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Review

Digital biomarkers of poor gait and balance in diabetic foot, measurable by wearables: A review of literature

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Abstract: People with diabetic foot frequently exhibit poor gait and balance. However, there is no review to inform digital biomarkers of poor gait and balance related to diabetic foot, measurable by wearables outside traditional gait laboratories. Such information could assist in designing remote patient monitoring platform to track changes in gait and balance dysfunction among people with diabetic foot for timely referral and intervention. Accordingly, we conducted a web-based review using PubMed. Our search was limited to human subjects and English-written papers published in peer-reviewed journals. We identified 20 papers in this review. We found preliminary evidence of digital biomarkers of gait and balance dysfunction in people with diabetic foot, measured by wearables, such as slow gait speed, large gait variability, unstable gait initiation, and large body sway. However, due to heterogeneities in included papers in terms of study design, movement tasks, and small sample size, more studies are recommended to confirm this preliminary evidence. Additionally, based on our review, we recommend establishing appropriate strategies to successfully implement wearable-based assessment into clinical practice for diabetic foot care.

Keywords: Diabetic foot; Diabetic neuropathies; Peripheral arterial disease; Foot ulcer; Gait; Walking; Postural balance; Wearable electronic devices; Gait analysis; Digital technology

1. Introduction

The global epidemic of diabetes imposes significant burdens on health care systems [1]. The International Diabetes Federation estimated that in the year 2021, 537 million people were living with diabetes worldwide, and estimated that this number would increase to 643 million by the year 2030 and 783 million by the year 2045 [2]. Diabetes is a cause of 6.7 million deaths worldwide [2]. Medical expenditures for diabetes are enormous: more than $200 billion in the United States alone and nearly $1 trillion worldwide [2, 3].

Diabetes comprises a group of disorders that results in high blood glucose levels, namely hyperglycemia, caused by deficits in insulin response [4]. There are two main types of diabetes: type 1 diabetes, also known as insulin-dependent diabetes, and type 2 diabetes, characterized by insulin-resistance [5, 6]. More than 90% of people with diabetes have type 2 diabetes [6]. If poorly managed, diabetes causes a number of complications. Diabetic foot is one of the most common and devastating complications of diabetes, which affects 2-6% of people with diabetes annually [7, 8]. Diabetic foot accounted for more than

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100,000 lower-extremity amputations in the United States alone and more than 1,000,000 lower-extremity amputations worldwide each year [9, 10]. Remarkably, lower-extremity amputation is more fearful than death for people with diabetic foot [11].

Although diabetic foot is generally a consequence of multiple factors, common causal factors are sensory neuropathy causing sensory loss, motor neuropathy causing biomechanical abnormalities, autonomic neuropathy causing dry skin, and peripheral arterial disease causing claudication, rest pain and tissue loss in the lower-extremity [12]. All these factors inherently limit gait and balance [13].

Gait and balance dysfunction has significant negative impacts on survival and quality of life in people with diabetic foot [14]. For example, the risk of fall and likelihood to be injured from a fall in people with diabetic foot is 23 and 15 time greater, respectively, than in people without diabetic foot [15]. Gait and balance dysfunction in people with diabetic foot is associated with an onset or progression of fear of falling and restricts normal daily activities [16]. Furthermore, gait and balance dysfunction alters kinematics and kinetics such as excessive plantar pressure and shear stress, and may contribute to the development of a foot ulcer or leads to deterioration of an already developed foot ulcer [17, 18]. Thus, assessing gait and balance with valid and effective tools has been a critically important aspect of the management of diabetic foot.

Three-dimensional optoelectronic motion capture systems have been utilized to assess gait and balance in people with diabetic foot [19]. These motion capture systems are popular and have been considered as the "gold standard" in gait and balance assessment. However, as previously discussed in a number of articles, they are time-consuming and limited to primarily laboratory settings, and may not be suitable for translational research [20].

Recent technical advances enabled wearable-based gait and balance assessment outside traditional gait laboratories. These wearables often consist of inertial measurement units (IMUs), typically composed of an accelerometer and a gyroscope. IMUs have shown to provide repeatable and valid data in gait and balance assessment across clinical settings [21, 22]. Furthermore, recently, IMUs have been suggested as a viable option for gait and balance assessment in people with diabetic foot [23]. Nevertheless, we found no published review papers regarding these aspects. Accordingly, in this review, we aimed to summarize findings from published papers that assessed gait and balance in people with diabetic foot using wearables, mainly IMUs. Based on our review, we also aimed to discuss limitations from previous papers and suggest areas of future research in gait and balance assessment in people with diabetic foot using IMUs.

2. Materials and Methods

We performed a web-based, electronic search using PubMed for papers published before August 9, 2022. The following terms were used for PubMed search: "diabetic neuropathies", "diabetic foot", "peripheral arterial disease", "foot ulcer", "gait", "walking", and "postural balance". The full search query is described in Table 1. We limited our search to papers written in English and human subject studies.

