Contents lists available at [ScienceDirect](www.sciencedirect.com/science/journal/24058440)

Heliyon

journal homepage: www.cell.com/heliyon

Research article

5© CelPress

Knee proprioception, muscle strength, and stability in Type 2 Diabetes Mellitus- A cross-sectional study

Khalid A. Alahmari, Ravi Shankar Reddy

Department of Medical Rehabilitation Sciences, College of Applied Medical Sciences, King Khalid University, Abha, 61421, Saudi Arabia

ARTICLE INFO

Keywords: Type 2 Diabetes Mellitus Musculoskeletal health Proprioception Muscle strength Stability Physical activity Cross-sectional study

ABSTRACT

Background: The burgeoning prevalence of Type 2 Diabetes Mellitus (T2DM) has been linked to a spectrum of health complications, including those affecting the musculoskeletal system. Knee proprioception, muscle strength, and stability are essential for maintaining functional mobility and preventing falls, yet their relationship with T2DM is not fully elucidated. *Objectives:* This study aimed to compare knee proprioception, muscle strength, and limits of

stability (LOS) between individuals with T2DM and asymptomatic controls and to examine the moderating role of physical activity on these relationships.

Methods: In a cross-sectional design, 192 participants (96 with T2DM and 96 asymptomatic) underwent assessments for knee proprioception using a digital inclinometer, muscle strength via a handheld dynamometer, and LOS through dynamic posturography, graded as a percentage of maximum lean without losing balance.

Results: Our analysis revealed that individuals with T2DM demonstrated reduced knee muscle strength, with mean differences of 12.90 Nm (right) and 18.80 Nm (left) in 25◦ of flexion, and 25.78 Nm (right) and 26.36 Nm (left) in 40◦ of flexion, compared to asymptomatic controls. Proprioception errors were greater in the T2DM group (p *<* 0.001), with significant deficits noted in both knee 25◦ of flexion and 40◦ of flexion. Stability limits were also compromised, with the T2DM group displaying a decreased ability to maintain balance across all tested directions (p *<* 0.001). Physical activity emerged as a positive moderator, with higher activity levels correlating with improved muscle strength and stability.

Conclusion: T2DM significantly impairs musculoskeletal function, highlighting the need for integrated management strategies. The study underscores the importance of physical activity in mitigating T2DM-related musculoskeletal deterioration, suggesting that therapeutic interventions should include a focus on enhancing muscle strength and stability to improve the quality of life in this population.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) represents a growing global health concern, characterized by increasing prevalence rates worldwide [[1](#page-10-0)]. It is a metabolic disorder marked by insulin resistance and elevated blood glucose levels, leading to a range of systemic complications [[2](#page-10-0)]. According to the International Diabetes Federation, as of 2021, approximately 537 million adults (20–79 years)

Corresponding author. *E-mail addresses:* kahmarie@kku.edu.sa (K.A. Alahmari), rshankar@kku.edu.sa (R.S. Reddy).

<https://doi.org/10.1016/j.heliyon.2024.e39270>

Received 17 March 2024; Received in revised form 10 October 2024; Accepted 10 October 2024

Available online 18 October 2024
2405-8440/© 2024 The Authors.

Published by Elsevier Ltd. This is an open access article under the CC BY-NC license ([http://creativecommons.org/licenses/by-nc/4.0/\)](http://creativecommons.org/licenses/by-nc/4.0/).

were living with diabetes, with T2DM accounting for about 90 % of these cases [\[2\]](#page-10-0). This number is projected to rise to 783 million by 2045, indicating a significant public health challenge [[3](#page-10-0)]. T2DM predominantly affects the adult population, but an alarming trend is its increasing incidence in younger age groups. The disease is often associated with modifiable lifestyle factors such as obesity, physical inactivity, and poor diet, as well as non-modifiable factors like age and genetic predisposition [[3](#page-10-0)]. The increasing prevalence of T2DM globally presents a growing public health challenge, not only due to its well-known metabolic and cardiovascular complications but also because of its significant impact on musculoskeletal health [[3](#page-10-0)].

Knee proprioception, muscle strength, and stability are fundamental components of musculoskeletal health, playing a crucial role in overall physical functioning and quality of life [\[4,](#page-10-0)[5](#page-11-0)]. Proprioception refers to the body's ability to perceive its position and movement in space, a critical factor in coordinating movements and maintaining balance [\[6\]](#page-11-0). In the context of the knee joint, effective proprioception ensures accurate joint positioning, which is essential for activities such as walking, climbing stairs, and maintaining posture [\[7\]](#page-11-0). Muscle strength in the knee, particularly in the quadriceps and hamstrings, is vital for supporting the joint, facilitating movement, and absorbing impact during physical activities [[8](#page-11-0)]. Strong muscles around the knee not only enhance performance but also play a protective role, reducing the risk of injuries and degenerative joint conditions [[8](#page-11-0)]. Stability, encompassing both static and dynamic components, is crucial for preventing falls and injuries, especially in older adults or those with chronic conditions like osteoarthritis [\[9\]](#page-11-0). Good stability relies on a combination of muscle strength, proprioceptive acuity, and neuromuscular control [[10\]](#page-11-0). Together, these elements are essential for performing daily activities safely and efficiently, and their importance becomes even more pronounced in individuals with conditions that can impair musculoskeletal function, such as T2DM [\[10](#page-11-0)]. Maintaining knee proprioception, muscle strength, and stability is therefore key to preserving mobility and independence, particularly in aging populations [\[11](#page-11-0)].

The escalating prevalence of T2DM globally is not only a major concern due to its well-known metabolic and cardiovascular repercussions but also because of its emerging impact on musculoskeletal health [\[3\]](#page-10-0). There is a growing body of evidence suggesting that T2DM significantly impairs key components of musculoskeletal function, such as knee proprioception, muscle strength, and stability [\[10](#page-11-0)]. These impairments can lead to a decreased quality of life, increased risk of falls, and a consequent rise in healthcare burdens, particularly in the elderly population who are most commonly afflicted by both T2DM and musculoskeletal decline [\[12,13](#page-11-0)]. Despite this critical interplay, there is a lack of comprehensive understanding of the extent of T2DM's impact on these musculoskeletal parameters and the potential for modifiable factors like physical activity to mitigate these effects [[13\]](#page-11-0). This knowledge gap represents a significant problem in the holistic management of T2DM, necessitating a focused investigation to elucidate these relationships and inform more effective clinical interventions [\[14](#page-11-0)].

The primary objective of this study is to comprehensively assess and compare knee proprioception, muscle strength, and stability limits between individuals with T2DM and asymptomatic counterparts. This comparison aims to elucidate the specific impacts of T2DM on these crucial aspects of musculoskeletal health. Additionally, the study seeks to explore the interrelations among proprioception, muscle strength, and stability within the T2DM cohort, aiming to understand the compound effects of these variables. A further objective is to investigate the potential moderating role of physical activity on these relationships, thereby providing insights into possible intervention strategies. Based on the existing literature and the nature of T2DM, we hypothesize that individuals with T2DM will exhibit significant deficits in knee muscle strength, proprioception, and stability compared to their asymptomatic counterparts and that higher levels of physical activity will correlate with better musculoskeletal health outcomes in the T2DM group. The findings from this study are anticipated to contribute to a more holistic understanding of T2DM and its broader implications, ultimately informing more effective management strategies for individuals affected by this condition.

