)	<0.001	7.3(6.5;8.5)	6.6 (6.3;7.2)	0.002
Insulin (yes)	N/A	32 (35)		28 (52)	4 (11)	<0.001
Oral anti-diabetes agents	N/A	82 (89)		49 (91)	33 (87)	0.554
Fallers	6 (15)	33 (36)	0.019	19 (35)	14 (37)	0.870
Frequency of falls ^a	1 (0)	3 (2)	0.046	3 (2)	3 (2)	0.948
Falls Efficacy Scale, sum	17 (1)	22 (9)	<0.001	24 (10)	20 (7)	0.003
Instability index						
Average ST in neutral positions	23 (7)	39 (19)	<0.001	46 (21)	29 (9)	<0.001
Average ST in tilt/turn positions	29 (10)	52 (28)	<0.001	63 (31)	36 (12)	<0.001
Motor function						
FTSST (sec)	8.1 (2.1)	10.9 (3.5)	<0.001	11.7 (4.0)	9.6 (2.1)	0.003
6 MWT (m)	652.77 (85)	496.67 (125)	<0.001	555 (90)	455 (130)	<0.001
Muscle strength						
Average ankle plantar and dorsal flexion(Nm)	54 (14)	44 (13)	<0.001	41 (11)	48 (13)	0.011
Average knee extension and flexion (Nm)	109 (31)	98 (26)	0.041	98 (26)	99 (26)	0.888
Average ankle plantar and dorsal flexion (% of expected)	92 (13)	74 (19)	<0.001	66 (18)	85 (15)	<0.001
Average knee extension and flexion (% of expected)	93 (12)	78 (18)	<0.001	72 (16)	88 (17)	<0.001

N/A, not applicable.

Categorical data are frequencies (%); continuous data are medians (p25, p75) or mean (SD).

Continuous covariates were compared by the Wilcoxon rank sum test, and normally distributed data were compared by a *t*-test. Categorical variables and compared by the chi-square test. Data presented comparing all individuals with type 2 diabetes individuals and control individuals and comparing individuals with DPN to individuals without DPN.

^aThe frequency of falls was reported as the number of falls per individual during the preceding 12 months, Data are presented as mean (SD).

