
Objective: To quantify the muscle tone of upper limbs in patients with diabetic polyneuropathy (DPN).

Design: Case-control study. Quantitative upper-limb pendulum tests were conducted, and model analysis was performed.

Setting: Outpatient clinic of a medical center.

Participants: The experimental group consisted of patients with type 2 diabetes suffering from symptomatic but not disabling polyneuropathy. The diagnosis of polyneuropathy was based on symptoms, signs, and nerve conduction velocity (NCV) study. The control group consisted of age- and sex-matched normal subjects. In total, 181 subjects were recruited, including 128 controls and 53 DPN patients.

Interventions: Not applicable.

Main Outcome Measures: Quantitative biomechanic parameters (number of swings, relaxation index, stiffness constant and damping coefficient) were formulated and the differences between groups were investigated.

Results: The number of swings and stiffness constant showed no difference between groups. Relaxation index increased and damping coefficient decreased significantly in the DPN group.

Conclusions: Muscle tone, defined as passive resistance in the tested range, in DPN patients was shown to be decreased. The decrease was mainly due to a decrease in the velocity-dependent component. The decrease did not correlate with the decrease in NCV and could not be detected by the conventional manual pendulum test performed at the bedside.

Key Words: Diabetic neuropathies; Muscle hypotonia; Rehabilitation.

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Muscle Tone in Diabetic Polyneuropathy Evaluated by the Quantitative Pendulum Test

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MANY PATIENTS WITH DIABETIC polyneuropathy (DPN) complain about joint or muscle stiffness. Because polyneuropathy causes hyporeflexia and muscle wasting, however, it is natural to think that DPN leads to hypotonia. Whether the muscle tone is actually increased or decreased is important for management of DPN patients. Unfortunately, there were insufficient data to answer this question.

Muscle tone is the passive resistance of muscle under traction and is the joint display of neural control, muscle status, and connective tissue properties. More attention has been paid to hypertonia, because it is related to many common diseases, such as stroke and Parkinsonism, and can be evaluated semiquantitatively by manual tests. Furthermore, hypertonia can be quantified by electronic pendulum test and mechanical passive stretch. Hypotonia is less emphasized, because hypotonia can only be inferred from indirect evidence, such as hyperextensibility of joints and pendulum test. There is no recognized standard for quantifying hypotonia and this partly accounts for the relative lack of studies in investigating the muscle tone in DPN patients.

In previous studies, we designed a simple accessory apparatus to assist performing the pendulum test in the elbow joint and also proposed a biomechanic model of the elbow to formulate parameters for quantification. Initial results indicated that the parameters could differentiate between spasticity in stroke patients and normal muscle tone of healthy subjects. In another study, we also established the effects of age, sex, and body weight on muscle tone of normative subjects. The main purpose of the present study was, using our developed apparatus and analytic tools, to quantitatively investigate the effects of DPN on muscle tone. The results of this study not only quantify the muscle tone of DPN patients but also have implications for plans of treatment.

METHODS

Participants

This was a case-control study. We recruited subjects from the outpatient clinic of National Cheng Kung University Hospital (NCKUH). For the DPN group, subjects consisted of consecutive referrals to our neurology clinic due to DPN caused by type 2 diabetes from year 2000 to 2005. Diabetes mellitus was defined by the post fasting blood glucose level, glycosylated hemoglobin level, and the continued use of diabetes-specific medications. Polyneuropathy was defined by the symptoms and the nerve conduction velocity (NCV) studies of upper and lower limbs. We deliberately excluded stage 3 patients (ie, patients with disabling neuropathy), so the subjects in the experimental group all belonged to stage 2 (ie, symptomatic neuropathy). For the control group, subjects were chosen randomly from our database of normative subjects in the same years by matching the age range and sex. The sources of control subjects were (1) family members of patients who came to our hospital with the patients for electrophysiologic examinations and (2) patients that came for electrophysiologic examinations due to other problems, such as lumbosacral radiculopathy and headache. Subjects with a history of stroke, Parkinsonism, polyneuropathy due to other etiologies, or other neurologic diseases (particularly, those producing abnormal muscle tone, restricted range of motion or decreased muscle power) were excluded. Inclusion criteria for the control group included clear consciousness and cooperativity. No subject was
taking antispasticity medication or muscle relaxant at the time of study. The study protocol was approved by the NCKUH ethics committee on human subject study. Before an experiment, the purpose, the potential hazards and the procedure of the experiment were fully explained to the subjects. A written permission form was signed. The body weight, forearm length, and maximal forearm circumference were measured for the estimation of mass, center of mass, center of gyration, and inertia of the forearm and hand.7,8