2. Materials and methods

2.1. Study design, settings, and participants

In this cross-sectional study, we aimed to compare knee proprioception, muscle strength, and stability limits between individuals with T2DM and asymptomatic counterparts. Conducted within a specialized clinical physiotherapy environment, the study involved participants primarily recruited from endocrinology clinics and community health centers, offering a diverse and representative sample.

2.2. Inclusion and exclusion criteria

The selection criteria for the T2DM group in our study were meticulously delineated. Eligible participants needed a verified diagnosis of T2DM, confirmed through medical records or a physician's attestation. Additionally, the study focused on individuals aged 50 years or older, a demographic known for a higher incidence of musculoskeletal complications associated with T2DM. For the diagnosis of diabetes mellitus, we adhered to the American Diabetes Association's guidelines, which specify that an average blood glucose concentration over the previous two to three months, as reflected by a Hemoglobin A1c (HbA1c) level of 6.5 % or higher, is indicative of diabetes mellitus. The control group consisted of asymptomatic individuals who were age and sex-matched to the T2DM participants. Key criteria for the control group included the absence of a diabetes diagnosis and no history of major chronic conditions that could potentially impact musculoskeletal health, ensuring a fair comparison between the groups. A total of 192 participants were carefully selected, with equal distribution: 96 in the T2DM group and 96 in the control group. This sample size was determined to provide sufficient statistical power for detecting significant differences between the groups. Exclusion criteria for both groups were comprehensive to ensure the reliability of the study's outcomes. Individuals with any neurological disorders that could influence

proprioceptive or neuromuscular function were excluded. Also, participants with recent musculoskeletal injuries or surgeries (within the past six months) that could affect muscle strength or proprioception assessments were not included in the study.

2.3. Ethics

The study protocol was reviewed and approved by the KKU, DSR Review Board (ECM#2022–3567) on 23-03-2022, ensuring adherence to ethical standards and guidelines for research involving human subjects. All participants were informed about the objectives, procedures, potential risks, and benefits of the study. Written informed consent was obtained from each participant before their inclusion in the study. Participants were assured of confidentiality and the right to withdraw from the study at any point without any consequences. The study was conducted in compliance with the principles of the Declaration of Helsinki and local regulatory requirements.

2.4. Knee joint position sense evaluation

The assessment of knee joint position sense was conducted using a digital inclinometer. This evaluation was uniformly performed by a single investigator for both dominant and non-dominant limbs. The testing environment was controlled, ensuring it was quiet and well-ventilated, to facilitate optimal concentration and performance. During the assessment, participants were instructed to keep their eyes closed to negate the influence of visual cues.

The methodology employed for estimating knee joint position sense was the active target reposition technique. This involved defining target knee flexion positions at 25◦ and 40◦, angles chosen based on their relevance to proprioceptive input during normal walking patterns, thus serving as a functional measure [\[15](#page-11-0)]. The testing procedure commenced with the participant seated comfortably, hips and knees flexed at 90◦. The dual inclinometer was positioned strategically: one component (the secondary inclinometer) aligned along the joint line on the lower third of the lateral femur, and the other (the primary inclinometer) on the upper third of the lateral fibula, both secured with Velcro (Fig. 1).

The investigator guided the participant's knee from the initial 90 \degree flexion to the target position (25 \degree and 40 \degree) by extending the knee and holding it for 5 s, during which the participant memorized this position. After returning the leg to the starting position, the participant then actively extended their knee to replicate the target position as precisely as possible. The moment the participants believed they had reached the target, they indicated so verbally. The accuracy of this repositioning was quantified as the Joint Position Error (JPE), measured in degrees and displayed on the inclinometer. This procedure was repeated three times for each angle, and the absolute error was calculated as the difference between the actual target angle and the angle the participant perceived they had achieved. The JPE was determined by calculating the arithmetic mean of these absolute errors across the trials.

Fig. 1. Evaluation of knee joint proprioception employing dual digital inclinometers.

2.5. Knee muscle strength evaluation

In this study, a meticulous and uniform approach was adopted for the assessment of muscle strength in both knee flexors and extensors, employing a maximum voluntary isometric strength test with a handheld dynamometer [\[16](#page-11-0)]. For the quadriceps strength assessment, indicative of knee extensor strength, participants were seated on an examination table with knees bent at a 90◦ angle [[17\]](#page-11-0). An inelastic strap was used to secure the dynamometer in place, ensuring consistent knee angle maintenance during the assessment. Participants exerted maximum force by extending their knees against the dynamometer for 4 s, with the peak force recorded. Similarly, the knee flexor strength evaluation involved participants lying prone on the table with knees at a 90◦ angle over the edge. The dynamometer was positioned on the posterior aspect of the lower leg, above the heel. Participants flexed their knees against the dynamometer's resistance, again maintaining the exertion for 4 s. In both tests, three trials were conducted per participant, with the highest force from each recorded.

The average force values, measured in Newton-meter (Nm), from these trials were normalized relative to each participant's body mass, expressed in N/kg. This normalization step was crucial for accommodating body weight variations among participants, thus ensuring a fair comparison of muscle strength across the study population. This comprehensive assessment strategy, encompassing both knee flexors and extensors, provided a holistic view of the musculoskeletal implications of T2DM, particularly in lower limb strength.

2.6. Limits of stability assessment

The assessment of Limits of Stability (LOS) is a key parameter in the evaluation of balance and postural control [[18\]](#page-11-0). Current research methodologies leverage dynamic posturography, incorporating cutting-edge technology to measure the maximal distance or angle to which a person can lean without losing balance or altering their base of support $[18]$ $[18]$. This advanced technique employs a force plate within a mobile platform, offering a nuanced and accurate measurement of a person's LOS [\[19](#page-11-0)]. During the assessment, individuals stand on a stabilometric force platform, typically with feet positioned together to maintain a standard stance. The posturography system projects visual targets onto a screen, prompting the individual to lean toward these targets from their center of mass in a controlled manner, without moving their feet. This process challenges the participant in eight cardinal directions, providing a comprehensive evaluation of their balance control abilities in percentage. This system measures the amplitude and speed of the participant's sway as they attempt to reach each target, with the data being meticulously captured by the force plate sensors. These measurements are then utilized to compute an LOS score, reflecting the individual's ability to control their center of gravity over their base of support under dynamic conditions.

2.7. Sample size estimation

In determining the appropriate sample size for our investigation into the effects of T2DM on musculoskeletal health, G*Power statistical software was utilized to perform power analysis. Based on a previous study, an effect size of 0.4 was employed as a conservative estimate for detecting differences in LOS between T2DM subjects and asymptomatic controls [\[20](#page-11-0)]. The anticipated effect size reflects a moderate, yet clinically significant, difference between groups, which aligns with the common thresholds used in musculoskeletal research [[21\]](#page-11-0). Setting the alpha level at 0.05 and aiming for a power of 80 %, the analysis indicated that a total sample size of 192 participants was required to discern the stipulated effect size with sufficient statistical reliability.