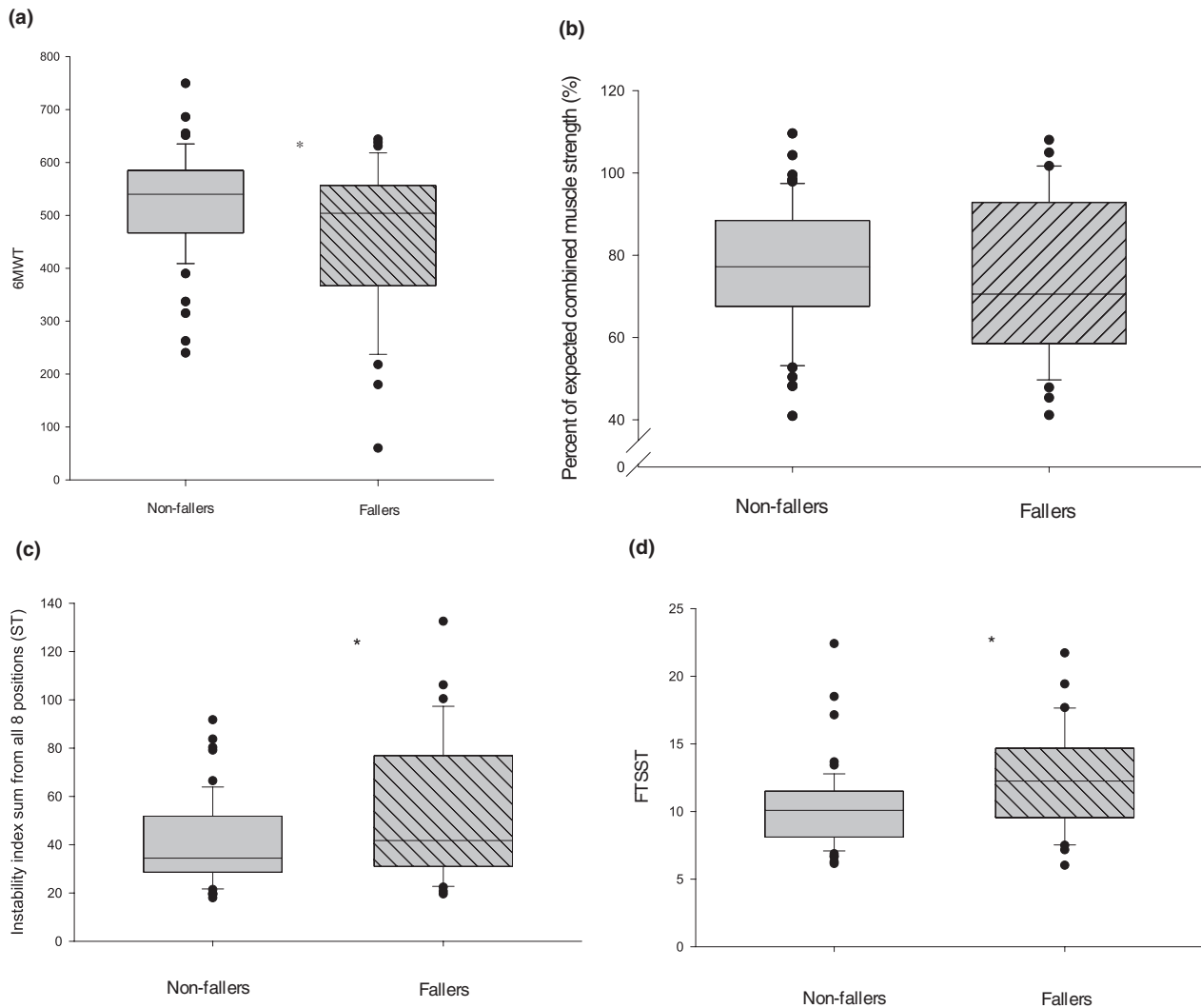


FIGURE 1 (a,b,c,d) The 6-minute walk test (6 MWT), percent of expected muscle strength (%), instability index (ST), five-time sit-to-stand test (FTSST) in 33 fallers versus 59 non-fallers with type 2 diabetes. * $p < 0.05$ comparing fallers and non-fallers

Unexpectedly, muscle strength and scores of DPN did not differ between fallers and non-fallers.

Several studies have assessed falling in individuals with type 2 diabetes and DPN.^{5–7} However, previous studies have not performed multifactorial assessments of risk factors for falling or have not included validated, quantitative methods for the assessments of muscle strength, postural stability and DPN.⁸ Furthermore, previous studies lack a control group or do not compare the results to individuals with diabetes without DPN. Some studies have only used vague definitions of DPN, without standardized clinical assessment and NCS.⁴ Due to a detailed assessment of clinical characteristics in individuals with type 2 diabetes and in an age-matched control group, our study allowed evaluation of the impact of both diabetes and DPN per se. The present study is the first to apply multiple validated examinations enabling detailed characterization of fallers with type 2 diabetes with and without DPN compared to healthy controls.

Previous studies have reported a higher incidence of falls in individuals with DPN compared to individuals without²⁶; however, this was not the case in our study. In line with previous studies we found an increased fear of falling in individuals with DPN (31). Despite the increased fear of falls, the incidence of falls was similar in individuals with type 2 diabetes with and without DPN. A potential explanation could be that individuals with DPN had an increased awareness of a tendency to fall, contributing to compensatory mechanisms preventing future falls. In our study only few individuals reported falling more than once within the previous year and our sample was too small to allow further analysis of the relation to the severity of diabetic neuropathy.

Multiple risk factors have been identified for falling including high BMI, older age, female gender and insulin use.²⁷ In our study, there were no differences in BMI, age, gender or insulin use comparing fallers with non-fallers, however, the low number of fallers limits the power of the analysis. In our individuals with type 2 diabetes, 36%

TABLE 2 Fallers versus non-fallers with type 2 diabetes

	Individuals with type 2 diabetes		
	Fallers (<i>n</i> = 33)	Non-fallers (<i>n</i> = 59)	<i>p</i> -value
With DPN	19 (58)	35 (59)	0.870
DD2 cohort (<i>n</i> , %)	18 (55)	30 (51)	0.733
Age (years)	64 (8.4)	63 (7.6)	0.817
Female gender (<i>n</i> , %)	17 (52)	19 (32)	0.069
BMI (kg/m ²)	34.6 (7.1)	32.6 (5.1)	0.295
Insulin (yes), <i>n</i> (%)	14 (42)	18 (31)	0.250
Orthostatic hypotension (yes), <i>n</i> (%)	3 (9.1)	7 (12)	0.682
Falls Efficacy Scale sum	26 (8.9)	21 (6.6)	0.002
Instability index			
Average ST in neutral head positions	45 (24)	35 (14)	0.016
Average ST in head tilt/turn positions	61 (36)	46 (21)	0.013
Neuropathy scores			
TCNS	9.5 (5.2)	8.0 (4.1)	0.146
UTAH	14 (8.8)	11 (7.5)	0.067
MNSI	4.0 (2.8)	3.0 (2.1)	0.230
MNSI-Q	4.0 (2.8)	3.0 (2.6)	0.071
Motor function			
Average ankle plantar and dorsal flexion strength (% of expected)	72 (19)	75 (19)	0.592
Average knee extension and flexion strength (% of expected)	78 (21)	79 (16)	0.818
6 MWT(m)	450 (153)	523 (97)	0.007
FTSST (sec)	11.9 (4.2)	10.3 (2.9)	0.032

Categorical data are presented as frequencies (%), continuous data as means (SD). Continuous covariates compared by a *t*-test, categorical variables and compared by the chi-square test. Data presented comparing all individuals with type 2 diabetes and control individuals and comparing individuals with DPN to individuals without DPN.