Study Design

The experimental setup and procedure was identical to that adopted in a previous study.5 In brief, an accessory apparatus was specifically designed to facilitate performing the pendulum test in the elbow joint (fig 1). The accessory apparatus consisted of a shaft, a weight, and a wrist fastening part. The steel shaft was connected at the mid point to the test bed through a pure rotary joint. An electronic goniometer at this joint measured the elbow joint angle. A weight was fastened to the lower end of the shaft to increase the total inertia and counterbalance the weight of the forearm. The subject lay comfortably on the test bed. The wrist was fixed to the accessory apparatus through the wrist fastening part. The upper part of the shaft was hooked to the test bed with a chain of predesigned length, such that the elbow joint angle was 130° (referencing full extension as 0°). Surface electromyography of the biceps and triceps brachii was collected with 2 pairs of standard cup electrodes and amplified 1000 times after band-pass filtering (1.59–300Hz) using a Polygraph 360 system.a The data collection was started and the chain was released swiftly without informing the subject. The forearm passively swung due to the weight at the lower part of the apparatus. After the swing motion stopped by visual inspection, the data collection was terminated. Six successful trials were collected.

The signals were sampled at 600Hz for 15 to 25 seconds depending on the duration of swing and stored in a personal computer for off-line analyses. The data collection was accomplished with LabView. The data were preprocessed and if (1) background electromyographic activity was observed and (2) the angle trajectories were inconsistent during the pendulum test, the data were excluded. Because there was no electromyographic activity, the signals were not further processed.

Data Analyses

To quantify the results, we formulated several parameters. Number of swings and relaxation index (RI) were determined from the averaged angle trajectory,9 where the RI was the ratio of maximal swing angle to the final steady-state angle and number of swings was the number of peaks and troughs during the swing (fig 1). In general, both number of swings and RI decreased as the muscle tone increased. Then, the angle trajectory was fitted to a previously proposed biomechanic model of the elbow joint,4

\[
1\dot{\theta} = -\tau - K(\theta - \theta_0) - C\dot{\theta}
\]

where \(\theta\) is the elbow joint angle, \(\tau\) is the gravitational torque, \(K\) is the stiffness coefficient of tissues, including muscles, around the elbow joint, \(\theta_0\) is the threshold angle, and \(C\) is the damping coefficient (also known as the coefficient of viscosity). From equation 1, it is clear that \(K\), related to the angle, is a measure of tendency to return to \(\theta_0\) position and \(C\), related to the angular velocity, is a measure of resistance to swing. In general, \(K\) is independent of muscle tone and is more related to the stiffness of tissue and \(C\) increases as muscle tone increases.4

The parameters (\(K, C\)) were estimated by recursive optimization technique. The goodness of parameter estimation was evaluated with root mean square error (RMSE) between the actual and estimated elbow angle trajectories. The full mathe-
Statistical Analyses

First, we calculated the group means and standard deviations (SDs) of the 4 quantitative parameters and tested the significance of difference between the 2 groups by Mann-Whitney U test with a significance level of α equal to .05. Next, the relationship among factors and parameters were evaluated and clustered by principal components analysis. Third, K and C as a linear function of weight and DPN were fitted by the multivariable regression technique. We also calculated the significance of correlation between factors by Fisher r to z transformation. Last, we computed the correlation between the parameters and NCV results. StatView was used for the above-mentioned statistical analyses.

