MANAGEMENT PERSPECTIVE

Advances in balance assessment and balance training for diabetes

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Practice Points

- Diabetic patients are more vulnerable to a minor trauma than a healthy individual, thus addressing fall prevention should be considered at an even younger age than people without diabetes.
- In addition to diabetes-associated comorbidities, which impact postural control in individuals with diabetes, many of the medications prescribed for diabetes could actually add to a patient's balance instability and, thus, should be prescribed with precaution in those at high risk of falling.
- The evaluation of the risk of falling is a necessary step towards the provision of preventive measures for individuals deemed to have a high risk of falling.
- The subtle, early findings that are indicative of postural instability are, however, difficult to accurately assess from a clinical examination, and gait laboratory assessment is not currently available or practical. Thus, unfortunately, many patients suffering from diabetes that are 'at risk for falls' are undiagnosed.
- The above point being the case, very few centers have practical gait laboratories at their disposal.
- Innovative technologies, such as wearable sensors (which may be deployed anywhere – in an unobserved fashion), may be used in clinical practice for assessing subtle deviation in gait and balance due to diabetes.
- New data have demonstrated a potential benefit of exercise training in improving balance in diabetes.
- Recent developments in motor learning and virtual reality have shown promise to help patients alleviate their sensory feedback and motor impairments and speed up motor function recovery and may be used by patients at home much as their younger family members use video games.

SUMMARY As clinicians, we have been searching for objective and widely available outcome measures for our care. We also prefer these measuring processes not to burden our busy clinics or patients' time. With this in mind, it seems that there are many challenges to treating patients with diabetes. Some of these are well recognized and some are not. For

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example, we know that balance deterioration affects this population. In addition, individuals with diabetes are more vulnerable to any minor trauma than a healthy individual. Any minor trauma causes a major wound, which can be very dangerous for this population. Thus preventive strategies for reducing the risk of falls in diabetes should be considered even before geriatric age. Evaluation of the risk of falling is a necessary step towards the provision of preventive measures. This paper reviews and provides a comprehensive outlook of current development and possible emerging technologies for addressing balance instability in diabetes.

Falling is among the most serious health problems associated with aging [1]. It is estimated that 32% of people aged 65 years and older and 75% of nursing home residents are expected to fall at least once a year, with a quarter of these cases leading to serious injuries [2]. Falls are one of the leading causes of injurious deaths among people aged 65 years and older [3], resulting in approximately 9600 deaths in 1998 in the USA [4]. Hip fractures are one of the most serious consequences of falls among the elderly and it is estimated that there will be 500,000 hip fractures per year by 2040 [5]. Falls have other negative consequences, such as loss of function or immobility. Even after injuries are healed, or in cases of falls that do not result in injury, the mere experience of a fall often leaves elderly individuals with a fear of falling, causing them to severely limit their physical activity [6]. Such restriction on activity can trap an individual in a vicious cycle leading to decreased functional mobility, which in turn further restricts activity, and so on [7]. The economical burden of fall-related injuries, together with the pretium doloris makes such injuries the first public health problem for the elderly population. Therefore, prevention of falls and fall-related injuries, specifically in the elderly, remains a key challenge for public health.

Individuals with diabetes are more vulnerable to any minor trauma than a healthy individual, thus addressing fall prevention should be considered at an even younger age than people without diabetes. For example, Reistetter *et al.* studied 79,526 persons with a first time hip fracture and demonstrated that younger patients with diabetes had poorer outcomes (e.g., length of stay in the medical rehabilitation unit or hospital) than patients with no diabetes [8]. Their results also suggest that the difference between diabetes and nondiabetes in recovery outcomes after hip fracture is more pronounced in younger subjects than older subjects.

In addition, several studies suggest that people with diabetes are more likely to fall than the same age-matched population of people without diabetes [9,10]. For example, Miller and colleagues demonstrated that individuals with diabetes are 2.5-times more likely to experience an accidental fall or a fall-related injury than age-matched controls [11]. In the Women's Health and Aging Study of 1002 women, Volpato and colleagues reported that diabetes status demonstrated a 44% increased risk of falls over 3 years in their multivariate model [10]. In the Study of Osteoporotic Fractures (n = 9249), Schwartz and colleagues reported a 68% increased in multiple falls risk in individuals with diabetes over 2-year follow-up, compared to aged-matched controls [9]. Incident falls are also increased in patients with previous foot ulceration compared to controls [12]. Interestingly, poor balance appears to describe more of the fall risk association than loss of sensation or decreased vibratory perception [9]. Other authors have also described loss of sensation falling out of a multivariate model for conservative gait patterns in persons with diabetes [13]. Schwartz and colleagues reported poor balance, as assessed by tandem gait and standing, describing 23 and 14% of the fall risk association compared with 3 and 6%, respectively, for monofilament insensitivity and decreased vibration perception [9].

Evaluation of the risk of falling is a necessary step towards the provision of preventive measures for individuals deemed to have a high risk of falling. The risk of falling is generally evaluated by using questionnaires (e.g., fall history, health-related quality of life [e.g., SF12 or SF36] and Fall Efficacy Scale [e.g., FES or FES-I]). These methods have numerous shortcomings such as subjectivity and limited accuracy in recall [14]. Risk of falling can also be evaluated using clinical and functional tests, such as assessments of posture and gait (e.g., Tinetti Gait and Balance Score, Romberg's Balance Test and gait intercycle variability), independence in daily life (Barthel Index), level of motor task functioning (e.g., Lawton's score), cognition and vision [15–21].