2.8. Data analysis

The SPSS software (version 24.0) was utilized for all analyses. To ensure the appropriateness of parametric tests, the normality of the data for each variable was first verified using the Shapiro-Wilk test. This test confirmed that our data followed a normal distribution. For demographic comparisons between the T2DM group and the control group, independent t-tests were used for continuous variables like age and BMI, while Chi-square tests were applied for categorical variables such as gender distribution and smoking

T2DM: Type 2 Diabetes Mellitus, BMI: Body Mass Index, HbA1c: Glycated hemoglobin.

status. When comparing knee muscle strength, proprioception errors, and limits of stability between groups, independent t-tests were again utilized. To quantify the effect size of the differences observed, we calculated Cohen's d values. Pearson's correlation coefficient (r) was used to explore the relationships between proprioception errors, muscle strength, and limits of stability within the T2DM group. Additionally, multiple regression analysis was conducted to perform moderation analyses, exploring the impact of various predictors on musculoskeletal health outcomes. This allowed for an adjustment of confounding variables and quantified the impact of each predictor. A p-value of less than 0.05 was set as the criterion for statistical significance.

3. Results

The demographic characteristics of the study population comprising individuals with T2DM and a control group ($n = 96$ in each group) are summarized in [Table 1.](#page-3-0) The average age for the T2DM group was 70.76 years with a standard deviation (SD) of 4.41, while the control group was slightly younger on average at 69.93 years (SD = 4.87), with no statistically significant difference between the groups (p-value $= 0.562$). The proportion of males in the T2DM group was 48.54 %, compared to 51.46 % in the control group, indicating a balanced gender distribution (p-value = 0.760). Body Mass Index (BMI) averaged lower in the T2DM group (25.17 \pm 4.23) than in the control group (27.05 \pm 3.77), but this difference was not statistically significant (p-value = 0.663). The T2DM group had a mean duration of diabetes of 9.9 years (SD = 3.22) and an average HbA1c level of 6.8 % (SD = 0.97). The prevalence of hypertension was slightly higher in the T2DM group (52.08 %) compared to the control group (47.92 %), though the difference was not significant (p-value = 0.413). Similarly, high levels of physical activity were reported slightly less frequently in the T2DM group (22.92 %) compared to controls (25.00 %), and higher education levels were also marginally lower in the T2DM group (30.21 % vs. 33.33 %), but these differences were not statistically significant. The majority of both groups were non-smokers, with 70.83 % in the T2DM group and 68.75 % in the control group not smoking, and a near-equal percentage of individuals living alone in both groups, all without significant differences between groups. Overall, the demographic variables showed no significant differences between the T2DM and control groups, suggesting a well-matched sample population for further analysis.

Table 2 compares knee muscle strength, proprioception errors, and LOS between individuals with T2DM and asymptomatic individuals, with 96 subjects. In terms of knee muscle strength, T2DM individuals showed significantly lower strength in both 25◦ of flexion and 40◦ of flexion compared to the asymptomatic group. The mean differences in knee muscle strength for 25◦ of flexion were 12.90 Nm (right) and 18.80 Nm (left), with corresponding Cohen's d values of 0.72 and 1.36, indicating a medium to large effect size. For 40◦ of, the differences were even more pronounced, with mean differences of 25.78 Nm (right) and 26.36 Nm (left) and high Cohen's d values of 2.20 and 2.67, reflecting a very large effect size. Regarding proprioception errors in 25◦ of flexion, T2DM subjects exhibited higher errors. The right knee showed a negligible difference (0.09°), while the left knee had a mean difference of $-1.75°$, with a significant Cohen's d value of −1.26. In 40° of, the T2DM group again had larger proprioception errors, with $-0.06°$ for the right knee and − 2.88◦ for the left knee, the latter showing a very large effect size (Cohen's d of − 3.24). In the assessment of limits of stability, the T2DM group consistently underperformed compared to the asymptomatic group across all directions. The forward LOS showed the largest mean difference of 37.69, with a Cohen's d of − 5.23, indicating an extremely large effect size. For other directions (right-forward, right, right-backward, backward, left-backward, left, left-forward), the mean differences ranged from 7.79 to 20.22, with Cohen's d values consistently indicating a moderate to large effect size. The total objective LOS also showed a substantial difference, with a mean difference of 17.74 and a Cohen's d of − 1.85.

[Table 3](#page-5-0) and [Fig. 2](#page-5-0) present the Pearson correlation coefficients delineating the relationships among proprioception in 25◦ of flexion and 40◦ of flexion, muscle strength in flexion and 40◦ of flexion, and the total objective for limits of stability (LOS) within individuals

Table 2

Comparisons of knee muscle strength, proprioception errors, and limits of stability in T2DM and asymptomatic individuals.

Nm: Newton meter (unit of torque), SD: Standard Deviation, LOS: Limits of Stability (referring to balance and stability), (°): Degrees (unit of angular measurement).

Table 3

Correlations between Proprioception, Muscle Strength, and Stability Limits in T2DM individuals ($n = 96$).

Nm: Newton meter (unit of torque), (°): Degrees (unit of angular measurement), LOS: Limits of Stability (referring to balance and stability), r: Pearson correlation coefficient.

Correlations between Proprioception, Muscle Strength, and Stability Limits in T2DM

diagnosed with Type 2 Diabetes Mellitus (T2DM). Coefficients nearing 1 denote robust positive correlations, while those nearing − 1 signify strong negative correlations. The significance of correlation coefficients is denoted by asterisks, with ** indicating p *<* 0.01. Notably, a significant positive correlation exists between proprioception and LOS, whereas muscle strength in 25◦ of flexion and 40◦ of flexion exhibits a noteworthy negative correlation with LOS, indicating divergent implications for stability control in T2DM patients. In the realm of proprioception, a moderate correlation is observed between errors during 25◦ of knee flexion and 40◦ of (r = 0.367, p *<* 0.01), indicating a consistent pattern of proprioceptive discrepancy across these movements in the T2DM population. The association

Table 4

Moderation analysis of the relationship between Type 2 diabetes mellitus and knee joint muscle strength.

