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A Clinical Comparison of Variable-Damping and Mechanically Passive Prosthetic Knee Devices

ABSTRACT

Objective: Although variable-damping knee prostheses offer some improvements over mechanically passive prostheses to transfemoral amputees, there is insufficient evidence that such prostheses provide advantages at self-selected walking speeds. In this investigation, we address this question by comparing two variable-damping knees, the hydraulic-based Otto Bock C-leg and the magnetorheological-based Össur Rheo, with the mechanically passive, hydraulic-based Mauch SNS.

Design: For each prosthesis, metabolic data were collected on eight unilateral amputees walking at self-selected speeds across an indoor track. Furthermore, kinetic, kinematic, and electromyographic data were collected while walking at self-selected speeds across a 10-m walkway in a laboratory.

Results: When using the Rheo, metabolic rate decreases by 5% compared with the Mauch and by 3% compared with the C-leg. Furthermore, for the C-leg and Rheo knee devices, we observe biomechanical advantages over the mechanically passive Mauch. These advantages include an enhanced smoothness of gait, a decrease in hip work production, a lower peak hip flexion moment at terminal stance, and a reduction in peak hip power generation at toe-off.

Conclusion: The results of this study indicate that variable-damping knee prostheses offer advantages over mechanically passive designs for unilateral transfemoral amputees walking at self-selected ambulatory speeds, and the results further suggest that a magnetorheological-based system may have advantages over hydraulic-based designs.

Key Words: Prosthesis, Hydraulic Knee, Magnetorheological Knee, Walking Metabolism
Recent advances in biomedical engineering have led to the introduction of computer-controlled, variable-damping prosthetic knees for transfemoral amputees. Motivated by the potential of such technology, researchers developed prototype knees, and these developments eventually led to marketable devices, such as the Blatchford Endolite Intelligent Prosthesis, the Otto Bock C-leg, and the Össur Rheo. Variable-damping prostheses offer several advantages over mechanically passive designs, including enhanced knee stability and adaptiveness to different ambulatory speeds.

Amputees subjectively report that variable-damping prosthetic knees decrease fatigue experienced during ambulation, are easier to maneuver, and allow for smoother movement than mechanically passive knees. Following these subjective reports by amputees, several scientific studies have been conducted to quantitatively compare mechanically passive knees with variable-damping devices using measures of gait metabolism, kinetics, and kinematics.

Several studies were performed in the early nineties following the introduction of the Blatchford Endolite Intelligent Prosthesis, a computer-controlled, variable-damping knee device that employs a pneumatic-based strategy for damping modulation. The introduction of this technology was viewed as revolutionary because, contrary to traditional, mechanically passive prosthetic knee designs, the Intelligent Prosthesis allowed for adaptation of knee damping during the swing phase of gait as a function of walking speed. Taylor et al. compared the Intelligent Prosthesis with two mechanically passive prostheses, the Mauch SNS and the Endolite pneumatic swing phase controller. They studied one transfemoral amputee walking on a treadmill at approximately 0.9 m/sec and showed that the Intelligent Prosthesis required about 10% lower oxygen uptake than the passive prosthetic knees. Tests at lower walking speeds were also performed and showed no significant difference in metabolic cost between the mechanically passive and variable-damping knees. Kirker et al. compared the metabolic cost of level ground walking at self-selected speeds when subjects used the Intelligent Prosthesis and a mechanically passive prosthesis. The study involved eighteen transfemoral amputees, and the results indicated that the Intelligent Prosthesis improved gait symmetry over the mechanically passive knee, but no significant difference was observed in metabolic cost at normal, self-selected walking speeds. Buckley et al. performed a study on three unilateral transfemoral amputees to compare the Intelligent Prosthesis with a mechanically passive, pneumatic-based prosthetic knee design (Endolite Stabilized Stance Flex). Compared with the mechanically passive design, the results showed a 5–10% reduction in metabolic cost when individuals walked with the Intelligent Prosthesis at slower and faster walking speeds than their normal, self-selected speed. However, at the normal speed, metabolic rate was not significantly different between the two knee designs.

Similar studies were performed following the introduction of the Otto Bock C-leg in the late nineteen-nineties. The C-leg was considered a step forward compared with the Intelligent Prosthesis because its computer-controlled hydraulic mechanism provided both swing and stance damping control. To assess this new device, Kastner et al. compared the C-leg with two mechanically passive, hydraulic-based designs, the Otto Bock 3R80 and 3R45. The study involved ten transfemoral amputees, and results indicated that the C-leg had smoother kinematics than the passive prostheses. Still further, the authors showed that subjects achieved the fastest time for a 1000-m walk test when using the C-leg. The study concluded that the C-leg provided significant advantages particularly at fast walking speeds. Schmalz et al. tested six transfemoral amputees wearing the C-leg and a mechanically passive prosthesis, the Otto Bock 3C1. Tests were performed by instructing subjects to walk on a treadmill at velocities ranging from 0.5–1.2 m/sec. Results showed a decrease in metabolic cost of about 6.5% for the C-leg over the mechanically passive prosthetic knee. Tests at higher walking speeds were also performed, but the difference in metabolic cost between the two knees was not statistically significant. The fact that there was no significant benefit in metabolic cost when using the C-leg at faster speeds was attributed to the fact that the swing phase damping of the mechanically passive prosthesis was already optimized for walking at those higher speeds.

The studies summarized above suggest that significant advantages are derived when using computer-controlled, variable-damping prostheses compared with nonadaptive, mechanically passive knee devices. For level ground ambulation, the main advantage seems to be the ability of variable-damping knees to adapt to different walking phases and speeds, allowing for early-stance knee flexion and smooth swing phase kinematics. These advantages substantially improve the mobility in individuals who live an active life. Consequently, variable-damping knees are generally prescribed to young and very active individuals. Conversely, the prescription of variable-damping knees is often discouraged in the remaining amputee population because, despite positive subjective reports, it is generally thought that there is insufficient evidence to support the hypothesis that variable-
damping knees provide advantages at self-selected walking speeds.\textsuperscript{18–20} Because it is well established that the metabolic cost of ambulation is significantly higher in lower extremity amputees than in nonamputees, even at self-selected walking speeds,\textsuperscript{17,21} researchers have sought improvements in prosthetic knee technology to gain better performance at comfortable walking speeds. This interest for improving prosthetic knee technology has recently generated a novel prosthetic knee device that relies on magnetorheological fluid and a user-adaptive control scheme.\textsuperscript{8} This approach has led to a commercially available device called the Össur Rheo knee. Preliminary results in four transfemoral amputees tested at different ambulatory speeds indicated that this variable-damping knee provided users with biologically realistic control of knee flexion during stance and swing.\textsuperscript{8}

Based on the enthusiasm generated by these preliminary results on the Össur Rheo knee, we designed a study aimed to investigate the impact of two distinct variable-damping knees, the Otto Bock C-leg and the Össur Rheo, on the metabolic cost and biomechanics of walking at comfortable, self-selected speeds. In addition, we compared these same knees to the Mauch SNS, a mechanically passive hydraulic knee. The Mauch SNS is one of the most common prosthetic knee designs in use today. It utilizes a hydraulic damper that dissipates mechanical energy during joint rotation. Like many commercially available knees, the Mauch SNS passively controls orifice size to adjust how knee damping changes with knee angular velocity.\textsuperscript{11} The C-leg is also based on a hydraulic design, but the hydraulic valves are controlled by a microprocessor.\textsuperscript{7} In distinction, the Rheo knee utilizes a magnetorheological fluid as the primary torque-producing strategy. Here damping is controlled by varying the magnetic field strength through the modulation of electric current passing through an electromagnet.\textsuperscript{8} The C-leg and Rheo have many similarities, but their distinctive torque-producing strategies (hydraulic vs. magnetorheological fluid) may yield differences in damping specifically at the minimum, or low-end torque region. Whereas the torque output of the hydraulic-based C-leg has a strong velocity dependence, the Rheo knee employees magnetorheological fluid in the shear mode and has a weak torque–velocity dependence due to the shear rate thinning properties of the carrier fluid.\textsuperscript{22}

Because of the differences between variable-damping and mechanically passive prostheses, we hypothesize that variable-damping devices offer an improved metabolic economy of gait compared with mechanically passive designs at self-selected walking speeds. Furthermore, we anticipate that the distinct torque-producing strategies of the investigated knees, hydraulic vs. magnetorheological, result in differences in metabolic gait economy at self-selected gait speeds. To test these hypotheses, oxygen uptake rate is measured on eight amputees (seven transfemoral and one knee disarticulation) walking at comfortable, self-selected speeds over an indoor track using each of the investigated knee prostheses.

Additionally, we hypothesize that gait biomechanics are significantly different between variable-damping and mechanically passive prostheses and between hydraulic and magnetorheological-based systems. To test this hypothesis, subjects are asked to ambulate at comfortable, self-selected speeds across a level walkway in a motion analysis laboratory. Kinematics and kinetics are estimated using a camera-based system equipped with force platforms for each of the knee prostheses.

Finally, we hypothesize that differences in movement and muscle activation patterns associated with the three knees can be captured by means of wearable sensors.\textsuperscript{23} Our interest in this technology originates from the expectation that wearable systems might one day allow for the assessment of prosthetic knees under real-life conditions.\textsuperscript{24} To this end, in this investigation we use EMG electrodes and accelerometers to monitor EMG activity and patterns of movement during the laboratory evaluations. EMG sensors and accelerometers could be used as part of a wearable system to monitor amputees in the field.\textsuperscript{23} Results are statistically compared across the three knees and associations are sought between the sensor data and kinematics and kinetics derived from the camera-based motion analysis system.

**METHODS**

**Data Collection**

Eight unilateral amputees participated in the study. The protocol was approved by the Spaulding Rehabilitation Hospital institutional review board, and written informed consent was obtained from each person before participation.

Amputee participants were experienced at prosthesis ambulation, could ambulate at least at a K3 level (i.e., the patient has the ability or potential for ambulation with variable cadence), and had no other musculoskeletal problems or any known cardiovascular, pulmonary or neurological disorders. The eight participants (seven male, one female) were 29–54 yrs old, 165–194 cm in height, and weighed 61–112 kg. Patient characteristics are summarized in Table 1.

Before the study began, each individual had approximately 10 hrs of acclimatization on each knee prosthesis that was not his or her usual prosthesis. Each amputee subject was asked to commit to three testing sessions. One session was per-
formed using an indoor track to assess metabolic cost of level walking for the three knee systems via oxygen uptake measures. The other two sessions were performed in a motion analysis laboratory to study differences in kinematics and kinetics associated with the three knees. Two prosthetic knees were studied in the first laboratory session and the third knee device was then investigated in the remaining session. The order in which the knee systems were evaluated was randomized. Before any testing, the subjects were fitted with three prosthetic knees by the same prosthetist. Manufacturer recommendations were followed when aligning each knee prosthesis. In addition, each subject used the same prosthetic socket, prosthetic foot, and shoe when testing each knee device. The Össur low profile, high-energy return Allurion foot was used with each knee prosthesis. By using the same prosthetic socket, foot, and shoe for all the tested knees, we assured that differences observed during the study were indeed caused by the different knee prosthetic designs. In other words, we avoided the use of different socket, foot, and shoe systems because they would have played the role of confounding factors. The three knees studied in this investigation are shown in Figure 1. The total mass of the prosthetic knee, shank, Allurion foot, and shoe system was 2.71 ± 0.24 kg, 2.72 ± 0.26 kg, and 3.03 ± 0.20 kg (average ± SD) corresponding to the Mauch SNS, C-leg, and Rheo, respectively. Furthermore, the distance between the knee rotational axis and the center of mass of the prosthetic knee, shank, Allurion foot, and shoe system corresponding to the Mauch SNS, C-leg, and Rheo was 27.07 ± 4.59 cm, 27.81 ± 3.53 cm, and 23.94 ± 3.49 cm (average ± SD), respectively.

Before the study began, each individual had approximately 10 hrs of acclimatization on each knee prosthesis that was not their usual prosthesis. In the session performed using the indoor track, oxygen uptake was measured in the amputee participants. Subjects walked at comfortable speeds over a quarter-mile track using a portable, lightweight, breath-by-breath telemetric system (Cosmed K4b2, IT). Before testing, each subject’s comfortable walking speed was determined. Then subjects were instructed to walk next to an electric vehicle programmed to move at their comfortable pace. The same speed was used for all the prosthetic knees and the order of testing was randomized. Time was given to allow each subject to become accustomed to each knee before being tested.

In the sessions performed in the laboratory, kinematic and kinetic data were collected using a motion analysis system (Vicon 512 system; Oxford Metrics, UK). Kinematics were derived by measuring the three-dimensional positions of reflective markers. The markers were placed at the following specific bony landmarks: bilateral anterior superior iliac spines, posterior superior iliac spines, lateral femoral condyles, lateral malleoli, second metatarsal heads, and the calcanei. Additional markers were also rigidly attached to wands and placed over the mid-femur and mid-shank. Kinetics were computed from measures of ground reaction forces derived using two staggered force platforms (AMTI).
EMG electrodes and accelerometers were also used during the laboratory experiments to monitor muscular activity and patterns of motion, respectively. Active EMG electrodes (Motion Labs, LA) were used to monitor bilaterally the activity of the gluteus maximus and gluteus medius muscles. We chose to monitor these two muscles because their activity has been related to hip control in the sagittal and coronal planes for both normal and amputee gait.\textsuperscript{26} In addition to the EMG measurements, uniaxial accelerometers were positioned bilaterally on both thighs and shanks. Accelerometer data were recorded using a VitaPort ambulatory system (Temec B.V., The Netherlands), and these data recordings were synchronized with the Vicon motion capture measurements.

Once the setup was complete, each subject was asked to walk at his/her comfortable walking speed across a 10-m walkway. The amputee subjects were tested in three conditions, each corresponding to a different knee prosthesis. For all subjects, bilateral lower extremity joint kinematic and kinetic data were collected over nine walking trials and averaged for each subject and condition. Each amputee participant was given time to acclimatize to each knee before testing. Amputee subjects were timed to ensure that they walked at the same speed with each prosthesis.

**Data Processing and Analysis**

Data recorded during indoor track testing were processed to evaluate the impact of different prosthetic knee technologies on the energetic cost of ambulating at a comfortable walking speed. Oxygen consumption (\(\text{VO}_{2}\)) as measured by the breath-by-breath telemetric system (K4b\textsuperscript{2}, Cosmed Srl., Italy) was averaged over three minutes of steady-state walking. The rate of oxygen uptake was then calculated by dividing \(\text{VO}_{2}\) by the mass of each individual.\textsuperscript{21} Results were analyzed to test for significant differences among the three knees (repeated measures ANOVA) and pairwise comparisons were performed using the least significant difference test.\textsuperscript{27} A significance level of 5\% was used for the analysis and estimated \(P\) values between 5 and 10\% were considered indicative of a trend.

Data recorded in the laboratory setting were processed to compare the biomechanical characteristics of ambulation across the prosthetic knee technologies. The following temporal parameters were estimated: walking speed, step time, step length, single support time, and double support time. Kinematic and kinetic trajectories, in the form of joint positions, torques and powers, were characterized by estimating peaks (i.e., maxima and minima) using custom-built software. The peak parameters were selected to capture differences across the prosthetic knees. In addition, work was estimated by integrating hip power to test the hypothesis that a different amount of work is associated with the tested knee technologies. We estimated total positive and negative work contributions for the stance and swing gait periods. Finally, we estimated foot compression on the affected side in the amputee individuals for each of the prosthetic knee technologies. This parameter was derived to capture different dynamic interactions of the prosthesis with the ground. Foot compression was calculated as the difference in vertical height of the shank marker and the malleolus marker. The malleolus marker was positioned on the lateral external surface of the shoe worn over the prosthetic foot. Hence, foot compression as measured here, included both prosthetic heel compression as well as shoe midsole compression. Average values for all the previously defined parameters were estimated for each subject over nine trials and statistically compared via repeated measures ANOVA’s and pairwise comparisons performed using the least significant difference test. Estimated \(P\) values smaller than 5\% were considered to be significant, whereas values between 5 and 10\% were considered to be indicative of a trend.

EMG and accelerometer measurements were performed during the same laboratory trials utilized to investigate the kinematics and kinetics of gait. EMG activities of the gluteus maximus and gluteus medius muscles were quantified by computing the root mean square value of the data recorded within a gait cycle. Average root mean square values were then estimated for each subject over nine trials and statistically compared via repeated measures ANOVA’s and pairwise comparisons performed using the least significant difference test. Significance level and values indicative of a trend were set as explained earlier. Additionally, accelerometer data were processed to explore the hypothesis that differences between prostheses could be measured using an ambulatory system equipped with accelerometer sensors, and to complement the biomechanical data measured with the stereophotogrammetric system. Accelerometer data were collected using wearable acceleration sensors positioned on the prosthesis shank, located distal to the prosthetic knee, and on the subject’s residual limb, located proximal to the prosthetic
From the accelerometer data, we computed the root mean square value of jerk about toe-off and in terminal swing. Jerk was calculated by differentiating the raw acceleration signal, and was used as a measure of gait smoothness. Average parameter values for each prosthesis were calculated and statistically compared using repeated measures ANOVAs and pairwise comparisons performed using the least significant difference test as per all other variables analyzed in the study.

RESULTS

Indoor Track Tests: Comparing Metabolic Cost Across Knee Prostheses

Metabolic cost during steady-state walking at a self-selected, comfortable speed was significantly different across the three tested knees ($P = 0.029$). The rate of oxygen consumption for each of the eight subjects and each of the three tested prostheses are shown in Figure 2. For six out of eight subjects, the rate of oxygen consumption when users wore the Rheo knee was lower compared with the Mauch. Statistical analysis showed a significant decrease in rate of oxygen consumption for the Rheo compared with the Mauch ($P = 0.009$) with an average decrease equal to 5% across the eight subjects. For six out of eight subjects, lower oxygen consumption rates were found for the Rheo as compared with the C-leg with an average decrease equal to 3%. A pairwise comparison revealed a trend, but no statistical significance, between the rate of oxygen consumption for the Rheo and the C-leg ($P = 0.092$). An average difference of 2% was shown between the rate of oxygen consumption for the C-leg and the Mauch, but the difference was not statistically significant ($P = 0.250$).

Laboratory Tests: Comparing Gait Data Across Knee Prostheses

Analysis of temporal parameters recorded in the laboratory setting showed few differences in the timing of ambulation among the three prosthetic knees. The results are summarized in Table 2. The walking speeds across the three prostheses were not statistically different. No statistical difference was demonstrated for the temporal parameters of the unaffected side. For the affected side, only step time demonstrated a statically significant difference among the three knees. Pairwise comparisons showed that the Rheo was associated with generally longer step times than the C-leg and the Mauch.

Analysis of kinematics and kinetics showed that significant differences mark the three knee technologies investigated in the study. An overview of kinematic and kinetic data for hip, knee, and ankle joints are shown in Figure 3. Average data across all the trials and subjects are shown for the affected side for each of the three knees. Differences are suggested by visual inspection of the plots. Conversely, the kinematics and kinetics of the unaffected side (not shown) did not demonstrate any obvious differences among the three knees. Consequently, statistical analysis was focused on parameters derived from hip, knee, and ankle data of the affected side (i.e., angle, torque, and power trajectories).

Results for the comparison of hip biomechanics across the investigated technologies are shown in Table 3. Differences in hip mechanics across the three prosthetic knees were characterized by statistically comparing the following parameters: peak hip extension angle about toe-off, peak hip flexion torque during terminal stance, peak hip extension torque during terminal swing, peak hip power generation during early stance, peak hip power absorption during mid to terminal stance, peak hip power generation about toe-off, hip work during stance, and hip work during swing. Compared with the C-leg and Rheo knees, the Mauch was found to be marked by greater stance period negative hip work production, greater swing period positive hip work production, larger peak hip flexion torque at terminal stance, and larger peak hip power generation at toe-off. Finally, the magnetorheological-based
Rheo showed a lower peak hip extension torque during late swing compared with the hydraulic knees, the Mauch and the C-leg (see Table 3).

Results for the comparison of prosthetic knee biomechanics across the investigated technologies are shown in Table 4. Differences in knee mechanics across the three prosthetic knees were characterized by statistically comparing the following parameters: peak knee extension angle at terminal swing, peak knee angular velocity about toe-off, peak knee torque during early stance, peak knee flexion torque at mid to terminal stance, peak knee extension torque about toe-off, peak knee flexion torque at terminal swing, and peak knee power absorption about toe-off. Compared with the Mauch and Rheo knees, peak knee extension angle during terminal swing was found to be significantly larger for the C-leg. Differences among the three knees were also found for peak knee angular velocity about toe-off. The C-leg had a significantly lower angular velocity compared with the Mauch and Rheo knees. Still further, analysis of peak knee torques and powers during the stance period demonstrated significant differences across the three knees, thus suggesting different stance phase control behaviors for the knees investigated. The mechanically passive Mauch had significantly higher values for peak knee extension torque and peak knee power absorption about toe-off compared with the variable-damping C-leg and Rheo knees. Finally, peak knee flexion torque during terminal swing was significantly lower for the magnetorheological-based Rheo compared with the hydraulic-based Mauch and C-leg knees.

Results for the comparison of prosthetic ankle biomechanics across the investigated technologies are shown in Table 5. Differences in ankle mechanics across the three prosthetic knees were characterized by statistically comparing the following parameters: peak ankle plantar flexion angle during early stance, peak ankle dorsiflexion angle during mid to terminal stance, peak ankle plantar flexion torque about 30% of the gait cycle, peak ankle power absorption at midstance, and peak prosthetic foot compression during early stance. Compared with the C-leg, the Mauch and Rheo had significantly greater peak ankle plantar flexion angles and peak foot compressions during early stance. In addition, compared with the C-leg, the Mauch and Rheo had significantly lower peak ankle dorsiflexion angles during mid to terminal stance, as well as lower peak ankle plantar flexion torques about 30% of the gait cycle.

**Laboratory Tests: Comparing EMG and Accelerometer Data Across Knee Prostheses**

EMG and accelerometer data were studied to explore the potential of wearable technology to capture biomechanical differences among the three knee technologies and to complement the results derived from the traditional kinematic and kinetic gait measures. Tables 6 and 7 summarize the results of the statistical analyses of EMG and accelerometer data. Comparisons of the RMS value of the EMG recordings from the gluteus medius muscle on the affected side showed significant differences among the three knees investigated in the study. Specifically, the magnetorheological-based Rheo was associated with a lower level of muscular activity compared with the hydraulic-based knees, the Mauch and C-leg. The analysis of accelerometer data showed significant differences among the

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**TABLE 2 Temporal parameters for the three prosthetic knees**

<table>
<thead>
<tr>
<th>Temporal parameter</th>
<th>Average Values</th>
<th>$P$ Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mauch</td>
<td>Cleg</td>
</tr>
<tr>
<td>Walking speed (m/s)</td>
<td>1.20</td>
<td>1.18</td>
</tr>
</tbody>
</table>

**Affected side:**

| Step time (s) | 0.66 | 0.65 | 0.69 | 0.019 | NS    | 0.038 | 0.007 |
| Step length (m) | 0.76 | 0.74 | 0.75 | NS    |       |       |       |
| Single support (s) | 0.42 | 0.42 | 0.43 | NS    |       |       |       |
| Double support (s) | 0.30 | 0.29 | 0.32 | NS    |       |       |       |

**Unaffected side:**

| Step time (s) | 0.57 | 0.58 | 0.59 | NS    |       |       |       |
| Step length (m) | 0.71 | 0.71 | 0.69 | NS    |       |       |       |
| Single support (s) | 0.51 | 0.52 | 0.53 | NS    |       |       |       |
| Double support (s) | 0.31 | 0.31 | 0.33 | NS    |       |       |       |

The average value over eight subjects is shown for each knee. $P$ values are shown when smaller than 10%, that is, when at least a trend was identified. Otherwise the differences were considered not significant (NS). $P$ values smaller than 5% are in bold type.
The RMS values of jerk estimated about toe-off from the accelerometer data recorded from the prosthetic shank showed a significant increase for the mechanically passive Mauch compared with the variable-damping Rheo. A trend was also shown with a higher RMS jerk value for the mechanically passive Mauch compared with the variable-damping C-leg. Still further, the RMS values of jerk estimated during terminal swing from the accelerometer data recorded from the thigh demonstrated a significant difference across the three knees investigated in the study. Pairwise comparisons showed a significantly higher RMS jerk value for the mechanically passive Mauch compared with the variable-damping C-leg and Rheo knee prostheses.

**DISCUSSION**

There is contrasting evidence in the literature concerning whether variable-damping knee prostheses provide a significant advantage over mechanically passive devices specifically at comfortable, self-selected walking speeds. In this investigation, we address this question by comprehensively comparing two distinct variable-damping knee devices, the Otto Bock C-leg and the Òssur Rheo, with the mechanically passive Mauch SNS. We hypothesize that variable-damping devices offer an improved metabolic economy of gait compared with mechanically passive designs. Although we find a 2% decrease in metabolic rate for the variable-damping C-leg compared with the mechanically passive Mauch, the difference is not statistically significant ($P = 0.250$). However, we do find that when using the variable-damping Rheo, energy expenditure decreases by 5% as compared with the Mauch ($P = 0.009$). We further hypothesize that the distinct torque-producing strategies of the investigated knees, hydraulic vs. magnetorheological, result in differences in metabolic gait economy. Our metabolic results support this hypothesis. When
using the magnetorheological-based Rheo, metabolic rate decreases by 5% compared with the hydraulic-based Mauch ($P = 0.009$) and by 3% compared with the hydraulic-based C-leg (trend; $P = 0.092$).

Additionally, we hypothesize that gait biomechanics are significantly different between variable-damping and mechanically passive prostheses and between hydraulic and magnetorheological-based systems. Our biomechanical results support these hypotheses. We observe several biomechanical advantages for the variable-damping devices compared with the mechanically passive Mauch. These advantages include an enhanced smoothness of gait as indicated by a lower jerk RMS, a decrease in hip work production during stance and swing phases, a lower peak hip flexion moment at terminal stance, and a reduction in peak hip power generation at toe-off. In addition to these biomechanical advantages, the magnetorheological-based Rheo offers an improved prosthetic foot-ground interaction and swing phase hip biomechanics. Compared with the C-leg, the Rheo knee allows for increased prosthetic heel compression, or energy storage, and a reduction in peak hip extension torque during terminal swing.

Finally, we hypothesize that differences in movement and muscle activation patterns associated with the three knees can be captured by means of wearable sensors. Our findings support this hypothesis. For the EMG measures, the magnetorheological-based Rheo is associated with a lower level of muscular activity in the gluteus medius muscle compared with the hydraulic-based knees.

### TABLE 3 Affected-side hip mechanics across the three prosthetic knees

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average Values</th>
<th>$P$ Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak hip angle in terminal stance (degrees)</td>
<td>-9.1  -3.9 -4.6</td>
<td>0.091 0.045 0.077 NS</td>
</tr>
<tr>
<td>Peak hip torque in terminal stance (Nm/kg)</td>
<td>-0.945 -0.801 -0.820</td>
<td>0.043 0.021 0.041 NS</td>
</tr>
<tr>
<td>Peak hip torque in terminal swing (Nm/kg)</td>
<td>0.163 0.163 0.092</td>
<td>&lt;0.001 NS &lt;0.001 &lt;0.001</td>
</tr>
<tr>
<td>Peak hip power in early stance (watts/kg)</td>
<td>0.67 0.76 0.69</td>
<td>NS</td>
</tr>
<tr>
<td>Peak hip power in mid-to-terminal stance (watts/kg)</td>
<td>-0.97 -0.76 -0.67</td>
<td>0.058 0.090 0.022 NS</td>
</tr>
<tr>
<td>Peak hip power about toe-off (watts/kg)</td>
<td>0.81 0.63 0.69</td>
<td>0.015 0.005 0.040 NS</td>
</tr>
<tr>
<td>Negative hip work during stance (joules/kg)</td>
<td>15.8 10.8 10.3</td>
<td>0.006 0.007 0.003 NS</td>
</tr>
<tr>
<td>Negative hip work during swing (joules/kg)</td>
<td>1.8 1.5 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Positive hip work during stance (joules/kg)</td>
<td>9.9 10.0 9.9</td>
<td>NS</td>
</tr>
<tr>
<td>Positive hip work during swing (joules/kg)</td>
<td>4.7 3.9 3.5</td>
<td>0.071 0.095 0.027 NS</td>
</tr>
</tbody>
</table>

Hip angle values are positive for hip flexion and negative for hip extension. Hip torque values are positive for internal hip flexion torque and negative for internal hip extension torque. Hip power values are positive for power generation and negative for power absorption. Torque, power, and work values are normalized by body mass. The average value over eight subjects is shown for each knee. $P$ values are shown when smaller than 10%, that is, when a trend was identified. Otherwise the differences were considered not significant (NS). $P$ values smaller than 5% are in bold type.