This review included papers that assessed gait and balance performance using IMUs in people with diabetic foot. If a paper utilized either an accelerometer or a gyroscope, we included the paper. Outcomes of this review were kinematic variables during gait and/or quiet standing such as spatiotemporal parameters during gait or center-of-mass displacement during quiet standing. An experienced reviewer (G.E.K.) conducted screening of the searched papers based on title and abstract. We excluded review papers, editorial comments, conference abstracts, and letters from the final paper selection. Furthermore, because the focus of this review is diabetic foot, if a paper included people with diabetes, assessed gait and balance performance using IMUs but did not specify the presence or a diagnosis of foot complications in the people of diabetes, the paper was excluded from the final selection.

Table 1. PubMed search query.

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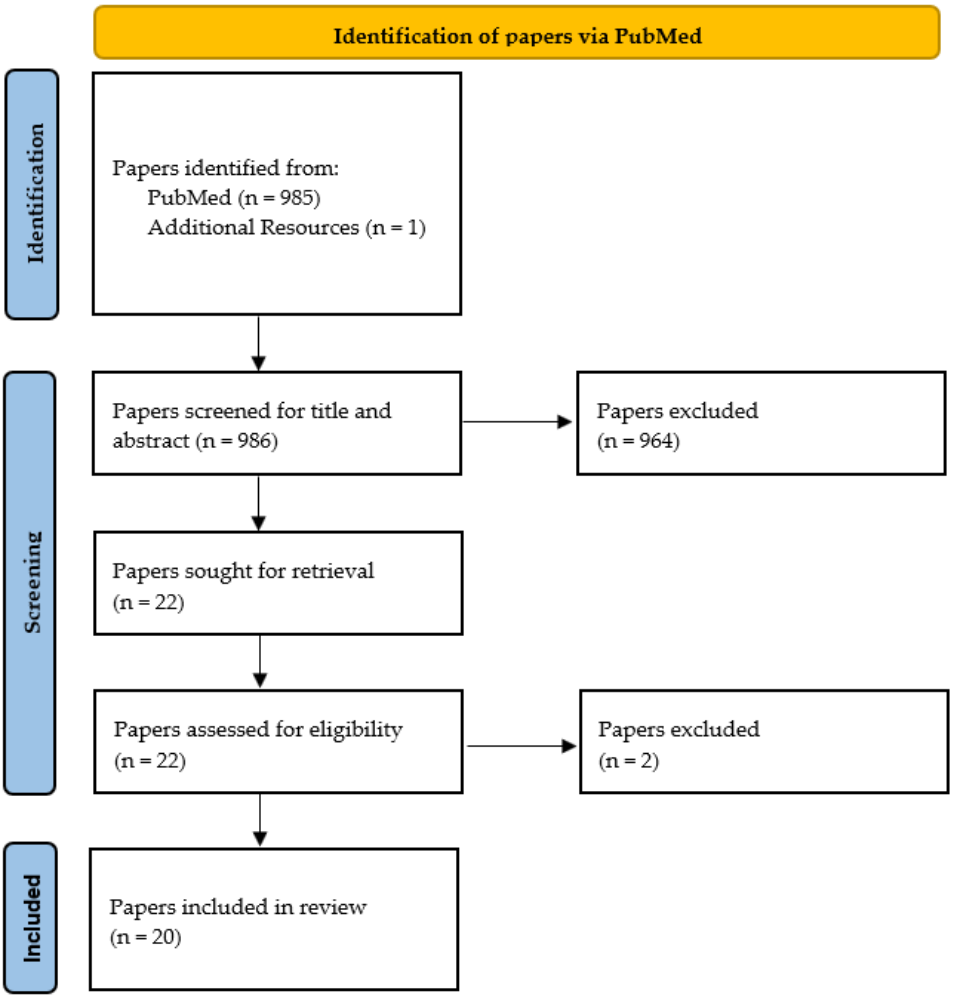
	Concept	Search Query
	Diabetic Foot	"Diabetic Neuropathies"[MeSH Terms] OR "Diabetic Foot"[MeSH Terms] OR "Foot Ulcer"[MeSH Terms] OR "Peripheral Arterial Disease"[MeSH Terms])
AND	Gait and Balance	"Gait"[MeSH Terms] OR "Walking"[MeSH Terms] OR "Postural Balance"[MeSH Terms])

3. Results

3.1. Search Results

The flow diagram for paper selection is shown in Figure 1. A total of 986 papers were identified through PubMed. After screening title and abstract, 964 papers were excluded. After evaluating eligibility for the other 22 articles, two more papers were excluded based on full-text review. Consequently, 20 papers were included in the current review [24-43].

Figure 1. Flow chart for selecting papers.



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3.2. Study Characteristics

We summarized findings from the final 20 papers in Table 2. All included papers were published between 2004 and 2021. Thirteen studies were conducted in USA, three studies were conducted in Switzerland, one study was conducted in Australia, one study was conducted in UK, and one study was conducted in China. One study was jointly conducted in USA and Qatar.

Table 2. Summary of included papers. A list of abbreviations was added at the bottom of this table.