The subtle, early findings that are indicative of postural instability are, however, difficult to accurately assess from a clinical examination, and gait laboratory assessment is not currently available or practical for the clinical environment. Thus, unfortunately, many patients suffering from diabetes that are 'at risk for falls' are undiagnosed. The conventional methods for assessment of gait and balance have been limited to gait laboratories equipped with motion tracking systems [22–26], which may not be suitable for a clinical environment [27,28]. This review aims to provide an overview of new advances in technologies and methods that may allow clinicians to evaluate gait and balance alteration due to diabetes outside of a gait laboratory and appropriately for routine clinical assessment. To better look at the appropriate technology for assessing gait and balance, first the impact of diabetes on gait and balance is briefly overviewed.

Diabetes & balance control

Traditionally, balance control is defined by an individual's ability to control deviations of the center of mass (COM) within the base of support (or center of pressure [COP]) [29], and balance deficits defined by deviations that lie outside normal age-matched reference limits [30].

Balance deficit is a key concern for individuals with diabetes and is associated with high morbidity and mortality. According to the National Diabetes Information Clearinghouse [201], 20.8 million people in the USA – at least 7% of the population – have diabetes and the number is steadily growing and estimated to increase by 122% by 2025 to reach a total of 300 million individuals [202]. Approximately 50% of individuals with diabetes over the age of 60 years exhibit diabetic neuropathy, making this the most common symptomatic complication. Diabetic peripheral neuropathy (DPN) is a serious complication, predisposing diabetic patients to foot complications. Individuals with DPN often suffer from postural instabilities, leading to falls, depression, anxiety and a decreased quality of life [31–33].

Balance disorder in DPN has been found to be associated with abnormal somatosensory feedback (proprioceptive and tactile), which is used in the formation of an internal representation of body position and motion (internal model) in the CNS [31,34–36]. It has been well established that in healthy subjects, this internal model is formed and tuned with practice, based on error-dependent learning of rules between the prior motor action and desired action [37,38]. In spite of long sensory delays, noise from multiple sources and many interdependent muscles to control, this internal model enables individuals to produce motor commands (feedforward prediction) appropriate for arbitrary actions. DPN individuals may compensate for the lack of sensory feedback through intact sensory systems and through prior experience (e.g., feedforward prediction). Although, this is a very positive phenomenon for reducing the risk of falling, especially during clinical evaluation, this capability may be enhanced and mask the impact of sensory impairment for maintaining balance in those conditions in which subjects are naive. Therefore, a potential postural disorder may not be recognized during a clinic visit. The novel technology based on body-worn sensors with a suitable biomechanical model of the human body offer a new objective tool that allows assessing both biomechanical (e.g., body sway) and neurological (e.g., postural compensatory strategy) aspects of balance control in DPN patients.

Deficit in somatosensory feedback due to peripheral neuropathy is not the only cause of balance instability in individuals with diabetes. Several studies have hypothesized that deficits in vision due to retinopathies, vestibular system due to polyneuropathy and orthostatic intolerance due to diabetes could be important contributors to postural instabilities in this population [39–44]. In addition, alteration in the CNS due to autonomic neuropathy may also contribute to abnormalities in gait and balance in individuals with diabetes [42,44,45].

Diabetes & gait

Proper gait function (i.e., quality of gait) requires the ability to maintain safe gait while navigating in complex and changing environments, and to conform one's gait to different task demands. Furthermore, a person's quality of gait is closely linked to his or her overall state of health. For example, walking speed inversely correlates with an individual's ability to live independently, perform various activities of daily life (such as safely crossing a traffic intersection) and risk of falling [27,46,47].

Patients with diabetes experience a high incidence of injuries while walking and have a low level of perceived safety [31,43,48]. Furthermore, aberrations in some spatio-temporal gait parameters have been linked with increased fall risk among elderly patients [48–51]. Cavanagh *et al.* found that patients with DPN are 15-times more likely to report a fall accident during walking or standing than aged-matched controls [48]. Therefore, a better understanding of the impact of peripheral neuropathy on spatio-temporal parameters of gait may be of key importance in preventing falls in this patient population.

Several studies have previously addressed gait alterations that occur in patients with diabetes. Patients with diabetes tend to take shorter steps with a wider base of support [43,52]. They also walk slower and demonstrate a longer double support time [43,52]. There may be psychological factors that influence one's gait pattern beyond aging alone [53]. Nonetheless, patients with diabetes and peripheral neuropathy have been described to have gait instability [54]. Petrofsky and colleagues studied this potential area in 15 patients with diabetes and no strength deficits via manual muscle testing or loss of protective sensation using 10 g monofilaments [52]. Gait was assessed in a linear path as well during two turning tasks (0.66 m and 0.33 m). They demonstrated slower speed and wider step length in patients with diabetes compared to aged-matched controls, coupled with greater motor error at the joints. The authors suggested that the deterioration in gait observed in individuals with diabetes is due to damage in the vestibular, autonomic and somatic nervous systems [52]. Other authors have observed gait impairment preceding sensory loss [55,56].

Diabetes & reaction time

Aging slows reflexes and increases the time to react to a number of external stimuli of different modalities [57]. In movement-related research fields, the reaction time test is used to estimate the attention demand required to perform the main motor task [58]. Several studies suggest that diabetes slows psychomotor responses and has cognitive affect on those individuals without proper metabolic control, all of which may affect reaction times. The additional slowing of reaction times may affect every day tasks such as balance, increasing the probability of a slip or fall.