Predictor	B (SE)	Beta		p-value	95 % CI
Age (years)	$-0.02(0.01)$	-0.15	-1.65	0.110	$[-0.04, 0.01]$
BMI (kg/m^2)	$-0.05(0.02)$	-0.22	-2.10	$0.035*$	$[-0.09, -0.01]$
Duration of Diabetes (years)	$-0.08(0.02)$	-0.29	-3.60	$0.003**$	$[-0.12, -0.04]$
HbA1c (%)	$-0.03(0.02)$	-0.17	-1.70	0.085	$[-0.07, 0.01]$
Physical Activity Level (High)	0.10(0.02)	0.35	4.50	${<}0.001**$	[0.06, 0.14]

B (SE): Beta coefficient (Standard Error), Beta: Standardized Beta coefficient, t: t-statistic (a measure of the relative magnitude of the standard error to the Beta coefficient), BMI (kg/m²): Body Mass Index (measured in kilograms per square meter), HbA1c (%): Hemoglobin A1c (measured as a percentage, an indicator of average blood sugar levels over the past 2–3 months).

between proprioceptive errors and muscle strength manifests as moderate negative correlations. Specifically, errors in knee flexion exhibit moderate inverse relationships with muscle strength in both 25◦ of flexion (r = − 0.346, p *<* 0.01) and 40◦ of flexion (r = − 0.432, p *<* 0.01). Similarly, proprioceptive errors during knee 40◦ of flexion show moderate negative correlations with muscle strength in 25 \degree of flexion (r = -0.421, p < 0.01) and 40 \degree of flexion (r = -0.398, p < 0.01), implying a concurrent decline in proprioceptive accuracy and muscle strength. Conversely, the limits of stability (Total Objective) display robust positive correlations with proprioceptive errors in both 25 \degree of flexion (r = 0.513, p < 0.01) and 40 \degree of flexion (r = 0.498, p < 0.01), indicating a significant association between increased proprioceptive errors and expanded postural sway boundaries. In contrast, moderate negative correlations are observed between the limits of stability and muscle strength in 25◦ of flexion (r = − 0.412, p *<* 0.01) and 40◦ of flexion (r = − 0.378, p *<* 0.01), suggesting that individuals with greater knee muscle strength exhibit a reduced range of postural sway.

[Table 4](#page-5-0) and Fig. 3 moderation analysis delineates the relationship between T2DM and knee joint muscle strength, with a focus on various predictors. Age displayed a negative association $(B = -0.02, SE = 0.01; Beta = -0.15)$, yet was not statistically significant (t = -1.65 , p = 0.110). Body Mass Index (BMI) showed a significant negative correlation (B = -0.05 , SE = 0.02; Beta = -0.22 ; t = -2.10 , $p = 0.035[*]$), as did the duration of diabetes (B = -0.08, SE = 0.02; Beta = -0.29; t = -3.60, p = 0.003). Conversely, higher levels of physical activity were positively related to knee joint muscle strength (B = 0.10, SE = 0.02; Beta = 0.35; t = 4.50, p *<* 0.001). HbA1c percentage indicated a negative trend $(B = -0.03, SE = 0.02; Beta = -0.17; t = -1.70, p = 0.085)$, but this was not statistically significant.

[Table 5](#page-7-0) and [Fig. 4](#page-7-0) offer insights into the moderation analysis concerning the relationship between T2DM and proprioception. The analysis highlights that age has a minor, non-significant negative correlation with proprioception ($B = -0.01$, $SE = 0.01$; Beta = -0.11 ; t = -1.00 , p = 0.230). Body Mass Index (BMI) similarly indicates a negative but not statistically significant relationship (B = -0.04 , SE = 0.02; Beta = -0.19 ; t = -1.90 , p = 0.055). Notably, the duration of diabetes is negatively associated with proprioception and is statistically significant (B = -0.07 , SE = 0.02; Beta = -0.25 ; t = -2.80 , p = 0.008). The HbA1c percentage shows a negative trend (B = -0.02 , SE = 0.01; Beta = -0.14 ; t = -1.40 , p = 0.150), which is not significant. In contrast, high levels of physical activity correlate positively and significantly with proprioception ($B = 0.08$, $SE = 0.02$; Beta = 0.30; t = 3.40, p = 0.002).

[Table 6](#page-7-0) and [Fig. 5](#page-8-0) provides a comprehensive moderation analysis on the relationship between T2DM and limits of stability, revealing several significant correlations. Age shows a minor, non-significant negative correlation with limits of stability ($B = -0.01$, $SE = 0.01$; Beta = -0.09; t = -0.90, p = 0.350). Body Mass Index (BMI) presents a more substantial negative association that is statistically significant (B = -0.06, SE = 0.02; Beta = -0.27; t = -3.00, p = 0.015*). The duration of diabetes exhibits a notable negative correlation with limits of stability, which is highly significant (B = −0.09, SE = 0.02; Beta = −0.31; t = −4.50, p = 0.001). The HbA1c percentage also indicates a significant negative trend (B = −0.04, SE = 0.02; Beta = −0.20; t = −2.00, p = 0.040^{*}). In contrast, high levels of physical activity correlate positively and significantly with better limits of stability ($B = 0.12$, $SE = 0.03$; Beta = 0.40; $t = 4.00$, $p < 0.001$).

Scatter Plot with Diverse Color Regression Lines for T2DM Knee Joint Muscle Strength Analysis

Fig. 3. Impact of various predictors on knee joint muscle strength in T2DM patients: A moderation analysis.

Table 5

Moderation analysis of the relationship between T2DM and proprioception.

B (SE): Beta coefficient (Standard Error), Beta: Standardized Beta coefficient, t: t-statistic (a measure of the relative magnitude of the standard error to the Beta coefficient), BMI (kg/m²): Body Mass Index (measured in kilograms per square meter), HbA1c (%): Hemoglobin A1c (measured as a percentage, an indicator of average blood sugar levels over the past 2–3 months).

Scatter Plot with Diverse Color Regression Lines for T2DM Proprioception Analysis

Fig. 4. Analyzing the predictors of proprioception in T2DM patients: A moderation analysis with regression lines.

Table 6

Moderation analysis of the relationship between T2DM and limits of stability.

B (SE): Beta coefficient (Standard Error), Beta: Standardized Beta coefficient, t: t-statistic (a measure of the relative magnitude of the standard error to the Beta coefficient), BMI (kg/m²): Body Mass Index (measured in kilograms per square meter), HbA1c (%): Hemoglobin A1c (measured as a percentage, an indicator of average blood sugar levels over the past 2–3 months).

4. Discussion

In our investigation, we set out with distinct objectives to enhance the understanding of the musculoskeletal consequences of T2DM in the elderly. Primarily, we aimed to compare knee proprioception, muscle strength, and stability limits between elderly individuals with T2DM and their asymptomatic peers. Our results indicated significant disparities, with the T2DM group exhibiting notably weaker muscle strength, compromised proprioception, and reduced stability limits [\[22](#page-11-0)]. Furthermore, we sought to elucidate the

Scatter Plot with Diverse Color Regression Lines for T2DM Limits of Stability Analysis

Fig. 5. Analyzing the Predictors on the relationship between T2DM and limits of stability: A Moderation Analysis with Regression Lines.

correlations between proprioception, muscle strength, and stability within the context of T2DM, uncovering moderate to strong associations that signify the interdependent nature of these musculoskeletal attributes in diabetic conditions [[23](#page-11-0)]. Lastly, we aimed to explore the moderating role of physical activity on T2DM-associated musculoskeletal health. In this regard, our findings were particularly enlightening, revealing that regular physical activity potentially serves as a protective factor, attenuating the adverse effects of T2DM on musculoskeletal function [[24\]](#page-11-0). These insights collectively underscore the critical influence of T2DM on musculoskeletal health and the potential of physical activity as a mitigating factor.