RESULTS

One hundred eighty-one subjects (128 controls, 53 DPN patients) completed the pendulum test. The basic data of subjects are listed in Table 1. The estimated inertia and total weight of forearm and hand are also listed. Subjects were not matched on body weight and the DPN group was slightly heavier. Motor and sensory NCV was only performed in the DPN group. The NCV was slower than the normative data from our electrophysiology lab (Table 2).

An example of the angle trajectory during the pendulum test along with the simulation result is shown in Figure 2. A summary and comparison of parameters are listed in Table 3. Although there was no significant difference between the 2 groups for parameters number of swings and K, the differences for both RI and C were significant. The pooled mean and SD of RMSE in model fitting was 2.9°.

We did principal components analysis to evaluate the relationship among parameters and the respective contribution of the clustered factors (Table 4). The results show that the parameters were clustered into 4 factors. Factor 1 (consisting mainly of number of swings, RI, and C) contributed 30.8%, factor 2 (consisting mainly of weight, forearm length, and sex) 32.4%, factor 3 (consisting mainly of age and K) 19.5%, and factor 4 (consisting mainly of DPN) 15.9% to the total variance, respectively. In other words, there were 4 independent clusters of parameters, the first one being related to viscosity, the second one to body weight and sex, the third one to stiffness and age, and the last to polyneuropathy.

According to one of our previous studies, K and C were relatively independent of age, and the effects of sex and forearm length on K and C were related to the difference in body weight. When all the subjects in the 2 groups were pooled together, K was fitted as a function of weight (W) and P (DPN) by stepwise multiple linear regression,

\[ K = 0.039W + 0.182, \]

where P equals 1 represents the control group and P equals 2 represents the DPN group, and \( r^2 \) equals .19 (P < .001). P was dropped because of nonsignificant contribution (P = .28). Similarly, C was fitted as

\[ C = 0.009W - 0.218P + 0.424, \]

where \( r^2 \) equals .09 (P < .001). The effect of interaction between weight and P was checked by adding W × P in the regression analyses and the results showed that the interaction was nonsignificant.

The linear correlations between weight versus K and C (Figure 3) were calculated (K: \( r^2 = .436, P < .001; \) C: \( r^2 = .184, P = .13 \)). The difference between the 2 correlation coefficients was significant (P < .001). The results indicated that K was more dependent on body weight. The linear correlations between parameters and NCV results were very low (Figure 4), indicating the correlation between the joint stiffness and NCV results was very weak in the DPN patients that we recruited.

Table 1: Anthropometric Data of Subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control</th>
<th>DPN</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>58.1±11.1</td>
<td>58.4±9.5</td>
<td>.768</td>
</tr>
<tr>
<td>Sex (men/women)</td>
<td>80/48</td>
<td>34/19</td>
<td>.615</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>63.9±9.3</td>
<td>67.6±12.1</td>
<td>.016</td>
</tr>
<tr>
<td>Forearm circumference (cm)</td>
<td>28.4±2.5</td>
<td>28.6±3.1</td>
<td>.251</td>
</tr>
<tr>
<td>Forearm length (cm)</td>
<td>30.3±1.9</td>
<td>30.8±1.9</td>
<td>.200</td>
</tr>
<tr>
<td>Estimated weight of FA (kg)</td>
<td>1.40±0.20</td>
<td>1.49±0.27</td>
<td>.016</td>
</tr>
<tr>
<td>Estimated inertia of FA (kg/m²)</td>
<td>0.10±0.02</td>
<td>0.11±0.03</td>
<td>.015</td>
</tr>
</tbody>
</table>

NOTE. Values are mean ± SD or as otherwise indicated.

Abbreviation: FA, forearm and hand together.

Table 2: NCV Results of DPN Group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>NCV (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median motor</td>
<td>47.4±5.3</td>
</tr>
<tr>
<td>Ulnar motor</td>
<td>47.7±6.8</td>
</tr>
<tr>
<td>Median sensory</td>
<td>23.2±17.7</td>
</tr>
<tr>
<td>Ulnar sensory</td>
<td>24.8±18.7</td>
</tr>
</tbody>
</table>

NOTE. Values are mean ± SD.