In the gait study by Petoskey and colleagues in 15 patients with diabetes [52], reaction times were assessed as the time taken to stop walking in response to a strobe flash. The results suggest that the reaction time is twofold longer in individuals with diabetes versus age-matched controls. Courtemanche and colleagues observed similar findings in a study of 12 patients with DPN compared with seven age-matched controls. Neuropathy was defined using a clinical scoring system and authors found prolonged reaction time in patients suffering from diabetes and peripheral neuropathy. This was measured using an upper extremity reaction time test to auditory stimulus. These results led the authors to conclude that increased attentional demands with more conservative gait patterns suggest lack of proprioception affecting control of gait [59].

Prescribed medication & its impact on balance

Theoretically, many of the medications prescribed for DPN could actually add to a patient's balance instability. For example, amitriptyline has been reported to cause sedation in 43% of patients [60]. In a comparison trial with gabapentin, 79% of patients treated with amitriptyline reported sedation, dizziness, ataxia, postural hypotension or lethargy and there were 31 reports of these conditions in 28 patients treated with gabapentin [61]. In another report, Biesbroeck and colleagues reported somnolence and musculoskeletal complaints in 46 and 23% of DPN patients, respectively [62]. Similar adverse event rates have been reported in trials of newer agents. In a trial of duloxetine, 43% reported somnolence, fatigue or dizziness [63]. In a trial of pregabulin, 61% reported somnolence, dizziness, ataxia or asthenia [64]. The point of this discussion is not to diminish the high clinical value of treating neuropathic pain with effective agents. The point is that many of these reported adverse events are difficult to quantify in a patient's health-related quality of life. More objective measures, such as modeling the COM and postural control strategy during a Romberg's test could be helpful in understanding how balance has responded to a therapy [65]. Also, measuring one's quality of activity at home and the duration of their postural transitions outside of the gait laboratory or under the watchful eyes of a clinician could also be helpful in understanding response to treatment [66].

Objective assessment of balance instability

During normal quiet stance, humans sway slightly. This sway is indicative of a sensorimotor control system maintaining imperfect equilibrium of an inverted pendulum model of upright posture [67]. The control generally relies on input from multiple sensory modalities, and sway, practically defined either as motion of the body's COM or the COP of vertical ground reaction forces onto a subject's feet [68], increases when some sensory inputs are disrupted [69]. In addition, subjects with a variety of neurological disorders exhibit greater sway than healthy subjects [70–72]. For these reasons and because the of ease of measurement, sway and other quantifiers of quiet stance have been proposed as useful measures for detecting balance disorders or determining the risk of falling. These measures are, however, limited in their ability to either diagnose contributing factors or provide insight concerning underlying mechanisms [73,74]. In fact, increasing sway is not a good predictor of postural instability since many very unstable patients, such as patients with Parkinson's disease, show smaller than normal sway in stance [75]. Gill *et al.* for example showed that elderly subjects did not exhibit greater sway than younger subjects in some conditions [76]. The inaccuracy of current technologies based on measuring body sway for assessing postural control is mostly owing to the following reasons:

- They do not take into account the postural compensatory strategy, which represents how a voluntary oscillation of a body segment is compensated by involuntary movement of other segments;
- They study the postural response without altering the sensory feedback systems (e.g., under low light condition, during which false visual cues may make things worse) [77];
- Sway is measured based on using a single inverted pendulum rotating around the ankle joint, under the assumption that movement around the hip joint is quite small;
- Most importantly, balance is assessed under conditions that do not challenge the feedforward control system and hence the role of motor adaptation to compensate the impairment in sensory feedback through re-weighting or using other intact sensory systems is unclear.

Thus, for a more accurate assessment of balance and its potential improvement postintervention a combination of more sensitive tools and paradigms of test is required. More specifically, balance should be assessed by the evaluation of how different body segments are interacting with each other and whether this interaction helps to stabilize COM within the base of support (or COP). Additionally, balance should be tested under conditions in which individuals with diabetes may have more difficulty to interact with sensory feedback such as standing on an irregular surface (vulnerability due to foot insensation) or an ankle reaching task (vulnerability due to limited lower extremity flexibility and lack of prioprioception feedback).

Postural strategy & sensory alteration

Body sway itself may not be accurate enough to evaluate postural control. An individual may have a significant sway in the COP or ankle without moving his/her COM through an appropriate reciprocal coordination between his/her body segments [65]. This is the strategy that is often used in acrobatics performance (e.g., tightrope walking). On the other hand, a slight motion of ankle segment may substantially move COM out of the base of support and thus cause a fall if, for example, the hip moves in the same direction as the ankle movement. The best postural anticipatory strategy is defined as best joint reciprocal coordination to minimize the motion of COM. Balance assessment should evaluate how postural anticipatory strategy is modified owing to diabetes. For example, poor strength and poor sensory response at the ankles due to diabetes may lead to a compensatory strategy of excessive hip/trunk motion for control of the postural equilibrium [78]. The identification of the strategies used by a patient to compensate for his/her impairments enables clinicians to determine whether more optimal strategies are potentially available.Thus, an objective assessment helps clinicians know whether or not their patients are performing optimally given their current set of primary impairments, and whether intervention can improve the strategies used to accomplish balance tasks. It would also be helpful to assess reciprocal postural response with changes in support and sensory conditions, an individual's expectation and experience, and task constraints. Balance assessments should also differentiate between different types of balance control, including the ability to respond to external perturbations, the ability to anticipate postural demands associated with voluntary movements, and the ability to voluntarily and efficiently move the COM through space, since patients may be affected differently in these different types of balance control [75,78]. A balance assessment system must also evaluate the compensatory strategies used by individuals during balancing tasks.