Falls over the past year recorded at the visit.

6 MWT: 6 Minute walk test. FTSST: Five-time sit-to-stand test. Orthostatic hypotension was defined as a drop in systolic BP ≥ 20 mm Hg or diastolic BP ≥ 10 mm Hg.

Average ST in neutral positions: (NOST+NCST+POST+PCST)/4.

Average ST in lateral positions: (HRST+HLST+HBST+HFST)/4.

Percentage of expected muscle strength after correction for the influence of gender, age, weight and height.

reported falls which is similar to previous studies.²⁸ Our sample of individuals was younger than in previous studies²⁸ and it is therefore unexpected that we found similar incidence of falls in our population. Poor peripheral nerve function combined with motor dysfunction, in DPN, are associated with low physical performance, muscle weakness and impaired balance in diabetes, particularly during active movements.¹² In sensorimotor polyneuropathy, proprioception is impaired, affecting balance during ambulation

through inaccurate initiation of appropriate muscular responses with delayed muscle activation²⁹ has also been considered a key contributing factor to falling. Although, we did not find pronounced muscle weakness among fallers, fallers had shorter walking distance and slower sit to stand movements, reflecting motor dysfunction at a functional level. The 6 MWT represents muscular endurance, aerobic capacity and muscle strength of the lower body and the axial skeletal muscles, and the FTSST represents a