Study **Title** **Country**	**Study design** **Participants**	**Tasks**	**Sensor type** **(Manufacturer)** **Placement** **Sampling frequency**	**Measures**	**Key findings**
Menz et al. 2004 [24] Walking stability and sensorimotor function in older people with diabetic peripheral neuropathy Australia	Observational DPN n=30 (22 men; 8 women) Age (years) = 73.5 ± 8.3 BMI (kg/m²) = 28.2 ± 6.0 Duration of DM (years) = 12.3 ± 8.4 HbA1c (%) = 7.6 ± 1.3 VPT (Volts) = 37.6 ± 11.4 HC n = 30 (22 men; 8 women) Age (years) = 73.9 ± 9.0 BMI (kg/m²) = 25.6 ± 3.4	Gait 20 meters Two surface conditions • Level • Irregular	3D Accelerometer n = 2 Head (n = 1) Sacrum (n = 1) Frequency not reported	Gait speed Cadence Step length Step time variability Smoothness (harmonic ratio)	↓ Gait speed, cadence, step length, and smoothness on both surfaces in DPN vs. HC ↑ Step time variability on irregular surface in DPN vs. HC
Allet et al. 2009 [25] Gait alterations of diabetic patients while walking on different surfaces Switzerland	Observational DPN n = 15 (sex ratio not reported) Age (years) = 61.29 ± 6.52 Height (m) = 1.67 ± 0.08 Weight (kg) = 86.94 ± 9.13 Duration of DM (years) = 8.83 ± 4.60 Blood sugar level not reported VPT (Scale) = 2.63 ± 1.58 DM (without neuropathy) n = 15 (sex ratio not reported) Age (years) = 55.83 ± 8.20 Height (m) = 1.72 ± 0.12 Weight (kg) = 90.30 ± 22.15 Duration of DM (years) = 9.87 ± 7.78 Blood sugar level not reported VPT (Scale) = 5.65 ± 1.14 HC n=15 (sex ratio not reported) Age (years) = 57.42 ± 4.31 Height (m) = 1.73 ± 0.10 Weight (kg) = 79.93 ± 11.53 VPT (Scale) = 6.80 ± 0.86	Gait Distance not reported Three surface conditions • Tar • Grass • Stones	IMU (BioAGM, Switzerland) n=4 Shin (n = 2; right and left) Thigh (n = 2; right and left) Frequency = 200 Hz	Gait speed Cadence Stride length Stance phase Double support Gait cycle time Step time variability	↓ Gait speed, cadence, and stride length in DPN vs. HC, but not DPN vs. DM ↑ Stance phase, double support, gait cycle time, and stride time variability on all surfaces in DPN vs. HC, but not DPN vs. DM
Allet et al. 2010 [26]	Interventional (RCT): IG (Exercise intervention	Gait Distance not reported	Gyroscope n = 4 Shin (n = 2; right and left)	Gait speed Cadence Stride length Stance time	All gait and balance variables were similar between IG and CG at baseline

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An exercise intervention to improve diabetic patients' gait in a real-life environment Switzerland	60 minutes per session; two sessions per week; 12 weeks) DPN n = 35 (sex ratio not reported) Age (years) = 63.0 ± 8.0 BMI (kg/m2) = 30.5 ± 6.0 Disease duration not reported Blood sugar level not reported VPT (Scale) = 3.2 ± 1.3 CG (No treatment or advice) DPN n = 36 (sex ratio not reported) Age (years) = 64.0 ± 8.9 BMI (kg/m2) = 31.5 ± 5.3 Disease duration not reported Blood sugar level not reported VPT (Scale) = 3.3 ± 1.3	Two surface conditions • Tar • Cobblestone	Thigh (n = 2; right and left) Frequency = 200 Hz	Gait cycle time Step time variability Time points: Baseline 12-week 6-month	↑ Gait speed, cadence, and stride length in IG at 12-week and 6-month vs. baseline on both surfaces ↓ Gait cycle time and stance time in IG at 12-week and 6-month vs. baseline on both surfaces
Crews et al. 2012 [27] Impact of strut height on offloading capacity of removable cast walkers USA	Observational DPN with diabetic foot risk classification: Grade 1 (n = 8) Grade 3 (n = 1) Grade 4 (n = 2) n = 11 (7 men, 4 women) Age (years) = 51.4 ± 10.0 BMI (kg/m2) = 33.9 ± 7.3 Duration of DM (years) = 14.5 ± 9 Blood sugar level not reported VPT value not provided	Gait 20 meters Four shoe conditions • Ankle-high RCW • Knee-high RCW • Shoe RCW • Standard athletic shoe	IMU (BioAGM, Switzerland) n = 5 Shin (n = 2; right and left) Thigh (n = 2; right and left) Lumbar region (n = 1) Frequency = 200 Hz	Gait speed Stride length Stride time Double support Gait speed variability	↓ Gait speed and stride length in ankle-high RCW and knee-high RCW vs. standard athletic shoe ↑ Stride time, double support, and gait speed variability in ankle-high RCW and knee-high RCW vs. standard athletic shoe
Najafi et al. 2013a [28] The impact of footwear and walking distance on gait stability in diabetic patients with peripheral neuropathy USA	Observational DPN n = 12 (8 men; 4 women) Age (years) = 60 ± 12 BMI (kg/m2) = 33.2 ± 6.4 Duration of DM (years) = 10 ± 13 Blood sugar level not reported VPT (Volts; right foot) = 56 ± 25 VPT (Volts; left foot) = 61 ± 29 HC n = 8 (6 men; 2 women) Age (years) = 60 ± 6 BMI (kg/m2) = 27.0 ± 3.2 VPT (Volts; right foot) = 19 ± 4 VPT (Volts; left foot) = 20 ± 3	Gait Four conditions (two distance × two footwear) • Short (7 meters) • Long (20 meters) • Barefoot • Regular shoes	IMU (BioSensics, USA) n = 5 Shin (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency = 100 Hz	Gait initiation steps Gait initiation speed Gait speed Stride length Stride time Double limb support Gait speed variability CoM sway	All variables were similar between DPN and HC in the short distance condition regardless of footwear conditions ↓ Gait initiation speed, gait speed, and stride length in DPN vs. HC in the long distance condition regardless of footwear conditions ↑ Gait initiation steps, stride time, double limb support, and gait speed variability in the short distance condition regardless of footwear conditions CoM sway was similar between DPN and HC in all conditions
Najafi et al. 2013b [29] A novel plantar stimulation technology for	Interventional (RCT) IG (Electrical plantar stimulation; 30 min per treatment; 5 treatments per week; 6 weeks)	Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 2 Shin (n = 1) Lower back (n = 1)	CoM sway area Time points: Baseline 2-week 4-week	All variables were similar between IG and CG at baseline. ↓ CoM sway area at weeks 2, 4, and 6 vs. baseline in IG