### TABLE 4 Affected-side knee mechanics across the three prosthetic knees

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average Values</th>
<th>$P$ Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak knee angle in terminal swing (degrees)</td>
<td>-2.4 2.7 -0.8</td>
<td>0.004 0.001 NS NS 0.017</td>
</tr>
<tr>
<td>Peak knee angular velocity about toe-off (degrees/s)</td>
<td>354 353 395</td>
<td>0.001 0.001 NS NS &lt;0.001</td>
</tr>
<tr>
<td>Peak knee torque in early stance (Nm/kg)</td>
<td>-0.015 0.003 -0.021</td>
<td>NS</td>
</tr>
<tr>
<td>Peak knee torque in mid-to-terminal stance (Nm/kg)</td>
<td>-0.539 -0.427 -0.565</td>
<td>0.031 0.037 NS 0.014</td>
</tr>
<tr>
<td>Peak knee torque about toe-off (Nm/kg)</td>
<td>0.127 0.093 0.076</td>
<td>0.005 0.023 0.002 NS</td>
</tr>
<tr>
<td>Peak knee torque in terminal swing (Nm/kg)</td>
<td>-0.122 -0.125 -0.097</td>
<td>0.003 NS 0.004 0.002</td>
</tr>
<tr>
<td>Peak knee power about toe-off (watts/kg)</td>
<td>-0.72 -0.51 -0.45</td>
<td>0.001 0.004 &lt;0.001 NS</td>
</tr>
</tbody>
</table>

Knee angle values are positive for knee flexion and negative for knee (hyper-)extension. Knee torque values are positive for internal knee extension torque and negative for internal knee flexion torque. Knee power values are positive for power generation and negative for power absorption. Torque, power, and work values are normalized by body mass. The average value over eight subjects is shown for each knee. $P$ values are shown when smaller than 10%, that is, when a trend was identified. Otherwise the differences were considered not significant (NS). $P$ values smaller than 5% are in bold type.
the C-leg and the Mauch. The analysis of accelerometer data show significant differences among the three knees tested about toe-off and terminal swing. The variable-damping knees generally show lower jerk values about toe-off compared with the mechanically passive Mauch, indicating a smoother transition for the variable-damping devices from stance to swing. Further, the variable-damping knees generally show lower jerk values during terminal swing compared with the Mauch, indicating a smoother transition from swing to stance.

The results of this study indicate that variable-damping knee prostheses have significant advantages over mechanically passive designs for unilateral transfemoral amputees walking at self-selected ambulatory speeds. Moreover, the study results suggest that a magnetorheological-based system may have advantages over hydraulic-based designs. In the following sections, we discuss various biomechanical mechanisms for the observed metabolic differences between the three knee prostheses.

Biomechanical Mechanisms for Metabolic Cost Differences: Rheo vs. Mauch

By actively modulating knee joint damping, the Rheo offers increased stance stability compared with the mechanically passive Mauch. Consequently, since the Mauch is mechanically passive and cannot actively modulate joint damping, the knee is typically aligned anteriorly (i.e., the ground reaction force is anterior to the knee center of rotation when the subject is in a quiet stance position) so as to limit the tendency of the knee to flex at heel strike when weight is applied to the prosthesis. In distinction, the Rheo knee is typically aligned in a neutral or posterior manner, and early stance stability is then achieved by increasing knee joint damping. Although the anterior alignment makes the Mauch knee more stable during early stance, that alignment makes rapid knee flexion during preswing more difficult compared with the posteriorly aligned, variable-damping Rheo prosthesis.

Numerous biomechanical differences were observed from the analysis of the laboratory data that seem to be related to the different prosthetic

### TABLE 5

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average Values</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mauch</td>
<td>Cleg</td>
<td>Rheo</td>
</tr>
<tr>
<td>Peak ankle angle in early stance (degrees)</td>
<td>−9.6</td>
<td>−6.2</td>
</tr>
<tr>
<td>Peak ankle angle in mid-to-terminal stance (degrees)</td>
<td>6.1</td>
<td>9.8</td>
</tr>
<tr>
<td>Peak ankle torque about 30% of gait cycle (Nm/kg)</td>
<td>0.701</td>
<td>0.978</td>
</tr>
<tr>
<td>Peak ankle power in mid-stance (watts/kg)</td>
<td>−0.84</td>
<td>−0.79</td>
</tr>
<tr>
<td>Foot compression in early stance (mm)</td>
<td>23.8</td>
<td>17.1</td>
</tr>
</tbody>
</table>

Ankle angle values are positive for ankle dorsiflexion and negative for ankle plantar flexion. Ankle torque values are positive for internal ankle plantar flexion torque and negative for internal ankle dorsiflexion torque. Ankle power values are positive for power generation and negative for power absorption. Torque, power, and work values are normalized by body mass. The average value over eight subjects is shown for each knee. P values are shown when smaller than 10%, that is, when a trend was identified. Otherwise the differences were considered not significant (NS). P values smaller than 5% are in bold type.

### TABLE 6

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Average Values</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mauch</td>
<td>Cleg</td>
<td>Rheo</td>
</tr>
<tr>
<td>Gluteus maximus (RMS, μV)</td>
<td>38.8</td>
<td>56.4</td>
</tr>
<tr>
<td>Gluteus medius (RMS, μV)</td>
<td>54.5</td>
<td>55.7</td>
</tr>
</tbody>
</table>

The average value over eight subjects is shown for each knee. P values are shown when smaller than 10%, that is, when a trend was identified. Otherwise the differences were considered not significant (NS). P values smaller than 5% are in bold type.

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alignment and damping control strategies of the Rheo and Mauch knee prostheses. When subjects wore the Mauch, they utilized a hip control strategy marked by exaggerated hip movement components compared with the Rheo as shown by larger peak hip torque during terminal stance, peak hip power during mid-to-terminal stance, peak hip power about toe-off, and negative hip work during stance. In addition, a trend was observed indicating a larger peak hip extension angle during terminal stance for the Mauch compared with the Rheo. Still further, the larger peak knee moment and peak knee power absorption about toe-off found for the Mauch compared with the Rheo seems to reflect the relative ease of rotation during preswing for the Rheo.

In addition to differences during the stance period of walking, biomechanical observations between the two knees suggested that the Rheo required less effort during the swing phase compared with the Mauch. A significantly larger peak hip flexion moment during terminal swing and a greater swing phase positive work production was found for the Mauch compared with the Rheo. This seems to point to an exaggerated hip control needed when subjects wore the Mauch compared with Rheo. Also, a larger peak knee moment during terminal swing was found for the Mauch compared with the Rheo, further suggesting that the Rheo required less effort during the swing phase of walking.

The wearable sensors employed in the study seem to have captured at least some aspects of the aforementioned differences between the Mauch and Rheo knees. A larger RMS value marked the EMG recordings from the gluteus medius muscle when subjects wore the Mauch compared with the Rheo. Additionally, accelerometer data from the affected shank captured the ease of initiating swing for the Rheo knee compared with the Mauch. The observed difference in rate of oxygen uptake corresponds to about 20% of the difference between above-knee amputees and healthy adults. Thus, the Rheo knee prosthesis fills in a significant percentage of the gap between the Mauch prosthetic knee and the one expected for a control group of healthy adults. Based on this observation, we think that it is reasonable to hypothesize that the Rheo prosthetic knee has a significant impact on mobility in above-knee amputees compared with the Mauch prosthetic knee. Future studies performed in the field (i.e., the home and the community settings) by relying on wearable technology seem to be the most appropriate way to investigate this hypothesis.

### Biomechanical Mechanisms for Metabolic Cost Differences: Rheo vs. C-leg

Both the Rheo and C-leg are variable-damping prosthetic knees and thus provide stability during early stance. Due to their posterior alignment, the variable-damping Rheo and C-leg do not require the use of an exaggerated hip strategy to facilitate swing leg smoothness for the Rheo compared with the Mauch. The RMS value of jerk about terminal swing was significantly larger for the Mauch compared with the Rheo.

These biomechanical differences observed in the laboratory setting via analysis of data gathered using a video camera–based system, as well as wearable sensors, seem to account for the differences in metabolic cost between the Mauch and Rheo knee prostheses. It is worth emphasizing that an average difference of 5% in the rate of oxygen uptake was demonstrated, thus suggesting that the combination of variable-damping and magnetorheological technologies leads to a significant advantage over mechanically passive, hydraulic-based knees. The observed difference in rate of oxygen uptake corresponds to about 20% of the difference between above-knee amputees and healthy adults. Therefore, the Rheo knee prosthesis fills in a significant percentage of the gap between the Mauch prosthetic knee and the one expected for a control group of healthy adults.

### TABLE 7 Root-mean-square jerk parameters derived from accelerometer data for the affected thigh and shank

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average Values</th>
<th>P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMS of thigh jerk about toe-off (m/s³)</td>
<td>Mauch: 2.358</td>
<td>Cleg: 2.154</td>
</tr>
<tr>
<td>RMS of shank jerk about toe-off (m/s³)</td>
<td>Mauch: 1.962</td>
<td>Cleg: 1.541</td>
</tr>
<tr>
<td>RMS of thigh jerk in terminal swing (m/s³)</td>
<td>Mauch: 3.340</td>
<td>Cleg: 1.769</td>
</tr>
<tr>
<td>RMS of shank jerk in terminal swing (m/s³)</td>
<td>Mauch: 2.886</td>
<td>Cleg: 2.231</td>
</tr>
</tbody>
</table>

The average value over eight subjects is shown for each knee. P values are shown when smaller than 10%, that is, when a trend was identified. Otherwise the differences were considered not significant (NS). P values smaller than 5% are in bold type.
knee flexion during preswing as observed with the anteriorly aligned Mauch knee. However, differences do exist between these two knee prostheses. The Rheo and C-leg are distinct in their torque producing strategies, or magnetorheological vs. hydraulic, respectively. In addition, the knees are distinct in their peak extension angle. Upon full extension, the C-leg assumes a slightly flexed knee posture whereas the Rheo is set at zero flexion (see Table 4). The different torque producing strategies seem to influence hip behavior during swing. The Rheo knee is marked by a smaller peak hip moment during terminal swing and a lower gluteus medius muscle activity compared with the C-leg, suggesting an easier swing control for the Rheo. Still further, the fact that the C-leg knee is set in slight flexion seems to influence prosthetic foot-ground interactions during early stance. We find that the C-leg has a significantly smaller heel compression, or prosthetic foot energy storage, compared with the Rheo. The results of this study suggest that differences in hip swing phase behavior and prosthetic foot energy storage are contributing factors for the observed difference in walking metabolism between the Rheo and C-leg knee prostheses.

Concluding Remarks

The results of this study indicate that variable-damping knee prostheses have significant advantages over mechanically passive designs for unilateral transfemoral amputees walking at self-selected speeds. For the investigated variable-damping devices, the Rheo and C-leg knee prostheses, we observe biomechanical advantages over the mechanically passive Mauch. These advantages include an enhanced smoothness of gait, a decrease in hip work, a lower peak hip flexion moment at terminal stance, and a reduction in peak hip power generation at toe-off. The study results further suggest that the magnetorheological-based Rheo may have advantages over the hydraulic-based C-leg. When using the Rheo, metabolic rate decreases by 5% compared with the Mauch and by 3% compared with the C-leg. In distinction, when using the C-leg, metabolic rate decreases by 2% compared with the Mauch but the difference is not statistically significant. We consider these differences to be clinically relevant and anticipate a significant impact of such differences on mobility. It is our hope that this work will lead to further studies linking prosthetic design to clinical outcomes, resulting in an even wider range of locomotory performance advantages for contemporary prostheses.

ACKNOWLEDGMENTS

We would like to thank the following individuals for their contribution to the study: Matthew Lazzara, Roberto Reif, Melvin Meister, and Ugo Della Croce. A special recognition goes to Bob Emerson (Next Step Orthotics and Prosthetics, Manchester, NH), who performed all the procedures for the fitting and alignment of the prostheses. Last but not least, we would like to thank the subjects who participated in the research. Their dedication and generosity in volunteering their time to advance the field of prosthetics via objective assessment of different prosthetic technologies is very much appreciated.

REFERENCES

18. Flynn K, Alligood E: Computerized lower limb prostheses. VA Technology Assessment Program Short Report; 2000, pp. 1–11
Perceived Barriers to Exercise in People with Spinal Cord Injury

ABSTRACT


Objective: To identify barriers to physical fitness faced by individuals with spinal cord injury preventing them from participating in a physical fitness program.

Design: In this cross-sectional study, a survey of barriers to exercise was administered to 72 individuals with spinal cord injury.

Results: Although 73.6% of the participants expressed an interest in an exercise program, less than half (45.8%) were currently active in an exercise program. Less than half (47.2%) reported that their physician had recommended an exercise program for them. The most frequently cited concerns about barriers to exercise fell into three areas: (1) intrapersonal or intrinsic (e.g., lack of motivation, lack of energy, lack of interest), (2) resources (e.g., cost of an exercise program, not knowing where to exercise), and (3) structural or architectural (e.g., accessibility of facilities and knowledgeable instructors). More individuals with tetraplegia reported concerns over exercise being too difficult and that health concerns kept them from exercising. Greater number of concerns was significantly related to higher levels of perceived stress.

Conclusions: People with spinal cord injury face multiple barriers to physical fitness in functional, psychological, and architectural domains. Identification of these barriers can facilitate the participation of individuals with spinal cord injury in an exercise program, improving long-term health and wellness.

Key Words: Spinal Cord Injury, Exercise, Physical Fitness, Rehabilitation
As both the number of people and life expectancy increase for people with spinal cord injuries (SCIs), many health concerns related to aging start to play a significant role in their overall health. Estimates for the incidence of new SCI remain approximately 11,000/yr, and the prevalence is approximately 230,000 and growing. Although still below that of the general population, improved emergent and long-term management techniques have increased life expectancies after SCI. Accordingly, mitigating the effects of aging with lifestyle changes have become more prominent.

Rimmer suggests that health promotion for those with disabilities, including those with SCI, has historically been directed at primary prevention of disability rather than prevention of secondary conditions; however, the benefits of exercise in improving outcomes after SCI are increasingly recognized. Exercise has been shown to improve functional capacity, bone density in upper limbs, endurance, muscle strength, pain, and psychological well-being and to reduce stress. Despite these numerous benefits, there are physiologic, psychological, and environmental barriers to exercise that can impede participation in exercise after SCI, thereby increasing health risks associated with inactivity and a sedentary lifestyle.

Cardiovascular health also is a major concern after SCI, despite increased life expectancies. Heart disease has been found to be one of the leading causes or contributing factor to deaths among people with SCI. Carbohydrate metabolism and percentage of body fat are adversely affected by lack of physical fitness and contribute to accelerated cardiovascular disease in the SCI population. For example, Bauman and Spungen found that among their sample of individuals with SCI, 22% had diabetes vs. 6% of the able-bodied controls, and another 34% had glucose intolerance, a prediabetic condition, compared with 12% of the control group.

In addition to the effects of a sedentary lifestyle on glucose metabolism, cardiovascular physiology also has been shown to deteriorate after SCI. Although low-density lipoprotein levels are comparable in individuals with SCI vs. the nondisabled population, high-density lipoprotein levels, believed to decrease risk of cardiovascular disease, are lower in individuals with SCI. Obesity also is a major contributor to altered lipid profiles and carbohydrate metabolism. In general, people with SCI have lower metabolic demands and thus decreased energy expenditure. As a consequence, excessive weight gain is not uncommon, with increased percentages of body fat and decreased lean body mass, all of which are exacerbated by a sedentary lifestyle.

Despite the salutary effects of exercise on the overall health of those with SCI, there are physical and psychological barriers preventing them from participating in a fitness program and reaping its benefits. Much of the literature discussing barriers to physical activity is aimed toward adults with disabilities. Healthy People 2010 outlined that individuals with disabilities were more likely to encounter problematic barriers than the nondisabled population (55% vs. 43%). Recently, Rimmer et al. conducted focus groups in ten regions of the United States to identify barriers and facilitators of physical activities among people with disabilities. Focus group participants consisted of people with disabilities, architects, fitness/recreation professionals, and city planners and park district managers. Participants were instructed to address access issues related to fitness centers, swimming pools, parks, and trails. Factors such as the natural and built environment, economic, emotional and psychological, equipment suitability, perceptions and attitudes toward disability, and availability of resources were some of the themes identified.

Barriers other than the physical also exist. Health professionals often focus on a person’s disability vs. the individual as one who needs counseling on appropriate benefits of a healthy lifestyle. Many may think that because their doctors are not encouraging them to participate in fitness programs that they may not benefit. This may also affect the emotional well-being of the individual. Putnam et al. reported that physical activity was a crucial component to the overall well-being and that barriers to physical fitness affected the mental and physical states of those with disabilities.

Identification of barriers to exercise among individuals with SCI is the first step to reducing such barriers to facilitate participation in exercise and improve health outcomes. The primary purpose of this study was to describe perceived barriers to exercise in a sample of individuals with SCI who participated in a Wellness with SCI educational program at a large Midwestern university medical center. In addition, differences in perceived exercise barriers between those with paraplegia vs. tetraplegia and the relationship between barriers to exercise and perceived stress were explored.

**METHODS**

**Sample**

Subjects were recruited for participation in a randomized, controlled trial to test the efficacy of a Wellness with SCI intervention. A total of 717 individuals were drawn from the University of Michigan Model SCI Care System database, the Ann Arbor Center for Independent Living, University of Michigan Physical Medicine and Rehabilita-
A total of 98 subjects expressed interest in participating in the study, and 84 were admitted; 72 subjects completed the prestudy survey, which included information about their experience of barriers to exercise.

Inclusion criteria included: (1) diagnosis of SCI with neurologic level of injury at C5 and below, (2) age between 18–80 yrs, and (3) ≥1 yr postinjury. Exclusion criteria included: (1) any medical conditions that would impose a significant health risk to participation in the study (e.g., heart condition), (2) cognitive dysfunction that would limit ability to complete written surveys or participate in workshops, or (3) a primary disability unrelated to SCI. Selected characteristics of subjects are given in Table 1.

### Measures

A comprehensive survey composed of standardized measures and individual items was used in the Wellness with SCI intervention and completed by these subjects at baseline. The survey covered a variety of topics related to health behavior, health, and well-being. Selected standardized measures and demographic information drawn from this survey were analyzed for this current study.

#### Level of Injury

Neurologic classification of SCI was ascertained by a physical examination using the International Standards for Neurological and Functional Classification of Spinal Cord Injury.24 Subjects were classified by level of injury (tetraplegia vs. paraplegia), completeness of injury (complete vs. incomplete), and those who were ambulatory.

#### Barriers to Exercise

The Barriers to Physical Exercise and Disability was developed by Rimmer et al.25 to gather information about barriers individuals with disabilities experienced in regard to exercise. The Barriers to Physical Exercise and Disability consists of a total of 34 items. Fourteen items are related to availability of exercise facilities, participation in an exercise program, and financial and transportation resources related to exercise programs. Each item is rated as “yes,” “no,” or “don’t know.” There are another 14 items related to concerns that may limit involvement in exercise, such as cost of an exercise program, lack of motivation or energy, or lack of interest. Each item is rated dichotomously as either “yes” or “no”.

Five open-ended follow-up questions ask respondents to elaborate on affirmative responses to issues such as health problems keeping them from exercising, having been injured while exercising, concerns about exercising at a community facility like the YMCA, and the ability of exercise instructors at such facilities to meet their needs. A final item asks respondents about any additional reasons why they may not be involved in an exercise program or not exercising as much as they would like.

Test-retest reliability and interrater reliability was evaluated by Rimmer et al.25 and found to be within acceptable limits (Cohen’s kappa = 0.76, interrater reliability kappa = 0.86, respectively). Only baseline data are used in this current study, and therefore, test-retest reliability information is not available. However, a concern index was created by summing “yes” responses (scored as a 1) to the 14 Barriers to Physical Exercise and Disability items related to concerns surrounding exercise such that higher scores indicated a greater number of concerns. Internal consistency of this index (Cronbach’s alpha) was 0.70.

### TABLE 1 Demographic characteristics of subjects

<table>
<thead>
<tr>
<th>Demographic Variable</th>
<th>n = 72</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current age, mean (SD)</td>
<td>44.1 (13.0)</td>
</tr>
<tr>
<td>Years since injury, mean (SD)</td>
<td>13.1 (10.6)</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>69.4</td>
</tr>
<tr>
<td>Marital status, %</td>
<td></td>
</tr>
<tr>
<td>Single (never married)</td>
<td>37.5</td>
</tr>
<tr>
<td>Married</td>
<td>47.2</td>
</tr>
<tr>
<td>Divorced</td>
<td>15.3</td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>88.9</td>
</tr>
<tr>
<td>African American</td>
<td>8.3</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1.4</td>
</tr>
<tr>
<td>Education, %</td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td>5.6</td>
</tr>
<tr>
<td>High school degree</td>
<td>23.9</td>
</tr>
<tr>
<td>Some college</td>
<td>35.2</td>
</tr>
<tr>
<td>College degree</td>
<td>21.1</td>
</tr>
<tr>
<td>Professional or postgraduate degree</td>
<td>14.1</td>
</tr>
<tr>
<td>Work status, %</td>
<td></td>
</tr>
<tr>
<td>Employed, full-time</td>
<td>25.0</td>
</tr>
<tr>
<td>Employed, part-time</td>
<td>6.9</td>
</tr>
<tr>
<td>Unemployed</td>
<td>25.0</td>
</tr>
<tr>
<td>Retired</td>
<td>22.2</td>
</tr>
<tr>
<td>Homemaker</td>
<td>9.7</td>
</tr>
<tr>
<td>Student</td>
<td>8.3</td>
</tr>
<tr>
<td>Volunteer/other</td>
<td>2.8</td>
</tr>
<tr>
<td>Neurological classification of injury, %</td>
<td></td>
</tr>
<tr>
<td>Paraplegic, complete</td>
<td>36.1</td>
</tr>
<tr>
<td>Paraplegic, incomplete</td>
<td>11.1</td>
</tr>
<tr>
<td>Tetraplegic, complete</td>
<td>19.4</td>
</tr>
<tr>
<td>Tetraplegic, incomplete</td>
<td>16.7</td>
</tr>
<tr>
<td>Ambulatory</td>
<td>16.7</td>
</tr>
</tbody>
</table>
Perceived Stress

The Perceived Stress Scale\(^{26}\) is the most widely used measure of the degree to which situations in one's life are appraised as stressful. Items were designed to tap into how unpredictable, uncontrollable, and overloaded respondents find their lives. A total of 14 items are rated on a Likert scale ranging from 0 (never) to 4 (very often) using a 1-mo time frame. Scores range from 0 to 56 such that higher scores indicate higher levels of perceived stress. Internal consistency has been reported as 0.85;\(^{26}\) in the current study, internal consistency was 0.86.

Analysis

All statistical analyses were performed using SPSS 12.0 (SPSS, Chicago, IL). Data from the Barriers to Physical Exercise and Disability were analyzed using descriptive and summary statistics. Bivariate correlations (Pearson’s $r$) were used to assess relationships between continuous variables. $\chi^2$ analysis was used to ascertain significant differences between groups (i.e., paraplegia vs. tetraplegia or exercisers vs. nonexercisers) on categorical variables and independent $t$ tests were used to compare groups on continuous variables.

RESULTS

Description of Perceived Barriers to Exercise

As shown in Table 2, although the majority of the subjects (73.6%) in this sample indicated they would like to be involved in an exercise program and thought an exercise program would help them (79.2%), less than half (45.8%) were currently involved in one. Approximately half of the sample reported being told by their doctor to exercise and had participated in an exercise program before. A relative minority had been injured from exercising (22.2%) and had health problems that caused them to stop exercising (37.5%). Barriers such as transportation, availability of facilities and financial resources for transportation and joining a program, or fear of leaving home were least problematic for this sample.

Examination of open-ended responses indicated that those who said they had health problems causing them to stop exercising cited pain and fractures most often; four respondents cited their SCI itself as the reason. For those who were injured exercising, pulled muscles and strains were cited most often. For those respondents who indicated facilities as a perceived barrier, accessibility, privacy, and discomfort being watched by others were cited as potential problems.

Concerns about Exercise

The top concerns about exercise were lack of motivation, lack of energy, cost of an exercise program, not knowing where to exercise, and lack of interest. Although respondents did not indicate paying for transportation as a barrier, 40% did indicate the cost of a program was a concern.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Perceived barriers to exercise (values are percentages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barriers</td>
<td>Yes</td>
</tr>
<tr>
<td>If a fitness center was in your area, would you have a means of transportation?</td>
<td>93.0</td>
</tr>
<tr>
<td>Do you feel an exercise program could help you?</td>
<td>79.2</td>
</tr>
<tr>
<td>Would you like to begin an exercise program?</td>
<td>73.6</td>
</tr>
<tr>
<td>If you had to pay for transportation, would you be willing to spend that amount of money?</td>
<td>73.6</td>
</tr>
<tr>
<td>If you had to pay for transportation, could you afford to spend that amount of money?</td>
<td>70.8</td>
</tr>
<tr>
<td>Do you know a fitness center you could get to?</td>
<td>66.7</td>
</tr>
<tr>
<td>Have you ever participated in an exercise program?</td>
<td>51.4</td>
</tr>
<tr>
<td>Do you feel that an exercise instructor at a center like a YMCA would know how to set up an exercise program to meet your needs?</td>
<td>48.6</td>
</tr>
<tr>
<td>Has your doctor ever told you to exercise?</td>
<td>47.2</td>
</tr>
<tr>
<td>Do you currently exercise?</td>
<td>45.8</td>
</tr>
<tr>
<td>Did you ever have any health problems that caused you to stop exercising?</td>
<td>37.5</td>
</tr>
<tr>
<td>Would you have any concerns about exercising in a facility like a YMCA?</td>
<td>31.9</td>
</tr>
<tr>
<td>Have you ever gotten injured from exercising?</td>
<td>22.2</td>
</tr>
<tr>
<td>Would you have to pay to be transported to the exercise facility?</td>
<td>16.7</td>
</tr>
<tr>
<td>Are you ever afraid to leave your home?</td>
<td>6.9</td>
</tr>
</tbody>
</table>
Approximately a third of respondents indicated that exercise was boring, that they were too lazy, and that they did not know how to exercise. Far fewer respondents indicated concerns about whether exercise would worsen their condition, that exercise would not improve their condition, or that they had health conditions that would prevent them from exercising.

Concern Index

The mean score on the concern index was 4.03 (SD = 2.8). Using independent-sample t test, exercisers had a statistically significantly lower concern index than nonexercisers (3.19 vs. 4.72, respectively; \( t = 2.47, P = 0.016 \)). There were no significant differences between nonambulatory tetraplegia (n = 26) and paraplegia (n = 34) groups. Subjects who were ambulatory (n = 12) were excluded from analysis because of sample size.

Relationship between Injury Level and Exercise Participation and Perceived Barriers to Exercise

\( \chi^2 \) analysis was used to compare nonambulatory tetraplegia and paraplegia groups on their current participation in exercise and the 14 items regarding concerns about exercise. Ambulatory subjects were again excluded in this analysis due to sample size. The primary difference between those with tetraplegia and paraplegia was in regard to health problems terminating exercise (39.4% vs. 15.4%, respectively; \( \chi^2 = 4.09, P = 0.043 \)). There also were statistically significant differences between groups in terms of concern over exercise being too difficult (26.9% vs. 5.9%, respectively; \( \chi^2 = 5.12, P = 0.024 \)) and that health concerns prevented them from exercising (38.5% vs. 14.7%, respectively; \( \chi^2 = 4.43, P = 0.035 \)). All other comparisons were nonsignificant. Frequencies of affirmative responses to each of the 14 concerns for all three groups are given in Table 3.

Relationship of Barriers to Exercise and Stress

The mean Perceived Stress Scale score was 31.26 (SD = 6.0). There was a statistically significant correlation between perceived stress and the concern index, such that a greater number of concerns over exercise was associated with higher perceived stress (\( r = 0.257, P = 0.036 \)), although this was a modest relationship (\( r^2 = 0.06 \)). There were no differences in perceived stress levels between those who reported currently exercising compared with those who were not.