Motor learning & sensory compensation

Recent studies support the hypothesis that postural compensation for sensory feedback loss can involve sensory substitution, predictive mechanisms and increased sensitivity to the remaining intact sensory information [79]. For example, in a case study of an unusual patient with total body loss of large fiber sensory afferents, Horak *et al.* found that auditory cues indicating perturbation onset can trigger functional postural responses when the direction of perturbation is predictable [72]. In a subsequent study, they showed that patients with partial loss of somatosensory information from the feet due to DPN can substitute light touch from a fingertip to reduce sway and improve scaling of postural response magnitude [80]. Interestingly, in another study, Horak *et al.* demonstrated that control subjects standing on any sway-referenced surface swayed significantly more than neuropathy subjects who stood on a firm surface [34]. This suggests that sway-referencing disrupts more somatosensory information than is disrupted by severe neuropathy [32,48]. A similar observation was reported by Najafi *et al.* by comparing balance control between healthy subjects standing on a soft surface (alteration in somatosensory feedback) and DPN patients [65]. These findings may indicate that in DPN patients, CNS forms a new motor adaptation mechanism to predict the alteration and hence compensate for the distorted somatosensory information. The details of this compensation mechanism, however, are not well understood. Additionally, these studies may suggest that although DPN patients may show a relatively good balance during their clinical visit, they may be vulnerable when maintaining balance in conditions that are new to them. Therefore, novel techniques/paradigms should also be designed to examine the feedforward component underlying balance control prior to compensation of the lack of sensory feedback for appropriate therapeutic decision-making.

Current methods for assessment of balance instability

Currently available technologies for assessing postural control can be divided into four categories (see **Figure 1**). A variation of COM can be estimated using camera-based systems (e.g., Vicon) incorporated with several reflected markers attached to different body segments, as **Figure 1A** shows; such technologies, however, are expensive. Given that they require installation of particular infrastructures, and that the overall process, including marker attachment and data extraction, are time consuming, these systems are impractical for use in routine clinical practice; the most widely-used method for evaluation of a patient's ability to maintain postural stability (posturography) is based on the measurement of ground reaction forces and variation of COP **(Figure 1B)**. Forceplate (e.g., Kistler) provides an accurate estimate of the ground reaction forces and the COP. These technologies, however, are

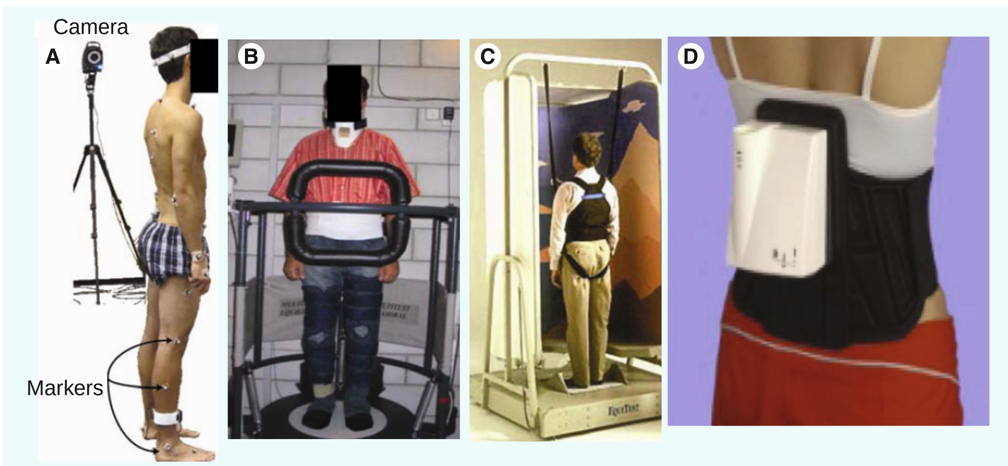

Figure 1. Current methods for assessment of postural instability. (A) Camera-based systems: these technologies could be used for estimation of center of mass sway. **(B)** Force Platform: a force plate could be used for measuring the variation of center of pressure as the subject stands on the platform. **(C)** Computerized dynamic posturography: using a computerized and movable platform, balance can be assessed under altered sensory conditions; **(D)** recently some innovative technologies based on micro-electro-mechanical systems technology has been introduced to measure body segment oscillation.

relatively expensive, and often require specific infrastructure installation and are not ambulatory. Additionally, standing on an instrumented platform makes it difficult to examine balance on different types of surfaces, which make difficult the assessment of type of standing surface, footwear on balance. Therefore, they are also less practical for small clinic/hospital environments. Furthermore, they do not provide any information about the movement of body segments as well as compensatory strategy. **Figure 1C** shows computerized dynamic posturography attempts to provide quantitative information about the patient's ability to maintain balance [203]. The patient wears a harness to prevent falls and stands on an enclosed platform surrounded by a visual field. By altering the platform angle, or by shifting the visual field, the test assesses movement coordination and the sensory organization of visual, somatosensory and vestibular information relevant to postural control. The results of posturography have been used to determine what type of information (e.g., visual, vestibular and proprioceptive) can and cannot be used to maintain balance. Although such a technology enables the study of postural control in altered sensory conditions, these systems are expensive and require a dedicated space and installation of particular infrastructures. They are therefore unsuitable for in-home and small clinics/hospital applications. Recently several technologies have been developed to measure body sway based on MEMS technology (e.g., SwayStar™ [204]) **(Figure 1D)**. However, they are unable to evaluate postural compensatory strategy since they lack a suitable biomechanical model – most studies model the human body as a single inverted pendulum rotating around the ankle joint, under the assumption that movement around the hip joint is quite small. However, a recent study suggests that the movement around hip joint is not only not negligible, but is also of key importance for maintaining balance [81].