The observed reductions in knee muscle strength, proprioception accuracy, and LOS in individuals with T2DM could be attributable to several interrelated factors. Chronic hyperglycemia in T2DM is known to contribute to advanced glycation end-product (AGE) formation, which can negatively affect collagen properties in musculoskeletal tissues, leading to stiffness and decreased muscle function, as suggested by previous studies [\[25](#page-11-0)]. This may explain the significant disparities in muscle strength between T2DM patients and their asymptomatic counterparts [\[26](#page-11-0)]. The elevated proprioception errors observed among T2DM subjects align with findings from Ettinger et al. [\[27](#page-11-0)], which postulate that diabetic neuropathy impairs sensory feedback mechanisms, essential for joint position sense [[27\]](#page-11-0). These proprioceptive deficits are further corroborated by the study of Sienko et al. [[28\]](#page-11-0), indicating that sensory degradation in T2DM can lead to compensatory reliance on visual and vestibular inputs, which are less precise than somatosensory feedback for proprioceptive tasks [\[28](#page-11-0)]. Moreover, the compromised LOS in T2DM individuals resonates with the findings by Lang et al. [[29\]](#page-11-0), who report that balance and stability are often compromised in diabetic populations due to both neural and musculoskeletal factors [\[29](#page-11-0)]. This is exemplified by reduced joint mobility and alterations in postural reflexes, which collectively diminish an individual's ability to maintain or recover stability [\[30](#page-11-0)]. The pronounced effect sizes (Cohen's d) for the differences in muscle strength, proprioception, and LOS underscore the clinical relevance of these findings. Such effect sizes have been echoed in prior research, including the work of Wettasinghe et al. [[24\]](#page-11-0), which noted substantial variations in muscle strength and proprioceptive acuity between diabetics and non-diabetics [\[24](#page-11-0)].

The interplay between proprioceptive accuracy, muscle strength, and stability limits in individuals with T2DM reflects complex neuromuscular dynamics that are influenced by the diabetic condition [[31](#page-11-0)]. The observed moderate negative correlations between proprioceptive errors and muscle strength may be indicative of the progressive nature of diabetic neuropathy, which affects both sensory and motor nerves, leading to decreased proprioceptive sensitivity and muscle weakening [\[32](#page-11-0)]. This is consistent with findings by Felicetti et al. [[33](#page-11-0)] which demonstrated that sensory impairment due to neuropathy in diabetic patients is closely associated with muscle weakness, particularly in lower limbs [[33\]](#page-11-0). The strong positive correlations between proprioceptive errors and stability limits suggest that as proprioceptive deficits increase, so does the challenge of maintaining postural control, potentially heightening the risk of falls [[34\]](#page-11-0). This relationship has been substantiated by studies such as those by Ahmad et al. [\[35](#page-11-0)], which highlighted that proprioceptive deficits can significantly affect balance and stability in T2DM individuals [\[35](#page-11-0)]. The increase in postural sway boundaries with proprioceptive errors could be the body's compensatory mechanism to maintain balance despite sensory loss, as suggested by the

research of Phapatarinan [\[36](#page-11-0)].

Conversely, the moderate negative correlations between muscle strength and stability limits point towards the protective role of muscle strength against instability [\[37](#page-11-0)]. Stronger muscles, particularly around the knee, are fundamental in providing joint stability and shock absorption, crucial for balance maintenance [[38\]](#page-11-0). This corroborates with findings from Willemse [\[39](#page-11-0)], indicating that muscle strength, especially in the lower extremities, is paramount in reducing the risk of falls by enhancing postural control mechanisms [\[39](#page-11-0)]. The relationship between proprioception and muscle strength in T2DM could also be affected by factors such as glycation of connective tissues and microvascular changes, which are prevalent in diabetic pathology and can impair muscle function and sensory feedback systems, as discussed by Maugeri et al. [\[40](#page-11-0)]. These microvascular changes might lead to a reduction in muscle oxygenation and nutrient delivery, further contributing to muscle weakness, as suggested by the work of Mendelson et al. [[41\]](#page-11-0). Overall, the intricate correlations revealed in this study underscore the need for integrated management strategies in T2DM, which not only focus on glycemic control but also on enhancing proprioception and muscle strength to improve stability and minimize fall risk [\[42](#page-12-0)]. Such strategies may include targeted physical therapies and exercise programs that are specifically designed to address the multifactorial aspects of musculoskeletal health in diabetic populations [[42\]](#page-12-0).

The analysis of the moderating effects on the relationship between T2DM and various aspects of musculoskeletal health provides insights into the multifactorial impact of the disease [[43\]](#page-12-0). The lack of a statistically significant relationship between age and musculoskeletal parameters such as muscle strength, proprioception, and LOS may indicate that while aging is associated with a decline in these parameters, T2DM may be a more dominant factor in the observed musculoskeletal impairments [[44\]](#page-12-0). This aligns with studies by Kushkestani et al. [[45](#page-12-0)], which suggest that diabetic complications can exacerbate age-related musculoskeletal decline [[45\]](#page-12-0).

The significant negative associations between BMI and musculoskeletal health measures reflect the additional mechanical and systemic stresses imposed by higher body mass on the musculoskeletal system, consistent with findings from previous research by D'Onofrio et al., [[46\]](#page-12-0). The duration of diabetes showing a strong negative correlation with muscle strength and stability can be attributed to the cumulative effects of chronic hyperglycemia on muscle and nerve function over time, as supported by studies such as those by Ballinger et al., [\[47](#page-12-0)]. The negative trend observed with HbA1c levels, particularly in relation to stability, could be reflective of the impact of glycemic variability on muscle and nerve function, where higher levels of HbA1c are indicative of poorer glycemic control, leading to complications that affect musculoskeletal health, as seen in studies by Abdelhafiz et al. [\[48](#page-12-0)]. Conversely, the positive influence of physical activity on musculoskeletal health parameters across the analyses is consistent with the protective and adaptive responses elicited by regular exercise, which can improve muscle strength, enhance proprioceptive feedback, and increase LOS, as found in research by Ras et al. [[49\]](#page-12-0). These adaptive responses may include improved insulin sensitivity, enhanced muscle glucose uptake, and reduced inflammation, which contribute to the maintenance or improvement of musculoskeletal function in individuals with T2DM [\[49](#page-12-0)]. Overall, the findings suggest that while T2DM and its duration are detrimental to musculoskeletal health, interventions aimed at increasing physical activity could serve as a vital component in managing the musculoskeletal complications associated with T2DM [[50\]](#page-12-0). This perspective is supported by comprehensive reviews like that by Shawahna et al. [\[50](#page-12-0)], emphasizing the need for lifestyle modifications as part of diabetes management plans.

4.1. Clinical significance

The clinical significance of this study is grounded in its demonstration that T2DM significantly impairs musculoskeletal health, affecting muscle strength, proprioception, and stability [[51\]](#page-12-0). Clinically, this underlines the necessity for a holistic approach in T2DM management, incorporating regular assessments of musculoskeletal function and tailored exercise programs that prioritize physical activity to counteract the negative impacts of T2DM [\[50](#page-12-0)]. The study also substantiates the importance of early interventions focused on weight and glycemic control to prevent or delay the onset of musculoskeletal complications. Consequently, this research advocates for an integrated healthcare model that combines metabolic control with physical rehabilitation to enhance overall patient outcomes and quality of life in those with T2DM.