DISCUSSION

The primary objective of this study was to describe perceived barriers to exercise in a sample of individuals with SCI. In this study, the majority of participants indicated they would like to be participating in some type of exercise program; however, less than half of them were currently doing so. No single perceived barrier stood out as being most problematic. In fact, factors such as transportation (i.e., availability and cost), which are commonly cited in the literature as one of the most persistent barriers facing people with disabilities and access to the community, did not seem to be highly problematic for this sample. This may be explained by living in a relatively affluent region with many community resources. In comparison, in the study by Rimmer et al.25 in which the Barriers to Physical Exercise and Disability was first developed, the SCI sample of African American

| Concerns about exercise\(^a\) (values are percentages) |
|-----------------|-----------------|-----------------|-----------------|
| Concerns        | Total Group     | Tetraplegia     | Paraplegia      | Ambulatory      |
| Lack of motivation | 54.2            | 57.7            | 50.0            | 58.3            |
| Lack of energy  | 41.7            | 42.3            | 41.2            | 41.7            |
| Cost of exercise program | 40.3 | 50.0 | 35.3 | 33.3 |
| Do not know where to exercise | 36.1 | 42.3 | 41.2 | 8.3 |
| Lack of interest | 33.3            | 32.0            | 35.3            | 33.3            |
| Lack of time    | 31.9            | 30.8            | 35.3            | 25.0            |
| Exercise is boring | 31.9 | 23.1 | 35.3 | 41.7 |
| Too lazy        | 31.9            | 23.1            | 32.4            | 50.0            |
| Do not know how to exercise | 27.8 | 23.1 | 38.2 | 8.3 |
| Health conditions prevent exercising | 25.0 | 38.5\(^b\) | 14.7\(^b\) | 25.0 |
| Exercise will make condition worse | 16.7 | 23.1 | 8.8 | 25.0 |
| Exercise will not improve condition | 15.3 | 12.0 | 14.7 | 25.0 |
| Exercise is too difficult | 15.3 | 26.9\(^b\) | 5.9\(^b\) | 16.7 |
| Lack of transportation | 8.3            | 11.5            | 5.9             | 8.3             |

\( \chi^2 \) analysis was used to compare nonambulatory tetraplegia and paraplegia groups on their current participation in exercise and the 14 items regarding concerns about exercise. Ambulatory subjects were again excluded in this analysis due to sample size. The primary difference between those with tetraplegia and paraplegia was in regard to health problems terminating exercise (39.4% vs. 15.4%, respectively; \( \chi^2 = 4.09, P = 0.043 \)). There also were statistically significant differences between groups in terms of concern over exercise being too difficult (26.9% vs. 5.9%, respectively; \( \chi^2 = 5.12, P = 0.024 \)) and that health concerns prevented them from exercising (38.5% vs. 14.7%, respectively; \( \chi^2 = 4.43, P = 0.035 \)). All other comparisons were nonsignificant. Frequencies of affirmative responses to each of the 14 concerns for all three groups are given in Table 3.

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women living in inner-city Chicago indicated greater fear about leaving home (39% vs. 6.9%), cost of an exercise program (84% vs. 40%), and a lack of transportation (61% vs. 8.3%). In addition, the need for the participants to attend several workshops for their participation in the Wellness with SCI study required transportation, possibly eliminating several people who did not have readily available transportation from enrolling in the study.

Less than half of the sample indicated their physicians had recommended exercise to them; however, these rates are generally commensurate with national estimates. Glasgow et al.27 examined physician advice and support for physical activity in a diverse national sample and found that 28% reporting having received physical advice to increase their activity level. Using information gathered by the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey, a modest ascending trend in rates of diet and physical activity counseling for at-risk adults was found, but these rates were still below expectations, with <45% of visits including diet counseling and <30% including physical activity counseling.28 Several investigators suggest that primary care physicians have the influence to improve the participation, duration, and confidence in a physical fitness programs.27,29–31 As physiatrists and other rehabilitation-related healthcare workers are often integrally involved in the everyday lives of those with SCI, they have a tremendous opportunity to intervene and counsel on the benefits and importance of physical fitness.

In regard to other barriers to exercise, participants expressed concern over a lack of experience among fitness center staff to meet their needs. Poor accessibility, lack of privacy, fear of injury, and public exposure were other concerns identified by the study sample. Although this study did not verify the existence of these perceived barriers, these findings are generally consistent with other studies examining barriers to exercise for people with disabilities. For example, Cardinal et al.32 identified that fitness facilities in general are accessible, but only 8% provided adequate accessibility to and around the actual exercise equipment. Participants also expressed concern over a lack of experience among fitness center staff to meet their needs and concern about poor accessibility, lack of privacy, fear of injury, and public exposure. It is not surprising that the vast majority of fitness center staff members would not have experience working with people with SCI.

Despite the numerous benefits afforded by regular exercise, particularly in light of a narrower margin of health among individuals with SCI, the desire to exercise does not often match the actual behavior. This is true of the general population, with motivation as a ubiquitous barrier to exercise.25 Kinne et al.33 found that motivation barriers and exercise self-efficacy were more powerful predictors of exercise maintenance among people with mobility impairments than demographic or disability-related characteristics and environmental barriers. Directly addressing motivation and barriers in the environment in facilitating exercise among individuals with SCI is an important consideration.

In this study, significantly more individuals with tetraplegia indicated that exercise was too difficult and that health concerns prevented them from exercising, concomitant with the greater architectural barriers they face in accessing exercise programs. However, there is literature to suggest that although individuals with paraplegia have a greater advantage in this regard, they do not necessarily avail themselves of it. For example, Nash and Hortorff28 assert that that those with paraplegia, despite their functional capacity to exercise, are only marginally more fit compared with those with tetraplegia, suggesting more than accessibility itself influences participation in exercise programs after SCI. Nevertheless, this does not diminish the importance of increasing accessibility to exercise programs for people facing substantial physical limitations associated with tetraplegia.

Options for exercise and SCI include neuromuscular electrical stimulation, which has been quite promising for therapeutic exercise for those with substantial functional limitations. The use of neuromuscular electrical stimulation in the lower limbs has been shown to increase many cardiovascular variables, including oxygen uptake, submaximal heart rate, and aerobic capacity.34 Numerous other exercise and recreational programs (e.g., handcycling, swimming, and tennis) also are becoming more available to those with SCI.34 These new advances will require specialized centers to provide the proper equipment and the knowledgeable personnel to make sure each program is safe and appropriate for the individual.

The relationship between number of concerns about exercise and perceived stress was statistically significant, albeit modestly. The direction of this relationship cannot be determined from these data. However, it is likely to be bi-directional in nature. For example, concern over exercise may be part of a larger set of concerns in regard to health and well-being, which in turn increase stress levels. Perceived stress levels may exacerbate concerns regarding exercise such that they are out of proportion to what are realistic concerns for an individual.

Encouraging fitness facilities to comply with American Disabilities Act standards for accessibility is crucial to reversing some of the types of con-
cerns expressed among individuals in this sample. Individual rehabilitation centers also can provide information to their patients on facilities that are able to accommodate their needs. In addition, fitness instructors need to be well trained and comfortable in assisting people with SCI in their fitness programs, which will take the efforts of specialists in SCI to provide such training. Specifically, instructors should be aware of both functional limitations of those with SCI and the potential to develop secondary conditions (e.g., pressure ulcers, autonomic dysreflexia, and overuse injuries).

Limitations

There are several limitations to this study that should be taken into account when considering its results. This study involved a relatively small sample size, although of average size compared with other SCI studies. Furthermore, individuals in this study lived in a generally affluent area of Michigan and had at their disposal more resources for transportation than would individuals living in larger urban areas with concomitant higher rates of poverty and crime, both of which adversely affect access to the community. This was highlighted in comparisons between this sample and the African American women who lived in inner city Chicago in the study by Rimmer et al.25. Further limiting generalizability is that this sample was predominately white and relatively well educated. The context in which these data were collected also is an important consideration. Participants were involved in a study evaluating the efficacy of a wellness program. As such, they were already likely to have stronger interest in exercise and wellness in general and therefore may not represent the larger SCI population.

Finally, it is important to emphasize that barriers identified by participants in this study were perceived rather than objectively measured, as no corroborating information was gathered to verify these perceptions. Future studies may examine the gap between perception of barriers and their actual presence for the individual.

CONCLUSIONS

In conclusion, as more emphasis is being placed on the health and wellness of a growing and aging population with SCI, exercise has been demonstrated to be a crucial part of this undertaking. This study has identified several perceived barriers to exercise in those with SCI that can minimize their effects on health and wellness. Future research is needed to further explore these perceived and identified barriers and to identify those strategies that will mitigate the negative effects of these barriers on the health of individuals with SCI and encourage physicians to work with their patients in reducing such barriers to optimize health and well-being.

ACKNOWLEDGMENT

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REFERENCES

17. Okuma H, Ogata H, Hatada K: Transition of physical fitness...
in wheelchair marathon competitors over several years. 

Paraplegia 1989;27:237–43


Transcutaneous Electrical Nerve Stimulation Versus Baclofen in Spasticity: Clinical and Electrophysiologic Comparison

ABSTRACT


Objectives: Clinical and electrophysiologic comparison of the efficacy of transcutaneous electrical nerve stimulation (TENS) and oral baclofen in the treatment of spasticity.

Design: Patients with spinal cord injury and spasticity were included in the study. Ten patients were assigned to oral baclofen and 11 to TENS groups. For the comparison of H-reflex variables, 20 healthy individuals were allocated to a control group. TENS was applied to the tibial nerve for 15 days at a frequency of 100 Hz. Clinical (spasm frequency scale, painful spasm scale, lower limb Ashworth score, clonus score, deep tendon reflex score, plantar stimulation response score) and electrophysiologic evaluations (H-reflex response at the highest amplitude, latency of maximum H-reflex, and ratio of H-reflex response at the highest amplitude to M response at maximum amplitude) of the lower limb and functional evaluations (functional disability score and FIM™) were carried out in baclofen and TENS groups before and after treatment. Posttreatment evaluation was made 24 hrs after the 15th session in the TENS group. In addition, clinical spasticity scores and electrophysiologic variables were measured 15 mins after the first application and 15 mins after the 15th session.

Results: Significant improvement was detected in lower limb Ashworth score, spasm frequency scale, deep tendon reflex score, functional disability score, and FIM in the baclofen (P = 0.011, P = 0.014, P = 0.025, P = 0.004, and P = 0.005, respectively) and TENS (P = 0.020, P = 0.014, P = 0.025, P = 0.003, and P = 0.003, respectively) group after treatment. Decrease in H-reflex maximum amplitude was significant in the TENS group (P = 0.026). Most marked improvement was observed in the third evaluation, 15 mins after the 15th session, particularly in lower limb Ashworth score (P = 0.006) and H-reflex maximum amplitude (P = 0.006) in the TENS group. The percentage change in clinical, electrophysiologic, and functional variables caused by baclofen was not different from that caused by repeated applications of TENS in the short- and long-term evaluations (P > 0.05).

Conclusion: TENS may be recommended as a supplement to medical treatment in the management of spasticity.

Key Words: Spinal Cord Injury, Spasticity, Baclofen, Transcutaneous Electrical Nerve Stimulation
The definition of spasticity according to the literature is as follows: (1) increased muscle tone, (2) increased tendon reflexes, (3) increased exteroceptive reflexes, and (4) pathologic radiologic reflexes. Its prevalence has been reported to be 12–37% in patients with spinal cord injury (SCI). When spasticity exceeds a certain degree, it becomes a difficult problem that should be dealt with by a neurological rehabilitation team. In spasticity treatment, the factors increasing spasticity should be eliminated first. Physical methods and medical treatment are the second step. One of the basic drugs used in the treatment of spasticity is baclofen, which is bound to γ-aminobutyric acid B receptors in the brain and neurons and acts on the terminals of primary efferents at the spinal level. In the therapeutic range, the presynaptic effects of baclofen suppress release of excitatory transmitters for both monosynaptic and polysynaptic pathways. Therefore, baclofen is frequently preferred, especially in the medical treatment of spasticity of spinal origin.

Physical treatment modalities that have been used in spastic hypertonia are, particularly, superficial heat and cold, diathermies, electrical stimulation, implanted spinal stimulation, and massage. The duration of the effects of most physical therapies is relatively short, which often may limit their application to immediate prestretch or pre-exercise periods. In the literature, the investigations on the effect of electric stimulation on spasticity report variable results. Some authors have reported that electrical stimulation decreases spasticity. However, stimulation patterns, application methods, measurement techniques, and the timing of the evaluation are quite variable. Among these, in studies investigating the short-term effects (<1 hr) after a single session in which high-frequency electrical stimulation is preferred, decrease in spasticity has been reported in clinical measurements. In some studies, it has been established that the improvement in spasticity was maintained through repeated applications of high-frequency electrical stimulation. At present, transcutaneous electrical nerve stimulation (TENS) is not used commonly in the treatment of spasticity. To our knowledge, there is no study comparing the efficacy of TENS in spasticity with drug treatment. However, TENS is a noninvasive and readily applicable method that has few side effects and no drug interactions, no potential toxicity, can be applied by the patient, and is less costly in the long term compared with drug treatment. Baclofen and similar drugs have limited efficacy in muscle relaxation and have side effects such as muscle weakness. Thus, if adequate improvement in spasticity is obtained with TENS, it may be used, per se, as an alternative to medical treatment or as an adjunct to it.

This study had two aims, namely, (1) determining the short- and long-term efficacy of TENS after repeated applications in patients with SCI on spasticity by means of clinical, electrophysiologic, and functional variables, and (2) comparing the short- and long-term efficacy of TENS with baclofen treatment.

**METHODS**

**Subjects**

A total of 21 adult patients with traumatic SCI and problematic spasticity, defined as being painful or restricting activities of daily life, or both, who were admitted to the Ankara Physical Medicine and Rehabilitation Center for rehabilitation between January 2000 and February 2001 were included in the study. Those with complications that can cause spasticity to increase (heterotopic ossification, urinary infection, pressure ulcer), those with systemic diseases that can cause peripheral neuropathy, or those diagnosed with lumbosacral radiculopathy, impairment in liver and kidney functions, and obesity were excluded from the study. Patients who had undergone any treatment for spasticity previously were not included in the study. The information about the patients and their clinical characteristics according to American Spinal Injury Association classification were recorded. Laboratory investigations, including liver and kidney function tests, complete blood count, and creatine clearance, were repeated every 2 wks throughout baclofen administration. To interpret the effect of treatments on electrophysiologic variables better, 20 volunteers matched for age were chosen as the control group for electrophysiologic evaluations. A control group comprised volunteering, healthy hospital staff and people accompanying patients. All procedures were approved by the Human Studies Research Committee of the Ankara Rehabilitation Center, and written informed consent was obtained from each subject before inclusion in the study. The patients were randomized into treatment groups considering the duration required for evaluation. Accordingly, the first ten patients were included in the baclofen treatment group and the second 11 patients in the TENS treatment group. All patients were inpatients and concomitantly received exercise therapy, including range of motion, every morning.

**Interventions**

The major goals of the treatments were to improve the signs of problematic spasticity (i.e., increased muscle tone, clonus, and the flexor spasm) in patients with SCI to a reasonable level.
Baclofen Administration

In the baclofen treatment group, the dose was increased by 5 mg every 3 or 5 days, considering the tolerance of the patient, until adequate clinical response was obtained or a maximum 80 mg/day was reached. The individual daily doses varied according to the patient’s tolerance and were divided into three oral doses. After 8 wks, posttreatment evaluation was made. All the patients in the baclofen treatment group were asked for side effects, including sedation, drowsiness, dizziness, nausea, dry mouth, fatigue, and muscle weakness. Neurological examination was performed on all the patients weekly.

TENS Application

In the TENS treatment group, the TENS System 2000 TENS device was used. Stimulation were provided with carbon electrodes and conducting gel on bilateral tibial nerves in a manner that would involve the gastrocnemius muscle. Biphasic square waves at the intensity of 50 mA, which would not cause contractions, were used at a frequency of 100 Hz and duration of 100 msecs. Treatment was organized as 15 sessions lasting for 15 mins and applied once a day.

Outcome Assessments

Clinical evaluations of spasticity were conducted by a physiatrist, and the electrophysiologic investigations were carried out by another physiatrist. They were not blinded to the interventions, but they were blinded to the evaluation results of each others. Outcome assessments of all patients were performed almost 8 hrs after the exercise therapy.

Clinical Assessment of Spasticity

Clinical evaluation of spasticity was carried out according by both self-reporting of the patient (self-report scores) and the examination of physiatrist (clinical examination scores). In the evaluation of self-report, the spasm frequency scale (SFS) modified from Penn and painful spasm scale were used. With SFS, the emergence pattern of spasm in the day and its frequency were inquired and evaluated on a scale ranging from 0 to 4 (0, no spasms; 4, spontaneous spasms occurring more than ten times per hour). To what degree spasms cause pain and disturbance was determined on a scale ranging from 0 to 2 (0, causes no discomfort or pain; 2, causes severe discomfort or severe pain) by painful spasm scale.

Clinical assessments of spasticity included examination of lower limb muscle tone, deep tendon reflex of Achilles, ankle clonus, and plantar stimulation. The lower limb overall muscle tone was calculated as follows: the muscle tone of the extensor and flexor muscles at the hip, knee, and ankle joints of the nondominant side were examined using the Ashworth score (0, no increase in tone; 4, limb rigid), and a total Ashworth score of those six muscle groups, described as the lower limb Ashworth score, with a maximum score of 24, was obtained. In the ankle, clonus score was evaluated between 0 and 3 (0, absent; 3, spontaneous/ provoked by light touch); in the Achilles, deep tendon reflex score was evaluated between 0 and 4 (0, no reflex; 4, very brisk, hyperactive, associated with clonus); and in the sole, plantar stimulation response score was evaluated between 0 and 3 (0, no visible activity/flexor response; 4, movement elicited by light touch). For the evaluation of disability related to functional status of the patients, the functional disability score, which evaluates pain, spasms, sitting position, body transfer, washing, and putting on clothes, which had an overall score of 20 and was developed for lower limbs, was employed as a global functional evaluation score. In addition, mobility, self-care, communication, and social and cognitive functions of patients were evaluated by FIM™, the scores of which ranged from 18 to 126.

Electrophysiologic Assessment of Spasticity

Electrophysiologic investigations included H-reflex variables of the nondominant lower limb, and the Medelec-MS92 electromyographic device (Medelec, London, UK) was used. Stimulation and recording was carried out with surface electrodes, at the range of 20 Hz to 10 KHz. Silver electrodes, 1 cm in diameter, were used for recording. Measurements were made at room temperatures of 20–22 degrees centigrade and with skin temperature around 31 degrees centigrade, with the patient in the prone position and with the feet suspended over the edge of the table. For the evaluation of H-reflex and M responses in the gastrocnemius muscle, the stimulating electrode was placed just medial to the midpoint of the knee crease in the popliteal fossa (the active stimulating electrode is proximally located), and the recording electrode was placed halfway between the popliteal crease and the proximal medial malleolus over the medial gastrocnemius. The ground electrode was connected between the active and passive electrodes. For stimulation, rectangular flow at the frequency of 0.5 Hz and duration of 0.5–1.0 msecs was used. Sweep speed of 10 msecs and sensitivity of 500 μV was chosen. First, M response at maximum amplitude (M_max) and then H-reflex response at the highest amplitude (H_max) was recorded by changing the intensity of stimulation without moving the stimulator. The latencies were measured from the stimulus onset to the beginning of the
initial deflection of compound motor action potential, and amplitude was measured from peak to peak. Afterward, $H_{\text{max}}/M_{\text{max}}$ (H/M) amplitude ratios were calculated.

Clinical, electrophysiologic, and functional evaluations were made before and after treatment in the baclofen group. In the TENS group, four evaluations were made, namely: a first evaluation before treatment (IE), a second evaluation 15 mins after the first session to determine the short-term effect after a single session (IIE), a third evaluation 15 mins after the 15th session to determine the short-term effect after repeated application (IIIE), and a fourth evaluation 24 hrs after the 15th session to determine the long-term effect after repeated application (IVE). IVE was defined as the posttreatment evaluation in the TENS group. Evaluations of functional status and evaluations of self-report were made only in IE and IVE.

**Statistical Analysis**

In the statistical analysis of the data, the SPSS for Windows 10.0 package program was used (SPSS, Chicago, IL). Descriptive statistical variables were calculated to document the characteristics of patients and controls. Comparison of age and time after injury between treatment groups was performed by using the Mann-Whitney $U$ test. Comparison of age between treatment and control groups was performed by using the Kruskal-Wallis test. Wilcoxon’s signed-ranks test was used in the comparison of before- and after-treatment values in the baclofen and TENS groups; in the comparison between both treatment groups and the control group and in the comparison of percentage change caused by both treatments, the Mann-Whitney $U$ test was used. A $P$ value of <0.05 was considered significant. In investigation of clinical examination scores and of H-reflex variables repeated multiple measurements in the TENS group, Friedman’s test and, afterward, Wilcoxon’s signed-ranks test were used. Because three pairs of comparisons were studied, with Bonferroni adjustment, the error rate allowed in each significance testing was 0.016 (i.e., 0.05 divided by 3).

**RESULTS**

**Descriptive Data**

The descriptive characteristics of patients in treatment groups are shown in Table 1. The baclofen group consisted of ten female patients with traumatic SCI. Of those, three had tetraplegia with cervical injury and seven had paraplegia with thoracic injury. The mean age of the baclofen group was 32.70 ± 16.30 yrs, and the time postinjury was 11.47 ± 11.70 mos, with a range of 4 – 44 mos. The TENS group consisted of 11 patients (five women, six men) with traumatic SCI. Of those, two had tetraplegia with the cervical injury and nine had paraplegia with thoracic injury. The mean age of the TENS group was 29.27 ± 7.33 yrs, and the time postinjury was 11.48 ± 13.92 mos, with a range of 2 – 49 mos. There was no statistically significant difference between the two treatment groups in terms of mean age and time postinjury ($P > 0.05$).

In the baclofen group, it was required to increase the dosage to maximum in all of the patients. Side effects due to baclofen included dryness of mouth in three patients and fatigue in two patients. In weekly routine neurological examination, weakness of muscles was not seen.

The control group consisted of 20 subjects (8 women, 12 men), with a mean age of 33.90 ± 11.44 yrs. There was no statistically significant difference

<table>
<thead>
<tr>
<th>TABLE 1 Characteristics of patients with spinal cord injury</th>
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<tr>
<td><strong>Baclofen Group</strong></td>
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<td><strong>TENS Group</strong></td>
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<td><strong>n = 10</strong></td>
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<tr>
<td>Sex</td>
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TENS, transcutaneous electrical nerve stimulation; ASIA, American Spinal Injury Association.
between the mean age of the control group and those of the treatment groups ($P > 0.05$).

### Clinical Indicators of Spasticity

Values of clinical findings of spasticity and functional status scales in both treatment groups before and after treatment are illustrated in Table 2. In both treatment groups, improvement was observed in SFS, lower limb Ashworth score, deep tendon reflex score, and functional status scales after treatment ($P < 0.05$). In repeated measurements of the TENS treatment group, comparison of the clinical examination scores of spasticity are shown in Table 3. When the short-term effect of TENS after a single session (IIE), short-term effect after 15 sessions (IIIE), and long-term effect (IVE) on clinical examination scores of spasticity were compared, the most pronounced change was observed in IIIE, especially in lower limb Ashworth score, and the least change was observed in IIE.

### Electrophysiologic Indicators of Spasticity

Baclofen treatment achieved a decrease in $H_{\text{max}}$ amplitude and $H/M$ amplitude ratios that was not statistically significant. The comparison of the electrophysiologic values obtained before and after baclofen treatment with each other and with the control group is given in Table 4. TENS reduced $H_{\text{max}}$ amplitude significantly. The comparison of the electrophysiologic values obtained before and after TENS treatment with each other and with the control group is given in Table 5.

When the effect of TENS on electrophysiologic variables in the IIE, IIIE, and IVE evaluations were compared with each other, the most prominent change was observed in IIIE, especially in $H_{\text{max}}$ amplitude ($P < 0.01$), and the least change was observed in IIE. In repeated measurements of the TENS treatment group, comparison of the electrophysiologic variables are shown in Table 6.

The percentage change in clinical, electrophysiologic, and functional variables caused by baclofen was not found to be different from that caused by repeated applications of TENS in short- and long-term evaluations ($P > 0.05$) (Table 7).

### DISCUSSION

There are many studies in the literature on baclofen treatment employed commonly in the treatment of spasticity. Duncan et al.\(^{18}\) established that in patients with chronic SCI, baclofen treatment decreased the frequency of involuntary flexor or extensor spasms and improved the increased resistance of leg to passive movements, but it did not influence gait, stretch reflex, or clonus. Milanov\(^{4}\) reported that in poststroke hemiplegic patients, baclofen treatment reduced increased muscle tension, depressed Babinski sign, and had no effect on muscle strength, ankle clonus, and deep tendon hyperreflexes. Nielsen and Sinkaer\(^{21}\) reported that in multiple sclerosis patients with spasticity, oral baclofen administration decreased ankle tension by 20%. In the present study, in the group administered baclofen, when spasticity was evaluated clinically, significant improvements in SFS, lower limb Ashworth score, and deep tendon reflex score were observed. In addition, there were significant improvements in FIM and functional disability scores, which evaluated functional status. Our findings have demonstrated that baclofen decreased spasticity in patients with SCI and were

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**TABLE 2** Comparison of self-report scores, clinical examination scores, and functional status scales of spasticity pretreatment and posttreatment in baclofen and transcutaneous electrical nerve stimulation (TENS) groups

<table>
<thead>
<tr>
<th></th>
<th>Baclofen Treatment</th>
<th>TENS Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (n = 10)</td>
<td>Post (n = 10)</td>
</tr>
<tr>
<td>SRS</td>
<td>3.3 ± 0.9</td>
<td>2.3 ± 0.3</td>
</tr>
<tr>
<td>PSS</td>
<td>1.2 ± 0.9</td>
<td>1.1 ± 0.9</td>
</tr>
<tr>
<td>CES</td>
<td>19.2 ± 3.7</td>
<td>14.4 ± 6.4</td>
</tr>
<tr>
<td>LLAS</td>
<td>2.3 ± 1</td>
<td>1.9 ± 0.9</td>
</tr>
<tr>
<td>CS</td>
<td>3.8 ± 0.4</td>
<td>3.3 ± 0.6</td>
</tr>
<tr>
<td>DTRS</td>
<td>2.2 ± 0.9</td>
<td>1.9 ± 0.7</td>
</tr>
<tr>
<td>PSRS</td>
<td>11.4 ± 2.2</td>
<td>8.5 ± 2.4</td>
</tr>
<tr>
<td>FDS</td>
<td>67 ± 11.6</td>
<td>75.7 ± 12.6</td>
</tr>
</tbody>
</table>

SRS, self-report scores; SFS, spasm frequency scale; PSS, painful spasm scale; CES, clinical examination scores; LLAS, lower limb Ashworth score; CS, clonus score; DTRS, deep tendon reflex score; PSRS, plantar stimulation response score; FSS, functional status scores; FDS, functional disability score.

*Data are expressed as mean ± SD; level of significance set at $P < 0.05$, Wilcoxon’s signed-ranks test, with bold type indicating significance.*
found to be congruent with other studies reporting that baclofen reduced clinical spasticity, particularly flexor spasms. Although baclofen has a favorable effect on spasticity, it has some side effects. In the present study, no major side effect requiring the study to be discontinued was observed.

To determine the role of TENS in the treatment of spasticity, short- and long-term effects of TENS should be known. Studies in the literature on application of TENS mostly evaluate the short-term activity after a single session. Bajd et al. established that there was a decrease in spasticity after a 20-min, single session of TENS (100 Hz, 0.3-msec pulse duration, 50 mA) administered on L3-L4 dermatomes. Hui-Chan et al. determined a reduction in clinical spasticity score in the dermatome measurements they made at 20, 40, and 60

#### TABLE 3 Comparison of the clinical examination scores of spasticity in repeated measurements of the transcutaneous electrical nerve stimulation treatment group

<table>
<thead>
<tr>
<th>IE (n = 11)</th>
<th>IIE (n = 11)</th>
<th>IIE (n = 11)</th>
<th>IVE (n = 11)</th>
<th>P Value</th>
<th>P Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CES</td>
<td>LLAS</td>
<td>PSRS</td>
<td>DTRS</td>
<td>Pre-Post</td>
<td>Pre-Post</td>
<td>Pre-Post</td>
</tr>
<tr>
<td>20.1 ± 4</td>
<td>17.4 ± 1.8</td>
<td>13.6 ± 3.8</td>
<td>16.3 ± 2.8</td>
<td>0.059</td>
<td>0.006</td>
<td>0.020</td>
</tr>
<tr>
<td>CS</td>
<td>2.6 ± 1</td>
<td>2.2 ± 0.9</td>
<td>2.3 ± 0.6</td>
<td>2.1 ± 0.8</td>
<td>0.046</td>
<td>0.257</td>
</tr>
<tr>
<td>DTRS</td>
<td>3.6 ± 0.5</td>
<td>3.3 ± 0.5</td>
<td>3 ± 0.7</td>
<td>3.1 ± 0.4</td>
<td>0.083</td>
<td>0.020</td>
</tr>
<tr>
<td>PSRS</td>
<td>2.6 ± 0.8</td>
<td>2.5 ± 0.5</td>
<td>2 ± 0.8</td>
<td>2.2 ± 0.4</td>
<td>0.564</td>
<td>0.034</td>
</tr>
</tbody>
</table>

IE, evaluation before treatment; IIE, evaluation 15 mins after first application; IIE, evaluation 15 mins after 15th session; IVE, evaluation 24 hrs after 15th session; CES, clinical examination scores; LLAS, lower limb Asworth score; CS, clonus score; DTRS, deep tendon reflex score; PSRS, plantar stimulation response score.