Table 3: Parameters and Comparisons of 2 Groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>DPN</th>
<th>( \Delta )</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of swings</td>
<td>4.10±1.92</td>
<td>4.25±1.71</td>
<td>-0.16</td>
<td>.492</td>
</tr>
<tr>
<td>RI</td>
<td>1.43±0.17</td>
<td>1.56±0.25</td>
<td>-0.13</td>
<td>.001</td>
</tr>
<tr>
<td>K (Nm·s)</td>
<td>2.64±0.88</td>
<td>2.93±0.99</td>
<td>-0.29</td>
<td>.098</td>
</tr>
<tr>
<td>C (Nm·s/rad)</td>
<td>0.78±0.44</td>
<td>0.59±0.29</td>
<td>-0.24</td>
<td>.16</td>
</tr>
</tbody>
</table>

NOTE. Values are mean ± SD.
DISCUSSION

Comparison With Other Studies

As described above, there is very little objective data on muscle tone in DPN. Nielsen et al\textsuperscript{10} reported that ankle joint stiffness decreased in long-term type 1 diabetic patients. The decrease was very subtle. Stiffness in the report was not defined as the elastic component, but as the gross resistance to passive stretch. Nielsen did not investigate the changes in individual stiffness components. Our results also indicated that the total resistance to passive stretch was decreased and, furthermore, the decrease was in the damping component (C in table 3), whereas the elastic component showed no difference from the control group. Duquette et al\textsuperscript{11} studied the viscoelastic properties of knee ligaments in congenital diabetes mellitus rats and reported that the storage compliance (corresponding to 1/K) did not differ significantly from that in the control group but the loss compliance (corresponding to 1/C) was increased. The results were compatible with ours. The authors also commented on many previous studies, noting problems in study design that resulted in the inconsistency of results.\textsuperscript{12,13} Athanasiou et al\textsuperscript{14} studied the effects of diabetes on biomechanic properties of human ankle cartilage and found that the cartilage became softer. The authors did not analyze the changes in stiffness components, either.

Many studies\textsuperscript{15,16} reported that the range of motion (ROM) of joints decreased in diabetic patients, which seemed to be contradictory to the trend of hypotonia and our results. This point is discussed in detail below.

Factors Contributing to Muscle Tone

Neural control, muscle status, and biomechanic properties of connective tissue are 3 main factors affecting the magnitude of muscle tone. Traditionally, neural control has been thought to be the most dominant factor. Polyneuropathy affects mainly the spinal segmental reflexes. Stretch reflexes with afferents from muscle spindles and Golgi tendon organs are thought to play a key role in the spinal segmental neural control of muscle tone. The effects of muscle status on muscle tone are less well defined. Though it is known that a larger muscle produces a larger muscle force, no data show whether, in the passive state, C is larger in a larger muscle or joint. Wiegner and Watts,\textsuperscript{17} in a small series, showed that K of the elbow joint correlated linearly with the volume of the arm. Chleboun et al\textsuperscript{18} also reached a similar conclusion by measuring elbow flexor volume and angular stiffness of the elbow joint. We calculated the correlation between weight versus K and C, and the results indicated that K was more dependent on body weight. When
the product of forearm length and circumference was used as an indicator of forearm volume, the correlation of this indicator versus K and C was similar to the above conclusion. Last, though the resistance to the passive stretch is defined as the muscle tone, in addition to muscle, connective tissue around the joint is also stretched in the testing process. More and more data indicate that the biomechanic properties of muscle and connective tissues around the joint, including tendons and ligaments, also affect the grossly perceived muscle tone.11,12

The extreme case is the complete joint contracture. One study20 showed that muscle tone and joint ROM were related, that is, smaller ROM was associated with hypertonia.

