ABSTRACT

**Background:** Polyneuropathy is one of the most common chronic complications associated with diabetes mellitus, it is a damage of the peripheral nerves and manifested by signs and symptoms as numbness, irritation, and pain in the upper and lower limbs. This study aimed to evaluate muscular performance and proprioception at the ankle in diabetic neuropathic patients with quantitative and standardized tools and correlate these findings with those of sural nerve conduction velocity (sural NCV) and amplitude.

**Methods:** Fifteen male patients with diabetic neuropathy participated in this study, with age ranged from 40 to 55 years, and fifteen age-matched healthy subjects participated as a control group. Biodex Isokinetic System was used to assess the strength of ankle dorsiflexors and planter flexors and ankle reposition accuracy. Berg balance test was used to assess balance. Sural nerve conduction velocity (NCV) and amplitude were examined by diabetic polyneuropathy check (DPN-check) device.

**Results:** The results showed a significant decrease in the mean peak torque values of the plantar flexors and dorsiflexors and a significant increase in the reposition error in the diabetic neuropathic group (p=0.0001). The results also revealed a significant decrease in the mean values of the Berg balance scores in diabetic neuropathy group (p=0.0001). Sural NCV and amplitude tests revealed abnormal values (p<0.05).

**Conclusion:** It was concluded that the isokinetic system is an objective and sensitive tool to detect the motor and sensory changes of the diabetic neuropathic patients, also an examination by DPN-check device help in the determination of the severity of the disease. Moreover, it can be concluded that there are strong correlations between duration of diabetes and sural nerve NCV and amplitude and the peak torque of the muscles around the ankle.

**Keywords:** Isokinetic, Polyneuropathy, Diabetic neuropathy, Nerve conduction velocity, Proprioception, Reposition accuracy.
Peripheral neuropathy caused by diabetes is a damage of the peripheral nerves and manifested by signs and symptoms as numbness, irritation, and pain in the upper and lower limbs. Diabetic neuropathy is one of the most common complications associated with diabetes mellitus. It affects up to fifty percent of diabetic patients [1,2,3]. The incidence of peripheral neuropathy in diabetic patients increases with age and long duration of diabetes. As well, the incidence increases with poor glycemic control. It is more common in patient with altered blood glucose level, high levels of blood fat, and hypertension [4].

Proprioception is the neural input to the higher centers from the mechanoreceptors, which are sensory neurons in the joint, joint capsules, muscles and ligaments [5]. It is important for functional joint stability, coordinated movements, maintenance and regulation of posture, balance, and gait [6,7]. Proprioception can be assessed by examining joint position sense (JPS) and movement sense. JPS can be assessed by reproduction of passive and active positioning [8].

Peripheral neuropathy is contributing to decreased proprioception and increased reaction time [9]. It has been considered as a risk factor for disturbance of balance, gait abnormality and falling [10]. Gait impairment includes lower gait velocity, decrease in cadence, shorter stride length and increase in stance time [11].

Isokinetic dynamometers can be used to examine neuromuscular function as they can provide detailed data about torque, velocity, and position with high reliability [12]. Under intrarator and interrater situations, Isokinetic dynamometers are reliable tools for assessment of peak torque for ankle plantar flexors and dorsiflexors in the adult healthy population [13,14]. As well, it shows high reliability in measurement of the strength of ankle muscles in older adults [15].

Simoneau et al., 1996, studied the ankle joint movement perception and its relation to cutaneous sensory function in diabetic subjects with lower extremity cutaneous sensory neuropathy using traditional methods and techniques [9]. Also, simple clinical tests were used in previous studies carried out on the motor and sensory functions in diabetic neuropathy [16,17,18]. So, this study was conducted using quantitative isokinetic techniques to measure muscle strength and proprioception and to determine the severity of diabetic polyneuropathy through examination of sensory NCV. The objectives of this study were to evaluate muscular performance and proprioception at the ankle joint in diabetic neuropathic patients with quantitative and standardized tools and correlate these findings with those of sural nerve conduction velocity (sural NCV) and amplitude.