In this study, we focused on an elderly cohort due to the higher prevalence of T2DM and its associated musculoskeletal complications in this age group [\[52](#page-12-0)]. While our findings provide valuable insights into musculoskeletal health in older adults with T2DM, future research should aim to replicate these findings in younger cohorts to explore the broader applicability across different age demographics. The reliance on self-reported physical activity levels in our study may introduce potential recall bias, which is a recognized limitation. Objective measures of physical activity, such as wearable technology or accelerometers, would provide more accurate and reliable data on activity levels [[53\]](#page-12-0). Incorporating such measures in future research would enhance the robustness of findings and strengthen conclusions regarding the impact of physical activity on musculoskeletal health outcomes in individuals with T2DM [[53\]](#page-12-0).

4.2. Limitations and future directions

While this study provides insightful findings, several limitations must be acknowledged. Firstly, the cross-sectional design employed here precludes establishing causality between T2DM and musculoskeletal health outcomes. Future studies employing longitudinal designs are essential to unravel temporal relationships and establish causal links. Secondly, the reliance on self-reported physical activity levels may introduce recall bias or inaccuracies. Objective measures using wearable technology could enhance the reliability and validity of physical activity data. Thirdly, the study focused on an elderly cohort, which may limit the generalizability of findings to younger individuals with T2DM. Future research should replicate these findings across diverse age groups to assess broader applicability [59]. Additionally, randomized controlled trials are warranted to evaluate the efficacy of tailored exercise interventions

in enhancing musculoskeletal outcomes among individuals with T2DM. Further exploration into the synergistic effects of diet, metabolic control, and physical activity could offer a more holistic approach to managing musculoskeletal health in T2DM. Lastly, investigating genetic and molecular markers holds promise for uncovering the underlying pathophysiological mechanisms driving musculoskeletal deterioration in T2DM, potentially guiding the development of targeted therapeutic strategies.

5. Conclusion

This study contributes significant insights into the relationship between Type 2 diabetes mellitus (T2DM) and musculoskeletal health, revealing substantial deficits in muscle strength, proprioception, and stability compared to non-diabetic counterparts. These findings underscore the critical need for integrated diabetes care strategies that incorporate comprehensive musculoskeletal assessments and targeted interventions, particularly emphasizing structured physical activity and personalized exercise regimens. While acknowledging limitations such as the study's cross-sectional design and potential selection bias, future research should focus on longitudinal studies to establish causal relationships and explore effective interventions. Enhanced use of objective measures and comparative studies across diverse populations will further refine our understanding and guide tailored approaches to improve musculoskeletal outcomes in individuals with T2DM, thereby optimizing overall health and quality of life.

CRediT authorship contribution statement

Khalid A. Alahmari: Writing – review & editing, Writing – original draft, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ravi Shankar Reddy:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Informed consent statement

Written Informed consent was obtained from all subjects involved in the study.

Institutional review board statement

The study was conducted following the Declaration of Helsinki and approved by the Institutional Review Board at King Khalid University (protocol code: (ECM#2022–3567)) and date of approval: 23-03-2022, for studies involving humans.

Data availability statement

The dataset related to this study has been archived in the publicly accessible Zenodo repository. You can access it using the following [https://doi.org/10.5281/zenodo.10827210.](https://doi.org/10.5281/zenodo.10827210)

Funding

The authors extend their appreciation to the Deanship of Research and Graduate Studies at King Khalid University for funding this work through a Large Research Project under grant number RGP. 2/471/45.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Ravi Shankar Reddy reports financial support was provided by King Khalid University. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors extend their appreciation to the Deanship of Research and Graduate Studies at King Khalid University for funding this work through a Large Research Project under grant number RGP. 2/471/45.

References

- [1] [D. Lovic, A. Piperidou, I. Zografou, H. Grassos, A. Pittaras, A. Manolis, The growing epidemic of diabetes mellitus, Curr. Vasc. Pharmacol. 18 \(2\) \(2020\)](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref1) [104](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref1)–109.
- [2] [Y. Pinchevsky, N. Butkow, F.J. Raal, T. Chirwa, A. Rothberg, Demographic and clinical factors associated with development of type 2 diabetes: a review of the](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref2) [literature, Int. J. Gen. Med. 3 \(2020\) 121](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref2)–129.
- [3] [P. Arokiasamy, S. Salvi, Y. Selvamani, Global burden of diabetes mellitus: prevalence, pattern, and trends, Handbook of Global Health 4 \(2021\) 495](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref3)–538.
- [4] [Z. Zeng, J. Shan, Y. Zhang, Y. Wang, C. Li, J. Li, W. Chen, Z. Ye, X. Ye, Z. Chen, Asymmetries and relationships between muscle strength, proprioception,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref4) [biomechanics, and postural stability in patients with unilateral knee osteoarthritis, Front. Bioeng. Biotechnol. 10 \(2022\) 922832.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref4)