Recent advances in assessing balance

Human body motion is traditionally captured using standard optic, magnetic or sonic technologies [82]. However, in recent years, body-wearable sensor technology based on electromechanical sensors (MEMS) has provided a new avenue for accurately detecting and monitoring body motion and physical activity of an individual under free conditions [50,82,83]. In particular thanks to the integration of MEMS in a new generation of smart cell phones, the application of MEMS for motion analysis and mobile health application has sharply increased in recent years.

Unlike laboratory-based instruments, which need a dedicated controlled space, the wearable sensors can be used just about anywhere [82]. These are highly transportable and do not require stationary units such as a transmitter, receiver or cameras. In addition, these sensors are much cheaper than sonic, magnetic and optical motion capture devices [82]. They are easy to set up and use, and do not require highly skilled operators. Wearable sensors can be used in real time, since the processing phase of detected signal is much shorter than the computing time of some standard systems using image processing and marker tracking algorithms [82]. In particular, the combination of multiple accelerometers, angular rate sensors (gyroscopes) and a magnetometer show a promising design for a hybrid kinematic sensor module for measuring the 3D kinematics of different body segments [65]. These sensors incorporated with a high speed data acquisition system enable the measuring and recording of 3D body segment motion with sample frequency (up to several hundred Hz) with a lower cost than camera-based systems. The high sample frequency is essential for virtual reality and motor adaption applications, where assessing subjects' postural response against an alteration is required (e.g., assessing involuntary response or feedforward and motor adaptation ability). In addition, real-time processing is highly beneficial to the creation a bio-feedback signal from body segment motion or COM for both rehabilitation and evaluation of gait and postural control mechanisms [84].

Using body-worn sensor for assessing postural control & postural control strategy in diabetes

The application of wearable sensors based on MEMS technology for assessing balance has been described in the past. For example, postural sway can be measured by using accelerometers placed at the back of a subject. Adlerton *et al* assessed the changes in postural control strategy after fatiguing exercise using accelerometers on a hip belt and compared the results with a force platform [85]. Results suggest that both COP movements and truck accelerations are increased post fatigue. Body sway can also be measured using angular velocity sensor (gyroscope), for example, Allum *et al.* quantified trunk sway during balance tasks using two angular velocity sensors mounted on a belt and attached to the lower back [86]. The results suggest that measuring trunk sway allows the identification of vestibular deficit subjects from normal healthy controls [86].

A key challenge for using wearable sensors is their ability to extract useful clinical data along with a restriction on the number of sensor attachments and ease of management. Naturally, if the wearable sensor poses any hindrance to a subject's movements, due to either the complexity of sensor attachments (e.g., multiple sensor units or the location of sensor attachment) or device management (e.g., limited battery life), its application for outdoor monitoring and routine clinical assessment will be limited [82]. Therefore, a simplified biomechanical model of the human body with the requirement of a minimum number of sensor attachments should be integrated with such technology to make them suitable for various clinical applications. On the other hand, model simplification may alter system accuracy. Therefore, an optimum tradeoff between system accuracy and the minimum number of sensor attachment should be provided. Previous studies addressing MEMS technology for assessing balance often assumed that measuring sacral or lower back motion (e.g., one link) is sufficient to estimate the COM sway, assuming that the hip joint movement is quite small [65,81,85,86].

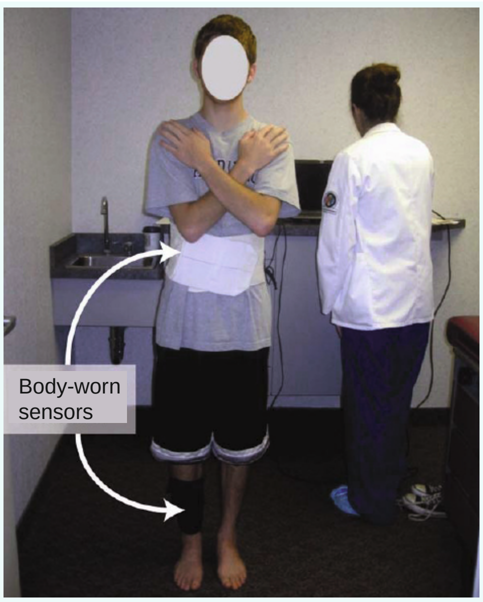

Figure 2. Wearable sensors for assessing balance. By attaching two wearable sensors to a patient's shin and lower back, balance as well as reciprocal interaction between ankle and hip motion can be assessed accurately. One of the key advantages of this method is the ability to assess balance in any environment independent of type of surface and base of support.

In a recent study, our team has designed and validated a biosensor technology named BalanSens™ [65]. The system is based on widely available kinematic sensors (i.e., accelerometer, gyroscope and magnetometer). The system measures ankle and hip motion in 3D **(Figure 2)**. We have also integrated the resulting data into a two-link biomechanical model of the human body for estimating the 2D sway of the COM in anterior–posterior (AP) and medial–lateral (ML) directions **(Figure 3)**. To evaluate the best postural strategy for maintaining balance, a reciprocal compensatory index (RCI) was defined, which quantifies how the movement around the hip could compensate for the movement around the ankle for reducing the variation of COM [65]. RCI values near to zero represent a good postural control strategy (i.e., negative correlation between hip and ankle movements), RCI values more than one represent inappropriate postural control strategy (i.e., positive correlation between hip and ankle movements leading to an increase in the variation of COM and consequently fall accident) and RCI values near to one indicate that there is no correlation between the movement of ankle and hip joints [65].