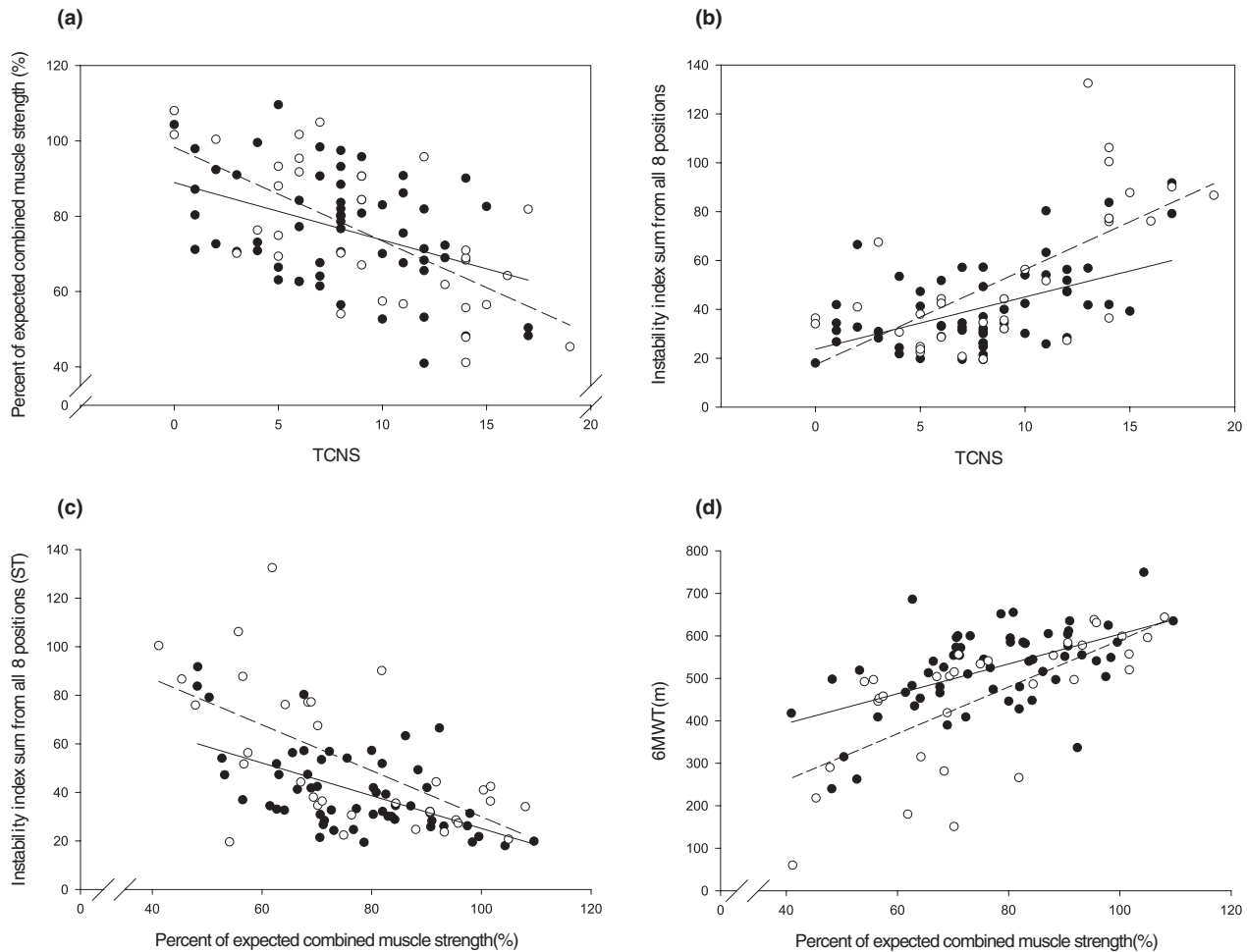


FIGURE 2 Empty circles and dashed line: Fallers. Filled circles and solid line: Non-fallers. (r = Pearson correlation coefficient). (a) Toronto Clinical Neuropathy Score (TCNS) in relation to percent of expected total muscle strength. Fallers ($r = -0.66$, $p < 0.001$), non-fallers ($r = -0.41$, $p < 0.001$). (b) Toronto Clinical Neuropathy Score (TCNS) in relation to the stability index sum from all eight positions. Fallers ($r = 0.72$, $p < 0.001$), non-fallers ($r = 0.59$, $p < 0.001$). (c) Percent of expected total muscle strength in relation to the stability index sum from all eight positions. Fallers ($r = -0.61$, $p < 0.001$), non-fallers ($r = -0.56$, $p < 0.001$). (d) Percent of expected total muscle strength in relation to 6-minute walk test (6 MWT). Fallers ($r = 0.68$, $p < 0.001$), non-fallers ($r = 0.54$, $p < 0.001$).

compound movement of the lower body, including flexion and extension of the hip, knee and ankle joints.

Postural instability in DPN occurs due to deficits in numerous systems working together to control balance.² Thus, causation is most likely multifactorial and could explain the lack of association between DPN and falls in our findings. In our study, postural instability was highest in individuals with DPN and in fallers when compared to non-fallers during lateral, forward and backward head movements. Using static posturography, Oppenheim described similar findings in individuals with DPN with larger sway excursions in the lateral planes and during backward head tilts.³⁰ One could speculate that larger instability in those planes could be due to unilateral stress on the opposing leg, which could be less responsive in the presence of somatosensory disturbances. In support of this, we found that individuals with DPN had lower walking speed and slower transitional movements, indicating

that muscle weakness and postural instability directly affect gait performance and motor function. We did not perform dynamic posturography, which is a better measure of balance problems during activities of daily living and during walking. Static posturography is less expensive and less complex as it does not require individuals to be secured in a harness.²¹

4.1 | Limitations and strengths

There are limitations to our study. First, a cross-sectional design does not allow conclusions on causality and effects over time. Second, the study consisted of a convenience sample as individuals with DPN were included primarily from the outpatient clinic at Aarhus University Hospital, which may have introduced bias. Individuals had to be self-sufficient and live in some proximity to our hospital,

leaving out individuals with more advanced disease. Third, falls were recorded retrospectively over the past year. This period could lead to recall bias that could have left out fall incidences, however, 12 months is the optimal time frame to obtain self-reported falls ruling out any seasonal influence and this method has been applied in previous studies.²⁸ Fourth, hypoglycaemia and insulin treatment may cause postural instability and falls. We did not obtain data on hypoglycaemic episodes, however a clinician ensured that individuals concurred on the definition of a fall excluding other causes such as syncope, external forces, hypoglycaemic episodes, etc. Lastly, our individuals were not examined for foot deformities, which is also associated with falling in the diabetes population.²⁸

The strengths of our study are inclusion of a fairly large cohort of individuals with type 2 diabetes and healthy controls, all being examined by the same physician during the same time of the day using standardized quantitative techniques to measure motor function and balance. Furthermore, the presence of DPN was confirmed by both clinical examinations and NCS was performed by a physician.

In summary, individuals with type 2 diabetes reported more falls within the preceding year compared to healthy controls, irrespective of the presence of DPN. Major risk factors for falls were increased postural instability, shorter walking distance and slower sit to stand movements. Therefore, 6 MWT, FTSST and posturography should be considered in future screening programs in identification of individuals at risk for falls.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

Khan KS was involved in study design, data collection, statistical analysis, interpretation of data and writing of first manuscript draft. **Pop-Busui R** was involved in analysis, interpretation of data and writing and revision of manuscript. **Devantier L, Kristensen AG and Tankisi H** were involved in data collection and revision of manuscript. **Dalgas U and Overgaard K** were involved in study design, interpretation

of data and revision of manuscript. **Andersen H** was involved in study design, analysis and interpretation of data and writing and revision of manuscript. All authors approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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