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improving protective sensation and postural control in patients with diabetic peripheral neuropathy: A double-blinded, randomized study USA	DPN n = 25 (sex ratio not reported) Age (years) = 61.6 ± 8.3 BMI not reported Disease duration not reported HbA1c (%) = 7.6 ± 1.6 VPT (Volts) = 46.8 ± 23 CG (Sham stimulation) DPN n = 29 (sex ratio not reported) Age (years) = 61.4 ± 8.2 BMI not reported Disease duration not reported HbA1c (%) = 7.1 ± 1.5 VPT (Volts) = 37.6 ± 22	Measured in a subsample	Frequency not reported	6-week 6-month	↑ CoM sway area at weeks 2, 4, and 6 vs. baseline in CG
Grewal et al. 2013 [30] Diabetic peripheral neuropathy and gait: Does footwear modify this association? USA	Observational DPN with active DFU n = 16 (sex ratio not reported) Age (years) = 58.3 ± 4.4 BMI (kg/m2) = 29.5 ± 3.7 Disease duration not reported Blood sugar level not reported VPT value not provided DPN without active DFU n = 15 (sex ratio not reported) Age (years) = 54.2 ± 11.3 BMI (kg/m2) = 31.2 ± 5.9 Disease duration not reported Blood sugar level not reported VPT value not provided HC n = 8 (sex ratio not reported) Age (years) = 59.6 ± 6 BMI (kg/m2) = 27 ± 3.2	Gait 200 feet Habitual pace	IMU (BioSensics, USA) Sensor placement not reported Sampling frequency not reported	Gait initiation steps Gait initiation distance Gait speed Stride length Gait cycle time Double stance Gait speed variability CoM sway Knee RoM	↑ Gait initiation steps, gait speed variability in DPN groups vs. HC ↓ Knee RoM in DPN groups vs. HC
Kelly et al. 2013 [31] Fear of falling is prevalent in older adults with diabetes mellitus but is unrelated to level of neuropathy USA	Observational DPN n = 16 (10 men; 6 women) Age (years) = 73 ± 8 BMI (kg/m2) = 30.6 ± 5.7 Duration of DM (years) = 17 ± 11 HbA1c (%) = 8.9 ± 2.7 VPT (Volts) = 49.7 ± 21.9 DM without neuropathy n = 18 (5 men; 13 women) Age (years) = 62 ± 7 BMI (kg/m2) = 31.2 ± 5.9 Duration of DM (years) = 13 ± 13 HbA1c (%) = 7.2 ± 1.6 VPT (Volts) = 18.3 ± 4.5	Gait 20 meters Habitual pace	IMU (BioSensics, USA) n = 5 Shin (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency not reported	Gait initiation steps Gait speed Stride length Stride time Double stance Gait speed variability CoM sway	↑ Gait initiation steps and double stance in DPN vs. DM without neuropathy Gait initiation steps and double stance was significantly correlated with VPT