Data are expressed as mean ± SD; bold type indicates statistical significance.

Level of significance set at $P < 0.01$, Wilcoxon signed-ranks test with Bonferroni adjustment.

#### TABLE 4 Comparison of the electrophysiologic values obtained before and after baclofen treatment with each other and with the control group

<table>
<thead>
<tr>
<th>Control (n = 20)</th>
<th>Before Baclofen (n = 10)</th>
<th>After Baclofen (n = 10)</th>
<th>P Value$^a$</th>
<th>P Value$^a$</th>
<th>P Value$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_{max}^a$, mV</td>
<td>3.7 ± 2.7</td>
<td>5.5 ± 3.6</td>
<td>4.3 ± 2.9</td>
<td>0.048</td>
<td>0.322</td>
</tr>
<tr>
<td>H$_{max}^a$, latency, msecs</td>
<td>29.6 ± 1.9</td>
<td>30.7 ± 2.4</td>
<td>31.1 ± 2.6</td>
<td>0.217</td>
<td>0.117</td>
</tr>
<tr>
<td>H/M</td>
<td>0.1 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>0.4 ± 0.3</td>
<td>0.001</td>
<td>0.009</td>
</tr>
</tbody>
</table>

C-Pre, control–before treatment; C-Post, control–after treatment; Pre-Post, before treatment–after treatment; H$_{max}^a$, H-reflex response at the highest amplitude; H$_{max}^a$, latency of maximum H-reflex; H/M, ratio of H-reflex response at the highest amplitude to M response at maximum amplitude.

Data are expressed as mean ± SD; level of significance set at $P < 0.05$, with bold type indicating statistical significance.

$^a$ Mann-Whitney $U$ test.

$^b$ Wilcoxon’s signed-ranks test.

#### TABLE 5 Comparison of the electrophysiologic values obtained before and after transcutaneous electrical nerve stimulation (TENS) treatment with each other and with the control group

<table>
<thead>
<tr>
<th>Control (n = 20)</th>
<th>Before TENS (n = 11)</th>
<th>After TENS (n = 11)</th>
<th>P Value$^a$</th>
<th>P Value$^a$</th>
<th>P Value$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_{max}^a$, mV</td>
<td>3.7 ± 2.7</td>
<td>3.1 ± 2.7</td>
<td>2.3 ± 2.3</td>
<td>0.322</td>
<td>0.032</td>
</tr>
<tr>
<td>H$_{max}^a$, latency, msecs</td>
<td>29.6 ± 1.9</td>
<td>30.4 ± 2.5</td>
<td>30.2 ± 3.2</td>
<td>0.331</td>
<td>0.142</td>
</tr>
<tr>
<td>H/M</td>
<td>0.1 ± 0.2</td>
<td>0.4 ± 0.7</td>
<td>0.4 ± 1</td>
<td>0.186</td>
<td>0.773</td>
</tr>
</tbody>
</table>

C-Pre, control–before treatment; C-Post, control–after treatment; Pre-Post, before treatment–after treatment; H$_{max}^a$, H-reflex response at the highest amplitude; H$_{max}^a$, latency of maximum H-reflex; H/M, ratio of H-reflex response at the highest amplitude to M response at maximum amplitude.

Data are expressed as mean ± SD; level of significance set at $P < 0.05$, with bold type indicating statistical significance.

$^a$ Mann-Whitney $U$ test.

$^b$ Wilcoxon’s signed-ranks test.
mins after a single session of TENS (99 Hz, 0.125-
msec pulse duration; 2× sensory threshold) lasting
for 45 mins and administered on the median and
common peroneal nerves in patients with spastic
hemiparesis. Han et al.12 administered low-
and high-frequency TENS for 30 mins once a day to the
acupuncture points on the feet and hands of pa-
tients with muscle spasticity of spinal origin and
reported a reduction in spasticity in <30 mins in
the group administered high-frequency (100 Hz,
0.3-msec pulse duration, 0–50 mA). Yu11 has pro-
posed that high-frequency electrical stimulation to
the acupuncture points in the treatment of spinal
spasticity immediately exerted an antispastic effect,
which could be maintained for 3 mos with daily
administration. Potisk et al.13 reported that appli-
cation of TENS at 100 Hz for 20 mins on the sural
nerve in hemiplegic individuals reduced clinical
spasticity in the short term and inhibited stretch-
reflex excitability. Goulet et al.14 reported that
when TENS (99 Hz, 250-msec pulse duration, 15
mA) was applied to the common peroneal nerve in
patients with SCI for 30 mins, the evaluations at 10
and 30 mins later demonstrated reduction in Achil-
les tendon reflex and modified Ashworth scores.
Wang et al.15 established that sensory stimulation
to T12-L1 spinal muscles for 45 mins at 250 Hz
lowered spasticity in hemiplegic patients. In the
present study, at IIE, which evaluated short-term
effect 15 mins after a single session, a decrease was
observed in all measurements in clinical examina-
tion scores compared with pretreatment values.

### Table 6: Comparison of electrophysiologic variables in repeated measurements of the transcutaneous electrical nerve stimulation treatment group

<table>
<thead>
<tr>
<th></th>
<th>IE (n = 11)</th>
<th>IIE (n = 11)</th>
<th>IIIE (n = 11)</th>
<th>IVE (n = 11)</th>
<th>P Value I–II</th>
<th>P Value I–III</th>
<th>P Value I–IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hmaxamp, mV</td>
<td>3.1 ± 2.7</td>
<td>2.4 ± 2.1</td>
<td>2.1 ± 2.5</td>
<td>2.3 ± 2.3</td>
<td>0.021</td>
<td>0.006</td>
<td>0.026</td>
</tr>
<tr>
<td>Hmaxlat, msecs</td>
<td>30.4 ± 2.5</td>
<td>31.2 ± 2.8</td>
<td>30.5 ± 3.4</td>
<td>30.2 ± 3.2</td>
<td>0.086</td>
<td>0.878</td>
<td>0.876</td>
</tr>
<tr>
<td>H/M</td>
<td>0.4 ± 0.7</td>
<td>0.3 ± 0.5</td>
<td>0.3 ± 0.8</td>
<td>0.4 ± 1</td>
<td>0.021</td>
<td>0.155</td>
<td>0.328</td>
</tr>
</tbody>
</table>

IE, evaluation before treatment; IIE, evaluation 15 mins after first application; IIIE, evaluation 15 mins after 15th session; IVE, evaluation 24 hrs after 15th session; Hmaxamp, H-reflex response at the highest amplitude; Hmaxlat, latency of maximum H-reflex; H/M, ratio of H-reflex response at the highest amplitude to M response at maximum amplitude.

Data are expressed as mean ± SD; level of significance set at *P* < 0.01 (with bold type indicating statistical significance), Wilcoxon’s signed-ranks test with Bonferroni adjustment.

### Table 7: Comparison of percentage changes in outcome measurements of spasticity obtained by baclofen and transcutaneous electrical nerve stimulation (TENS) treatments

<table>
<thead>
<tr>
<th></th>
<th>Baclofen (n = 10)</th>
<th>TENS (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Post</td>
<td>IE–IIE</td>
</tr>
<tr>
<td>SFS</td>
<td>-28 ± 30</td>
<td>NE</td>
</tr>
<tr>
<td>PSS</td>
<td>-10 ± 32</td>
<td>NE</td>
</tr>
<tr>
<td>FDS</td>
<td>-26 ± 12</td>
<td>NE</td>
</tr>
<tr>
<td>PIM&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>13 ± 6</td>
<td>NE</td>
</tr>
<tr>
<td>LLAS</td>
<td>-28 ± 22</td>
<td>-32 ± 19</td>
</tr>
<tr>
<td>CS</td>
<td>-14 ± 50</td>
<td>0 ± 38</td>
</tr>
<tr>
<td>DTRS</td>
<td>-13 ± 14</td>
<td>-17 ± 18</td>
</tr>
<tr>
<td>PSRS</td>
<td>-10 ± 16</td>
<td>-19 ± 24</td>
</tr>
<tr>
<td>Hmaxamp, mV</td>
<td>-15 ± 46</td>
<td>-30 ± 33</td>
</tr>
<tr>
<td>Hmaxlat, msecs</td>
<td>2 ± 6</td>
<td>0 ± 9</td>
</tr>
<tr>
<td>H/M</td>
<td>-11 ± 48</td>
<td>-29 ± 40</td>
</tr>
</tbody>
</table>

IE, evaluation before treatment; IIE, evaluation 15 mins after 15th session; IVE, evaluation 24 hrs after 15th session; SFS, spasm frequency scale; NE, not evaluated; PSS, painful spasm scale; FDS, functional disability score; LLAS, lower limb Ashworth score; CS, clonus score; DTRS, deep tendon reflex score; PSRS, plantar stimulation response score; Hmaxamp, H-reflex response at the highest amplitude; Hmaxlat, latency of maximum H-reflex; H/M, ratio of H-reflex response at the highest amplitude to M response at maximum amplitude.

Data are expressed as mean ± SD; level of significance set at *P* < 0.05, Mann-Whitney *U* test.

<sup>a</sup> Comparison of percentage change in clinical examination and electrophysiologic outcome measurements of baclofen before and after treatment and TENS IE–IIE.

<sup>b</sup> Comparison of percentage change in all outcome measurements of baclofen before and after treatment and TENS IE–IVE.
However, the difference was not statistically significant. Our findings were not consistent with those of studies\(^7,10,12-15\) reporting that high-frequency, single-session TENS improves clinical variables in the short term. It is reported that the longer the duration of TENS, the longer its effects last.\(^10\) The fact that the difference obtained in our study was not significant, unlike other studies, may be attributed to the short duration of TENS in our study (15 mins vs. 30–45 mins). In addition, a low number of cases, differences of stimulation variables, and evaluation methods may be other factors influencing treatment outcome.

In the literature, there are studies reporting that the decrease brought about by electric stimulation is not maintained in the long term (up to 24 hrs).\(^6,7\) However, Han et al.\(^12\) in their study investigating long-term effect after repeated application, reported that the decrease in spasticity they obtained in the short term continued for 18 hrs after the last session—they applied TENS for 30 mins, twice a day, for 3 mos. In the present study, no significant change was observed in any clinical examination score after a single-session TENS application. However, after repeated applications of TENS, significant decrease was observed in lower limb Ashworth and deep tendon reflex scores in short-term measurements. These results suggest that repeated applications in TENS treatment increase short-term efficacy. There were significant improvements in SFS, functional disability score, and FIM at IVE; these variables were evaluated only in IE and IVE. Although improvement in all clinical examination scores was observed in repeated measures in IVE when compared with IIE, there was no significant difference in any score after Bonferroni adjustment \(P > 0.016\). Increasing the duration and frequency of daily sessions may cause a significant increase in long-term efficacy, which is a postulate that should be investigated in another study.

In both treatment groups, the improvement in FIM and functional disability scores may be considered as a sign of the favorable developments in the clinical symptoms of spasticity. However, the improvements observed in both treatment groups could not be attributed to only the particular effect of those treatments because all patients also received exercise therapy concomitantly. This condition may be considered as a limitation of this study.

The influence of treatment method on spinal neurone and segmental reflexes is mostly evaluated by electrophysiologic methods.\(^1,25\) It is known that many mechanisms play a role in the development of spasticity. Among these, primary and secondary increases in alpha motor neurone activity are the most implicated, and it is considered that H-reflex and F-wave variables represent these mechanisms in electrophysiology.\(^25,26\)

In a study evaluating the efficacy of baclofen electrophysiologically, it has been reported that baclofen reduced the H/M ratio.\(^27\) In the present study as well, in the baclofen treatment group, H\(_{\text{max}}\) amplitude values and H/M ratio was significantly higher compared with the control group; after treatment, no difference was observed with the control group in terms of H\(_{\text{max}}\) amplitude values. Although there was a decrease in H/M amplitude ratios compared with pretreatment values, it was not significant.

The results obtained in studies investigating the efficacy of TENS electrophysiology are controversial. In patient groups with spasticity, after a single-session, high-frequency TENS application, in the short term, Goulet et al.\(^14\) reported that H\(_{\text{max}}\) amplitude and H/M amplitude ratios remained unchanged, Hui-Chan et al.\(^10\) reported that H\(_{\text{max}}\) latency was sustained and H/M amplitude ratios remained the same, and Joodaki et al.\(^28\) reported that H\(_{\text{max}}\) amplitude, H/M amplitude ratio, and F-wave/M-response amplitude ratio decreased. Levin and Hui-Chan\(^9\) reported that they did not find any change in H/M amplitude ratios after repeated TENS application. In the present study, there was significant reduction in H\(_{\text{max}}\) amplitude in measurements after treatment compared with pretreatment values. When repeated measurements were compared with each other, the most significant decrease was in the short-term evaluation (IIIE) after repeated measurements. H/M ratio decreased in all measurements, even if not significantly.

In both treatment methods, the improvement in electrophysiologic measurements was less marked than that obtained clinically. Although it is thought that a single mechanism may be adequate for the development of spasticity, it is also regarded that two or more of these mechanisms are observed in spasticity.\(^25,26\) H-reflex variables represent limited neural physiologic mechanisms of spasticity. Clinical scales may be considered a general reflection of these mechanisms. Hence, a complete correspondence between clinical expression of spasticity and individual electrophysiologic variables cannot be expected. Actually, most of the studies evaluating clinical expression of spasticity could not find a correlation between clinical expression and electrophysiologic variables.\(^3,14,26,29\) So, it should not be considered surprising that alterations in electrophysiologic variables that evaluate only alpha motor neurone activity were not as substantial as those in clinical variables.

The effect of TENS was observed most markedly in the short-term evaluation after repeated applications. Although this effect lessened 24 hrs after the last application, it was still maintained. The effect obtained in the short and long term after repeated applications was not different from that obtained with baclofen.
There were some other limitations in this study such that only electrophysiologic evaluation was used as the objective outcome assessment method. In addition, the validity of clinical tests used in this study may be a concern of limitation. Although the Ashworth scale is used widely and is validated, other clinical tests may be poor for validity, except for SFS. Another limitation was the lack of blinding of physiatrists to the interventions due to the frequent repeated measurements in the TENS treatment group.

In conclusion, TENS may be recommended as an adjuvant treatment before stretch and range of motion exercises and in periods before sleep when an increase in hyperreflex activity is observed. In addition, due to its effect in the long term after repeated applications, it may be used as a supplement to medical treatment in spasticity.

In current literature, it is reported that the chosen frequency and intensity in electrical stimulation exerts different effects in different regions of the nervous system through different receptors. Therefore, it is our proposition that further studies using different stimulation variables or daily stimulation periods, or both, are warranted to determine if the short-term effect of repeated TENS application can be maintained in the long term.

REFERENCES

Referred Pain Pattern of the Abductor Pollicis Longus Muscle

ABSTRACT

Objective: To determine the referred pain pattern of the abductor pollicis longus muscle.

Design: Intramuscular hypertonic saline was injected into the abductor pollicis longus of 15 healthy adults to induce muscle pain. Subjects completed pain drawings depicting the pain distribution. The drawings were transferred into the Pain Chart System for analysis.

Results: Referred pain distributions were as follows: the radial aspect of the wrist (61.9%), the dorsal aspects of the third and fourth fingers (14.3%), and a combination of the two distribution patterns (23.8%).

Conclusion: Referred pain patterns of the abductor pollicis longus resemble the C6, 7, and 8 dermatomes, the superficial radial sensory nerve distribution, and are very similar to the area of pain experienced in de Quervain’s tenosynovitis. Thus, identification of the abductor pollicis longus trigger point should be considered in pain of the radial aspect of the wrist and thumb, especially when no other neurologic abnormalities or inflammatory conditions are present.

Key Words: Abductor Pollicis Longus, Referred Pain, Myofascial Trigger Point, Hypertonic Saline
Myofascial pain syndrome (MPS) is a common disorder that can involve any skeletal muscle in the human body to produce pain and dysfunction. The outstanding feature of MPS is the source of pain, the myofascial trigger point (TrP) and its referred pain. Referred pain is defined as pain that arises in a trigger point but is felt at a distance, often entirely remote from its source.1 The patterns of pain referred from the TrPs in a muscle are reproducible and predictable by either manual compression or needle stimulation.1–3 Knowledge of these patterns is used to locate the muscles most likely to be causing the spontaneous pain. The importance of acknowledging MPS and its referred pain patterns lie in the fact that they produce symptoms very similar to other disorders, such as angina pectoris (pectoralis major), C6 radiculopathy (pectoralis minor), appendicitis (lower rectus abdominis), or epicondylitis (wrist extensors).1

Review of the pain patterns of muscles reveal a tendency of referral to be related to the muscle’s bony attachment sites, even extending beyond the anatomic insertion sites in many cases. Through the pioneering works of Simons et al.1, over 300 referred pain patterns of the more than 100 different skeletal muscles, including those of the head and hand intrinsic muscles, have been described and documented. Although the referred pain patterns of most forearm and hand muscles have been accounted for, there are no published reports of the referred pain pattern of the abductor pollicis longus (APL) muscle. The APL arises from the middle third of the posterior surface of the radius and the lateral part of the posterior surface of the ulna below the anconeus muscle, and it has multiple tendinous insertions in structures around the carpometacarpal joint, including the base of the first metacarpal.4,5 The APL is active in all movements of the thumb, including thumb abduction and pinch grasp,6,7 and thus is susceptible to overload stress, which may lead to MPS.

The objective of this study was to determine the referred pain pattern of the APL muscle and to recognize MPS of the APL as a possible cause of pain in the wrist and hand areas.

METHODS
Subjects
A total of 15 healthy adults with no history of neck or arm pain, upper limb paresthesia, cervical radiculopathy, or physical findings suggestive of MPS in the shoulder or upper limb regions participated in the study. The group consisted of 13 men and two women with an average age of 26.3 yrs (range, 23–45 yrs). All subjects gave written informed consent to participate in the study, which was approved by the local ethics committee.

Muscle Pain
Experimental muscle pain was produced to mimic pain of the myofascial TrP with hypertonic saline injection into the muscle. The subject lied in the supine position with arms to the side and in full pronation so that the palm of the hand was facing downward. A point was marked at the midpoint between the lateral epicondyle and radial styloid process as the site of injection. This point was palpated while the subject actively abduced his or her first metacarpal to confirm muscle contraction of the APL. After skin sterilization, a Teflon-coated syringe electromyography needle was inserted into the marked point and progressed perpendicularly through the extensor digitorum communis muscle into the APL. Needle placement into the APL was confirmed electromyographically by observing the presence and recruitment of motor unit action potentials in response to active abduction of the first metacarpal. Extension of the middle finger was also performed with the needle in place to confirm that it was not placed in the extensor digitorum communis. Caution was taken to avoid neurovascular trauma, which might have induced pain other than muscle pain and have led to contamination of the APL’s pain referral distribution. The subject was instructed to immediately inform the examiner should he or she experience paresthesia or electric sensation during the injection procedure. After electromyographic confirmation of needle placement, the subject relaxed, and 0.3 ml of 6% hypertonic saline solution was slowly injected into the muscle to induce muscle pain. Gentle manual pressure was applied for 10 secs after needle removal for hemostasis. Among the 15 subjects, both arms were injected in six, and only the nondominant arm was injected in nine subjects, for a total of 21 arms included in this study.

Pain Drawing
Immediately after the hypertonic saline injection, the subjects were instructed to draw in the area of pain experienced in a pain diagram. Pain areas were differentially depicted according to the intensity of pain such that areas of more intense pain were shaded in more darkly than the less painful areas. The injected forearm was kept on the level surface during the drawing process so as to prevent any possible effect of gravity on the injected solution.

The subjects’ pain drawings were then transferred into the Pain Chart System (ilisoft, Korea) for analysis. The Pain Chart System is a computer program developed for digital three-dimensional representation of the human body into which areas of pain can be drawn in with a computer mouse.8 It was originally developed to assist general practitioners in locating myofascial TrPs related to the...
areas of pain input into the program. The Pain Chart System also serves as a database for pain drawings in which pain areas can be analyzed or compared according to timed intervals. All pain drawings were transferred into the Pain Chart System by a single researcher (M. Hwang) experienced in using the program, and the most common pain patterns were analyzed by the program.

RESULTS

The main pain referral pattern after intramuscular injection of hypertonic saline into the APL was seen to spread distally to the radial aspect of the wrist. Most intense pain was localized to the area overlying the radial styloid process and anatomic snuffbox (pattern 1). This pattern was observed in 13 out of the 21 arms (61.9%). Of these 13 arms, pain referral to the radial side of the wrist was continuous with the injection site (pattern 1a) in seven arms and discrete to the radial wrist (pattern 1b) in six arms (Figs. 1 and 2). Pain referral from the injection site to the dorsal aspect of the third and fourth fingers (pattern 2) was observed in three arms (14.3%) (Fig. 3A), and a combination of isolated pain patterns to the radial aspect of the wrist and the third and fourth fingers (pattern 3) was found in five arms (23.8%) (Fig. 3B).

In all subjects, pain onset began shortly after needle removal at the injection site, and pain intensity increased with the manual compression. All subjects described the pain as deep aching or throbbing in character, both at the site of injection and at the referred areas. There were no complaints of electric shock–like sensations or involuntary muscle contractions to indicate nerve irritation during or after the injection. Pain symptoms gradually subsided within minutes after the injection, and no adverse effects were noted in any of the subjects.

DISCUSSION

The APL muscle is a long, tendinous muscle located in the deep extensor surface of the forearm. It arises from the middle third of the posterior surface of the radius and the lateral part of the posterior surface of the ulna and is known to have multiple tendinous insertions around the carpometacarpal area of the thumb.⁴ The muscle consists of two heads, each with its own insertion site.⁵ The superficial head inserts into the radial side of the first metacarpal to act as a thumb abductor in conjunction with the abductor pollicis brevis muscle. The deep head tendon inserts into the trapezium or the fascia of the abductor pollicis brevis muscle and mainly functions to stabilize the basal joint of the thumb during its movements.⁵,⁹,¹⁰ Although its main joint action is to abduct the thumb, the APL is active in all actions of the thumb, including key pinch and opposition activities,⁶,⁷ and thus may be susceptible to overload stress. Repetitive activities leading to overload stress of skeletal muscles are known to be the main causative factor in the development of MPS.¹,³ Thus, identification of muscle pain patterns for each individual muscle is crucial for accurate diagnosis and effective treatment. Although the referred pain patterns for myofascial TrPs of most of the forearm muscles have already been elucidated,
to date, there have been no publications on the referred pain pattern originating from the APL.

The most predominant referral pattern of the APL (pattern 1) was in the distribution of the radial aspect of the wrist, extending distally to the metacarpophalangeal joint of the thumb. The most intense pain was described to be located over the radial styloid process at the base of the anatomic snuffbox. This area overlaps the first extensor compartment under the extensor retinaculum through which the APL and extensor pollicis brevis tendons pass. When considering the fact that referred pain from muscular trigger points tend to be closely related to the muscle’s bony attachments, it is quite obvious that pattern 1 follows the direction of the APL muscle and its tendinous insertion. The pain distribution of pattern 1 is also very similar to that of the C6 dermatome, the superficial radial nerve territory, and the area of pain experienced in de Quervain’s tenosynovitis. Patterns 2 and 3 display pain referral to the dorsal aspects of the third and fourth fingers, extending only as far as the proximal interphalangeal joint, which interestingly also coincides with the superficial radial nerve’s sensory territory. These areas also overlap with the C7 (third finger) and C8 (fourth finger) dermatomes. Although there is no definite anatomic correlation between the APL and the referral patterns to the third and fourth fingers, the deep-seated location of the APL in the forearm may be a factor for such findings. Review of referred pain patterns from TrPs of other deep-seated muscles such as the subscapularis, brachialis, and gluteus minimus reveal pain areas distant from the muscle with no definite relationship to their bony attachments.

The referral pain patterns described may assist in diagnosing MPS of the APL in cases of pain symptoms in the C6, 7, or 8 dermatomes or the superficial radial nerve territory that are unaccompanied by motor involvement. Such patterns, pattern 1 in particular, should also be kept in mind for the differential diagnosis of de Quervain’s tenosynovitis. However, it is important to acknowledge that the pain referral patterns of a myofascial TrP are not exclusive to a single muscle and that TrPs in different muscles may have similar referral patterns. For example, pain referral areas similar to pattern 1 of the APL can be found in the brachialis, supinator, brachioradialis, and even the subclavius muscles. The extensor digitorum communis and scalenus minimus muscles have pain referral patterns resembling the APL’s pattern 2. Thus, all possibilities must be considered before a conclusive diagnosis is made. This is especially true when one considers the possibility that the pain referred to muscle may originate from other structures such as articular joints, internal viscera, and even the central nervous system.

Induction of muscle pain with hypertonic saline injection has been studied extensively and is considered to be a safe and valid model of experimental muscle pain with good reproducibility. Intramuscular injection of hypertonic saline produces not only a local area of transient pain similar in quality and intensity to clinical myalgia, but also referred pain as well. The intensity and spatial distribution of such pain are related to the volume of saline injected. Other algogens, including endogenous substances such as substance P, bradykinin, and serotonin and exogenous agents like capsaicin and mustard oil, are also used in experimental muscle pain models. The ready availability, in addition to its safety and effectiveness in pain production, was the main factor for the use of 6% hypertonic saline in this study. The duration of pain after the injection of 0.3 ml was long enough for the subject to describe the pain areas in drawings yet not so long as to cause prolonged discomfort. Pain after intramuscular injection of hypertonic saline resolved completely within a few minutes, with no side effects in any of the subjects tested. Accurate localization for injection into the APL was confirmed by electromyography, and pain induced by the injection was consistent with the characteristics of muscle pain. The injection was performed in the APL deep to the extensor digitorum communis, rather than the more superficial portion in the distal forearm, as it has a greater muscle mass and is more proximal to the muscle’s motor point. Proximity to the motor point is an important factor when one considers the etiologic definition of a central trigger point: a cluster of electrically active loci, each of which is associated with a contraction knot and a dysfunctional motor endplate in skeletal muscle. Injection into the deep portion is also advantageous because there is a lesser possibility of inadvertent trauma to the adjacent extensor tendons and neurovascular structures that might have led to pain that was not purely of muscular origin.

CONCLUSION

The pain referral patterns of the APL muscle can be described as follows: (1) pain in the radial aspect of the wrist, extending to the metacarpophalangeal joint of the thumb; (2) pain in the dorsal aspects of the third and fourth digits; and (3) a combination of the aforementioned patterns. In patients with a clinical history of pain symptoms in such areas as the anatomic snuffbox, the C6, 7, or 8 dermatomes, and superficial radial nerve territories in the absence of other neurologic or active inflammatory findings, MPS of the APL muscle should be included in the differential diagnosis.
REFERENCES


Slowed Conduction Velocity of the Median Sensory Nerve Across the Carpal Tunnel in Normal Adults

ABSTRACT


Objective: To examine the difference of using onset or peak latency in the segmental conduction study of the median nerve in normal adults without carpal tunnel syndrome.

Design: We investigated 60 hands of 30 young healthy adults (15 men and 15 women; mean age, 27.1 yrs; range, 18–36 yrs). We performed the mid-palm segmental conduction study using antidromic and orthodromic techniques in the median sensory nerves of the second and third digits and the onset and peak latencies of the proximal (wrist-palm) and distal (palm-digit) segments were measured. The distoproximal latency ratios were compared between onset and peak latencies and were compared with the ratios of the superficial radial sensory nerve.

Results: Distoproximal peak latency ratios in the median and superficial radial sensory nerves were always >1.0 in both the antidromic and orthodromic conduction studies. However, distoproximal onset latency ratios in the median sensory nerve were >1.0 in only 35% and 21.7% of second digits and in only 25% and 11.7% of third digits in orthodromic and antidromic studies, respectively (P < 0.05). The results of distoproximal onset latency ratios in the superficial radial sensory nerve were 93.3% in the orthodromic study and 86.7% in the antidromic study (P < 0.05).