The validity and reliability of the suggested system were examined by several measurements [65]. First, the COM estimated using BalanSens was compared with COP measured using a standard pressure platform in 21 healthy subjects. Results suggested a relatively high correlation ($r = 0.92$) between the two measurements during both eyes-open (EO) and eyes-closed (EC) conditions. The clinical validity of the system was assessed by comparing the balance control of healthy subjects with a group of 17 individuals with DPN [65]. Results demonstrated that DPN patients exhibit significantly greater COM sway than healthy subjects for both EO and EC conditions ($p < 0.005$). The difference becomes highly pronounced while eyes are closed. Furthermore, the results showed that postural compensatory strategy assessed using RCI is significantly better in healthy subjects compared to DPN subjects for both EO and EC conditions, as well as in both medial-lateral and anterior–posterior directions ($p < 0.05$). Interestingly, alteration in somatosensory feedback in healthy subjects by standing on a soft surface resulted in diminished RCI values that were similar to those seen in the DPN subjects ($p > 0.05$). These results suggest that a low-cost technology based on inertial sensors similar to those sensors used in the new generation of smart phones (e.g., iPhone® 4S, Apple Inc., CA, USA) can provide accurate information about a patient's balance without using an elaborate gait lab infrastructure [65]. This strategy also appears to be more sensitive and responsive as the changes are approximately 12-times larger than using traditional COP techniques. This degree of discrimination could detect clinically subtle yet meaningful changes in a patient's balance.

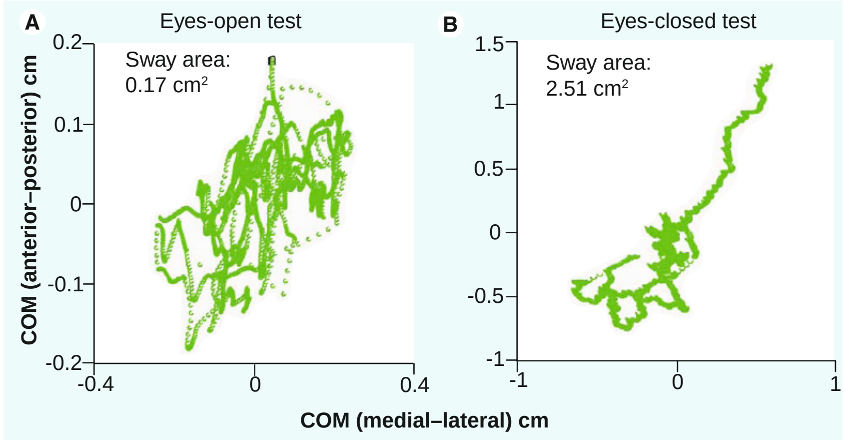

Figure 3. Measuring center of mass sway during Romberg test. Center of mass sway in a typical patient with diabetic peripheral neuropathy during **(A)** eyes-open and **(B)** eyes-closed condition.
COM: Center of mass.

New advances in assessing gait

Many of the previous studies explored gait alteration due to diabetes in gait laboratories, which have inherent space restrictions, making use of targeting forceplates and requiring the speed, rythmicity, and path of the subject to be regulated by treadmills. These laboratory conditions do not always replicate the natural environments in which patients are usually active [28,50,87,88]. Advances in the technology of wearable sensors during the last decade have opened new avenues for exploration into gait assessment outside of the confines of the gait laboratory [83].

The reliability of gait parameters can change at varying distances and gait speeds [50]. Najafi and colleagues studied 24 elderly patients over shorter (<10 m) and longer walking distances (>20 m). They compared the results of gait assessment inside of a gait laboratory over a traditional walking test distance (~10 m) and outside of a gait laboratory. They found that the reliability of spatio-temporal parameters of gait improved with longer walking distances [50]. Surprisingly, their results suggest that gait parameters measured outside of a gait laboratory and over a longer walking distance are significantly different from those measured inside of a gait laboratory [27,50]. Recent studies also suggest that patients with diabetes will change their gait strategy based on differences in terrain [89]. Outside of gait perturbation studies, this is difficult to assess in a laboratory environment. Allet and colleagues studied 16 patients with diabetes with and without neuropathy. Patients wore wearable sensors including four uniaxial gyroscopes attached to each shank and thigh segments using elastic bands. They were asked to walk with their habitual speed over three different surfaces including tarred, grass and cobbled stone. The order of walking surface was randomized by subject to remove any potential bias due to learning or fatigue. After 8 days, they were tested again. They reported excellent reliability across the three different conditions. Their results suggested that surfaces have an effect on spatio-temporal parameters of gait in diabetic subjects ($p < 0.05$). Specifically, the enrolled subjects tended to walk slower on stones by 8% on average compared to walking on grass surface (1.12 ± 0.23 m/s on stones vs 1.21 ± 0.21 m/s on grass). On the same note, they walked slower on grass than on the tarred surface (1.25 ± 0.20 m/s on tar vs 1.21 ± 0.21 m/s on grass) [89].