In the case of DPN in this study, spinal segmental reflexes, including stretch reflexes, decreased, contributing to decreased muscle tone. Diabetes, through biochemical actions, changes the molecular interactions of connective tissues and also contributes to the decreased muscle tone.13 The relative immobilization, however, due to poor physical condition may cause contracture of joints, leading to a smaller ROM, and increased passive resistance. We did not match body weight in the control and study groups. The greater body weight of the DPN groups may also have contributed to elevated tone. The paradox between decreased ROM and decreased muscle tone may have been secondary to the movement range over which the test was performed. In measuring ROM, whole ROM was evaluated, whereas in our pendulum test, the pendular swing was from 130° to about 60°, that is, part of the extension was not tested. In summary, many factors with variable degree of influence contributed to the final gross manifestation of muscle tone. In the DPN subjects in our study that we chose and the movement range over which the joint was tested, the factors leading to decreased muscle tone dominated over those that may have led to increased tone.

As described in the Methods section, all subjects in the DPN group were rated as having stage 2 diabetic polyneuropathy. We expect that muscle tone in some DPN patients may change from hypotonia to hypertonia as polyneuropathy becomes more severe and the joints are more immobilized and develop contracture.

**Comments on the Parameter Results**

Although the parameters number of swings, RI, and C were clustered together as a factor in the principal components analysis, number of swings, in contrast to RI and C, did not show a significant difference between the 2 groups. The possible explanation is that number of swings, representing the number of swings and being an integer, was a discrete variable, whereas RI and C were continuous variables. Discrete variables were less powerful in detecting subtle changes. Because number of swings was not increased in the DPN group, it indicates that the conventional manual pendulum test performed at the bedside is ineffective in detecting the subtle hypotonia in DPN. Le Cavorzin et al21 showed, by model simulation, that the weight of forearm and hand has an effect on angle trajectory similar to C. In other words, RI can be increased by increasing the weight of forearm and hand without changing C. Because weight of forearm and hand was estimated from body weight by multiplying a constant, we tested the effects of body weight on the RI by similar model simulations (fig 5). First, the pendulum angle trajectory of the control group was calculated by incorporating the mean K, C, weight, and forearm length of the control group. Then, weight was changed by ±10% and ±20% and simulations were repeated. For ±20% change in W, the changes in the RI are only 3.7% (1.42±0.03). If we increased weight by 20% and assumed the variance of the RI was identical, the statistical difference between the RI of the control and DPN groups was still significant. Because the difference in the mean body weight between the 2 groups was only 6%, the above results indicated that the difference between the RI of the control and DPN groups was not due to the difference in body weight. Parameter RI has the advantage of being independent of model and easy to calculate. On the other hand, C has a definite physical meaning and interpretation.

**Clinical Implications**

One of our previous studies3 showed that C was increased and K remained constant in stroke patients with spasticity. This study showed that C was decreased and K remained constant in DNP patients. Combined, these results strengthen the concept that testing of muscle tone is more stretch-velocity–dependent and that the damping coefficient, C, can be a quantitative indicator of muscle tone. In contrast, the stiffness constant, K, intuitively representing the stiffness of the joint, is not a primary factor in determining muscle tone. In the previous study, it was also shown that C was linearly correlated with the scores on the Modified Ashworth Scale. Because we have found no comparable scale or other relevant quantitative studies about hypotonia in the past, we do not know the linear correlation between the clinical severity of hypotonia and C. To our knowledge, this is the first quantitative study of hypotonia.

In addition to the application of these findings to DPN patients, accurate muscle tone quantification can also clarify the effects of many drugs on muscle power and muscle tone. The decomposition of damping (velocity-dependent) and stiffness (position-dependent) components by model analysis assists in the search of underlying mechanisms of altered muscle tone in pathologic conditions.

**CONCLUSIONS**

The present study showed that muscle tone, defined as the passive resistance in the tested range, was decreased in stage 2...
DPN patients. The decrease was mainly due to a decrease in the velocity-dependent component.

References

Suppliers
a. NEC, 7-1, Shiba 5-chome, Minato-ku, Tokyo 108-8001, Japan.
c. SAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.