Conclusion: Prolongation of onset latency across the carpal tunnel during segmental conduction study of the median sensory nerve was common in healthy adults. When comparing proximal and distal segments for diagnosis of carpal tunnel syndrome, using onset latency as a diagnostic variable may cause greater reporting of false positives.

Key Words: Carpal Tunnel Syndrome, Median Nerve, Nerve Conduction, Nerve Fibers, Action Potentials
Carpal tunnel syndrome (CTS) is the most common peripheral mononeuropathy and is the result of structural change in the median nerve caused by the carpal ligament. The largest and fastest conducting fibers are usually affected first in CTS, and electrodiagnostic medicine studies have been found to be highly sensitive and specific for diagnosis of this disease.\(^2-8\) The American Association of Electrodiagnostic Medicine recommends that if median sensory nerve conduction studies across the wrist with a conduction distance of 13–14 cm show abnormal data, then the standard practice should include median nerve conduction studies across the wrist over a short (7–8 cm) conduction distance. Also, comparison of median sensory conduction across the wrist with other sensory nerves in the same limb or comparison of proximal and distal segments of the median nerve in the same limb is recommended.\(^2,3\)

The mid-palmar (7 cm) stimulation technique\(^9\) of the median sensory nerve is well known for diagnosis of CTS. Padua et al.\(^10\) reported a similar simple technique based on evaluation of the ratio of orthodromic median sensory nerve conduction velocity from the third digit to the palm to that of the palm-wrist segment. During this technique, transcarpal conduction time should always be less than the time for the distal segment in normal condition, most likely due to tapering of the axonal diameter.\(^11\) However, this is not universally found for all nerves, and other investigators suggested significantly shorter internodal length without remarkable fiber diameter as a possible cause of slower conduction velocity along the fingers in median and ulnar nerves.\(^12,13\) Under the authors’ observation, slower conduction time in the wrist-to-palm (W-P) segment than palm-to-digit (P-D) segment is common when onset latency is measured. In our search, there were no known reports dealing with our observation and the discrepancy between onset and peak latency measurements in segmental conduction study of the median sensory nerve.

We hypothesized that the conduction time of the median sensory nerve is always faster in the proximal (W-P) segment than distal (P-D) segment, regardless of whether the onset latency or peak latency is used as a variable in healthy adults. We investigated this hypothesis using orthodromic and antidromic techniques in segmental conduction studies of the median sensory nerve.

**MATERIALS AND METHODS**

We examined 60 hands of 30 healthy volunteers (15 men and 15 women) who had no symptoms or signs of neuromuscular disease, no history of trauma of the wrist or hand, and no general metabolic disease. Mean height of subjects was 167.2 cm (men, 173.8 cm; women, 160.5 cm; range, 155–181 cm). We performed motor and sensory examinations, including Phalen’s test and Tinel’s signs to screen for CTS. The study used relatively young subjects (mean age, 27.1 yrs; range, 18–36 yrs), as they have less chance of having asymptomatic CTS. Subjects gave informed consent for the procedures, which were approved by the Health Service Human Research Ethics Committee and Committee on Experimental Procedures Involving Human Subjects of the Asan Medical Center.

The test protocol was designed to compare differences between onset and peak latency measurements using orthodromic and antidromic techniques in median sensory nerves of second and third fingers and to compare the results with another nerve not passing through the carpal tunnel. The segmental conduction studies are presented in Figure 1. The 7-cm mid-palium stimulation technique\(^14\) of the median sensory nerve was performed antidromically, and the sensory nerve action potentials (SNAPs) were obtained from the second and third digits using ring electrodes. An active recording electrode was secured around the proximal phalanx, and an interelectrode separation with the reference electrode was always maintained at 4 cm. Stimulus was delivered supramaximally at the mid-palmar and wrist, 7 cm and 14 cm proximal to the active recording electrode, respectively, and the distances were measured with a caliper. We also performed orthodromic segmental conduction studies, which require the same stimulus intensity compared with antidromic studies. To avoid using a different stimulus intensity during the orthodromic study, we used simultaneous two-channel recording with disk electrodes placed on the mid-palm and wrist. We examined the superficial radial sensory nerve in the same limb, applying the same techniques used for the median sensory nerve, to compare the results of median nerve conduction. In antidromic conduction of the superficial radial sensory nerve, an active recording electrode was positioned around the first metacarpophalangeal joint to maintain an interelectrode separation of 4 cm. The stimulation and recording sites of antidromic conduction were always the recording and stimulation sites of the orthodromic study.

One author (S. Pyun) performed all nerve conduction studies, and another electromyographer measured the variables of the SNAPs. All data were obtained using a Medelec Synergy electromyograph (Medelec, Surrey, England), and the instrument settings were: sensitivity of 20 μV/division, sweep speed of 1 msec/division, and filter settings of 20 Hz to 5 kHz. A supramaximal stimulation of 0.1 msec in duration was delivered to the stimulation site, and the ground electrode was attached between the stimula-
tion and recording sites. During stimulation, hands were placed with the wrist in a neutral position, the digits were relaxed, and anodal rotation was permitted to reduce stimulation artifacts. All SNAPs were recorded after averaging ten times, and the onset and peak latency and the onset to peak amplitude were measured. We measured skin temperature at mid-palm, and it was maintained at >33°C using a hydrocollator pack.

To compare the conduction times between P-D and W-P segments, we calculated the distoproximal ratio (D/P ratio) using the method of Padua et al.,

\[
\frac{L_{P,D}}{L_{W,D}} = \frac{L_{P,D}}{L_{W,D}},
\]

in which \(L_{P,D}\) is the P-D latency and \(L_{W,D}\) is the wrist-to-digit latency.

D/P ratio data were classified into three categories: a ratio of 1 meant the W-P and P-D segment conduction times were the same; a ratio of <1 meant the W-P segment conduction time was slower than that for the P-D segment; and a ratio of >1 meant the W-P segment conduction time was faster than that for the P-D segment. We defined a reversed D/P ratio as when the ratio was ≤1, based on the null hypothesis. Statistical analysis was performed using SPSS+ 10.0 software (SPSS, Chicago, IL). The distributions of D/P ratios according to three categories in individual nerves were assessed using \(\chi^2\) tests. The correlation between latency and age of subjects was assessed using Pearson’s correlation.

RESULTS

We examined onset and peak latency using both the antidromic and orthodromic techniques and found no significant differences between data generated using these two techniques. Amplitudes of median SNAPs were significantly larger for palm stimulation compared with wrist stimulation in the antidromic study and were larger in palm recording compared with wrist recording in the orthodromic study (\(P < 0.05\)). The differences of amplitude ranged from 18% to 24%.

For all hands, the D/P peak latency ratio was always >1 during median and superficial radial nerve sensory conduction studies. However, in the antidromic study, the D/P onset latency ratio was ≤1 (reversed D/P ratio) in 45 hands (75%) in the third digit and in 39 hands (65%) in the second digit, whereas a reversed D/P onset latency ratio was observed in only 4 hands (6.7%) for the superficial radial sensory nerve (\(P < 0.05\)). The orthodromic conduction results were similar to those obtained in the antidromic study (Table 1).

Most onset and peak latencies of median SNAPs in wrist stimulation in the antidromic study and in wrist recording in the orthodromic study showed a positive correlation with age (\(P < 0.05\)). However, these correlations were not clearly observed for latencies of the P-D segment and for the superficial radial nerve (Table 2).

DISCUSSION

In compressive lesions, the large-myelinated and fast-conducting fibers are affected first and to the greatest degree.\textsuperscript{4,14} Numerous techniques \textsuperscript{1,4–6,10,11,15–21} have been developed to increase the sensitivity of testing for CTS, and the results of electrodagnostic
medicine studies show this approach to be highly sensitive and specific, with sensitivities ranging from 49% to 84%, with specificity of ≥93%. Median sensory and mixed nerve conduction studies comparing W-P segment and P-D segment conduction show very high pooled specificity (98%) and relatively good sensitivity (85%). The mid-palm stimulation (7 cm) of the median sensory nerve is very useful in the diagnosis of CTS, and similar techniques measuring the D/P ratio have been reported.2

Recently, onset latency measurement of SNAPs increased in popularity because onset latency reflects the function of the fastest conducting fibers and has relatively even distribution, whereas peak latency has relatively uneven distribution due to temporal dispersion. However, measurement of onset latency is not always easy due to contamination of SNAPs by stimulus artifacts over short distances, an unclear take-off point during antidromic stimulation, and by multiple factors affect-

| TABLE 1 | Distribution of distoproximal (D/P) ratio in antidromic and orthodromic conduction study |
| --- | --- | --- |
| | Median Nerve (n = 60) | Superficial Radial Nerve (n = 60) |
| | Third Digit | Second Digit | First Digit |
| | Onset Latency | Peak Latency | Onset Latency | Peak Latency | Onset Latency | Peak Latency |
| **Antidromic conduction (%)** | | | | | | |
| 1 > D/P | 51 (85.0) | 0 (0) | 42 (70.0) | 0 (0) | 5 (8.3) | 0 (0) |
| 1 = D/P | 2 (3.3) | 0 (0) | 5 (8.3) | 0 (0) | 3 (5.0) | 0 (0) |
| 1 < D/P | 7 (11.7) | 60 (100.0) | 13 (21.7) | 60 (100.0) | 52 (86.7) | 60 (100.0) |
| **Orthodromic conduction (%)** | | | | | | |
| 1 > D/P | 38 (63.3) | 0 (0) | 29 (48.3) | 0 (0) | 1 (1.7) | 0 (0) |
| 1 = D/P | 7 (11.7) | 0 (0) | 10 (16.7) | 0 (0) | 3 (5.0) | 0 (0) |
| 1 < D/P | 15 (25.0) | 60 (100.0) | 21 (35.0) | 60 (100.0) | 56 (93.3) | 60 (100.0) |

*P < 0.05 for onset latency vs. peak latency.
TABLE 2. Correlation coefficients between age and latency of median and superficial radial nerves

<table>
<thead>
<tr>
<th></th>
<th>Median Nerve</th>
<th>Superficial Radial Nerve</th>
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<tbody>
<tr>
<td></td>
<td>Third Digit</td>
<td>Second Digit</td>
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<tr>
<td></td>
<td>Onset Latency</td>
<td>Peak Latency</td>
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<tr>
<td>Antidromic conduction (P value)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist stimulation</td>
<td>0.414* (0.023)</td>
<td>0.450* (0.013)</td>
</tr>
<tr>
<td>Palm stimulation</td>
<td>0.301 (0.106)</td>
<td>0.455* (0.012)</td>
</tr>
<tr>
<td>Orthodromic conduction (P value)</td>
<td></td>
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<tr>
<td>Wrist recording</td>
<td>0.313 (0.076)</td>
<td>0.400* (0.029)</td>
</tr>
<tr>
<td>Palm recording</td>
<td>0.169 (0.371)</td>
<td>0.232 (0.218)</td>
</tr>
</tbody>
</table>

Numbers in parentheses are P values.

* P < 0.05 for correlation between age and latency.

ing baseline measurements. Many studies developed for diagnosis of CTS do not clearly document which latency measurement is more valid and reliable for early diagnosis of CTS. There are a number of median sensory conduction studies of wrist-to-digit and palm stimulation techniques that provide data regarding onset, peak, and both latencies.5,16,22,23

Under normal circumstances, the transcarpal conduction time should be less than the time for distal segments during mid-palm stimulation technique of the median nerve.5,10 This principle was upheld in the peak latency data of the present study but not with the measurement of onset latency. There are no reports dealing with this discrepancy in segmental conduction studies of the median nerve. We chose relatively young subjects (18–36 yrs) who had no symptoms or signs of CTS, and who were at low risk of having underlying subclinical CTS due to their age. In general, the aging nervous system demonstrates loss of large fibers, and there is evidence suggesting progressive segmental demyelination and remyelination, and this is especially evident in individuals in their sixth decade.24 –26 However, we found that even in this younger population, the proportion of reversed D/P onset latency ratio was frequent in the median sensory nerve. The positive correlation between latency of the wrist-to-digit segment and age in the median sensory nerve, but not the superficial radial nerve, adds more supportive evidence to the possible physiologic changes of median sensory nerve fibers at the carpal tunnel.

We considered whether technical factors might have affected the present results, such as errors in determining the onset point of SNAPs or the use of inappropriately high stimulus intensity at the palm during antidromic conduction. However, such factors would be less likely using the orthodromic conduction technique.27 During the orthodromic conduction study, the onset points of SNAPs were more easily identifiable than in antidromic studies, and the orthodromic conduction study avoids issues relating to differences in the stimulation intensity, which can frequently arise in antidromic studies. The results of orthodromic and antidromic conduction studies were similar in terms of the distribution of the D/P ratio, and superficial radial nerve data were also similar, even when using the antidromic technique. These observations indicate that measurement error in determining onset latency or stimulus intensity differences were not likely to be the causes of the observed reversed D/P ratio in the median nerve.

Another factor we considered was the effect of distal tapering of the nerve axons on slower conduction in the distal limb than in the proximal one.28 Caruso et al.12 obtained postmortem samples of either the median or the ulnar nerve from the finger, palm, and wrist and forearm in five young adults and five newborn boys and they investigated the size distribution of the axonal diameters and internodal lengths. They argued that slower conduction velocity in the distal hand is not caused by a change of axonal diameter but that the short internodal length seemed to play an important role in myelinated peripheral nerve fibers in median and ulnar nerves. These physiologic factors could not function over a short conduction distance. However, our superficial radial sensory nerve results showed D/P ratios of >1.0 in almost all hands, regardless of onset or peak latencies, making this assumption less likely.

We also examined median sensory nerve conduction at the second and third digits, as finger selection affects sensitivity in diagnosis of CTS. An earlier report argued that the middle finger was the most suitable digit,29 and although the present results suggest a higher frequency of reversed D/P ratios in segmental nerve conduction studies of the third digit, statistical analysis indicated this was not a significant difference.
In this study, we have chosen the superficial radial nerve for comparison with the median nerve because it does not pass through the carpal tunnel and because of the rarity of entrapment neuropathy around the wrist. However it is much easier to measure the distance accurately in the superficial radial sensory nerve than in the more deeply located median nerve within the carpal tunnel. This might cause a distance measurement error between the median and superficial radial nerves. Additional evaluation of the ulnar nerve might give more information because, like median nerve, it is on the volar aspect of the hand and passes through similar changes in the configuration of the volume conductor.

In summary, we found that prolonged onset latency of the median sensory nerve across the carpal tunnel was common in healthy adults who were not CTS patients, whereas studies on the superficial radial sensory nerve fulfilled the null hypothesis. The reversed pattern regarding the onset latency measurement in this study suggests that the results were not simply related to technical factors but might be a result of chronic physiological or structural changes of the fastest conducting fiber at the carpal tunnel. More studies will be needed to verify this hypothesis using elaborate control of temperature at the wrist, palm, and fingers and known risk factors for CTS, such as body mass index.

The present data suggest that onset latency is not recommended as a diagnostic variable for CTS when comparing conduction times between W-P and P-D or when calculating D/P ratio, as it may cause greater reporting of false positives in CTS diagnosis.

REFERENCES

15. Buchthal F, Rosenfalck A: Sensory conduction from digit to palm and from palm to wrist in the carpal tunnel syndrome. J Neurol Neurosurg Psychiatry 1971;34:243–52
Stroke Impairment Predictors of Discharge Function, Length of Stay, and Discharge Destination in Stroke Rehabilitation

ABSTRACT


Objectives: This article presents analytic results from a prospective study of 313 stroke rehabilitation patients, looking at the relative contributions of different stroke impairments toward prediction of discharge function, rehabilitation length of stay, and discharge destination after inpatient rehabilitation. The relationship between number of stroke risk factors and recurrence of strokes during rehabilitation was also evaluated.

Methods: A total of 313 subjects were enrolled consecutively. Information on type of stroke and individual stroke-related impairment was collected prospectively. Recurrent stroke, rehabilitation length of stay, discharge destination, discharge function, and available family support at discharge were documented.

Results: Rates of impairment occurrence and coexistence are presented. Analysis using linear (length of stay, discharge function) and logistic (discharge destination) regression revealed significant contributory predictive effects of admission balance, aphasia, number of impairments, and family support on length of stay; admission balance and number of impairments on discharge function; and admission balance, body neglect, and presence of family support on discharge destination.

Conclusion: In addition to admission function and balance, other factors to consider in predicting length of stay for patients should include the number of stroke-related impairments and family support. For discharge destination prediction, the presence of body neglect should be considered in addition to balance and family support. Evaluation of patients for right-sided neglect and left-sided neglect is important.

Key Words: Cerebrovascular Accident, Outcomes Research, Rehabilitation, Perceptual Disorders
Patient and family education about expectations after stroke is often a focus in inpatient stroke rehabilitation. Patient and family knowledge and expectations for functional recovery have been demonstrated to be limited, and further opportunities for improved education in this area have been identified. Strokes can cause a variety of impairments; more severe or extensive neurological involvement is associated with greater disability and handicap. The more information that health professionals have regarding the relationship between specific stroke-related impairments and outcomes that might be of interest to patients and families, the more knowledge can be imparted in patient and family education.

The literature has identified that potential predictors of function include urinary continence, motor impairment, cognition, and other stroke-related impairments such as hemianopsia. Some complications such as early seizures have predictive properties after stroke. Most published articles on the topic of stroke impairment predictors examine the effects of single impairments. A multivariable analysis conducted in a community-based study indicated that incontinence, coma, dysphagia, cognitive impairment, and gaze paresis were independently associated with severe disability and death at 3 mos. It is acknowledged that cumulative deficits after stroke affect functional outcomes, and it is recommended that measures of both physical and cognitive function be used in studies of stroke outcome and care of stroke patients. Despite such recommendations, clarity is lacking in regard to which stroke impairments are most useful for determining prognosis in inpatient stroke rehabilitation.

Results of balance as a predictor of discharge function, in-hospital length of stay (LOS) and discharge destination (DD) in stroke rehabilitation have previously been published by Wee et al. That article also reported family support as a strong contributor in allowing discharge to home. This article builds on the previous publication by describing other important stroke impairments in predicting such outcomes to better inform health professionals, patients, and their families of expectations during and after inpatient stroke rehabilitation. This observational study attempts to measure neurological impairments caused by stroke in a comprehensive manner and examines associations between such impairments and outcomes. It documents all clearly recognized stroke-related impairments, namely, aphasia, dysphagia, dysarthria, apraxia, hemianopsia, diplopia, and poor visual acuity resulting from stroke, inattention/neglect, poor balance, and motor and sensory deficits, in a prospective cohort of stroke rehabilitation inpatients and reports on relative prognostic properties of the most influential predictors of function, LOS, and DD. Clinical experience has been that certain impairments lead to poorer outcomes as compared with other impairments; this study was conducted to clarify which impairments might have the greatest contribution toward such outcomes.

METHODS

Ethical approval for this prospective observational study was obtained through the hospital ethics committee, according to national guidelines, before commencement of the study. Data were obtained prospectively from 313 subjects who had been recruited from 325 patients consecutively admitted for stroke rehabilitation to a tertiary rehabilitation center in Vancouver, British Columbia, Canada. This center is a provincial referral center, and often, referral and admission to rehabilitation may occasionally take longer than expected, particularly from rural areas, because potential candidates cannot be assessed in person. Admission criteria included ability to follow gestural or verbal commands, sit unsupported at the edge of a bed for 30 secs, sit in a chair for ≥2 hrs, and participate in several 30-min therapy sessions, in addition to being medically stable. Strokes must have occurred within 6 mos before admission, and strokes were defined according to World Health Organization criteria. Excluded were patients who sustained hemiparesis as a result of trauma or tumor and those who could not complete rehabilitation because of medical complications requiring acute hospital admission or because of death during hospitalization. Recurrent strokes were distinguished from new-onset strokes because it is generally acknowledged that those with recurrent strokes do not fare as well as those with first-onset stroke. Type of stroke, namely, hemorrhagic or nonhemorrhagic, was noted.

Types of stroke-related impairments were documented by stroke rehabilitation team members within 1 wk of admission. All patients were screened for motor and sensory impairments and for difficulties in swallowing, perception, cognition, balance, and language. Urinary incontinence is not reported in this article, as most patients with incontinence at admission were no longer incontinent at discharge. Furthermore, urinary incontinence may not necessarily be due to stroke but could also be influenced by communication, equipment, and staffing. Cognition was measured with the Folstein Mini-Mental Status Examination (MMSE) when possible. This examination could not be completed in some aphasic subjects. Cut-off scores were chosen based on existing literature. Generally, a score of 23 or 24 of a maximum of 30,
is used to identify presence of dementia, with a sensitivity of 87%, specificity of 92%, and positive predictive value of 69%. Severe cognitive impairment is thought to be present if scores are less than 17 or 18. Balance was measured through the Berg Balance Scale (BBS). Other impairments documented included aphasia (expressive, receptive, mixed), apraxia, inattention to body (body neglect) or environment (visual inattention), hemianopsia and other visual impairments resulting from stroke, motor and sensory impairments, dysarthria, and dysphagia. The term “neglect” is often used interchangeably with “inattention” in stroke rehabilitation, though neglect implies greater severity of impairment. A description for detection of these impairments is found in the Post-Stroke Rehabilitation clinical practice guideline. Presence or absence of impairments was entered into a database by one individual at the beginning of each subject’s admission. The number of impairments was determined by totaling them. We chose this method instead of a weighting system for the sake of clinical utility in the event that number of impairments is a significant predictor. Because balance was affected in all subjects, the total impairment score included impairments other than balance, for a maximum possible score of 10.

Admission BBS scores, presence or absence of individual stroke impairments, total number of impairments, and presence of support at home were examined as explanatory variables; the dependent variables (outcomes) included rehabilitation LOS in days, discharge functioning as measured through the FIM instrument, and DD (home vs. institutional supported living). Determination of discharge FIM scores was a shared team effort, with each member of the team responsible for completing a portion of the scale. The team was appropriately trained to collect these data. Scores were tallied after discharge by the person inputting the data and entered into the database. Decisions regarding DD and LOS on this Canadian rehabilitation unit were made through a consensual process—by patients, their families, and treating team members. Patients usually have ultimate decision-making power. The LOS reported is active rehabilitation LOS. Once rehabilitation was completed, subjects were deemed to be at alternate levels of care and returned to referring facilities if beds in care facilities were not imminently available. Financial resource availability (indicated by patients as poor or adequate) and presence of family support (an able and available caregiver at home) were also collected for individuals because these might affect DD. The following possible DDs were recorded: home, intermediate care (able to transfer independently), extended care (requiring assistance with basic activities of daily living), acute care (requiring acute medical care); however, these were collapsed into home vs. other to create a binary outcome for analysis.

**Statistics**

Data were entered into an Excel spreadsheet and transferred into SPSS for Windows (version 11.0.1, SPSS, Chicago, IL) for analysis. Descriptive statistics (mean and standard deviation values for continuous data, frequencies and proportions for categorical data) were generated for all variables. The distribution of both LOS and discharge FIM score were plotted to assess the normality of the underlying distribution. To examine the relationships between the independent variables and LOS and discharge FIM scores, independent samples t tests, one-way analyses of variance (categorical data), and correlation (continuous data) were used. For analyses of variance, Tukey’s post hoc tests were used to adjust for multiple comparisons. The relationships between the independent variables and DD were examined by means of χ² tests (categorical variables) and independent samples t tests (continuous data). These tests were also used to evaluate the relationship between the independent variables in some cases to assess colinearity between the predictors. Multivariable stepwise linear regression modeling was used to identify the predictors of LOS and discharge FIM scores, and logistic regression was used to identify predictors of DD. Variables were offered into the models on the basis of the significance of the bivariate relationships (criteria of $P < 0.20$).

**RESULTS**

During the study period, a total of 325 patients were admitted to the stroke rehabilitation unit. A total of 12 were excluded (eight nonrehabilitation candidates admitted for family education to facilitate discharge home, two died, and two had acute medical complications requiring hospital admission [gastrointestinal bleed, urosepsis]). The results from 313 subjects are presented. The sample included 162 men and 151 women. Mean age was 76 ± 8 yrs. The subjects were equally represented with respect to hemisphere affected. Average time from stroke onset to admission was 37 ± 22 days. A total of 110 subjects had recurrent stroke compared with 203 subjects with first-time stroke. Thirty-five subjects incurred hemorrhagic stroke, and the rest had nonhemorrhagic mechanisms, with documented hemorrhagic transformation in two.

**Stroke Impairments**

A total of 224 subjects (71.6%) could complete the MMSE. They were divided into three groups: 14...
subjects (6%) had severe cognitive difficulty (MMSE score, 0–17), 33 subjects (15%) were classified as having moderate cognitive difficulty (MMSE score, 18–23), and 176 (79%) were within the mild to normal category (MMSE score, 24–30). A total of 89 subjects with communication impairments could not complete the test. Some impairments were found to frequently occur in conjunction with others (Table 1): dysarthria and dysphagia, left visual inattention and left sensory impairment, right visual inattention and right sensory impairment, right visual inattention and right-sided body neglect, left visual inattention and left-sided body neglect, apraxia and right visual inattention, apraxia and cognitive impairment, and visual inattention and cognitive impairment. Neglect of both body and environment, and body neglect and sensory impairment, coexisted in a third of the patients. A total of 207 of the 313 patients (66.1%, \( P = 0.09 \)) had both weakness and sensory impairment. Table 2 outlines the frequency of stroke-related impairments. All subjects had some impairment in balance, with admission BBS scores of <56. The normally distributed number of impairments (other than impaired balance) ranged from 0 to 9, with a mean of 4.59.

Discharge FIM scores and LOS were sufficiently normally distributed to permit the use of parametric statistics. Mean FIM score at discharge was 104.3 (SD, 16.7) and mean LOS was 54.8 days (SD, 23.3). A total of 178 subjects (79.5%) were discharged to home, 9 (4.0%) to intermediate care, 23 (10.3%) to extended care, and 14 (6.3%) to acute care hospitals. No differences were found with respect to functioning, LOS, or DD for those with hemorrhagic compared with nonhemorrhagic strokes. Admission balance scores, as measured by the BBS, were significantly lower for those with recurrent stroke (mean of 20/56 compared with 24/56, \( P = 0.03 \)) than for those with a first-time stroke. LOS, on average, was 3 days longer for those with a previous stroke, but this fell short of statistical significance (\( P = 0.15 \)). No significant difference was found in DD (\( P = 0.56 \)) or discharge function (\( P = 0.68 \)) for those with and without a previous stroke. \( \chi^2 \) tests were used to examine the associations between impairments and recurrent or first-time strokes. There being no differences, for the purposes of examining the relationship between impairments and outcomes, data from all subjects were combined.

Table 2 describes the associations of stroke-related impairments with discharge FIM score, LOS, and DD. There was a trend for those with right-sided body neglect to have longer LOS (64 ± 24 days) than those with left-sided body neglect (57 ± 22 days; \( P = 0.07 \)). Right visual inattention was significantly associated with prolonged LOS as compared with left visual inattention (61 ± 26 days and 52 ± 25 days, respectively, \( P = 0.02 \)).

There was no association between MMSE and LOS (\( F = 0.36, P = 0.70 \)). Post hoc (Tukey’s) analyses of discharge FIM scores indicated significant differences between the mild to normal (mean FIM score, 107.3) and severe (mean FIM score, 92.0) groups (\( P = 0.003 \)). The moderately impaired group (mean FIM score, 101.3) was not significantly different from the other two. A statistically significant effect of cognitive impairment was also found on DD (\( P = 0.015 \)), with 82.0% of unimpaired subjects being discharged home as compared with 69.7% of the moderately impaired and 71.4% of the severely impaired. Twenty-one percent of the severely impaired were discharged to extended care, compared with only 3% of the moderately impaired, and 11% of the mild to normal group.

Some differences were found with respect to functioning in those with different types of aphasia. A total of 49 subjects (15.7%) had expressive aphasia.