Virtual reality & its application for assessing alteration in motor performance due to diabetes

Restricted joint mobility and alteration in sensory feedback due to diabetes can contribute to misjudgments while crossing obstacles [90]. In certain cases the impaired judgment – mainly due to impaired proprioceptive feedback in subjects with DPN – can cause obstacle collision leading to falls or even serious injuries. It should be noted that it is not only patients with moderate-to-severe DPN who walk with altered gait patterns [88,89,91], those with no to minimal DPN also show degraded postural control and gait performance [90]. Apart from deviations in gait, other changes are also present in patients prior to clinical expression of DPN including reduced ankle muscle strength [92] and impaired joint position sense of the distal joints, which have been shown to affect gait performance [93]. Therefore, during the early development of DPN or prior to its diagnosis, assessing motor performance during an obstacle negotiation task may be helpful for assessing the associated risk of falling, especially in challenging environments, including obstacle avoidance [94].

However, the conventional methods for assessment of obstacle crossing ability have been limited to gait laboratories equipped with motion tracking systems [22–26], which may not be suitable for a clinical environment [27,28,83,95]. In addition, assessing gait and balance in a real condition such as using an actual obstacle could be risky for DPN patients and may cause injury during the test. Since even a small accident (e.g., hitting a real obstacle) could cause a serious adverse event such as a diabetic foot ulcer, which is difficult to heal, the obstacle crossing test using an actual obstacle should be avoided. The new technologies based on virtual reality can replace the assessments performed in a gait laboratory without imposing any risk to patients and without the requirement of expensive motion analyzer systems and/or devoting a big gait laboratory space, which is often unaffordable for many small clinics.

In a recent study, we proposed virtual reality paradigm using wearable sensors for quantifying a subject's ability for successfully crossing a series of virtual obstacles (Figure 4) [84]. The implemented portable system provides real-time joint position feedback from lower limbs and uses virtual obstacles, thereby posing minimum risk of injury to participants. Sixty seven participants (age: 55.4 ± 8.9 years; BMI: 28.1 ± 5.8) including diabetes with and without DPN, as well as aged-matched healthy controls, were recruited. The severity of neuropathy was quantified using the vibratory perception threshold (VPT) test. The ability to perceive the position of lower extremities was quantified by measuring obstacle crossing success rate, toe–obstacle clearance and reaction time while crossing a series of virtual obstacles with heights at 10 and 20% of the subject's leg length. All three parameters were deteriorated in individuals with diabetes compared to healthy controls. Results suggest that DPN subjects have a longer reaction time in response to approaching virtual obstacles than aged-matched controls and diabetes without neuropathy. Interestingly, results suggest a relatively high correlation with neuropathy severity (r = 0.5) quantified using a vibratory perception threshold test. The delay becomes more pronounced by increasing the size of the obstacle. Using a regression model, results suggest that the change in reaction time between obstacle sizes of 10 and 20% of leg length is the most sensitive predictor for neuropathy severity with an odds ratio of 2.70 (p = 0.02). The increased reaction time seen in this modality for subjects with diabetes may be one cause of increased slips and falls in this group, and thus its assessment may provide useful information for assessing the risk of falling in individuals with diabetes. Additionally, the developed technique could be used by diabetics at home to assess their motor function deterioration caused by diabetes and neuropathy, which in turn may help to prevent falls and other associated trauma caused by progression in neuropathy severity.

Figure 4. Virtual reality can be used for assessing lower-extremity joint perception in individuals with diabetes.

Methods for improving balance in diabetes

In order to improve postural balance, a number of studies have been conducted incorporating balance training exercises to reduce the risk of falling among subjects with poor balance control. A recent study by Morrison *et al.* examined the effect of balance training on reduction of fall risk in Type 2 diabetic individuals [96]. The participants performed balance/strength training tasks over a period of 6 weeks and with a training schedule of 3 days a week. The results showed that, after balance training tasks, individuals with diabetes had a significantly greater amount of leg strength, faster reaction time and decreased amount of sway.

In a randomized control trial study, Allet and colleagues showed that gait speed and balance can be improved by exercise training in individuals with diabetes [97]. A 12-week program (twice a week for 1 h) of warm up, circuit training and ten exercise tasks: balance and walking, functional strength and endurance, stable and unstable surfaces, increased step height exercises and interactive games, such as badminton and obstacle races in teams, and feedback sessions suggesting what exercises to do at home was followed. After training, individuals with diabetes had an increase in gait velocity, balance, muscle strength, joint mobility and a decrease in fear of falling. A follow-up measurement was made after 6 months and subjects were encouraged to continue the exercises for that period of time. The Sway Index was reduced by approximately 33% (from 6 to 4); however, at follow-up measurements, the Sway Index reduction was approximately 16.6% compared with baseline. Knerl *et al*. examined the effect of 6 weeks single and combined training on dynamic balance including the 8-Foot-Up and Go Test and the combined score on the Fullerton Advanced Balance Scale (FAB-Scale) with 51 elderly individuals divided into three groups. The authors concluded that the 6-week period was not sufficient to reduce significant improvement in dynamic balance regardless of the training paradigm [98]. The possible reason for contrary results could be the recruitment of participants who were well above cutoff scores for the test being involved in the measurement protocol as reported by the authors themselves.

Interestingly, from the above discussions it can be argued that the conventional balance assessment techniques might not be as efficient outside the vulnerable population. Thus, there is also a need to explore systems that can identify the subtlety of balance improvement/deterioration among individuals at the early stage of balance deterioration to prevent future trauma. Objective assessment of gait and balance may provide the necessary sensitivity to compare the benefit of different balance training paradigms and examine the benefit of balance training in a short period of time.