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Wrobel et al. 2014 [32] A novel shear reduction insole effect on the thermal response to walking stress, balance, and gait for diabetic neuropathy USA	Interventional DFO; immediate effect DPN n = 27 (14 men; 13 women) Age (years) = 65.1 BMI (kg/m2) = 33.9 Disease duration not reported Blood sugar level not reported VPT value not provided	Gait 200 steps Two conditions • Habitual pace • Dual task Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) Sensor placement not reported Frequency not reported	Gait Gait initiation steps Gait initiation speed Gait initiation double stance Gait speed Stride length Stride time Double stance Gait speed variability CoM sway Quiet standing CoM sway area	↓ Gait initiation double stance for DFO vs. standard shoe during habitual walking
Grewal et al. 2015 [33] Sensor-based interactive balance training with visual joint movement feedback for improving postural stability in diabetics with peripheral neuropathy: A randomized controlled trial USA	Interventional (RCT) IG (Balance training exercise with real time visual feedback; twice a week; 4 weeks) DPN n = 19 (male = 8, female = 11) Age (years) = 62.58 ± 7.98 BMI (kg/m2) = 31.78 ± 7.53 Duration of DM (years) = 17.17 ± 10.08 HbA1c (mmol/mol) = 65.23 ± 19.65 VPT (Volts) = 34.28 ± 8.16 CG (Not specified) DPN n = 16 (male = 8, female = 8) Age (years) = 64.90 ± 8.50 BMI (kg/m2) = 29.58 ± 4.24 Duration of DM (years) = 17.40 ± 9.42 HbA1c (mmol/mol) = 65.40 ± 29.91 VPT (V) = 33.52 ± 6.16	Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 2 Shin (n = 1) Lower back (n = 1) Frequency = 100 Hz	CoM sway Ankle sway Hip sway Time points: Baseline 4-week	↓ CoM, ankle and hip sway at 4-week vs. baseline in IG during eyes open
Toosizadeh et al. 2015 [34] The influence of diabetic peripheral neuropathy on local postural muscle and central sensory feedback balance control USA	Observational DPN n=18 (11 men; 7 women) Age (years) = 65 ± 8 BMI (kg/m2) = 29.3 ± 5.4 Duration of DM (years) = 19 ± 11 Blood sugar level not reported VPT (mV) = 34.6 ± 7.0 HC n=18 (7 men; 11 women) Age (years) = 69 ± 3 BMI (kg/m2) = 27.0 ± 4.1	Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 2 Sensor placement not reported Frequency not reported	CoM sway Local control balance Central control balance	↑ CoM sway, local control balance, and central control balance in DPN vs. HC for both conditions
Toosizadeh et al. 2016 [35] Alterations in gait parameters with peripheral artery disease: The importance of pre-	Observational PAD n = 17 (10 men; 7 women) Age (years) = 74 ± 8 BMI (kg/m2) = 26.8 ± 3.5 ABI = 0.83 ± 0.04	Gait 25 steps Two conditions • Habitual pace • Fast pace	IMU (BioSensics, USA) n = 5 Shin (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1)	Gait initiation steps Gait initiation distance Gait speed Stride length Gait cycle time Double support	↑ Gait initiation steps, gait initiation distance, and trunk sway in PAD vs. HC for both paces ↑ Gait speed in PAD vs. HC for both paces

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frailty as a confounding variable USA	HC n = 24 (12 men; 12 women) Age (years) = 76 ± 7 BMI (kg/m2) = 27.9 ± 5.7		Frequency not reported	Gait speed variability Trunk sway Knee RoM	↓ Stride length, ↑ Gait cycle time and double support in PAD vs. HC for habitual pace ↑ Knee RoM and gait speed variability in PAD vs. HC for fast pace
Thiede et al. 2016 [36] Gait and balance assessments as early indicators of frailty in patients with known peripheral artery disease USA	Observational Pre-frail PAD n = 9 (4 men; 5 women) Age (years) = 74.4 ± 7.5 BMI (kg/m2) = 27.1 ± 3.1 ABI = 0.79 ± 0.14 Non-frail PAD n = 8 (6 men; 2 women) Age (years) = 73.4 ± 9.9 BMI (kg/m2) = 26.4 ± 4.1 ABI = 0.88 ± 0.12 Note: Fried criteria for frailty measurement	Gait 25 steps Three conditions • Habitual pace • Dual task • Fast pace Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 5 Shin (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency not reported	Gait Gait speed Stride length Gait cycle time Double support Trunk sway Gait speed variability Quiet standing CoM sway Ankle sway Hip sway	↓ Gait speed, ↑ Gait cycle time, double support, gait speed variability in pre-frail PAD vs. non-frail PAD for dual task walking ↑ Double support and trunk sway in pre-frail PAD vs. non-frail PAD for fast pace No significant difference in quiet standing
Najafi et al. 2017 [37] Using plantar electrical stimulation to improve postural balance and plantar sensation among patients with diabetic peripheral neuropathy: A randomized double blinded study USA and Qatar	Interventional (RCT) IG (Wearable plantar electrical stimulation; 1 hour daily; 6 weeks; at home) DPN n = 17 (12 men; 5 women) Age (years) = 56 ± 11 BMI (kg/m2) = 28.7 ± 5.9 HbA1c (%) = 8.8 ± 1.9 Disease duration not reported VPT (Volts) = 41 ± 7 CG (Sham stimulation) DPN n = 11 (9 men; 2 women) Age (years) = 64 ± 10 BMI (kg/m2) = 31.5 ± 8.0 HbA1c (%) = 9.6 ± 2.2 Disease duration not reported VPT (Volts) = 40 ± 10	Gait 10 meters Two conditions • Habitual pace • Fast pace Quiet standing Two conditions • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 2 (gait) Shin (n = 2; right and left) n = 2 (quiet standing) Shin (n = 1) lower back (n = 1) Frequency not reported	Gait Gait speed Cadence Stride length Stride time Quiet standing CoM sway Ankle sway Hip sway Time points: Baseline 6-week	All variables were similar between IG and CG at baseline ↑ Gait speed, cadence, and stride length ↓ stride time at 6-week vs. baseline in IG ↓ Ankle sway at 6-week vs. baseline in IG
Esser et al. 2018 [38] Single sensor gait analysis to detect diabetic peripheral neuropathy: A proof of principle study UK	Observational DPN n = 17 (14 men; 3 women) Age (years) = 63 ± 9 BMI (kg/m2) = 33.6 ± 7.6 Duration of DM (years) = 24 ± 13 HbA1c (%) = 8.8 ± 1.0 HC n = 42 (30 men; 12 women) Age (years) = 61 ± 4 BMI (kg/m2) = 31.6 ± 3.9	Gait 10 meters Habitual pace	IMU n = 1 Lower back (n = 1) Frequency = 100 Hz	Gait speed Cadence Stride length Stride time	↓ Gait speed, cadence, and stride length ↑ stride time in DPN vs. HC
Kang et al. 2019 [39] The effect of daily use of plantar mechanical stimulation through micro-mobile foot	Interventional: Micro-mobile foot compression; 4 hours daily; 4 weeks Severe DPN n = 30 (11 men; 19 women)	Gait 10 meters Three conditions • Habitual pace • Dual task • Fast pace Quiet standing	IMU (BioSensics, USA) n = 5 (gait) Shins (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1)	Gait Gait speed Stride length Stride time Double support Quiet standing CoM sway	↑ Gait speed and stride length at 4-week vs. baseline for habitual pace ↑ Gait speed and stride length ↓ stride time and double support at 4-week vs. baseline for dual task walking