<table>
<thead>
<tr>
<th>Impairment Pairs</th>
<th>n</th>
<th>%a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphagia/dysarthria</td>
<td>62</td>
<td>57% (dysarthria), 52% (dysphagia)</td>
</tr>
<tr>
<td>Visual inattention/sensory impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>74</td>
<td>67% (sensory impairment), 69% (visual inattention)</td>
</tr>
<tr>
<td>Right</td>
<td>39</td>
<td>43% (sensory impairment), 53% (visual inattention)</td>
</tr>
<tr>
<td>Body neglect/sensory impairment</td>
<td>100</td>
<td>32% of entire sample</td>
</tr>
<tr>
<td>Visual inattention/body neglect</td>
<td>115</td>
<td>37% of entire sample</td>
</tr>
<tr>
<td>Left</td>
<td>68</td>
<td>84% (body neglect), 63% (visual inattention)</td>
</tr>
<tr>
<td>Right</td>
<td>45</td>
<td>76% (body neglect), 62% (visual inattention)</td>
</tr>
<tr>
<td>Right visual inattention/apraxia</td>
<td>41</td>
<td>56% (visual inattention), 34% (apraxia)</td>
</tr>
<tr>
<td>Cognitive impairment/apraxia</td>
<td>24</td>
<td>11% of 224 who completed MMSE</td>
</tr>
<tr>
<td>Cognitive impairment/visual inattention</td>
<td>36</td>
<td>16% of 224 who completed MMSE</td>
</tr>
</tbody>
</table>

*a* Percentage of those with the impairment in parentheses who also have the other impairment of the impairment pair indicated.
sia, and 51 (16.3%) had mixed expressive and receptive aphasia (only two subjects had pure receptive aphasia). Mean discharge FIM score was 106.1 ± 15.6 for subjects without aphasia. Compared with those without aphasia, discharge function was poorer for those with mixed aphasia (discharge FIM scores averaged 97.7 ± 18.7, \( P = 0.006 \)) but not significantly lower for those with expressive aphasia (104.3 ± 17.6). The two subjects with receptive aphasia demonstrated a mean discharge score of 88.5 ± 10.6, the lowest of the aphasic subgroups. For subsequent analyses, the two subjects with receptive aphasia were included with those with mixed aphasia (discharge FIM scores, 97.3 ± 18.5).

For subsequent analyses, the two subjects with receptive aphasia were included with those with mixed aphasia (discharge FIM scores, 97.3 ± 18.5). Aphasic subjects as a whole showed a trend for longer LOS (\( P = 0.116 \)). When the aphasic subjects were separated into receptive/mixed or expressive, there was no association between expressive aphasia and LOS, but the relationship between mixed or receptive aphasia and LOS was significant both in bivariate testing (\( P = 0.030 \)) and in multivariable regression (Table 3).

Table 3 contains the linear regression models for discharge FIM score and rehabilitation LOS. Three variables were predictors of discharge FIM score, accounting for 51.2% of the variation in outcome. The best predictor was admission BBS score: a higher admission BBS score was associated with a higher discharge FIM score. A similar trend was observed for length of stay, with admission BBS score and mixed/receptive aphasia being significant predictors of LOS.

### Table 2: Significance levels for bivariate associations between impairment and outcomes

<table>
<thead>
<tr>
<th>Impairment</th>
<th>No. of Subjects (% of Total)</th>
<th>Discharge Functioning (FIM)</th>
<th>Length of Inpatient Rehabilitation</th>
<th>Discharge Destination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness</td>
<td>310 (99)</td>
<td>0.920</td>
<td>0.247</td>
<td>0.472</td>
</tr>
<tr>
<td>Sensory disturbance</td>
<td>207 (66)</td>
<td>0.035(^a)</td>
<td>0.046(^a)</td>
<td>&lt;0.001(^a)</td>
</tr>
<tr>
<td>Balance</td>
<td>313 (100)</td>
<td>&lt;0.001(^a)</td>
<td>&lt;0.001(^a)</td>
<td>&lt;0.001(^a)</td>
</tr>
<tr>
<td>Hemianopsia,(^b) poor visual acuity, diplopia(^c)</td>
<td>108 (35)</td>
<td>0.049(^a)</td>
<td>0.411</td>
<td>0.641</td>
</tr>
<tr>
<td>Expressive aphasia</td>
<td>49 (16)</td>
<td>0.983</td>
<td>0.822</td>
<td>0.650</td>
</tr>
<tr>
<td>Receptive/mixed aphasia</td>
<td>53 (17)</td>
<td>0.001(^a)</td>
<td>0.030(^a)</td>
<td>0.579</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>108 (35)</td>
<td>0.034(^a)</td>
<td>&lt;0.001(^a)</td>
<td>0.191</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>119 (38)</td>
<td>&lt;0.001(^a)</td>
<td>0.044(^a)</td>
<td>0.669</td>
</tr>
<tr>
<td>Apraxia</td>
<td>121 (39)</td>
<td>0.002(^a)</td>
<td>0.099</td>
<td>0.324</td>
</tr>
<tr>
<td>Visual inattention(^d)</td>
<td>181 (58)</td>
<td>0.001(^a)</td>
<td>0.040(^a)</td>
<td>0.039(^p)</td>
</tr>
<tr>
<td>Body neglect(^e)</td>
<td>134 (43)</td>
<td>&lt;0.001(^a)</td>
<td>0.001(^a)</td>
<td>0.001(^a)</td>
</tr>
<tr>
<td>Impaired cognition(^f)</td>
<td>47 (15)</td>
<td>0.002(^a)</td>
<td>0.668</td>
<td>0.049(^p)</td>
</tr>
<tr>
<td>No. of impairments</td>
<td>Mean, 4.59, SD, 1.92</td>
<td>&lt;0.001(^a)</td>
<td>&lt;0.001(^a)</td>
<td>0.104</td>
</tr>
</tbody>
</table>

\(^a\) Statistically significant.

\(^b\) Total of 68 with hemianopsia (22%).

\(^c\) Total of 39 with poor visual acuity/diplopia (12%).

\(^d\) Total of 73 with right visual inattention (23%) and 108 left-side visual inattention (35%).

\(^e\) Total of 59 with right-sided body neglect (19%) and 75 left-side body neglect (24%).

\(^f\) Defined as a Mini-Mental Status Examination score of <24; 89 (28%) could not complete the Mini-Mental Status Examination.

### Table 3: Linear regression models for discharge FIM score and length of stay

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>( P ) Value</th>
<th>Change in ( R^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discharge FIM score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>100.73</td>
<td>&lt;0.001</td>
<td>NA</td>
</tr>
<tr>
<td>Admission BBS score</td>
<td>0.66</td>
<td>&lt;0.001</td>
<td>0.423</td>
</tr>
<tr>
<td>No. of impairments</td>
<td>-1.94</td>
<td>&lt;0.001</td>
<td>0.074</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>-5.46</td>
<td>0.010</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>Length of stay</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>67.16</td>
<td>&lt;0.001</td>
<td>NA</td>
</tr>
<tr>
<td>Admission BBS score</td>
<td>-0.75</td>
<td>&lt;0.001</td>
<td>0.277</td>
</tr>
<tr>
<td>Receptive/mixed aphasia (yes = 1)</td>
<td>7.33</td>
<td>0.019</td>
<td>0.023</td>
</tr>
<tr>
<td>No. of impairments</td>
<td>1.30</td>
<td>0.033</td>
<td>0.010</td>
</tr>
<tr>
<td>Support at home (yes = 1)</td>
<td>-4.21</td>
<td>0.057</td>
<td>0.008</td>
</tr>
</tbody>
</table>

BBS, Berg Balance Scale.
with a higher FIM score, accounting for 42.3% of the variation in outcome. Although ten individual impairments (other than balance) were associated with discharge FIM score in the bivariate analysis, and offered into the regression model, only the presence of cognitive impairment and the total number of impairments were selected when admission BBS score was included in the model. The reason for this is the high degree of association (collinearity) between the admission BBS score and the impairments. As a result, when admission BBS score was entered into the model, it accounted for most of the variance that was shared with other variables.

Four variables were predictors of LOS, accounting for 31.8% of the variation in outcome. This model is based on the regression equation obtained when all variables that were associated with LOS in bivariate analyses \((P < 0.20)\) were offered into the model. A stepwise process was used to determine the best combination of variables, accounting for the highest percentage of variation in outcome. Ten impairments (Table 2), admission BBS, the number of impairments, presence of family support, and whether this was a new or recurrent stroke were offered into the model. Again, admission BBS score was by far the best predictor of LOS, accounting for 27.7% of the variation in outcome. When considering contributions of receptive/mixed aphasia \((1 = \text{yes})\), the number of stroke impairments besides balance, and family support \((\text{available} = 1, \text{not available} = 0)\) to LOS, the previously published model\(^2\) of LOS was \(72.3 - (0.77 \times \text{admission BBS score}) + 20 \text{ becomes becomes LOS} = 67.2 - (0.75 \times \text{admission BBS score}) + (1.3 \times \text{number of other impairments}) + (7.3 \times \text{receptive/mixed aphasia}) - (4.2 \times \text{caregiver support}) + 19.2\).

In other words, predicted LOS starts at 67.2 days, drops by 7.5 days for every 10-point increase in admission BBS scores, increases by 1.3 days for every additional impairment, and if receptive or mixed aphasia is present, increases by 7.3 days. Those with support at home have a LOS that is 4.2 days less than those without support, although the significance of this variable is borderline \((P = 0.057)\), and it accounts for only 0.8% of the variation in outcome.

Table 4 contains the logistic regression for the two-level variable of DD (coded as home = 0, other = 1). Seventy-nine percent of subjects were discharged to home, as opposed to an institution, after inpatient rehabilitation. Higher admission BBS score was associated with an increased likelihood of being discharged home. For every 10-point increase in admission BBS score, subjects were 10.8 times more likely to go home \((1/0.92, \text{multiplied by} 10; 95\% \text{ confidence interval}, 10.4 –11.2)\). Those with support at home were 3.2 times more likely to go home \((1/0.31; 95\% \text{ confidence interval}, 1.45 –7.14)\), whereas those with body neglect were 2.2 times more likely to be discharged to a destination other than home \((95\% \text{ confidence interval}, 1.00 –4.84)\). Patients with cognitive impairment were 2.6 times more likely to be discharged elsewhere \((95\% \text{ confidence interval}, 1.04 –6.39)\). This model accounted for 21.2% of the variation in outcome. Effect of sensory disturbance was significant in bivariate analysis, but because it correlated with balance, it did not have a significant effect once there was a control for balance. Financial status did not seem to affect DD. Therefore, the most important predictors for discharge to home seem to be good balance, caregiver support, and absence of body neglect or cognitive impairment.

There is a noticeable overlap of predictors in the models, likely because the outcomes themselves are not independent. Admission BBS score was present in all three models. Number of impairments, family support, and cognitive impairment were included in two of the three models. Discharge FIM score was correlated with LOS \((-0.346, P < 0.001)\). DD was associated with both discharge FIM score and LOS. Those who went home had a mean FIM score of 107.9, whereas those who were discharged elsewhere had a mean score of 90.7 \((P < 0.001)\). LOS was 51.6 days for those discharged home and 67.1 for those who went to other destinations \((P < 0.001)\).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>P Value</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.06</td>
<td>0.881</td>
<td>0.94</td>
<td>NA</td>
</tr>
<tr>
<td>Admission BBS score</td>
<td>-0.08</td>
<td>&lt;0.001</td>
<td>0.92</td>
<td>0.89–0.96</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>0.95</td>
<td>0.036</td>
<td>2.58</td>
<td>1.04–6.39</td>
</tr>
<tr>
<td>Body neglect (yes = 1)</td>
<td>0.79</td>
<td>0.045</td>
<td>2.20</td>
<td>1.00–4.84</td>
</tr>
<tr>
<td>Support at home (yes = 1)</td>
<td>-1.16</td>
<td>0.003</td>
<td>0.31</td>
<td>0.14–0.69</td>
</tr>
</tbody>
</table>

BBS, Berg Balance Scale.
Model Cox and Snell \(R^2 = 0.212\).
DISCUSSION

Stroke-related impairments are important in defining individual rehabilitation goals. They are helpful in discussions with patients and their families regarding expected discharge functioning, length of rehabilitation stay in hospital, and possible DD. One might ask why look at impairments when one could use FIM scores to help with such predictions? It is already known that admission FIM scores correlate with these outcomes. Such scores are often not available in acute care settings, where a bedside assessment of impairments can be made to determine prognosis. This article presents the rate of various stroke-related impairments in a rehabilitation unit and their associations with discharge outcomes, supporting and building on existing literature, by further examining relationships between stroke impairment predictors.

Impaired balance and motor weakness were by far the most frequently occurring impairments in this population, followed by sensory impairments, which, in 66% of subjects, coexisted with motor impairments. This is not surprising, as cortical infarctions tend to encompass both motor and sensory territories. In decreasing order of frequency, other impairments that resulted from stroke were visual inattention (58%), body neglect (43%), apraxia (39%), dysphagia (38%), dysarthria (35%), visual disturbance (35%), and aphasia (33%). Also, 21% of those who could complete a standardized cognitive assessment (72% of subjects) demonstrated moderate to severe cognitive impairment. We recognize that the MMSE measures cognition only at the time of administration and cannot be completed by many aphasic patients; however, it is a standard tool used in most Canadian rehabilitation units. Impaired cognition in study subjects was thought to be a result of stroke in most, whereas in some, preexisting cognitive difficulties were known. The three most frequent impairments after motor and sensory disturbance were perceptual impairments that might easily be missed clinically in incomplete examinations. It is important to know which impairments to look for when assessing stroke patients referred to rehabilitation units.

We presented the tendency of some impairments to coexist: dysarthria and dysphagia, neglect of body and environment, left visual inattention/body neglect and left sensory impairment, right visual inattention/body neglect and right sensory impairment, apraxia and right visual inattention, cognitive impairment and apraxia or visual inattention, weakness and sensory impairment. It is important for clinicians to be aware of these associations and to assess stroke patients for these impairments so that rehabilitation and patient/family education may be appropriately guided.

Based on clinical observations, it is not surprising that almost 70% of subjects with either left visual inattention or left sensory dysfunction also had the other impairment present and that around 40–50% of those with right visual inattention or right sensory impairment also had the other impairment. Around 75–85% of those with body neglect also demonstrated ipsilateral visual inattention, suggesting that the perceptual mechanisms involved are likely related. Each of these three impairments—visual inattention, body neglect, sensory dysfunction—when considered separately, tends to lengthen LOS and decrease likelihood of discharge to home.

In our stroke rehabilitation population, we found a 23% prevalence of right visual inattention and 19% prevalence of right-sided body neglect. The literature contains several publications that discuss visual inattention, but only one article reported on percentage of subjects with right visual inattention (19%) in a sample of 90 subjects with visual inattention. In our study, 40% of 181 subjects with visual inattention demonstrated right-sided inattention. Most reported body neglect in the literature has been left-sided neglect. No publications were found reporting incidence or prevalence of right-sided body neglect. In our study, 43% of subjects demonstrated body neglect; 59 (44%) of these experienced right-sided neglect. Clinically, we had the impression that right-sided body neglect after stroke occurs at a higher rate than previously reported. This unexpectedly high percentage of those with right-sided neglect after stroke has not been previously reported. Because both these impairments are associated with longer LOS, poorer discharge functioning, and lower discharge to home, it is important to screen for them when performing neurological examinations, as the recognition of many stroke-related impairments depends on a specific search for them.

Most impairments seemed to affect discharge function. Naturally, the more severe the impairments, the greater their effect. For example, our study showed that those with severe cognitive impairment functioned more poorly and were less likely to be discharged home at the completion of inpatient rehabilitation compared with those scoring 24/30 or higher on the MMSE. One limitation of this study is in the nominal reporting of most impairments (other than balance and cognition). This is in part due to a lack of appropriately validated instruments that grade severity of specific impairments such as apraxia, inattention, and aphasia. Further development of such tools may be beneficial. In the absence of these, presence or absence of impairments must suffice.
As previously indicated, we wanted to determine if a simple method of counting number of impairments could help in the prediction of outcomes. Indeed, we found that higher numbers of impairments correlated with lower FIM score at discharge. We have shown that one can use this simple method to help describe prognosis to patients and their family members. In addition, presence of mixed or receptive aphasia and presence of cognitive impairment also correlated with lower FIM scores when taking all variables into account through multivariable regression modeling. In multivariable regression modeling, the best predictor of function was balance, with lower admission BBS scores predicting worse discharge functioning. We recognize that assessment of these impairments occurred, on average, >30 days after stroke. Future studies could look at whether these relationships hold closer to the time of stroke onset.

We also recognize that additional factors, such as depression and endurance, might affect rehabilitation outcomes. Although we did collect this information, such factors did not occur with sufficient frequency to have substantial effect on our outcome measures, and their effect is not the focus of this article. Throughout inpatient rehabilitation stay, optimizing medical status should remain an important goal if patients are to benefit maximally from the rehabilitation program.

Active rehabilitation duration on inpatient rehabilitation units in Canada depends substantially on goals that are set for the inpatient stay. When each impairment was examined individually through bivariate analysis, the most statistically significant associations between longer LOS and impairment presence were seen in persons with decreased balance, body neglect, and dysarthria. However, after adjusting for balance, these impairments were not found to be significantly associated with longer LOS. These results further emphasize the importance of balance. Other predictors that were found after adjusting for balance included receptive or mixed aphasia (longer stay with compromised comprehension), the number of impairments (longer stay with more impairments), and caregiver support at home (shorter stay). These findings support clinical experience.

We recognize that LOS on any rehabilitation unit depends on the environment encompassing the unit. In recent years, inpatient rehabilitation LOS has decreased, and this trend is expected to continue with ongoing fiscal pressures. Undoubtedly, the availability of care facilities in any given community could affect in-hospital LOS, as would payment mechanisms for in-hospital stay. A user pay system would not be expected to have in-hospital rehabilitation durations comparable with those of a society that provides comprehensive medical coverage. As the pressure for shorter hospitalization duration continues, society will depend more on the availability of outpatient rehabilitation services to maintain individuals in the community.

Persons with previous strokes began with lower balance (BBS) scores and stayed 3 days longer on average. The mean BBS admission score of 20/56 for those with previous strokes is at the level that seems to discriminate poor from good outcomes, confirming previous observations. These results are in keeping with expectations of poorer outcomes after recurrent strokes.

Impairments that had the strongest association with DD included sensory disturbance, balance, and body neglect in bivariate analysis. When we used logistic regression, we found that those with body neglect were 2.2 times less likely to be discharged home. It has already been described that those with poor balance are less likely to be discharged home and that without family support, one is more likely to be discharged to a destination other than home. We also found that subjects with cognitive impairment were 2.6 times less likely to be discharged home. Therefore, in addition to impaired balance, which often coexists with sensory disturbance, assessment for body neglect and impaired cognition is important in realistic considerations of DD.

Balance seems to have the greatest predictive ability of all the impairments studied. Although balance has been found to be a prognostic indicator, the full importance of impaired balance as a predictor of stroke rehabilitation outcomes had not been clearly established in the literature. It clearly affects discharge functioning, LOS, and DD.

CONCLUSION

Many stroke-related impairments affect functioning. Important impairments that affect discharge function include balance, cognitive impairment, and the total number of impairments. Factors other than balance and admission functioning to consider in predicting LOS for inpatients in stroke rehabilitation should include the number of stroke-related impairments, receptive or mixed aphasia, and the presence of caregiver support at home. For DD prediction, the presence of body neglect or cognitive impairment should also be considered, in addition to balance and family support. We also report the occurrence of right-sided body neglect and visual inattention in our study as higher than previously published.

REFERENCES


27. Elliott J: The clinical uses of the Berg Balance Scale [commentary]. *Physiotherapy* 1997;83:363
Changes in Stroke Rehabilitation Outcomes After the Implementation of Japan’s Long-Term Care Insurance System: A Hospital-Based Study

ABSTRACT

Objective: To explore the changes in stroke rehabilitation outcomes after the introduction of Japan’s long-term care insurance (LTCI) system.

Design: Stroke patients discharged during a 3-yr period before and after the implementation of LTCI were compared (before-LTCI vs. after-LTCI). Outcome measures included onset to admission interval, length of stay, and correlation between discharge site and functional level at discharge.

Results: A total of 201 patients in the before-LTCI group and 252 patients in the after-LTCI group were eligible for the study. Shorter mean length of stay ($P < 0.01$) and higher rates of discharge to a rehabilitation facility ($P < 0.01$) were found in the after-LTCI group. Logistic regression analysis revealed that the patients with higher activities of daily living scores or ambulatory status at discharge were more likely to be discharged to home after inpatient rehabilitation in both groups ($P < 0.01$). The rate of discharge to home was similar in both groups.

Conclusions: Within this rehabilitation hospital’s experience, the mean length of stay was reduced after the implementation of the LTCI. Although it was one of the primary goals of the LTCI, the rate of discharge to home did not significantly increase. Further evaluation and modification of the LTCI and more efforts to improve a patient’s activities of daily living and ambulatory status at discharge will be necessary to promote in-home care in Japan.

Key Words: Long-Term Care Insurance, Cerebrovascular Accident, Rehabilitation, Outcome, Japan
The median age of the world’s population is increasing as the average life span increases and birthrate decreases. In Japan, the proportion of the population aged ≥65 yrs has increased from 7.9% in 1975 to 17.3% in 2000. This is expected to reach 28.7% by 2025 and 35.7% by 2050.1 The rate and magnitude of this increase are unprecedented.

In 1961, the Japanese healthcare system established a mandatory fee schedule that allowed the entire nation to be covered for medical services.2 Between 1973 and 1982, Japanese citizens aged ≥70 and those bedridden between 65 and 69 all received free health care. In 1982, this was amended to include a low-cost copayment system.

Most families chose readily available inpatient hospital care instead of pursuing formal home care services or nursing homes, as these invariably were associated with long waiting times for admission due to a major shortage of beds and available services.3 As a result, most of the elderly population became institutionalized, as their stay was covered by medical insurance. Three quarters of them were in hospitals, although they did not require close medical care, and about half of them elected to stay in the hospital for >1 yr, thereby creating an “epidemic” of Japan’s social hospitalization.3–5

This created serious problems with Japan’s healthcare finances and also placed the traditional system of informal caregiving in crisis. Within this traditional system of caregiving, the spouse and daughter-in-law had been the typical caregivers for their frail elders. This practice is now becoming obsolete because there are fewer three-generation families living together. This is also accentuated by the lack of living space for the elders in their children’s home; more women working outside the home, and caregivers themselves are aging and less able to provide care to others.3 Furthermore, the national medical care expenditure has increased to >30 trillion yen (285.7 billion United States dollars: 1 dollar = 105 yen) in 1999, whereas just 10 yrs ago, it had been <20 trillion yen (190.5 billion United States dollars). Japan has also encountered an economic depression since the early 1990s.6

Under these circumstances, a national caregiving system obligating societal participation was considered necessary. Therefore, in April 2000, the long-term care insurance (LTCI) system was initiated to meet the needs of the growing elderly population.

All citizens age ≥65 are automatically eligible for LTCI, regardless of their income status or family situation, but those between 40 and 64 are only eligible if their condition is a result of chronic “age-related disease” (e.g., stroke, presenile dementia, or severe osteoarthropathy).3 An on-site assessment is conducted by certified examiners to evaluate the applicant’s physical and cognitive status. Based on their assessment, a government computer program automatically classifies applicants into six categories (or may reject them). The executive committee reviews the patient’s initial computer-generated classification, along with descriptive statements and reports from the attending physician, and subsequently determines the appropriate level of subsidy to be provided. The monetary amounts of each eligibility level range from 61,500 yen (586 United States dollars) to 358,300 yen (3412 United States dollars) per month. The insured individuals are responsible for a 10% copayment. Additional services can be purchased through "out of pocket" expenses. Insurance benefits cover most institutional services, including respite care and home care services, and they provide financial assistance to help improve the home environment.3,4

The aim of this study is to assess the effect of LTCI on rehabilitation outcomes in Japanese stroke patients. Stroke is one of the major diseases affecting the elderly, with a high mortality rate, and it is a leading cause of significant long-term disability. In Japan, it accounts for 27.7% (42.9% for men and 20.2% for women) of all causes requiring medical care and 11.7% of the total medical costs for persons aged ≥65 in 2000.6 Comparing stroke rehabilitation outcomes before LTCI and after LTCI may reveal problems with the LTCI system or reveal further unforeseen issues related to the frail elderly population of Japan.

METHODS

Hospital and Treatment

Asagi Hospital is a community-based, 58-bed, freestanding rehabilitation hospital in Fukuoka, Japan. Most stroke patients are transferred from various surrounding acute care hospitals. More than 90% of all stroke referrals for rehabilitation are accepted, regardless of severity, medical condition, or discharge plan. Patients were admitted as early as possible after referral to expedite comprehensive rehabilitation by an interdisciplinary team, which consists of the physiatrist, psychiatrist, rehabilitation nurse, physical therapist, occupational therapist, speech-language pathologist, medical social worker, and case manager. There are eight physical therapists, five occupational therapists, and one speech-language pathologist within the hospital. Patients were instructed to perform various functional exercises, including muscle strengthening, range of motion, and passive stretching activities. An intensive sitting-standing exercise was especially stressed during the physical therapy interventions. They also received activities of daily living training or speech therapy as warranted for their stroke impairments. Patients received reha-
bilitation for 4–5 hrs/day, 6 days/wk. The methods and time given for therapies remained the same before LTCI and after LTCI. Patients were discharged either when they regained the ability to walk independently, if they stayed in the hospital for >60 days, or when they had reached a relative plateau in functional recovery. The severely disabled patients were often permitted to stay up to 3 mos in rehabilitation. Patients and their families determined the appropriate discharge site in conjunction with recommendations made by the rehabilitation team.

**Patient Selection**

This study was performed by retrospective chart review. Institutional review board approval was obtained; informed consent was exempted. There were 758 consecutive stroke patients discharged from the hospital between April 1, 1997, and March 31, 2003. Among them, 472 patients met the selection criteria, which included patients that (1) had a principal diagnosis of a new stroke confirmed by a neurologist’s clinical assessment and supported by neuroradiologic findings (either computed tomography or magnetic resonance imaging), (2) was independent in performing activities of daily living before the stroke, (3) had been directly admitted to the rehabilitation hospital from an acute care unit, and (4) had complete data available in the medical records. A total of 19 of these patients were omitted in accordance with our exclusion criteria: (1) transient ischemic attack, (2) death during inpatient rehabilitation, (3) stroke from subdural or epidural hemorrhage, (4) stroke caused by trauma, or (5) presence of co-morbidities due to previous stroke or other chronic disabling pathologic conditions such as limb amputation or central nervous system metastases. Finally, 453 stroke patients were enrolled in this study.

**Study Design**

The patients were divided into two groups. Patients discharged from the hospital between April 1, 2000, and March 31, 2003 (3-yr period after implementation of LTCI, the after-LTCI group) were compared with patients discharged between April 1, 1997, and March 31, 2000 (3-yr period before implementation of LTCI, the before-LTCI group).

**Measures**

The following data were extracted from chart review: age, sex, weight, height, type of stroke, medical history, type of paralysis, prestroke living conditions, interval from stroke onset to rehabilitation admission, length of hospital stay (LOS), and discharge site. Functional abilities were also assessed at admission and at discharge using the Barthel index (BI), composed of ten assessment items. There are several scoring methods for the BI; however, all of the patients in this study were assessed using the original guidelines, that is: (1) grooming and bathing rated on a 2-point scale of 0 and 5; (2) transfers and walking rated on a 4-point scale of 0, 5, 10, and 15; and (3) the other six items (feeding, dressing, toilet habits, stairs, bladder and bowel control) rated on a 3-point scale of 0, 5, and 10. The total best score of the BI equals 100, and the worst score is 0.7.

In this study, ambulatory status at discharge was a key variable because the ambulation item contributes toward the highest score on the BI and also represents the main item of functionality that patients hope to regain. Ambulatory status was divided into three categories: A (corresponding to BI score of 15: patient can walk for ≥50 yards [46 m] without help or supervision, may wear braces or prostheses, and use crutches, cane, or a walkerette, but not a rolling walker), B (corresponding to BI score of 10: patient needs supervision or some assistance), and C (corresponding to BI score of 0 or 5: patient cannot ambulate but may independently operate a wheelchair) to evaluate the correlation of ambulatory status with discharge site.

**Data Analysis and Statistics**

A comparison of BI between admission and discharge was computed by Wilcoxon’s signed-rank test. BI between before–and after–LTCI groups was analyzed with Mann-Whiney U test. To assess the correlation between discharge site and activities of daily living or ambulatory status at discharge, the data were analyzed using logistic regression. The significance levels were at 5%. Data were analyzed with SPSS version 11 for Windows (SPSS, Chicago, IL).

**RESULTS**

A total of 201 stroke patients met the criteria for the before-LTCI group, and 252 met the criteria for the after-LTCI group. Between the two groups, there was no statistical differences in age, sex, weight, height, type of stroke or type of paralysis, interval from stroke onset to rehabilitation admission, prestroke living condition, and co-morbidities (hypertension, diabetes mellitus, chronic atrial fibrillation, paroxysmal atrial fibrillation, ischemic heart disease; P > 0.05) (Tables 1 and 2). Only the prevalence of hyperlipidemia was found to be higher in the after-LTCI group (12.7% vs. 5.5%, P = 0.01).