SUBJECTS AND METHODS
Subject Selection:
This study was conducted at the Biodex Isokinetic dynamometer lab at the faculty of applied medical sciences, King Abdulaziz University, KSA through the period from April till December 2016. Fifteen male diabetic neuropathic patients participated in this study (group 1). Their age ranged between 40 to 55 years. As well, fifteen age-matched normal male subjects participated as a control group (group 2). The inclusion criteria included diabetic Patients with diabetic distal polyneuropathy as a neurologist diagnosed them, Their age ranged from 40 to 55 years, They were diabetic for more than 5 years and they were complaining of symptoms of polyneuropathy in the foot (as burning pain, tingling, numbness, aching pain sensations), While the exclusion criteria included Patients with marked deformities of the lower limbs, Patients with foot ulcers and Charcot foot, Patients with marked weakness or drop foot, Patients with any other neurological or orthopedic diseases that may affect balance and walking, Patients with amputation, Patients with marked cognitive impairment and Patients with liver or renal diseases. The ethical clearance was obtained from the ethics and Research Committee.

PROCEDURES
All participants signed an informed consent before sharing in the study. The aim and procedures of the study were explained to each subject before participation. All subjects in both groups were assessed for:

1. Proprioception of the ankle joint:
Proprioception accuracy as represented by repositioning accuracy was assessed for the ankle of the tested leg by the Biodex Isokinetic dynamometer system (Biodex Medical INC., Shirley, New York, USA) through active repositioning test which is testing the subject's capability to actively reproduce an angle at which the joint had been positioned before in weight-bearing position. The Isokinetic dynamometer was calibrated, and the attachment for the ankle was positioned by the specifications of the manufacturer. The subject was adjusted in sitting with knee flexion at 30 degrees (30°) while the ankle was in neutral position. Fixation was done by stabilizing each subject with mid-thigh straps, hip belts, and shoulder harnesses. As well, the subject was blindfolded to avoid visual input during the test. The foot of the subject was placed in a position that allows the alignment of the axis of ankle rotation with the axis of the dynamometer rotation. Two straps were used to fix the foot to the footplate, one distally to the ankle while the other on the metatarsal bones with the ankle positioned in a neutral position (Initial position of the Test) [19].

For consistency, the foot of the limb to be tested was permitted to go actively to target angle (15°) planter flexion at 30 degrees/second (30/sec) then stopped for 10 seconds as a process for teaching the subject so he could remember that position, and then the apparatus returned the foot to the initial position. Then the subject was ordered to actively move his foot to the target angle (15°) when the subject felt that the target angle was reached he would press the Hold/Release button to stop the apparatus. The protocol consisted of three trials with 10 seconds rest period after each trial [20]. The average of the angular differences of the three trials, between the position of the target angle (15°)
plantar flexion) and the end range position reached by the subject was measured in degrees and recorded as the repositioning accuracy deficit and was used in the statistical analysis.

2- Muscle strength of ankle dorsiflexors and ankle plantar flexors:
The strength of the dorsiflexors and plantar flexors muscles of the ankle were measured by Biodex Isokinetic dynamometer system (Biodex Medical INC., Shirley, New York, USA). The subject assumed the same position as in proprioception testing as the starting position with the knee at 30° of flexion and full plantar flexion at the ankle. Before starting the protocol, all subjects were instructed to “pull up and push down hard as fast as you can” and also were instructed during the test to cross their arms through the chest and holding on to the straps with the hands. A warming-up period of 5-min consisting of only 1 set including 6–8 submaximal repetitions performed at 45°/sec was done before starting the protocol [21]. After a 5-min rest period the test took place on the dominant leg to measure the peak torque and consisted of 4 maximal reciprocal trials at 45°/sec with a 10-sec rest period after each trial and the best trial was selected. Any bias deriving from the operator–subject interaction was avoided by preventing any verbal encouragements and feedback to the subject during testing [22].

3- Balance by Berg balance test:
The Berg balance test was used to examine balance. Berg balance test assesses 14 activities, indicating the capacity to sustain sitting and standing positions of graduated difficulty. This test evaluates 14 activities common in everyday life (sitting unsupported, sit to stand, stand to sit, transfers, stand without support, stand with one foot in front, stand with closed eyes, stand with feet together, stand on one foot, turn to look behind, retrieving an object from the floor, turning 360°, placing an alternate foot on a stool and reaching forward with an outstretched arm). Each task is evaluated from 0 to 4 [23]. Berg balance test is reliable test used for assessment of balance with high inter-rater reliability (ICC=0.98) and high intra-rater reliability (ICC=0.97) [24].

4- Nerve conduction velocity:
Diabetic polyneuropathy check (DPN-check) device was used to measure sural nerve conduction velocity and amplitude. This device is a valid and reliable device for assessment of sural NCV (ICC values=0.94) and sural nerve amplitude potential (ICC values=0.97) [25]. Additionally, Perkins et al.,2006, concluded that the sensitivity and specificity of the amplitude potentials of the sural nerve measured with the point-of-care device were 92% and 82%, respectively [26]. The patient was placed on the side lying with the tested leg on top. The position of the patient should be comfortable to allow for leg and foot relaxation during the test.