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compression device installed in shoe insoles on vibration perception, gait, and balance in people with diabetic peripheral neuropathy USA	Age (years) = 68.1 ± 9.7 BMI (kg/m2) = 33.4 ± 6.1 Disease duration not reported Blood sugar level not reported VPT (Volts) = 27.4 ± 12.6	Four conditions (two eyes conditions × two foot conditions) • Eyes open • Eyes closed • Double stance • Semi tandem stance	Frequency not reported n = 2 (quiet standing) Shin (n = 1) lower back (n = 1) Frequency not reported	Ankle sway Hip sway Time points: Baseline 4-week	↑ Gait speed ↓ double support at 4-week vs. baseline for fast pace ↓ CoM sway at 4-week vs. baseline for double stance eyes open and eyes closed
Kang et al. 2020 [40] Characteristics of the gait initiation phase in older adults with diabetic peripheral neuropathy compared to control older adults USA	Observational DPN n = 38 (20 men; 18 women) Age (years) = 72.6 ± 5.6 BMI (kg/m2) = 31.63 ± 6.07 Disease duration not reported Blood sugar level not reported VPT (Volts) = 32V ± 14 HC n = 33 (13 men; 20 women) Age (years) = 77.9 ± 8.2 BMI (kg/m2) = 27.05 ± 4.23	Gait 12 meters Two conditions • Habitual pace • Dual task	IMU (BioSensics, USA) n = 5 Shins (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency = 100 Hz	Gait initiation steps Gait initiation distance Gait speed CoM sway	↑ Gait initiation steps, gait initiation distance, and CoM sway, ↓ gait speed in DPN vs. HC for both walking
Ling et al. 2020 [41] The impact of diabetic foot ulcers and unilateral offloading footwear on gait in people with diabetes USA	Observational DPN with DFU wearing unilateral offloading n = 12 (10 men; 2 women) Age (years) = 55.6 ± 2.7 BMI (kg/m2) = 30.9 ± 1.3 Blood sugar level not reported Disease duration not reported VPT not reported DPN without DFU n = 27 (20 men; 7 women) Age (years) = 64.3 ± 1.5 BMI (kg/m2) = 30.9 ± 1.0 Blood sugar level not reported Disease duration not reported VPT not reported HC n = 47 (22 men; 25 women) Age (years) = 62.9 ± 2.3 BMI (kg/m2) = 29.0 ± 0.9	Gait 10 meters Habitual pace	IMU (BioSensics, USA) n = 5 Shins (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency not reported	Gait speed Stride length Gait cycle time Double support Gait speed variability Stride length variability Double support limp Step length limp	↓ Gait speed, and stride length, ↑ gait cycle time, double support limp, and step length limp in DPN with DFU wearing unilateral offloading vs. DPN without DFU and HC ↑ Double support, gait speed variability, stride length variability in DPN with DFU wearing unilateral offloading and DPN without DFU vs. HC
Du et al. 2021 [42] The feasibility and effectiveness of wearable sensor technology in the management of elderly diabetics with foot ulcer remission: A proof-of-concept	Observational Longitudinal DM with recently recovered from DFU n = 6 (sex ratio not reported) Offloading footwear group (n=3) Regular footwear group (n=3)	Gait 1 min Habitual walk Quiet standing Four conditions (two eyes conditions × two surface conditions) • Eyes open • Eyes closed	IMU (BioSensics, USA) n = 5 (gait) Shin (n = 2; right and left) Thigh (n = 2; right and left) Lower back (n = 1) Frequency = 100 Hz n = 2 (quiet standing)	Gait: Gait speed Stride length Double support Swing phase Quiet standing: CoM sway Ankle sway Hip sway	↑ Gait speed and stride length, ↓ double support in offloading footwear group Quiet standing remained similar