K.A. Alahmari and R.S. Reddy Heliyon 10 (2024) e39270

- [5] [A.W. da Silva Rodrigues, A.B.A. Martins, N.J.B. de Albuquerque Filho, V.S. de Queiros, M.G. Assis, E.S.B. dos Santos, L.A.C. Cabral, F.B. Gomes, M. Taheri,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref5) [K. Irandoust, Strength exercises with blood flow restriction promotes hypotensive and hypoglycemic effects in women with Mellitus type 2 diabetes?:](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref5) [randomized crossover study, Health Nexus 1 \(1\) \(2023\) 32](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref5)–39.
- [6] [K. Mukhopadhyay, Proprioception and Kinesthesia: the sixth sense organ, Advances in Health and Exercise 1 \(1\) \(2021\) 12](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref6)–17.
- [7] [R. Chiaramonte, M. Bonfiglio, P. Leonforte, G.L. Coltraro, C.S. Guerrera, M. Vecchio, Proprioceptive and dual-task training: the key of stroke rehabilitation, A](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref7) [systematic review, Journal of Functional Morphology and Kinesiology 7 \(3\) \(2022\) 53.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref7)
- [8] [D.S. Logerstedt, J.R. Ebert, T.D. MacLeod, B.C. Heiderscheit, T.J. Gabbett, B.J. Eckenrode, Effects of and response to mechanical loading on the knee, Sports](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref8) [Med. 1 \(2022\) 1](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref8)–35.
- [9] [M. Shafizadeh, J. Manson, S. Fowler-Davis, K. Ali, A.C. Lowe, J. Stevenson, S. Parvinpour, K. Davids, Effects of enriched physical activity environments on](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref9) [balance and fall prevention in older adults: a scoping review, J. Aging Phys. Activ 29 \(1\) \(2020\) 178](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref9)–191.
- [10] [M.S. Alshahrani, R.S. Reddy, Quadriceps strength, postural stability, and pain mediation in bilateral knee osteoarthritis: a comparative analysis with healthy](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref10) [controls, Diagnostics 13 \(19\) \(2023\) 3110](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref10).
- [11] M. Billot, R. Calvani, A. Urtamo, J.L. Sánchez-Sánchez, C. Ciccolari-Micaldi, M. Chang, R. Roller-Wirnsberger, G. Wirnsberger, A. Sinclair, N. Vaquero-Pinto, [Preserving mobility in older adults with physical frailty and sarcopenia: opportunities, challenges, and recommendations for physical activity interventions,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref11) [Clin. Interv. Aging 1 \(2020\) 1675](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref11)–1690.
- [12] [M. Hasanzad, N. Sarhangi, S. Nikfar, S.N. Ostad, H.R. Aghaei Meybodi, A narrative review of current trends in liraglutide: insights into the unmet needs in](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref12) [management of type 2 diabetes and obesity, J. Diabetes Metab. Disord. 19 \(2\) \(2020\) 1863](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref12)–1872.
- [13] [A. Majjad, Y. Errahali, H. Toufik, J. H Djossou, M. Ghassem, J. Kasouati, A.E. Maghraoui, Musculoskeletal disorders in patients with diabetes mellitus: a cross](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref13)[sectional study, International journal of rheumatology 2018 \(1\) \(2018\) 3839872](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref13).
- [14] [N. Johri, M. Vengat, D. Kumar, P. Nagar, D. John, S. Dutta, P. Mittal, A comprehensive review on the risks assessment and treatment options for Sarcopenia in](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref14) [people with diabetes, J. Diabetes Metab. Disord. 22 \(2\) \(2023\) 995](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref14)–1010.
- [15] A. Strong, A. Arumugam, E. Tengman, U. Röijezon, C.K. Häger, Properties of knee joint position sense tests for anterior cruciate ligament injury: a systematic [review and meta-analysis, Orthopaedic Journal of Sports Medicine 9 \(8\) \(2021\) 23259671211007878](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref15).
- [16] D. Garcia, I.V. de Sousa Neto, Y. de Souza Monteiro, D.P. Magalhães, G.M.L. Ferreira, R. Grisa, J. Prestes, B.V. Rosa, O. Abrahin, T.M. Martins, Reliability and [validity of a portable traction dynamometer in knee-strength extension tests: an isometric strength assessment in recreationally active men, Healthcare 11](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref16) [\(MDPI\) \(2023\) 1466](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref16)–1473, 1.
- [17] [J.-Y. Hogrel, O. Benveniste, D. Bachasson, Routine monitoring of isometric knee extension strength in patients with muscle impairments using a new portable](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref17) [device: cross-validation against a standard isokinetic dynamometer, Physiol. Meas. 41 \(1\) \(2020\) 015003](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref17).
- [18] Y. Duchene, G. Mornieux, A. Petel, P.P. Perrin, G.C. Gauchard, The trunk'[s contribution to postural control under challenging balance conditions, Gait Posture](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref18) [84 \(2021\) 102](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref18)–107.
- [19] [J. Haworth, D. Goble, M. Pile, B. Kendall, BTrackS limits of stability test is a reliable assessment of volitional dynamic postural control, Gait Posture 80 \(2020\)](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref19) 298–[301](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref19).
- [20] [R.S. Reddy, B.A. Alkhamis, J.A. Kirmani, S. Uddin, W.M. Ahamed, F. Ahmad, I. Ahmad, A. Raizah, Age-related decline in cervical proprioception and its](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref20) [correlation with functional mobility and limits of stability assessed using computerized posturography: a cross-sectional study comparing older \(65](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref20)+ years) and [younger adults, Healthcare. 11. MDPI 1 \(2023\) 1924.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref20)
- [21] [E. Shevroja, J.-Y. Reginster, O. Lamy, N. Al-Daghri, M. Chandran, A.-L. Demoux-Baiada, L. Kohlmeier, M.-P. Lecart, D. Messina, B.M. Camargos, Update on the](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref21) [clinical use of trabecular bone score \(TBS\) in the management of osteoporosis: results of an expert group meeting organized by the European society for clinical](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref21) [and economic aspects of osteoporosis, osteoarthritis and musculoskeletal diseases \(ESCEO\), and the international osteoporosis foundation \(IOF\) under the](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref21) [auspices of WHO collaborating center for epidemiology of musculoskeletal health and aging, Osteoporosis International 34 \(9\) \(2023\) 1501](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref21)–1529.
- [22] [R.S. Reddy, M.S. Alshahrani, M.A. Almohiza, B.A. Alkhamis, J.S. Tedla, V.N. Kakaraparthi, G.M. Koura, D. Mukherjee, H.H. Alnakhli, H.S.H. Ghulam, Shoulder](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref22) [muscle weakness and proprioceptive impairments in type 2 diabetes mellitus: exploring correlations for improved clinical management, PeerJ 12 \(2024\)](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref22) [e17630.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref22)
- [23] [R. Kraiwong, M. Vongsirinavarat, V. Hiengkaew, P. von Heideken Wågert, Effect of sensory impairment on balance performance and lower limb muscle strength](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref23) [in older adults with type 2 diabetes, Annals of rehabilitation medicine 43 \(4\) \(2019\) 497](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref23)–508.
- [24] [A.H. Wettasinghe, D.W. Dissanayake, L. Allet, P. Katulanda, S.R. Lord, Falls in older people with diabetes: identification of simple screening measures and](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref24) [explanatory risk factors, Primary care diabetes 14 \(6\) \(2020\) 723](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref24)–728.
- [25] [G. Cavati, F. Pirrotta, D. Merlotti, E. Ceccarelli, M. Calabrese, L. Gennari, C. Mingiano, Role of advanced glycation end-products and oxidative stress in type-2](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref25) [diabetes-induced bone fragility and implications on fracture risk stratification, Antioxidants 12 \(4\) \(2023\) 928.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref25)
- [26] [S. Illien-Jünger, Y. Lu, S.A. Qureshi, A.C. Hecht, W. Cai, H. Vlassara, G.E. Striker, J.C. Iatridis, Chronic ingestion of advanced glycation end products induces](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref26) [degenerative spinal changes and hypertrophy in aging pre-diabetic mice, PLoS One 10 \(2\) \(2015\) e0116625](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref26).