The mean LOS (in days) was significantly shorter in the after-LTCI group compared with the before-LTCI group (72.6 vs. 86.0, P = 0.004) (Table 2). However, there were no significant differences in either total BI scores or ambulatory status between the two groups (P > 0.05) (Table 3).
The discharge sites were different between the two groups \((P = 0.027)\) (Table 2). The rate of discharge to another rehabilitation facility was significantly increased in the after-LTCI group \(9.1\% vs. 2.5\%, P = 0.001\). There was no statistical difference in terms of the discharge to the other sites \(P > 0.05\).

The rate of discharge to home was lower in the after-LTCI group compared with the before-LTCI group, although this difference was not statistically significant \(64.3\% vs. 70.6\%, P > 0.05\) (Table 2, Fig. 1). The patients with higher scores for activities of daily living at discharge were more likely to be discharged home in both groups \(P < 0.01\) (Fig. 2). Moreover, the relationship between ambulatory status at discharge and discharge site is shown in Figure 3. In both groups, there was a higher percentage of patients discharged home among those with better ambulatory status \(P < 0.01\).

**DISCUSSION**

The primary objectives in establishing the LTCI program were to promote in-home care for the elderly and minimize the growth of inflating medical expenditures by eliminating the inappropriate practice of social hospitalization.\(^8\) This preliminary study, however, has apparently shown that the institution of LTCI did not significantly increase the rate of discharge to home after stroke rehabilitation but in fact showed an increase in the rate of patients transferred to another rehabilitation facility. Several issues with the LTCI system may have contributed to this. There may be insufficient provisions for financial assistance for patients to improve their home environment. Because of Japan’s limited land area for housing, typical Japanese home design is characterized by multilevel homes, overly narrow and restricted spaces, and high bathtub heights. Japanese prefer baths over showers, sitting or lounging on tatami mats directly on the floor instead of in chairs, and donning shoes while indoors. These features cause significant problems for those patients with disabilities. Therefore, a home’s structure, environmental barriers, and monetary resources to correct these obstacles need to be taken into consideration to remedy these practical and logistical problems that would otherwise prevent the disabled family member from successfully living at home. In addition, more comprehensive assessments of a patient’s cognitive status, especially in regard to safety and awareness of one’s deficits, need to be established to prevent unsafe behavior and injury within the home environment. Reassessment of the certification process for eligibilities may need to be reevaluated to establish more appropriate classifications and criteria for support.\(^9\) Perhaps waiving the 10% copayment for those with very low income may ease the expenditure for home modifications.\(^5\)

The mean LOS in this study significantly decreased from 86.0 days in the before-LTCI group to 72.6 days in the after-LTCI group. Japan’s stroke rehabilitation has been characterized by a relatively longer inpatient LOS in comparison with the United States. It has been reported to range from 95 to 138 days in Japan compared with the average of about 20 days in the United States.\(^2\). It is suggested that the LTCI promoted an earlier discharge from this rehabilitation hospital. A patient’s LOS can be shortened even further by continued reassessment of rehabilitation progress and by facilitating discharge to the next appropriate level of care.

Some authors note that among Japanese stroke survivors, patients with better baseline activities of daily living are more likely to be discharged to home.\(^2\) This study has concurred with this finding. There are numerous reports demonstrating a positive association between early initiation of rehabilitation interventions after stroke and improved functional outcomes.\(^14\)–\(^16\) Indredavik et al.\(^17\) stressed that a shorter period of time before mobilization/training was the most important factor associated with discharge to home. A delay in rehabilitation can lead to further deconditioning and atrophy, thus prolonging the LOS and hindering optimal recovery and functional gain.\(^2\) Unfortunately, one of the defining characteristics of Japanese stroke rehabilitation has been delayed admission to rehabilitation hospitals. The interval from stroke onset to admission to

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**TABLE 1** Demographics of inpatient stroke patients between before–and after–long-term care (LTCI) insurance groups

<table>
<thead>
<tr>
<th></th>
<th>Before-LTCI Group(^a)</th>
<th>After-LTCI Group(^b)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in yrs, mean ± SD</td>
<td>66.2 ± 11.1</td>
<td>65.8 ± 12.7</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male/female ratio</td>
<td>115:86</td>
<td>143:109</td>
<td>NS</td>
</tr>
<tr>
<td>Type of stroke, (n) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infarction</td>
<td>108 (53.7)</td>
<td>130 (51.6)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>85 (42.3)</td>
<td>107 (42.5)</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td>8 (4.0)</td>
<td>15 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Type of paresis, (n) (%)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Right hemiplegia</td>
<td>92 (45.8)</td>
<td>100 (39.7)</td>
<td></td>
</tr>
<tr>
<td>Left hemiplegia</td>
<td>94 (46.8)</td>
<td>114 (45.2)</td>
<td></td>
</tr>
<tr>
<td>Paraplegia</td>
<td>5 (2.5)</td>
<td>18 (7.1)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10 (5.0)</td>
<td>19 (7.5)</td>
<td></td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage.

Tests used were \(\chi^2\) analysis and independent \(t\) test.

\(^a\) April 1997 through March 2000.

\(^b\) April 2000 through March 2003.
rehabilitation hospitals was shortened from 47.0 days to 40.8 days in this study; however, it did not reach statistical significance. The mean LOS in acute hospitals in Japan has been reported to range from 40 to 83 days before subsequent referral to rehabilitation hospitals.2,10,12,18 This delay may be due to a lack of understanding among medical practitioners about the relative importance of early referral to rehabilitation; however, it is also confounded by the lack of rehabilitation hospitals in Japan.

Jørgensen et al.19 reported that well-organized

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Total Barthel index score of inpatient stroke patients between before— and after—long-term care insurance (LTCI) groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Barthel Index</td>
<td>Before-LTCI</td>
</tr>
<tr>
<td>(n = 201)</td>
<td>(n = 252)</td>
</tr>
<tr>
<td>At admission, mean ± SD</td>
<td>51.4 ± 31.0</td>
</tr>
<tr>
<td>At discharge, mean ± SD</td>
<td>77.9 ± 28.9</td>
</tr>
</tbody>
</table>

Comparison of Barthel index between admission and discharge was computed by Wilcoxon’s signed-rank test; Barthel index between before- and after-LTCI groups was analyzed with Mann-Whiney U test.

FIGURE 1 Discharge sites before and after long-term care insurance (LTCI). Long-term care facility (LTCF) includes all types of facilities for the elderly requiring long-term care, such as nursing homes, hospital beds designated for the care of the elderly, and healthcare facilities for the elderly.
stroke units could significantly increase rates of discharge to home, reduce the LOS, and potentially reduce costs. Unfortunately, very few hospitals possess such an organized stroke unit in Japan. To progress toward a more effective system, a more efficient communication system needs to be established between hospitals to expedite transfer and continued care of the stroke patient.

The major limitation of this study is that the data were based on analysis from a single hospital, and therefore, the findings cannot be generalized to all Japanese rehabilitation facilities. However, this is the first study to look at any potential effect of the LTCI on stroke rehabilitation in Japan. Stroke programs may differ in treatment methods and intensity. Discharge sites may vary between institutions in regard to preferred and available facilities and resources within that region. Furthermore, the data do not reflect the effect of the LTCI alone, as other health insurance reform policies have also been implemented during the after-LTCI period.

Japan is in the midst of an ongoing increase in the aging population. Changes in the social and economic environments are occurring, and Japan is facing more serious fiscal concerns. The LTCI system has been the first step toward a social security structural reform. The Japanese government may have to undergo a continual process of trial and error before optimizing health care for its progressively aging society. This may also provide lessons to other countries that are challenged with similar dilemmas in health care. Further studies, which would include surveying a broader extent of stroke units, will be necessary to evaluate the overall effect of the LTCI as future revisions are implemented.

CONCLUSION

The institution of the LTCI in 2000 was designed to help contain the expanding costs of hospitalization for the elderly in Japan. One of the main intentions of the LTCI was to increase the rate of patients discharged to home after hospitalization; however, this study did not demonstrate this. The mean LOS for stroke rehabilitation patients was, however, indeed shorter for those treated after the introduction of LTCI. Although this study was limited to one hospital, it invokes the awareness that further amendments in the LTCI may be necessary to more positively affect the future of rehabilitation patients (and perhaps other hospitalized patients) in the face of changing medical coverage in Japan.

ACKNOWLEDGMENTS

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REFERENCES

8. Niki R: *Long-Term Care Insurance and Medical Insurance Reforms*. Tokyo, Keisou Shobou, 2000
Long-Term Treatment of Sleep Apnea in Persons with Spinal Cord Injury

ABSTRACT

Objective: Although numerous studies have documented a high prevalence of sleep apnea in persons with spinal cord injury, relatively little has been published regarding treatment of sleep apnea in this population. The purpose of this study was to describe long-term treatment outcomes and side effects of sleep apnea treatment in persons with spinal cord injury.

Design: Descriptive, postal mail survey to spinal cord injury individuals with sleep apnea followed by a Veterans Affairs Spinal Cord Injury Service.

Results: The response rate to the mailed survey was 54%, with complete surveys obtained from 40 individuals with spinal cord injury and sleep apnea. The majority of participants (93%) had been diagnosed with sleep apnea through routine clinical care, and patients had been diagnosed a mean of 4 yrs earlier. Continuous positive airway pressure was the most commonly used treatment. Continuous positive airway pressure was tried by 80% of patients, and of these, 63% continued to use continuous positive airway pressure, with mean usage 6.5 nights per week and 6.9 hrs per night. Continuous positive airway pressure was rated as beneficial in comparison with its side effects. The most common side effects were nasal congestion and mask discomfort.

Conclusion: Many spinal cord injury individuals with sleep apnea become long-term users of continuous positive airway pressure and perceive a subjective benefit from the treatment.

Key Words: Spinal Cord Injuries, Sleep Apnea Syndromes, Continuous Positive Airway Pressure, Patient Compliance
Obstructive sleep apnea is a very common condition in the general population, in which it is associated with medical co-morbidities including hypertension, heart failure, and stroke.\textsuperscript{1,2} Continuous positive airway pressure (CPAP) is considered the therapy of choice for this disorder, though surgery and dental appliances are also used. CPAP provides positively pressurized air through a nasal or oral/nasal mask worn at nighttime. This lessens the collapse of the upper airway during inspiration, thereby reducing the frequency and severity of apneas. A variation on CPAP, commonly referred to as bi-level positive airway pressure, uses separate inspiratory and expiratory pressures. Dental appliances reduce apnea episodes by moving the mandible and tongue to a more anterior position. Surgical treatments such as uvulopalatopharyngoplasty reduce or reposition the soft tissues that cause upper airway occlusion. A large number of studies have been published on these treatments in the general population. Studies that objectively assess long-term acceptance and use of CPAP show 68–90% of patients prescribed CPAP continue to use it >6 mos later and those using CPAP average 5–5.8 hrs of daily use.\textsuperscript{3–6}

In comparison, very little has been published on treatment of sleep apnea in persons with spinal cord injury (SCI), a group known to have an extremely high prevalence of the disorder.\textsuperscript{7–14} A retrospective study of 53 SCI patients with sleep apnea, some of whom were using CPAP, relied on data derived from chart review; therefore, data on current CPAP usage, perceived benefits, and adverse effects from treatment were not documented consistently.\textsuperscript{9} In addition, the alternative treatments tried and the reasons why some patients were not receiving treatment were not ascertained. This study was performed to describe sleep apnea therapy in a case series of SCI patients. Our hypothesis was that long-term acceptance of and daily use of CPAP would be lower than what has been described in the patients without SCI due to a number of factors seen in persons with SCI, including impaired hand function, a high prevalence of nasal congestion, and expiratory muscle weakness.\textsuperscript{15,16}

\textbf{METHODS}

\textbf{Study Design}

All study participants were derived from a population of individuals with SCI who receive medical care through the Department of Veterans Affairs (VA) SCI Service at VA Puget Sound Health Care System in Seattle, WA. The service provides care for approximately 600 veterans with chronic SCI. Patients were offered participation if they had been diagnosed with sleep apnea syndrome, including obstructive, central, and mixed sleep apnea. Using multiple strategies, we identified 40 patients who agreed to participate in the study. First, we evaluated the 53 patients previously identified through retrospective review of medical records of 584 persons with SCI.\textsuperscript{9} Of these, eight had been identified through random screening studies,\textsuperscript{8} and the remainder had been identified through routine clinical care. In the 2 yrs between the medical record review and this survey, clinicians on the SCI service identified an additional 22 persons with SCI and sleep apnea. Demographic data from the electronic medical records were used to determine which patients in our intended participant sample were deceased, and all surviving patients (n = 64) were contacted for study participation. In addition, 252 persons with SCI not known to the investigators to have a diagnosis of sleep apnea were contacted in the process of identifying a control group for a future study. Of the 93 responding patients, eight identified themselves as having a history of sleep apnea. These eight patients also were included as participants in the current study. The study received approvals from the institutional review boards of the University of Washington and VA Puget Sound Health Care System. Written informed consent was obtained from all participants.

Participants received a survey by postal mail, with options for survey completion and return by mail or completion by telephone interview. Those who did not respond to the first mailing were sent a second survey. None of the participants requested the telephone interview for survey completion. All study data were collected through the survey, except for body mass index and level of injury (tetraplegia vs. paraplegia), which were determined from medical records. Primary survey components included demographic information, sleepiness, site where sleep apnea testing was performed, and for those with a diagnosis of sleep apnea, the treatments ever tried, treatments currently used, and perceived benefits from treatment. Sleepiness was assessed using the Epworth Sleepiness Scale (ESS) and a subset of sleepiness and fatigue-related items from the Sleep Apnea Quality of Life Index (SAQLI). The ESS is a commonly used eight-item self-administered questionnaire on the likelihood of falling asleep in each of eight daily situations on a scale of 0–3, in which 0 indicates no chance of dozing and 3 indicates a high chance of dozing.\textsuperscript{17} Examples of the daily situations assessed include watching television, sitting inactively in a public place, and traveling as a passenger in a car. The scores from the eight daily situations are summed to create the ESS. Studies indicate that adults without sleep complaints have an average ESS of 6–7, and an ESS score >10 is often used to rep-
resent an abnormal level of daytime sleepiness. The SAQLI is a validated disease-specific, health-related, quality-of-life questionnaire for sleep apnea. The full instrument includes 35 questions organized into three domains: daily functioning, social interactions, and emotional functioning; a fourth domain on 21 symptoms of sleep apnea; and a fifth domain, treatment-related symptoms, to record the possible negative effect of treatment. Due to the length of the SAQLI, the need for an interviewer for instrument administration, and the likelihood of SCI-related impairments influencing responses in some domains, we chose to administer only a subset of SAQLI items that involve fatigue and sleepiness.

We assessed which sleep apnea treatments had been tried by the participants and which treatments they currently used. We also determined whether adjuvant treatments such as avoidance of the supine position during sleep were recommended to participants. Participants currently using CPAP or bi-level positive airway pressure rated how helpful they found the treatment on a 0–10 scale, with 0 indicating “no help” and 10 indicating a “great deal of help.” They also rated the unpleasantness and discomfort associated with the treatment on a 0–10 scale, with 0 indicating “no problem” and 10 indicating “major problem.” Participants were provided with a description of an oral appliance for sleep apnea treatment (described as “similar to a dental retainer”) and that “some people prefer it to a CPAP or bi-level positive airway pressure mask”) and asked whether they would consider trying it.

Analysis

We calculated the response rate for the survey as the number of completed surveys received divided by the difference between the number of surveys mailed and the number of surveys returned as undeliverable. To assess whether the likelihood of study participation was related to current usage of CPAP or other treatments, we also calculated separate response rates for a subset of participants based on the treatment status previously determined from medical record review. Response rates for participants thought to be receiving treatment vs. not receiving treatment were compared using the $\chi^2$ test. For calculation of the proportion of participants currently receiving sleep apnea treatment, we considered participants treated if they reported ongoing use of any of the specified treatments. We considered all patients who had received airway surgery (e.g., uvulopalatopharyngoplasty) to be currently treated. Summated ESS scores and individual SAQLI items for sleepiness and cognitive fatigue were compared using a two-tailed unpaired t test (ESS) or the Mann-Whitney U test (SAQLI items). All statistical analyses were performed using SPSS version 10.0.5 (SPSS, Chicago, IL). A $P$ value of <0.05 was considered significant.

RESULTS

The survey was sent to 72 SCI patients with sleep apnea. Four mailed surveys were returned by the post office as undeliverable, and an additional survey was returned due to a patient death that was unknown to us before the mailing. We received 29 completed surveys from the first mailing and an additional three surveys from the second mailing, giving an adjusted response rate of 54% for surveys received by patients initially known to have sleep apnea. Completed surveys were also received from eight additional patients not initially identified as having a sleep apnea diagnosis, producing a total sample size of 40 participants. With the exception of three participants who had been identified in a prospective study on sleep apnea prevalence, 37 participants (93%) had been diagnosed as part of routine clinical care. A total of 22 participants in the current study were also included in the previous study that used chart review. Most participants (37 of 40) had tetraplegia, all were men, and their mean ± standard deviation body mass index was 29.2 ± 6.6 kg/m$^2$. The 37 tetraplegic participants comprise 13% of all patients with tetraplegia who are followed by our SCI service.

The primary indications for sleep testing, as reported by participants, are listed in Table 1. The most common were witnessed apnea events (44%), severe snoring (15%), and excessive daytime sleepiness (12%). Sleep apnea had been diagnosed a mean of 4.2 ± 3.0 yrs before the survey. Testing had been performed at our facility for 29 cases (73%), at a different VA hospital for three cases (8%), at a community hospital for five cases (13%), and at a community sleep lab for three cases (8%).

Table 2 shows the types of treatment tried by the participants and the treatment currently used. CPAP had been tried by 32 participants (80%). Of these, four participants had also tried bi-level positive airway pressure, but none continued to use it. In addition to the three participants who underwent airway surgery, one more participant indicated that surgical treatment had been recommended. Only one participant indicated that he had been told to avoid the supine position while sleeping. Finally, only six participants (15%) indicated that weight loss had been recommended as a treatment for sleep apnea. Overall, 17 participants (43%) indicated that they were not currently receiving any treatment, and of these, five participants (13% of total) reported never trying any treatment. The duration since sleep apnea diagnosis was similar in those currently receiving vs. not
receiving treatment (4.1 ± 3.3 vs. 4.3 ± 2.7 yrs), and age (60.1 ± 11.0 vs. 55.6 ± 10.3 yrs) and duration of injury (22.0 ± 18.5 vs. 15.3 ± 12.4 yrs) did not differ significantly between these groups (t test: \( P = 0.19 \) and \( t = -1.33, P = 0.18 \) and \( t = -1.38 \), respectively).

Of the 32 participants who tried CPAP, 20 (63%) continued to use it at the time of the survey. For these participants, self-reported frequency and nightly hours of usage were high. The mean number of nights per week with CPAP usage was 6.5 (range, 3–7), and participants reported using it for a mean of 6.9 ± 1.9 hrs per night. Participants using CPAP indicated a median helpfulness score of 10 (interquartile range, 7.75–10 points) on a 0–10 scale and a median unpleasantness score of 3 (interquartile range, 2–5 points). Side effects reported by current CPAP users are listed in Table 3. The most commonly reported side effects were nasal congestion in 12 (60%) and mask discomfort in eight (40%). Four participants (20%) indicated that they were unable to independently adjust and reposition their masks due to limited upper limb function.

For the 17 participants who were not currently receiving any treatment, 13 indicated they had been offered CPAP and 12 had tried it. The problems experienced while unsuccessfully attempting CPAP included an inability to fall asleep while using it for eight participants (67%), mask discomfort for five participants (42%), and claustrophobia for four participants (33%). Participants who attempted but were intolerant of CPAP indicated that they were currently not receiving it due to the inability to fall asleep while using CPAP (eight participants, 67%), lack of improvement in symptoms or reduction in apnea events (three participants, 25%), or patient belief that treatment was unnecessary (one participant, 8%). We provided all participants with a description of an oral appliance used for treatment of sleep apnea and asked whether they would consider trying this treatment. Overall, 28 of the 34 participants who answered the item (82% of item respondents, 70% of survey participants) indicated a willingness to try such a device. Only one participant had previously tried this device.

Sleepiness was assessed by the ESS and sleepiness-related items from the SAQLI. The mean ESS for the group was 9.1 ± 5.1 points. The mean ESS score was 8.6 ± 4.7 for the 23 participants receiving treatment and 9.8 ± 5.8 for the 17 participants not receiving treatment (t test: \( P = 0.5, t = 0.65 \)). Similarly, although the SAQLI items showed no significant difference between treated and untreated groups, complaints related to low energy and excessive sleepiness were common in both groups. Of the 39 respondents to these items, 21 (54%) had decreased energy and 14 (36%) had excessive fatigue. In addition, 55% endorsed more than “a small amount” of difficulty concentrating, and 38% endorsed more than “a small amount” of difficulty staying awake.

To ascertain whether patients currently receiving treatment and age (60.1 ± 11.0 vs. 55.6 ± 10.3 yrs) and duration of injury (22.0 ± 18.5 vs. 15.3 ± 12.4 yrs) did not differ significantly between these groups (t test: \( P = 0.19 \) and \( t = -1.33, P = 0.18 \) and \( t = -1.38 \), respectively).

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To ascertain whether patients currently receiv-
ing treatment were more likely to have participated in the survey than untreated patients, we calculated separate response rates based on the treatment status determined in our previous study. Thirty-eight patients with a previously determined treatment status were contacted for participation in this study and 18 participated. The response rate for patients anticipated to be using CPAP was 72% (13 of 18), whereas the response rate for those not anticipated to be using CPAP was 25% (5 of 20; \( P = 0.004, \chi^2 = 8.47 \)).

DISCUSSION

This study is the first to provide detailed long-term follow-up on the treatment of sleep apnea in a primarily clinically derived population of individuals with SCI. Previous studies on treatment of sleep apnea in persons with SCI have been limited to two case series (n = 3 and n = 2),7,11 retrospective review of medical records,9 or short-term follow-up on cases identified through screening rather than routine clinical care.8,10 Stockhammer et al.10 screened 50 patients with tetraplegia, detecting 31 cases with sleep-disordered breathing. Of the 16 who tried CPAP, 11 continued it for at least a few weeks, and nearly all of those continuing CPAP had previously experienced symptoms of excessive daytime sleepiness. The population investigated in the current study was primarily (93%) composed of patients who had been diagnosed through routine clinical care, and the mean follow-up duration was >4 yrs. Use of a survey allowed us to determine the benefit perceived by patients receiving treatment and the adverse effects experienced by those using and not currently using any treatment.

Contrary to our hypothesis, long-term use and self-reported daily hours of use compared favorably with what has been reported in non-SCI patients. Overall, 57% of participants were considered to be receiving some form of treatment for sleep apnea, and 63% of those who had tried CPAP continued to use it. McArdle et al.4 found a 68% acceptance rate for CPAP after 5 yrs in non-SCI patients, with 4.5% of cases refusing CPAP treatment initially and 20% discontinuing because of lack of effect. A retrospective study of men aged >65 yrs who were diagnosed and treated in a VA setting found that 20 of 33 (61%) continued to use CPAP.21 Our findings are likely an overestimate of the true proportion of SCI individuals who continue treatment because we found a differential response rate based on the anticipated treatment status. By comparing response rates for individuals previously included in our chart review study, we found that those thought to be receiving treatment were significantly more likely to participate in this study than those who we thought were receiving no treatment. If we assume that none of the nonrespondents were currently receiving treatment, the minimum rate of treatment in those thought to have received the survey would be 39% (23 treated out of 59 survey recipients).

Those currently using CPAP perceived the treatment to be greatly beneficial in comparison with the unpleasantness of treatment-related side effects. However, ESS and other measures of sleepiness and fatigue were not significantly lower in CPAP-treated patients. This may be explained by our small sample size and the role of other causes of sleepiness, including medications, in SCI patients. Because we had no measures of pretreatment sleepiness, we were unable to determine whether the ESS had decreased with treatment. Acceptance of treatment is more likely in those with greater pretreatment symptoms;3,4,10,22 therefore, treated participants may have had a reduction in sleepiness despite having similar sleepiness scores to the untreated participants. Prospective studies with standardized measures before and after treatment are needed to confirm that CPAP reduces sleepiness symptoms in this population. Complaints relating to reduced energy, excessive fatigue, difficulty concentrating, and difficulty staying awake were common in both treated and untreated groups.

The side effects reported by current CPAP users are somewhat similar to those reported for the general population. Janson et al.22 found problems in nose or pharynx, which increases with advanced aged, and lack of effect as important reasons leading to discontinuation of use. In this study, the most commonly reported reason for CPAP intolerance was an inability to fall asleep while using CPAP. Patients with SCI may experience barriers to treatment not seen in the general population. Mask-associated symptoms, which are a common barrier in the general population, were also relatively common in participants with SCI. Our previous work indicated that patients who lack adequate hand function to manipulate a CPAP mask may have a lower rate of CPAP acceptance.9 A number of strategies have been associated with improved CPAP acceptance and long-term acceptance in the general population. CPAP education and intensive follow-up and the regular use of heated humidification has been shown to improve objective CPAP usage in several studies.23–26 Sin et al.3 found 85% continued usage, defined as >4 hrs per day of use, after 6 mos with intensive follow up and support to resolve mask-related problems.

Relatively few patients had tried alternative treatments such as airway surgery or oral appliances. Although these treatments have some efficacy in the general population,20,27 data are not available on the efficacy and acceptance of these
treatments in individuals with SCI. The majority of participants expressed an interest in trying an oral appliance for treatment. Alternatives to CPAP, such as surgery and oral appliances need to be studied in this population to determine if they are reasonable options for SCI patient with obstructive sleep apnea.

In addition to the differential response bias based on current treatment status, there are a number of other limitations to this study. The adjusted response rate for the mailed surveys (54%) was somewhat low. The study relied on patient report, which may not be accurate for historical details regarding initial treatment after a mean duration of >4 yrs. We relied on self-report for data on CPAP usage. Patient report generally overestimates the duration of CPAP usage by 0.7–1.2 hrs per night when compared with objective measures. Finally, the findings may not generalize to other settings, in which sleep apnea may be diagnosed less frequently or with different testing methods. Study participants included 13% of all tetraplegic patients followed by our SCI service. Sleep studies and CPAP trials at our facility are performed by respiratory therapists who are not registered polysomnographic technicians and by using cardipulmonary monitors that lack electroencephalographic monitoring. The therapist is not present throughout the entire study. In the community setting, sleep studies typically include electroencephalographic monitoring and are fully attended by technicians who are specifically trained for this purpose. In addition, more varieties of mask interfaces, positive airway pressure devices and accessories, and more intensive education and follow-up may be available in other settings and may result in improved acceptance of CPAP. Our findings on CPAP acceptance are similar to those from a study in non-SCI patients diagnosed and treated in a different VA setting.

CONCLUSION

Many SCI individuals with sleep apnea become long-term users of CPAP and experience significant subjective benefit, with mild treatment-related side effects, despite potential barriers to treatment not present in patients without SCI. Those who do not tolerate treatment of CPAP report an inability to sleep while receiving the treatment. Strategies to improve treatment of sleep apnea in this population should include individualized assessment of factors interfering with treatment acceptance, combined with close follow-up, as shown to be beneficial in the general population. Future studies should assess the role of alternative treatments such as upper airway surgery and oral appliances.

REFERENCES

terizes patients who are unable to tolerate continuous positive airway pressure (CPAP) treatment? Respir Med 2000; 94:145–9


Advances in the Diagnosis of Neuromuscular Junction Disorders

ABSTRACT

Disorders of the neuromuscular junction have a wide range of clinical presentations, which frequently poses a diagnostic challenge to evaluating clinicians. This article describes the tests used in the diagnosis of diseases of the neuromuscular junction, reviews the evidence supporting the use of each test, and proposes guidelines for their efficient utilization. A focused review of the literature was employed. Reports from four main categories of diagnostic tests (pharmacologic, electrodiagnostic, immunologic, and miscellaneous tests) were reviewed, and the sensitivity and specificity of each test in the diagnosis of specific neuromuscular junction diseases were examined. The clinical presentation determines which diagnostic tests should be utilized in individual cases of suspected neuromuscular junction disease. However, knowledge of the sensitivity and specificity of each test can help to focus the diagnostic evaluation and maximize the diagnostic yield of each test.