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pilot study with six cases China	Age (years): between 55-80 Duration of DM: lasting for > 5 years Blood sugar level not reported VPT not reported	• Hard surface • Soft surface	Shin (n = 1) lower back (n = 1) Frequency = 100 Hz	Timepoints: Baseline 1-week 1-month 4-month 6-month	
Lanzi et al. 2021 [43] Supervised exercise training improves 6 min walking distance and modifies gait pattern during pain-free walking condition in patients with symptomatic lower extremity peripheral artery disease Switzerland	Interventional: Supervised exercise training PAD n = 29 (15 men; 14 women) Age (years) = 65.4 ± 9.9 BMI (kg/m2) = 28.7 ± 6.2 ABI = 0.79 ± 0.14	Gait 6 min walk test Habitual pace	IMU (GaitUp, Switzerland) n = 2 Sensor placement not specified Frequency not reported	Gait speed Stride length Stride time Stride frequency Double support Stance phase Swing phase Loading response Heel strike pitch angle Toe off pitch angle Max heel clearance First max toe clearance Second max toe clearance Minimum toe clearance Time points: Baseline 3-month	↑ Gait speed, stride length, swing phase, and loading response, ↓ stance phase at 3-month vs. baseline ↑ Toe off pitch angle at 3-month vs. baseline

Abbreviations: DM = Diabetes Mellitus; DPN = Diabetic peripheral neuropathy; DFU = Diabetic Foot Ulcer; BMI = Body-mass index; HC = Healthy controls; RCT = Randomized controlled trial; IG = Intervention group; CG = Control group; IMU = Inertial measurement unit; CoM = Center of mass; DFO = Dynamic Foot Orthoses; PAD = Peripheral Artery Disease; ABI = Ankle brachial index; RCW = Removable case walker; RoM = Range of motion.

3.3. Study Design and Participant Characteristics

Of the twenty included studies, seventeen studies included people with diabetic peripheral neuropathy, and three studies included people with peripheral arterial disease. Thirteen studies were non-interventional observational studies, and seven studies were interventional studies, among which four studies were randomized controlled trials.

Among the fourteen observational studies, eight studies compared people with diabetic peripheral neuropathy and healthy controls, among which two studies included those with active diabetic foot ulcer; and one study compared people with peripheral artery disease and healthy controls. Three studies included only one group of people with diabetic peripheral neuropathy, and one study included only one group of people with recently healed diabetic foot ulcer.

Four randomized controlled trials tested effectiveness of exercise or electrical stimulation within groups of people with diabetic peripheral neuropathy. Three non-randomized interventional studies tested effectiveness of diabetic foot orthoses and mechanical stimulation in people with diabetic peripheral neuropathy, and effectiveness of exercise in people with peripheral artery disease.

For the seventeen studies which included people with diabetic peripheral neuropathy, eleven studies reported vibration perception threshold to measure the severity of neuropathy, and six studies reported blood sugar level. The three studies which included people with peripheral artery disease reported ankle-brachial index to assess lower extremity blood flow.

3.4. Tasks and IMUs

Common tasks assessed with IMUs were gait and quiet standing in various conditions. Of the twenty studies included, twelve studies tested gait, three studies tested quiet standing, and the other five studies tested both gait and quiet standing.

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In terms of methods, of the twenty included studies, eighteen studies used IMUs, and two studies used either 3D accelerometers or gyroscopes. The number of sensors were between one and five. Sampling frequencies, if reported, were either 100 Hz or 200 Hz. Common sensor positions for gait assessment were the lower back, thighs, and shins for the five sensor system; the thighs, and shins for the four sensor system; the shins for the two sensor system; and the lower back for the one sensor system. One study that used 3D accelerometers for gait assessment attached the sensors to the head and lower back. For assessing balance during quiet standing, two IMUs were commonly used with the sensors attached to the lower back and shin.

3.5. Measures and Key Findings

The most popular gait measures were gait speed, stride length (or step length), stride time (or gait cycle time or step time), each of which was reported in 100% of gait studies. Gait variability measures (i.e., fluctuations in stride-to-stride) such as gait speed variability, stride time variability and stride length variability were reported in ten studies. Gait initiation variables including the number of steps and distance to be taken from standing posture to steady state walking were reported in six studies. One study quantified smoothness using harmonic ratio, and another study quantified limping during gait. One study reported foot kinematic variables such as toe clearance.

In terms of quiet standing, center of mass sway was the most popular measure, which was reported in 100% of quiet standing studies. Other variables of quiet standing included ankle sway and hip sway. One study reported local control balance and central control balance.