After positioning of the patient, preparation of the skin and placement of the device are essential. Insert the biosensor into the port then power on the device, press the button, and a green light will appear. A little amount of conductive gel is applied to each probe. Remove the backing from the biosensor. The long probe is placed just behind the patient’s outer ankle bone, maintain constant force and press the button to start the test. Normally the test takes about 10-15 seconds, and the results will be displayed on the screen once it is completed.

METHODS OF STATISTICAL ANALYSIS:
SPSS software, version 23 was used for statistical analysis in this paper. Descriptive statistical analysis has been made for all variables, and all data were expressed as mean ± SD. Normality test of data by using Kolmogorov-Smirnov test reflected that the data were normally distributed for all dependent variables. Therefore, Unpaired t-test performed to compare between group 1 (G1) and group 2 (G2) values. Level of significance is P< 0.05. Pearson correlation coefficient (r) was used to determine the relationship between different variables in this study.

RESULTS
1- General characteristics of the subjects:
- The diabetic neuropathy group (G1):
The subject’s ages ranged from 40 to 55 years with a mean value of 48.73±5.26 years. Their height ranged from 166 to 180 cm with a mean height of 172.93±4.74 cm. Their weight ranged from 63 to 90 kg with a mean weight of 78.13±6.91 kg and duration of illness ranged from 5 to 15 years with a mean duration of 8.93±4.2 years.
- The normal subjects group (G2):
The subject’s ages ranged from 41 to 55 years with a mean value of 46.47±4.42 years. Their height ranged from 168 to 185 cm with a mean height of 175.67 ±7.06 cm. Their weight ranged from 66 to 90 kg with a mean weight of 76.07±8.66 kg and duration of illness ranged from 5 to 15 years with a mean duration of 8.93±4.2 years.

2- Comparison between the mean values of the strength of ankle plantar flexors and dorsiflexors in both groups:
The mean peak torque values of the plantar flexors were 19.84±9.35 and 50.96±5.03 Newton meter (Nm) for G1 and G2 respectively. Comparisons between both groups showed a significant statistical difference in the mean peak torque values of the plantar flexors (p=0.0001). The mean peak torque values of the dorsiflexors were 10.6±4.28 and

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>G1 Mean±SD</th>
<th>G2 Mean±SD</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm.)</td>
<td>172.93±4.74</td>
<td>175.67 ±7.06</td>
<td>-1.245</td>
<td>0.223</td>
</tr>
<tr>
<td>Weight (kg.)</td>
<td>76.07±8.66</td>
<td>78.13±6.91</td>
<td>-0.723</td>
<td>0.476</td>
</tr>
</tbody>
</table>

*p≤ 0.05
24.94±2.89 Nm for G1 and G2 respectively. Comparisons between the two groups showed a statistically significant difference in the mean peak torque values of the dorsiflexors (p=0.001), as shown in the table (2).

3- Comparison between the isokinetic ankle reposition mean accuracy values in both groups:

The mean values of the difference between the target angle and performed angle which indicate the repositioning accuracy were 5.33±2.61 and 0.93±0.79 degrees for G1 and G2 respectively. Comparisons between the two groups showed a significant statistical difference in the mean values of the difference between target angle and the performed angle between both groups (p=0.0001), as shown in the table (2).

4- Comparison between the Berg balance scores mean values in both groups.

The mean values of the Berg balance test (BBT) were recorded as 42.27±4.89 and 52±2.27 for G1 and G2 respectively as shown in the table (2). Comparisons between the two groups showed a statistically significant difference in the mean values of the Berg balance scores (p=0.006).

5- Comparison between the nerve conduction velocity and amplitude of the sural nerve mean values in both groups:

The mean values of the nerve conduction velocity were recorded as 39.53±6.03 and 51.87±2.72 m/sec for G1 and G2 respectively as shown in the table (2). Regarding the amplitude of the sural nerve, the mean values were 4.73±2.89 and 10.93±2.46 µv for G1 and G2 respectively as shown in the table (2). Comparisons between the two groups regarding the sural NCV and amplitude showed a highly statistically significant difference in the mean values (p=0.0001) for both.