In addition, the discrepancies regarding the effect of type of training/exercise effective for balance training [96,98,99] have also been reported. Regardless of the contradictions discussed above, the improvement in balance depends on the training duration associated with it; usually weeks. And, it still seems unclear what period of training and what training exercises are most beneficial for improving balance control [98].

Retention is an important aspect of balance training, since training periods cannot last forever. Therefore, the benefits of training/learning must last. A number of studies have supported the fact that multiple exposures to a task will improve memory retention [100–103]. Several techniques have been developed to make memory retention more efficient, one such technique is spacing effect. Spacing effect states that memory retention can be significantly improved if one takes breaks between successive sessions. A study by Cepada *et al*. on memory retention showed that altering the time gaps between exposures influences retention [103]. The study concluded that the length of the time gap between the learning sessions had a significant effect on memory retention. By learning through shorter time gaps the participants were able to learn more; however, the information was not retained for a substantial length of time. The results indicated that there was an optimal time gap between sessions that changed on an individual case basis and was dependent on how long one wants to retain the information. Studies have shown that using a longer gap time between exposures or sessions is more beneficial than a shorter time gap [103].

Recent developments in the fields of robotics, neuroscience and physical therapy, have enabled a new wave of robotically assisted and virtual reality rehabilitation therapies that have shown promise to help patients alleviate their sensory feedback and motor impairments and speed up motor function recovery. Virtual reality gives clinicians more and better control over designing the paradigm to assess and improve balance without causing major risk to patients and without a dedicated big space (e.g., a gait laboratory) for testing the patient's motor function. For example, virtual reality can be implemented as a training tool for obstacle avoidance/crossing in a virtual environment. Such a motor learning-based virtual reality paradigm would be of greater benefit for patients than conventional balance training programs especially in a clinical environment. The visual information plays a significant role on foot elevation in the feedforward control of lower limbs locomotion during obstacle crossing [26]. Significant improvements in gait parameters and foot obstacle clearance using virtual obstacle and real-time feedback have been demonstrated in poststroke patients with hemiplegia [104]. During the actual phase of obstacle crossing an individual does not have complete visual information regarding clearance between the obstacle and the foot; thus they rely on proprioception of the leading limb and the feedforward mechanism of the trailing limb. Therefore, it can be hypothesized that providing visual feedback during obstacle crossing may be used as a motor learning paradigm to improve feedforward performance (improve in accuracy of prediction) via intact sensory feedbacks (e.g., visual, muscles, ligaments and so on).

In addition, the realistic graphical interface provided by virtual reality technology allows testing interaction of the patient with environment (e.g., obstacle crossing ability) with minimal physical effort. Navigating a 3D virtual reality landscape improves spatial awareness. Recent investigations showed that virtual reality combined with a motor learning paradigm can improve gait and balance [105,106]. Virtual reality also fosters motivation to work at improving health and physical and mental functioning during rehabilitation, because the person is having fun. Given the ad hoc nature of the current protocols, multiple questions, however, remain to be answered regarding how the motor system learns to maintain our balance in altered sensory conditions, how quickly that learning occurs, how it modifies motor plans when the motor output is not what is desired, how it is affected by sensory feedback deficiency such as in diabetic peripheral neuropathy and how motor learning procedures could be best designed to maximize the long-term effectiveness of the therapies based on motor learning and motor adaptation concepts. It is very important that we understand how the motor system operates/processes data before we can develop optimal rehabilitation strategies for improving the balance control in patients who suffer from sensory feedback impairment (e.g., individuals with diabetes).

Conclusion

People with diabetes frequently suffer from concomitant postural instability that can lead to falls, fracture, depression, anxiety and decreased quality of life. This is an often neglected problem, and has received little attention regarding development as well as testing of innovative strategies to improve balance and posture stability in individuals with diabetes. Evaluation of the risk of falling is a necessary step towards the provision of preventive measures for individuals deemed to have a high risk of falling. Current clinical methods for assessing static balance (e.g., Romberg's Sign) are too coarse, thus actionable findings occur too late for effective intervention. The subjective nature of these techniques lack the optimized sensitivity for diagnosing the presence of the condition early enough while simultaneously assessing its severity. Many strategies are also unsuitable for the busy clinical setting since they require substantial space and infrastructure. Furthermore, no simple, cost-effective and easy-to-use systems exist that can examine both biomechanical (e.g., body sway) and neurological (e.g., reciprocal postural coordination and feedforward mechanism) components of balance control. In recent years, body-wearable sensor technology based on electro-mechanical sensors has provided a new avenue for accurately detecting and monitoring body motion and proved promising for assessing body sway and postural coordination.

Future perspective

After identification of an individual with postural instability, the next step is to improve balance. Many studies proposed various balance training programs for improving postural control in diabetes. However, there is no guideline on training time and the activities to be incorporated into training. The training programs are time consuming, tedious and may not be ideal for subjects suffering from diabetes or other disorders affecting mobility. There seems to be no factor of motivation involved for patient compliance. After reviewing the literature and limitations of the current training paradigms it seems there is a need to develop more efficient training methods. The training methods need to be motivating enough to encourage the patients to participate and improve their balance control and to be able to retain the learning for a longer period of time. New advances in virtual reality and motor learning may be an alternative to overcome the abovementioned shortcomings. However, additional research should be conducted to validate the benefit of such technology for routine clinical usage.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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