In terms of key findings, gait studies reported slow gait speed, shorter stride length, greater gait variability, and longer gait initiation phase in people with diabetic foot compared to control subjects (e.g., healthy controls, people with diabetes but no diabetic foot). Similarly, studies that measured quiet standing reported larger sway in center of mass, ankle, or hip in people with diabetic foot compared to control subjects. Interventional studies also reported improvements in these gait and quiet standing measures at post-intervention compared to pre-intervention.

4. Discussion

We aimed to provide a review of the existing literature regarding assessment of gait and balance using wearables, mainly IMUs, in people with diabetic foot. Given the main role of the foot during gait (i.e., force absorption) and biomechanical deformities in diabetic foot, the importance of assessing gait and balance has been continuously emphasized in numerous review papers [13, 14, 44, 45]. Furthermore, gait and balance dysfunction is the key indicator of increased risk of falling in people with diabetic foot, which might in turn increase risk of hospitalization [46, 47]. Gait and balance dysfunction may facilitate ulceration because of abnormal loading pattern [48].

In this review, we identified a total of 20 papers that met our inclusion and exclusion criteria. Although there were some heterogeneities in gait and quiet standing protocols and findings, across the reviewed studies, IMU-based gait analysis and balance assessment demonstrated reasonably consistent patterns of gait speed, gait initiation, gait variability, and body sway in people with diabetic foot in comparison to non-diabetic people or in response to an intervention. Based on these findings, our review suggests IMUs indeed successfully measure kinematic aspects of gait and balance dysfunction in people with diabetic peripheral neuropathy, an active diabetic foot ulcer, or peripheral artery disease. Furthermore, wearable-based parameters could assist in designing remote patient monitoring platform to track changes in digital biomarkers of gait and balance dysfunction among people with diabetic foot. To our knowledge, this is the first review that focused on gait and balance assessment using IMUs in people with diabetic foot. Our review may also be used as the first step towards establishing a general agreement on gait metrics specifically described for people with diabetic foot.

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From this review, we noticed an agreed protocol for IMU-based gait assessment is urgently needed. Although most of the studies that tested IMU-based quiet standing used similar protocols basically adopted from the Romberg test [49], protocols for gait assessment varied significantly between studies in terms of distance, single or dual task conditions, speed conditions, and footwear conditions. These varied conditions might have resulted in heterogeneities in gait results. Furthermore, IMU-based gait outcomes that can indicate an important sub-phase of gait cycle such as propulsion phase or breaking phase would be beneficial. Because these phases account for the greatest shear and vertical pressure on the foot during gait, which is directly associated with an onset of an ulcer (i.e., skin breakdown) or progressing ulcerations, a way to assess characteristics of these phases will be particularly beneficial for people with diabetic foot.

Another important issue is the repeatability. Although repeatability of IMU-based gait analysis and balance assessment has been reported in general or other clinical populations [50, 51], we were unable to find evidence of this in people with diabetic foot. Small sample size in nearly every included study is another issue. Surprisingly, regardless of study design, the maximum number of participants in a group (either intervention group or control group if a randomized controlled trial) was 38. These two issues can lead to a subsequent question of generalizability of the findings. In terms of participant characteristics included in this review, the vast majority recruited people with diabetic peripheral neuropathy, the most common underlying etiology causing a diabetic foot ulcer [52], but reports are needed for different diabetic foot problems such as Charcot foot and diabetic foot in remission [53, 54].

Limitations of this review should be acknowledged. Due to the issues regarding study protocol, repeatability, and small sample size, we recommend considering our review as a preliminary review, not a confirmatory work. Another limitation is heterogeneity in IMUs. Although validities of the IMUs that were chosen in each paper have been reported previously, different IMUs may have slightly different results for sampling frequency and filtering techniques, though this has not been reported in the included papers.

Despite these limitations, based on the current status of using IMUs in assessing gait and balance in the management of diabetic foot, we believe the following examples are areas of future research. One primary area is to establish an implementation strategy. One strength of IMUs is the possibility of them being implemented into clinical practice. IMUs provide more detailed and necessary information about a person's functional status compared to a stopwatch and are more portable and translational compared to three-dimensional optoelectronic motion capture technology. In fact, the importance of implementation has been discussed previously [23, 55], and implementation has been attempted in another population [56]. We believe appropriate strategies such as IMU-based perioperative gait assessment will significantly advance the management of diabetic foot. Another primary area is to better identify people at the highest risk of diabetic foot ulceration. This may be particularly beneficial for those who recently recovered from a diabetic foot ulcer. IMU-based gait assessment during clinic visits on regular basis (e.g., every 3 months or 6 months according to established guidelines) may better identify those whose ulcers are likely to recur and those who will likely remain ulcer-free.

5. Conclusions

Assessing gait and balance dysfunction and investigating biomechanics have undoubtedly advanced our understanding of diabetic foot syndrome. Based on our review, it seems clear that IMUs can provide insightful and useful information about functional status in people with diabetic foot. Although our review also identified several issues and limitations of included studies, rapid developments in sensing technology and data analysis technology will further speed up the processes to successfully implement IMUs into clinical practice.

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