Table 2: Comparison between the mean values of the measured variables of both groups:

<table>
<thead>
<tr>
<th>Item</th>
<th>G1 Mean±SD</th>
<th>G2 Mean±SD</th>
<th>t-value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reposition accuracy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Planter flexors peak torque (Nm)</td>
<td>19.84±9.35</td>
<td>50.96±5.03</td>
<td>-11.353</td>
<td>0.0001</td>
</tr>
<tr>
<td>Dorsiflexors peak torque (Nm)</td>
<td>10.6±4.28</td>
<td>24.94±2.89</td>
<td>-10.749</td>
<td>0.0001</td>
</tr>
<tr>
<td>BBS</td>
<td>42.27±4.89</td>
<td>52±2.27</td>
<td>-6.992</td>
<td>0.0001</td>
</tr>
<tr>
<td>Sural NCV (m/sec)</td>
<td>39.53±6.03</td>
<td>51.87±2.72</td>
<td>-7.216</td>
<td>0.0001</td>
</tr>
<tr>
<td>Amplitude (µv)</td>
<td>4.73±2.89</td>
<td>10.93±2.46</td>
<td>-6.324</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*p≤ 0.05

Correlation analysis:

1- The correlation between reposition accuracy and other dependent variables in both G1 and G2:

Results concerning correlations between reposition accuracy and other dependent variables for the two groups are presented in table (3). The results showed a very strong negative correlation between BBS and reposition accuracy (r=-0.88 and p=0.0001) (in G1) and (r=-0.83 and p=0.001) (in G2) and between sural NCV and reposition accuracy (r=-0.82 and p=0.0001) (in G1) and (r=-0.75 and p=0.001) (in G2). As well, there was a strong negative correlation between planter flexors peak torque and reposition accuracy (r=-0.76 and p=0.001) (in G1) and (r=-0.77 and p=0.001) (in G2).

Table 3: Correlation between reposition accuracy and other dependent variables in both groups

<table>
<thead>
<tr>
<th>Item</th>
<th>G1 R</th>
<th>G1 p-value</th>
<th>G2 R</th>
<th>G2 p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sural NCV (m/sec)</td>
<td>-0.82</td>
<td>0.0001</td>
<td>-0.75</td>
<td>0.001</td>
</tr>
<tr>
<td>BBS</td>
<td>-0.88</td>
<td>0.0001</td>
<td>-0.83</td>
<td>0.0001</td>
</tr>
<tr>
<td>Planter flexors peak torque (Nm)</td>
<td>-0.76</td>
<td>0.001</td>
<td>-0.77</td>
<td>0.001</td>
</tr>
<tr>
<td>Dorsiflexors peak torque (Nm)</td>
<td>-0.75</td>
<td>0.001</td>
<td>-0.76</td>
<td>0.001</td>
</tr>
<tr>
<td>Amplitude (µv)</td>
<td>-0.71</td>
<td>0.003</td>
<td>-0.7</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*p≤ 0.05

2- The correlation between sural NCV and other dependent variables in both groups:

Results concerning correlations between sural NCV and other dependent variables in both groups are listed in table (4). Results showed strong positive correlations between sural NCV and BBS (r=0.71 and p=0.003) (in G1) and (r=0.81 and p=0.009) (in G2), sural NCV and planter flexors peak torque (r=0.78 and p=0.001) (in G1) and (r=0.76 and p=0.001) (in G2), sural NCV and dorsiflexors peak torque (r=0.79 and p=0.0001) (in G1) and (r=0.71 and p=0.003) (in G2), and between sural NCV and the amplitude of sural nerve (r=0.69 and p=0.004) (in G1) and (r=0.69 and p=0.004) (in G2).

Table 4: Correlation between nerve conduction velocity and other dependent variables in both groups

<table>
<thead>
<tr>
<th>Item</th>
<th>G1 R</th>
<th>G1 p-value</th>
<th>G2 R</th>
<th>G2 p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBS</td>
<td>0.71</td>
<td>0.003</td>
<td>0.81</td>
<td>0.009</td>
</tr>
<tr>
<td>Planter flexors peak torque (Nm)</td>
<td>0.78</td>
<td>0.001</td>
<td>0.76</td>
<td>0.001</td>
</tr>
<tr>
<td>Dorsiflexors peak torque (Nm)</td>
<td>0.79</td>
<td>0.0001</td>
<td>0.71</td>
<td>0.003</td>
</tr>
<tr>
<td>Amplitude (µv)</td>
<td>0.69</td>
<td>0.004</td>
<td>0.69</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*p≤ 0.05

3- The correlation between duration of illness and other dependent variables in G1:

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The results of this study revealed a significant decrease in proprioceptive accuracy in diabetic neuropathy group (p≤ 0.05) in agreement with the findings of Guneysu et al., 2013, who found decreased ankle joint position sense, which was measured as the ability to reproduce target ankle dorsiflexion and plantarflexion [31] actively. Furthermore, Hsu et al., 2009, compared the joint position sense of the lower limb in patients with diabetic neuropathy and normal controls and they found that distal joint involvement precedes that of proximal joints [32].