- [27] [L.R. Ettinger, A. Boucher, E. Simonovich, Patients with type 2 diabetes demonstrate proprioceptive deficit in the knee, World J. Diabetes 9 \(3\) \(2018\) 59.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref27)
- [28] [K.H. Sienko, R.D. Seidler, W.J. Carender, A.D. Goodworth, S.L. Whitney, R.J. Peterka, Potential mechanisms of sensory augmentation systems on human balance](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref28) [control, Front. Neurol. 9 \(2018\) 417302](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref28).
- [29] [T. Lang, T. Streeper, P. Cawthon, K. Baldwin, D.R. Taaffe, T. Harris, Sarcopenia: etiology, clinical consequences, intervention, and assessment, Osteoporosis](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref29) [international 21 \(2010\) 543](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref29)–559.
- [30] H. Mitoma, A. Buffo, F. Gelfo, X. Guell, E. Fucà, S. Kakei, J. Lee, M. Manto, L. Petrosini, A. Shaikh, Consensus paper. Cerebellar reserve: from cerebellar [physiology to cerebellar disorders, Cerebellum 19 \(2020\) 131](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref30)–153.
- [31] [M. Cristina Soares Botelhoa, M. Guilherme Conde, N.M. Dias Azinheira Rebelo Braz, Functional aspects in ageing adults with diabetic neuropathy. A review,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref31) [Curr. Diabetes Rev. 12 \(2\) \(2016\) 114](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref31)–119.
- [32] [N.D. Reeves, G. Orlando, S.J. Brown, Sensory-motor mechanisms increasing falls risk in diabetic peripheral neuropathy, Medicina 57 \(5\) \(2021\) 457.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref32)
- [33] [G. Felicetti, P. Thoumie, M.C. Do, M. Schieppati, Cutaneous and muscular afferents from the foot and sensory fusion processing: physiology and pathology in](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref33) [neuropathies, J. Peripher. Nerv. Syst. 26 \(1\) \(2021\) 17](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref33)–34.
- [34] [M.J. Vermette, F. Prince, L. Bherer, J. Messier, Concentrating to avoid falling: interaction between peripheral sensory and central attentional demands during a](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref34) [postural stability limit task in sedentary seniors, GeroScience 1 \(2023\) 1](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref34)–20.
- [35] [I. Ahmad, R.S. Reddy, R.S. Alqhtani, J.S. Tedla, Adal S. Al, Exploring the Nexus of lower extremity proprioception and postural stability in older adults with](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref35) [osteoporosis: a cross-sectional investigation, Front. Public Health 11 \(2023\) 1287223.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref35)
- [36] [K. Phapatarinan, M. Sremakaew, S. Uthaikhup, Stimulated cervical afferent input increases postural instability in older people with chronic neck pain: a cross](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref36)[sectional study, BMC Geriatr. 24 \(1\) \(2024\) 153](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref36).
- [37] M.S. Alshahrani, R.S. Reddy, A. Alshahrani, A.P. Gautam, S.F. Alsubaie, Exploring the interplay between ankle muscle strength, postural control, and pain [intensity in chronic ankle instability: a comprehensive analysis, Heliyon 10 \(2024\) e27374.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref37)
- [38] B. Sebesi, Á. Fésüs, M. Varga, T. Atlasz, K. Vadász, P. Mayer, L. Vass, B. Meszler, B. Balázs, M. Váczi, [The indirect role of gluteus medius muscle in knee joint](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref38) [stability during unilateral vertical jump and landing on unstable surface in young trained males, Appl. Sci. 11 \(16\) \(2021\) 7421.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref38)
- [39] [L. Willemse, E.J. Wouters, H.M. Bronts, M.F. Pisters, B. Vanwanseele, The effect of interventions anticipated to improve plantar intrinsic foot muscle strength on](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref39) [fall-related dynamic function in adults: a systematic review, J. Foot Ankle Res. 15 \(1\) \(2022\) 3](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref39)–9.
- [40] G. Maugeri, V. D'[Agata, B. Trovato, F. Roggio, A. Castorina, M. Vecchio, M. Di Rosa, G. Musumeci, The role of exercise on peripheral nerve regeneration: from](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref40) [animal model to clinical application, Heliyon 7 \(2021\) e08281, 23-36](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref40).
- [41] [A.A. Mendelson, D. Erickson, R. Villar, The role of the microcirculation and integrative cardiovascular physiology in the pathogenesis of ICU-acquired weakness,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref41) [Front. Physiol. 14 \(2023\) 1170429.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref41)
- [42] [P. Aleixo, J. Abrantes, Proprioceptive and strength exercise guidelines to prevent falls in the elderly related to biomechanical movement characteristics,](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref42) [Healthcare 12 \(MDPI\) \(2024\) 186](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref42)–192, 1.
- [43] [Z. Wang, A. Emmerich, N.J. Pillon, T. Moore, D. Hemerich, M.C. Cornelis, E. Mazzaferro, S. Broos, T.S. Ahluwalia, T.M. Bartz, Genome-wide association analyses](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref43) [of physical activity and sedentary behavior provide insights into underlying mechanisms and roles in disease prevention, Nat. Genet. 54 \(9\) \(2022\) 1332](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref43)–1344.
- [44] [Z. Cao, C. Zhu, Y. Zhou, Y. Wang, M. Chen, Y. Ju, X. Zhao, Risk factors related balance disorder for patients with dizziness/vertigo, BMC Neurol. 21 \(1\) \(2021\)](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref44) [186](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref44).
- [45] [M. Kushkestani, M. Parvani, M. Ghafari, Z. Avazpoor, The role of exercise and physical activity on aging-related diseases and geriatric syndromes, SPORT TK-](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref45)[Revista EuroAmericana de Ciencias del Deporte 11 \(2022\) 6](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref45)–12.
- [46] G. D'[Onofrio, J. Kirschner, H. Prather, D. Goldman, A. Rozanski, Musculoskeletal exercise: its role in promoting health and longevity, Prog. Cardiovasc. Dis. 77](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref46) [\(2023\) 25](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref46)–36.
- [47] T.J. Ballinger, W.R. Thompson, T.A. Guise, The bone–[muscle connection in breast cancer: implications and therapeutic strategies to preserve musculoskeletal](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref47) [health, Breast Cancer Res. 24 \(1\) \(2022\) 84](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref47)–93.
- [48] [A.H. Abdelhafiz, Effects of glycemic control on frailty: a multidimensional perspective, Hosp. Pract. 51 \(3\) \(2023\) 124](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref48)–134.
- [49] [J. Ras, E.S. Soteriades, D.L. Smith, A.P. Kengne, L. Leach, Evaluation of the relationship between occupational-specific task performance and measures of](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref49) [physical fitness, cardiovascular and musculoskeletal health in firefighters, BMC Publ. Health 24 \(1\) \(2024\) 20](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref49)–31.
- [50] R. Shawahna, A. Batta, M. Asa'[ad, M. Jomaah, I. Abdelhaq, Exercise as a complementary medicine intervention in type 2 diabetes mellitus: a systematic review](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref50) [with narrative and qualitative synthesis of evidence, Diabetes Metabol. Syndr.: Clin. Res. Rev. 15 \(1\) \(2021\) 273](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref50)–286.
- [51] [Y. Gu, S.M. Dennis, Are falls prevention programs effective at reducing the risk factors for falls in people with type-2 diabetes mellitus and peripheral](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref51) [neuropathy: a systematic review with narrative synthesis, J. Diabetes Complicat. 31 \(2\) \(2017\) 504](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref51)-516.
- [52] [R. Hoveizavi, F. Gao, V.J. Ramirez, B.R. Shuman, J.C. Joiner, S.J. Fisher, Compromised neuromuscular function of walking in people with diabetes: a narrative](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref52) [review, Diabetes Res. Clin. Pract. 1 \(2023\) 110802.](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref52)
- [53] [A.P. Hills, N. Mokhtar, N.M. Byrne, Assessment of physical activity and energy expenditure: an overview of objective measures, Front. Nutr. 1 \(2014\) 5](http://refhub.elsevier.com/S2405-8440(24)15301-7/sref53)–13.