Regarding the Berg balance test, the results of this study showed a significant decrease in the Berg balance scores in diabetic neuropathy group compared to control group (p≤ 0.05), which might be attributed to decreased proprioceptive input. This comes in agreement with Lafond et al., 2004. Turcot et al., 2009, who suggested that individuals with peripheral neuropathy show balance instability with a larger center of pressure displacement [33,34].

Regarding the examination of sural nerve conduction velocity and amplitude by DPN check, the results of the present study revealed that the mean values of the nerve conduction velocity and amplitude were decreased compared to the normal limits. This opinion is supported by the opinion of Dyck et al., 2011, who concluded that nerve conduction abnormality which may be without polyneuropathy signs or symptoms seems to be the first quantitative and objective indicator of diabetic sensory polyneuropathy (DSPN) and is essential for its confirmed diagnosis [35].

Nerve conduction velocity has been shown the most objective measure of nerve function [36], It is considered as the gold standard for diagnosis of DPN [37,38]. Moreover, Redmond et al., 1992, concluded that the sural sensory study is the best predictor of diabetic neuropathy [39]. DPN Check is a test for sural nerve conduction, which is a DPN standard and quantitative biomarker. It was concluded that assessment of Sensory Nerve Action Potential (SNAP) and NCV by the point-of-care nerve conduction device was accurate [19]. The measurements of sural nerve conduction by the DPN Check device are highly correlated to the presence of DPN [40]. This opinion is strengthened by the results of Sharma et al., 2015, who concluded that DPN Check device could be an excellent adjunctive diagnostic mean in the clinical settings for the diagnosis of DPN [41].

Correlation between NCV and duration of diabetes showed moderate correlation (r=−0.71, p<0.05). It is supported by the conclusion of Karki et al., 2016, who concluded that prevalence of diabetic neuropathy increased with duration of diabetes [42]. As well, the results showed a significant decrease in sural nerve amplitude than normal subjects. The findings of Charles et al., 2010, who found that in addition to the diabetes duration and A1C level, decreased NCV and amplitude is associated with the presence of other microvascular diabetes complications [43].

The results showed strong positive correlations between sural NCV and BBS (r=0.81, p<0.05) this come in agreement with the findings of Wang et al., 2017, who found
that NCV in the lower limbs showed a moderate to strong correlation with the balance tests in patients with diabetes [44]. This also come in agreement with the findings of Kakrani et al., 2014, who correlated the clinical findings of diabetic neuropathy with that of nerve conduction studies and found that the severity of the neuropathy can be determined by the findings of nerve conduction studies [45]. The results also revealed a very strong negative correlation between BBS and reposition accuracy (r=-0.88 and p<0.05). As well, there was a strong negative correlation between the ankle muscles peak torque and reposition accuracy (r=-0.76 and p<0.05), these findings are consistent with those of Fortaleza et al., 2013, who found that impairment in the balance function in patients with diabetic neuropathy is due to motor dysfunction, especially in the ankle's strategies for maintaining posture control, in addition to the change in the somatosensory system [46].

CONCLUSION

The Isokinetic system is an objective and standardized tool to detect the motor and sensory changes in patients with diabetic neuropathy. As well, it can be concluded that examination of sural nerve conduction velocity and amplitude by DPN-check device helps in determination of the severity of polyneuropathy in diabetic patients. Moreover, the Isokinetic assessment may serve as a predictor assessment tool for severity of neuropathy in diabetic patients. However, it is recommended that patients with diabetes mellitus especially those with long-standing diabetes should practice strengthening exercises for the distal muscle to guard against or delay muscle weakness that may affect those patients. Also, great attention should be paid to patients with long-standing diabetes to avoid dangerous complications as diabetic foot. On the other hand, other studies should be conducted involving a larger sample size to confirm the results and to allow generalization of findings.

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Abbreviations used

BBS - Berg Balance Scale
DM - Diabetes Mellitus
DPN - Diabetic Polyneuropathy
JPS - Joint Position Sense
µV - Microvolt
N/M - Newton's per Meter
NCV - Nerve Conduction Velocity
PT - Peak Torque

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**Citation**