Key Words: Neuromuscular Junction, Myasthenia Gravis, Lambert-Eaton Myasthenic Syndrome, Repetitive Nerve Stimulation, Single-Fiber Electromyography, Acetylcholine Receptor Antibodies, Muscle-Specific Receptor Tyrosine Kinase Antibodies
Disorders of the neuromuscular junction (NMJ) have a wide range of clinical presentations, which frequently poses a diagnostic challenge to evaluating clinicians. A common feature of these conditions is symptomatic muscle weakness that predominates in certain muscle groups and typically fluctuates in response to effort and rest. The diagnosis is usually suggested by these characteristic symptoms and by demonstrating this distinctive pattern of weakness. The major tools used to confirm the clinical diagnosis of a disorder of neuromuscular transmission may be divided into four main groups: pharmacologic, electrophysiologic, immunologic, and miscellaneous tests (Table 1). This article describes the tests used in the diagnosis of diseases of the NMJ, reviews the evidence supporting the use of each test, and proposes guidelines for their efficient utilization.

**PHARMACOLOGIC TESTS**

Clinical observation of the response to administration of pharmacologic agents that affect neuromuscular transmission forms the basis for a number of diagnostic tests. The most commonly performed are tests that demonstrate improved strength induced by cholinesterase inhibitors (i.e., edrophonium, neostigmine, pyridostigmine), which are most useful in the diagnosis of myasthenia gravis (MG).

**Edrophonium Chloride**

The use of edrophonium chloride (Tensilon) as a diagnostic test for MG was described in 1952.1 Its rapid onset (30 secs) and short duration of effect (5–10 mins) make it an ideal agent for this purpose. By inhibiting the normal action of the enzyme acetylcholinesterase, edrophonium and other cholinesterase inhibitors impede the breakdown of acetylcholine molecules, allowing them to diffuse more widely throughout the synaptic cleft and to have a more prolonged interaction with acetylcholine receptors, producing a larger endplate potential.2

The test consists of administering edrophonium intravenously and observing for improvement in muscle strength. A number of protocols for administration have been used, but most commonly, a test dose of up to 2 mg is given, followed by subsequent doses of 3–8 mg until there is a positive response or a total of 10 mg is given. The patient is observed for 60 secs between doses and for 3–5 mins after the full 10-mg dose has been administered.

The most important consideration in performance of the edrophonium test is the endpoint to be used. Only unequivocal improvement in strength of a sentinel muscle should be accepted as a positive result. In many muscle groups, particularly limb muscles, the observed strength is largely dependent on patient effort. For this reason, resolution of eyelid ptosis and improvement in strength of a single paretic extraocular muscle have been advocated as the only truly valid endpoints,3 observed function in these muscles being largely independent of voluntary effort.

Side effects from edrophonium include increased salivation and sweating, nausea, stomach cramping, and muscle fasciculations. Hypotension and bradycardia are infrequent and generally resolve with rest in the supine position. However, atropine should be available for injection (0.4–2 mg) if bradycardia is severe. In a survey of 357 physicians, mostly neuro-ophthalmologists, regarding the complication rate of edrophonium testing, the 199 responding physicians estimated that they had performed >23,000 edrophonium tests, of which 37 (0.16%) were associated with a serious complication, most often bradyarrhythmias and syncope.4

Published reports indicate that the sensitivity of the edrophonium test ranges from 60% to 95% for ocular myasthenia and 71.5% to 95% for generalized MG.5 The specificity of the test is not clear from available published information. However, a positive response to edrophonium has been reported in a variety of conditions other than MG, including other disorders of the NMJ, such as Lambert-Eaton myasthenic syndrome (LEMS) and botulism, as well as motor neuron disease,6 brainstem glioma,7 compressive aneurysm,8 Guillain-Barré syndrome,9 and end-stage renal disease.10 Positive
serves to maximally stimulating the motor nerve. RNS belonging to all the motor units activated by summation of the action potentials from muscle fibers is particularly useful in the evaluation of children.

Finally, administration of oral pyridostigmine (Mestinon) as a therapeutic trial may demonstrate increased muscle strength that is not apparent after a single dose of pyridostigmine or neostigmine. Caution is advised in interpreting such trials, which frequently rely on the patient’s subjective reports of benefit. Unlike most MG patients, many patients with muscle-specific receptor tyrosine kinase (MuSK)-positive MG (see below) do not improve and may even become worse with edrophonium or pyridostigmine.

**ELECTROPHYSIOLOGIC TESTS**

Electrophysiologic studies are performed in patients with suspected NMJ disease to confirm a defect in neuromuscular transmission and also to exclude other diseases of the motor unit that may contribute to the clinical findings. The two principal electrophysiologic tests used for this purpose are repetitive nerve stimulation studies and single fiber electromyography.

**Repetitive Nerve Stimulation**

Repetitive nerve stimulation (RNS) is the most commonly used electrophysiologic test of neuromuscular transmission. In 1895, Jolly described a technique in which an electric current was applied to excite a motor nerve while the force of muscle contraction was recorded. Harvey and Masland refined the technique in 1941 by recording the electrical signals from the muscle elicited by RNS to detect disorders of neuromuscular transmission. In this technique, a motor nerve is stimulated repetitively while recording compound muscle action potentials (CMAPs) from an appropriate muscle. The CMAP is the electrophysiologic summation of the action potentials from muscle fibers belonging to all the motor units activated by supramaximally stimulating the motor nerve. RNS serves to “stress” diseased NMJs by depleting the store of readily releasable acetylcholine, which causes failure of neuromuscular transmission in a portion of motor endplates, resulting in fewer muscle fibers contributing to the CMAP. This is the physiologic basis for the decremental response to RNS observed in NMJ disease.

A detailed description of the technical requirements for the optimal performance of RNS studies can be found elsewhere. Briefly, trains of supramaximal stimuli are delivered to a peripheral nerve at rates of 2–5 Hz. CMAPs are recorded from a muscle supplied by the nerve being stimulated. The decremental response is defined as the percentage of change between the amplitude or area of the fourth, fifth, or lowest potential compared with the first potential of each train. A decrement of >10% is usually considered abnormal, although the criteria for abnormality will vary to some degree among laboratories. Some laboratories require a decrement of >20% in proximal muscles to be considered abnormal because of baseline variability.

The diagnostic yield of RNS can be increased by techniques that activate the motor nerve. The most commonly employed is maximum isometric exercise of the tested muscle for a prescribed period of time. Activation may also be accomplished by rapid-rate nerve stimulation (20–50 Hz). The latter is used less frequently because it is painful and is mainly utilized in patients who cannot voluntarily exercise the muscle of interest. The physiologic effect of such activation results from accumulation of calcium in the nerve terminal, which enhances the release of acetylcholine. If the initial CMAP is small, as in a presynaptic disorder such as LEMS, this produces a marked increase in the CMAP amplitude. This phenomenon is termed postactivation facilitation. More sustained activation, such as maximum exercise for 30–60 secs or longer, depletes the readily releasable stores of acetylcholine, which overrides the effects of calcium accumulation in the nerve terminal and also depresses endplate excitability. This effect is most marked 2–4 mins after activation and is referred to as postactivation exhaustion. The electrophysiologic manifestation of this phenomenon is exaggeration of the decremental response compared with the pre-exercise values. The activation technique used depends on whether a presynaptic or postsynaptic NMJ disorder is suspected (Table 2).

**RNS in MG**

Characteristically in MG, the CMAP is normal, although in severely weak muscles, the amplitude may be reduced. The diagnostic pattern is a decremental response to trains of 2–5 Hz of stimulation and partial repair of the decrement after the third or fourth response of the train, which produces a characteristic U-shaped or saddle-shaped train envelope (Fig. 1). Postactivation exhaustion is commonly seen 1.5 to 3 mins after activation by maximum voluntary contraction for 30–60 secs or longer.

A literature review of electrodiagnostic testing
for MG and LEMS found the reported sensitivity of RNS for diagnosing MG to range from 53% to 100% in generalized MG and from 10% to 17% in ocular myasthenia.17 RNS is more likely to be abnormal in a proximal or facial muscle in MG. To obtain the maximal diagnostic yield, several muscles must be tested, including particularly those that are clinically weak. Studies report an abnormal decrement in a hand or shoulder muscle in approximately 75% of patients with generalized MG and in fewer than 50% of those with ocular myasthenia.18 Even with extensive testing of many muscles, RNS may be normal in many patients with generalized MG, especially if symptoms are mild or limited in distribution. Although the specificity of RNS is not clear from available data, it is important to remember that patients with primary neurogenic disease, particularly when associated with recent collateral sprouting, such as motor neuron disease, may have an abnormal decrement on RNS testing.19,20

**RNS in LEMS**

The pattern of abnormality on RNS in LEMS is characteristic (Fig. 2) and frequently forms the basis for the clinical diagnosis. The classic findings

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**Table 2. Repetitive nerve stimulation strategies for suspected presynaptic and postsynaptic neuromuscular junction (NMJ) defects**

<table>
<thead>
<tr>
<th>NMJ Defect Location</th>
<th>Stimulation Train</th>
<th>Stimulation Frequency</th>
<th>Expected Findings</th>
<th>Exercise</th>
<th>Expected Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postsynaptic</td>
<td>5–10 stimuli</td>
<td>2–5 Hz</td>
<td>&gt;10% decrement; normal CMAP amplitude</td>
<td>30–60 secs</td>
<td>PAE 2–4 mins</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10 secs</td>
<td>Repair of decrement immediately postexercise</td>
</tr>
<tr>
<td>Presynaptic</td>
<td>5–10 stimuli</td>
<td>2–5 Hz</td>
<td>&gt;10% decrement; low CMAP amplitude</td>
<td>10 secs</td>
<td>PAF &gt; 100% immediately postexercise</td>
</tr>
<tr>
<td></td>
<td>Stimulation for 5–7 secs</td>
<td>20–50 Hz</td>
<td>&gt;100% increase in intratrain CMAP amplitude</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

CMAP, compound muscle action potential; PAE, postactivation exhaustion; PAF, postactivation facilitation.

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**FIGURE 1** Example of A, a normal RNS study, and B, a decremental response in a patient with MG. Responses were obtained with repetitive stimulation of the ulnar nerve at 3 Hz, recording from the abductor digitii minimi muscle. The maximum decrement in B (30%) occurs after the fourth stimulation, producing the classic “U-shaped” or “saddle-shaped” envelope pattern. Reproduced with permission.69

**FIGURE 2** Classic electrodiagnostic findings in Lambert-Eaton myasthenic syndrome. Repetitive nerve stimulation of the ulnar nerve at 3 Hz, recording from the abductor digitii minimi muscle. A, repetitive nerve stimulation of resting muscle. Note low compound muscle action potential amplitude (1.1 mV) and decremental response at baseline (19%). B, repetitive nerve stimulation immediately after 10 secs of voluntary exercise. Note prominent facilitation of compound muscle action potential amplitude (>300%). Reproduced with permission.69
are low-amplitude CMAPs with an abnormal decrement with low-frequency stimulation.\textsuperscript{21–23} Immediately after a brief period of activation with exercise or during rapid-rate stimulation, there is a marked increase of CMAP amplitude (facilitation) of 100–1000\% or more. Although the predominant clinical feature of LEMS is proximal lower limb weakness, the characteristic electrophysiologic abnormalities are more readily detected in the hand muscles.\textsuperscript{24,25} In LEMS, facilitation of \( \geq 100\% \) is considered diagnostic, although this is not seen in all muscles, and it may be necessary to examine several muscles to demonstrate this feature. In proximal muscles, the CMAP amplitude is usually normal, there is usually a decremental pattern to low-frequency RNS, and the amount of facilitation is variable. Facilitation of \( >50\% \) in any muscle suggests LEMS, but this may also be seen in MG.\textsuperscript{24} If facilitation is \( >50\% \) in most muscles tested or is \( >400\% \) in any muscle, the patient almost certainly has LEMS. If facilitation is \( <50\% \) in all muscles tested, the patient still may have LEMS, especially if weakness has been present for only a short time or the patient has been partially treated. Practically speaking, it is preferable to assess for facilitation after brief voluntary exercise of the muscle rather than during high-frequency RNS because the former is less painful and just as effective for demonstrating postactivation facilitation.\textsuperscript{25} In a prospective study, the most sensitive electrophysiologic finding in a group of LEMS patients was a \( >10\% \) decrement in a distal hand muscle, which was found in 98\% of patients.\textsuperscript{25} In that study, 12\% of LEMS patients failed to demonstrate facilitation of \( >100\% \) in any of four tested muscles.

A simple screening test in patients suspected of LEMS is to elicit a single supramaximally activated CMAP from a warmed, rested hand muscle, and if it is low, to deliver a second supramaximal stimulus immediately after activating the muscle for 10 secs. In nearly all cases, there will be a marked facilitation of the CMAP amplitude (Fig. 3). More formal RNS studies can then be undertaken to demonstrate a decremental response to slow rates of stimulation and postactivation facilitation.

\textbf{RNS in Other NMJ Disorders.}

\textbf{Botulism}

Several patterns of RNS abnormalities may be observed in botulism, depending on the severity of the disease and whether the patient is an adult or an infant. The CMAP amplitude is low at rest in virtually all patients. RNS at 2–5 Hz may produce a decrement, but this may be minimal or absent if the baseline CMAP amplitude is very low. Postactivation facilitation after either brief isometric exercise or rapid-rate stimulation (20–50 Hz.) is common in children but is present in only approximately 60\% of adults. In patients with severe weakness who cannot produce maximal voluntary contraction of the muscle, rapid-rate stimulation is required to elicit postactivation facilitation. Facilitation may require more prolonged rapid-rate stimulation (10–20 secs) and also lasts longer (5–30 mins) compared with other endplate diseases. The degree of postactivation facilitation is characteristically less than that seen in LEMS, ranging from 40\% to 200\%.\textsuperscript{26} Postactivation exhaustion is not seen in botulism.

When present, the following four characteristic RNS findings are virtually diagnostic of botulism: (1) reduced resting CMAP amplitude, (2) \( \geq 40\% \) facilitation of CMAP amplitude after activation, (3) persistence of facilitation for \( \geq 2 \) mins after activation, and (4) the absence of postactivation exhaustion.\textsuperscript{26,27} However, hypermagnesemia may also have these electrodiagnostic features.

\textbf{Congenital Myasthenic Syndromes}

In many congenital myasthenic syndromes, the electrodiagnostic findings resemble those in autoimmune MG.\textsuperscript{28} In disorders that cause an increased duration of the endplate potential (congenital acetylcholinesterase deficiency and slow-channel syndrome) a repetitive CMAP is observed (Fig. 4).\textsuperscript{29} A single electrical stimulus elicits two or more CMAPs and results when suprathreshold depolarization at the endplate is prolonged beyond the absolute refractory period of the muscle fiber action potential. In certain other congenital myasthenic syndromes, high-frequency or prolonged stimulation may be required to produce a decremental response.\textsuperscript{29}
Single Fiber Electromyography

Single-fiber electromyography (SFEMG) is a selective recording technique in which a specially constructed concentric needle electrode is used to identify and record action potentials from individual muscle fibers. Measurement of jitter by SFEMG is the most sensitive clinical test for detection of a defect in neuromuscular transmission. This sensitivity allows for demonstration of abnormalities even in clinically unaffected muscles.30

During sustained activation of the motor nerve, the latency from nerve activation to muscle action potential varies from discharge to discharge. This variation is the neuromuscular jitter and is produced by fluctuations in the time it takes for the endplate potential at the NMJ to reach the threshold for muscle action potential generation. These fluctuations are in turn due to the normally varying amount of acetylcholine released from the nerve terminal after a nerve impulse. A small amount of jitter is seen in normal muscles due to this phenomenon. An increase in the jitter is the most sensitive electrophysiologic evidence of a defect in neuromuscular transmission. When the defect is more severe, some nerve impulses fail to elicit action potentials, and SFEMG recordings demonstrate an intermittent absence of one or more single muscle fiber action potentials on consecutive firings. This is called impulse blocking and represents neuromuscular transmission failure at the involved endplate. SFEMG studies can be performed during either voluntary activation of the muscle or with axonal stimulation. In the former, the examiner positions the recording electrode to record two or more time-locked potentials while the patient minimally contracts the muscle under study (Fig. 5). For jitter studies with axonal stimulation, the motor nerve is stimulated proximal to its entry into the muscle, or individual motor nerve branches may be stimulated within the muscle. The first technique is ideal for activating facial muscles because individual branches of the facial nerve can be stimulated with a monopolar needle electrode inserted through the skin anterior to the ear. For limb muscles, intramuscular axons are stimulated with a monopolar needle electrode inserted near the motor endplate zone (Fig. 6). Another needle or surface electrode is used as the anode. The stimulus intensity is adjusted to produce a slight twitch of the muscle. The SFEMG electrode is inserted into the twitching portion of the muscle and positioned to record clearly defined single fiber action potentials. As the stimulus intensity is increased, increasing numbers of single fiber action potentials are elicited, initially with high jitter and intermit-
tent blocking due to liminal stimulation. When a further increase in stimulus intensity no longer decreases the jitter, the jitter is measured between the stimulus and the action potentials from single muscle fibers. For accurate assessment of jitter during axonal stimulation, it is critical to distinguish neuromuscular jitter from the jitter and blocking that may be induced by liminal stimulation. Jitter measurements performed during voluntary activation are less subject to technical problems but are more dependent on patient cooperation.

Jitter is quantified by measuring the variation in the time interval between the two action potentials in the pair (interpotential interval) during voluntary activation. For axonal stimulation studies, the variation in latency from stimulus to individual action potentials is measured. Jitter measurements performed during voluntary activation are less subject to technical problems but are more dependent on patient cooperation. Jitter is calculated as the mean difference between consecutive interpotential intervals or action potential latencies (mean consecutive difference). The interpotential interval and action potential latency may be influenced by the preceding interdischarge interval. When the firing rate is not constant, this can introduce an additional degree of variability to these calculations due to changes in the velocity of action potential propagation in the muscle fibers. This is an important issue when jitter is measured during voluntary activation when firing rates may vary. This effect is minimized by sorting the interpotential intervals according to the length of the preceding interdischarge interval and then calculating the mean of the consecutive interval differences in the newly sorted data. This is called the mean sorted difference and should be used to express jitter when the mean consecutive difference/mean sorted difference ratio is >1.25.

The mean jitter of all fiber pairs and the percentage with normal jitter and impulse blocking are calculated and reported for each muscle tested. A study is abnormal if the mean jitter (mean consecutive difference) of all fiber pairs (or endplates) exceeds the upper limit of normal for that muscle or if >10% of pairs or endplates have jitter that exceeds the upper limit of normal for that muscle. Normal values for mean consecutive difference vary according to age and muscle, ranging between 10 and 50 μsec. For the extensor digitorum communis muscle, the mean consecutive difference should be <34 μsec, and the upper limit of normal for individual potential pairs is 55 μsec.

Reference values for jitter during voluntary activation have been determined for a number of muscles in a multicenter collaborative study. Normal jitter values for axonal stimulation studies have been determined for some muscles. For other muscles, the normal values for stimulated jitter can be calculated by dividing the values for voluntarily activated jitter by 1.4.

SFEMG in MG

The sensitivity of SFEMG for diagnosing MG ranges from 82% to 99%, with the highest sensitivity attained when several muscles are tested. Jitter is greatest in weak muscles but is usually increased even in muscles with normal strength. The finding of normal jitter in a clinically weak muscle essentially rules out a defect in neuromuscular transmission as a cause for the weakness in that muscle. The sensitivity of SFEMG for MG comes at the price of reduced specificity, as jitter may also be increased in primary nerve or even muscle disease. For this reason, nerve conduction studies and conventional electromyography should be done whenever SFEMG is abnormal to rule out disorders of nerve and muscle that may impair neuromuscular transmission.

SFEMG in Other NMJ Disorders

SFEMG demonstrates abnormal jitter in all patients with LEMS, usually with prominent impulse blocking. The magnitude of the increased jitter is often out of proportion to the relatively mild degree of clinical weakness. Jitter typically decreases with increasing firing rate in LEMS, although this is not seen in all patients. Neuromuscular jitter is usually increased in botulism and congenital myasthenic syndromes, with impulse blocking occurring particularly in clinically weak muscles.
IMMUNOLOGIC TESTS

Although not all NMJ disorders have an autoimmune pathogenesis, immunologic tests have become standard in the diagnosis of MG and LEMS and, when positive, have the advantage of being very disease specific.

Antiacetylcholine Receptor Antibodies
Acetylcholine Receptor Binding Antibodies

Antibodies that react with acetylcholine receptor (AChR) proteins are generally regarded as specific serologic markers for acquired MG. The AChR binding antibody assay has become a widely utilized diagnostic test for MG. The most commonly available assay uses purified AChR extracted from human skeletal muscle and labeled with radiiodinated α-bungarotoxin. The reported sensitivity of this test ranges from 70% to 95% for generalized MG and from 50% to 75% for ocular myasthenia.37–39 AChR antibody–positive patients with ocular or mild generalized MG tend to have antibody titers that are lower than those with generalized disease. However, the serum concentration of AChR antibodies varies widely among patients with similar degrees of weakness and does not reliably predict the severity of disease in individual patients.

In general, elevated AChR antibodies in a patient with compatible clinical features essentially confirm the diagnosis of MG. However, normal antibody measurements do not exclude the diagnosis. Although there are no published data on diagnostic specificity, the occurrence of false positives is believed to be rare. AChR antibodies may occasionally be found in autoimmune liver disease, systemic lupus, inflammatory neuropathies, amyotrophic lateral sclerosis, patients with rheumatoid arthritis receiving penicillamine, patients with thymoma without MG, and in first-degree relatives of patients with acquired autoimmune MG.40

AChR Blocking Antibodies

Blocking antibodies inhibit the binding of radiolabeled α-bungarotoxin to the AChR by competing for the acetylcholine binding site or by allosteric inhibition.40 They are directed against the acetylcholine binding site on the alpha subunit of the AChR. In most patients, relatively few of the circulating antibodies recognize this site, resulting in a lower sensitivity for this assay. When blocking antibodies are found, they usually occur in association with AChR binding antibodies, and add little diagnostic sensitivity because fewer than 1% of patients with MG have only serum blocking antibodies.41

AChR Modulating Antibodies

AChR antibodies crosslink the AChR in the membrane and increase their rate of degradation. The AChR modulating antibody test measures the rate of loss of labeled AChR from cultured human myotubes.42 A positive result is most useful when the AChR binding assay is negative, and this occurs in about 3–4% of patients.40,41 Therefore, for general clinical purposes, the AChR modulating antibody test should be reserved for patients with undetectable AChR binding antibodies. It is important to realize that false-positive results for this test may arise due to hemolysis, bacterial contamination, and exposure of the serum to ambient heat.40 MG patients with thymoma often have anti-AChR modulating antibodies of >90%, and it has been suggested that levels this high should raise the suspicion for an underlying thymoma.41,43 However, in one study, modulating antibody levels failed to distinguish patients with thymoma from those without thymoma: 38% of patients in each group had modulating antibody values of >90%.44

Striated Muscle Antibodies

Antibodies to striated muscle were the first autoantibody discovered in MG.45 These antibodies react with contractile elements of skeletal muscle and are found in 30% of all adult-onset MG. They are highly associated with thymoma, being found in ≥80% of MG patients with thymoma and 24% of patients with thymoma without MG.46 Their absence does not exclude thymoma, and they are found in many MG patients without thymoma, particularly in elderly patients.47 Striated muscle antibodies are most useful as a marker of thymoma in patients with MG onset before age 40. Striated muscle antibodies may also be a valuable marker for MG in middle-aged or elderly patients with mild disease, in whom they can be the only serologic abnormality. They are rarely found in patients without MG or thymoma but have been reported in patients with rheumatoid arthritis treated with penicillamine, in 3–5% of patients with LEMS, and in recipients of bone marrow allografts who develop graft-vs.-host disease.46

Approximately 95% of MG patients with thymoma have antibodies to the intracellular striated muscle protein titin, as do 50% of patients with late-onset nonthymomatus MG.48,49 Titin is a major muscle antigen and is at least partially responsible for the striational binding pattern of serum striational antibodies.

Some MG patients have immunoglobulin G antibodies that react with another muscle antigen, the ryanodine receptor. The ryanodine receptor is a calcium release channel located in the sarcoplasmic reticulum of skeletal muscle. Antiryanodine
antibodies are found in 75% of MG patients with thymoma and in approximately 10–20% of nonthymomatous, late-onset MG. These antibodies are found more often in patients with more severe myasthenia, who are less responsive to treatment, but their role in disease pathogenesis has not been determined.

**Anti-MuSK Antibodies**

Recent studies indicate that approximately 40–50% of anti-AChR antibody-negative, generalized MG patients have antibodies to MuSK (Table 3). MuSK is an NMJ protein that plays an important role in the clustering of AChRs during fetal development. Anti-MuSK antibodies are much more common in female compared with male MG patients. Some MuSK-positive patients have clinical features somewhat atypical for MG, with prominent facial and bulbar, or neck, shoulder, and respiratory muscle weakness, while sparing the ocular muscles. In many of these patients, particularly those with weakness restricted to facial, neck, or shoulder muscles, RNS or SFEMG testing may be abnormal only in weak muscles. Anti-MuSK antibodies may interfere with the aggregation of AChRs at the developing NMJ, but the mechanism of their pathogenic effect in patients has not yet been demonstrated.

**Antibodies to the Voltage-Gated Calcium Channel**

Up to 90% of patients with LEMS have antibodies directed against the voltage-gated calcium channel on the presynaptic nerve terminal. These antibodies are found more frequently in LEMS patients who have an underlying small-cell lung cancer. As is the case for MG, there is no correlation between the level of these antibodies and disease severity, and their absence does not exclude the diagnosis. Patients treated with immunosuppressive agents may become “seronegative;” thus, it is important to obtain these serological tests before instituting immunotherapy.

Although the sensitivity of voltage-gated calcium channel antibodies is quite high, they are also found in some patients with small-cell lung cancer without clinical evidence of LEMS. Furthermore, patients with paraneoplastic cerebellar ataxia with or without LEMS also may have these antibodies.

**MISCELLANEOUS TESTS**

**Ice-Pack Test**

A number of reports suggest that improvement in ptosis after application of ice to the ptotic eyelid is both sensitive and specific for the diagnosis of MG. In this test, an ice pack is placed over the ptotic eyelid, usually for a period of 2 mins. The response to local cooling is then assessed by observing whether ptosis improves. The precise onset and duration of cooling-induced improvement is not clear from published articles. Positive responses to the ice-pack test have been reported even when edrophonium tests are negative. A recent review of six studies in which the ice-pack test was performed in 76 patients with MG and in 77 controls showed it to have a sensitivity of 89% and a specificity of 100% in these patients, suggesting that it may be useful as an adjunctive diagnostic test in patients with lid ptosis, particularly if the edrophonium test is contraindicated or not available. Myasthenic ptosis also improves with rest, and this may account for some of the observed improvement after application of ice.

**Muscle Biopsy**

In autoimmune MG, the postsynaptic membrane visualized by electron microscopy is simplified, and the concentration of AChRs at the NMJ is reduced. Muscle biopsy studies to demonstrate the morphometric, immunocytochemical, and microphysiologic findings typical of MG have been used to confirm the diagnosis in patients without detectable AChR antibodies who have normal or equivocal electrodiagnostic findings. SFEMG has largely eliminated the need for these studies in the routine diagnosis of autoimmune MG, and few laboratories have the expertise to perform them. These tests may, however, be the only method to diagnose and characterize some congenital myasthenic syndromes.

Conventional muscle biopsy studies may demonstrate no obvious histologic abnormality in MG or may reveal type II fiber atrophy. A variety of nonspecific changes may be seen in muscle biopsy from patients with LEMS. Serial muscle biopsies in one such patient showed progressive atrophy and

**TABLE 3** Muscle-specific receptor tyrosine kinase (MuSK) antibodies in generalized, acetylcholine receptor–negative myasthenia gravis

<table>
<thead>
<tr>
<th>Reference</th>
<th>SN-MG</th>
<th>MuSK Positive</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanders et al., 2003</td>
<td>32</td>
<td>12</td>
<td>37.5</td>
</tr>
<tr>
<td>Evoli et al., 2003</td>
<td>78</td>
<td>37</td>
<td>47.5</td>
</tr>
<tr>
<td>McConville et al., 2004</td>
<td>66</td>
<td>27</td>
<td>41</td>
</tr>
<tr>
<td>Zhou et al., 2004</td>
<td>25</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Totals</td>
<td>201</td>
<td>86</td>
<td>43</td>
</tr>
</tbody>
</table>

SN-MG, seronegative myasthenia gravis.
loss of type I muscle fibers, resulting in a marked type II muscle fiber predominance.67

STRATEGY OF DIAGNOSTIC TESTING IN SUSPECTED NMJ DISEASE

The order in which the tests described above are performed depends on the presenting clinical picture, the sensitivity and specificity of the test for the suspected diagnosis, and the available expertise. The cost-effectiveness of the chosen approach should also be considered. Table 4 lists the NMJ tests that should be considered in different clinical presentations.

The edrophonium or ice-pack tests can confirm the diagnosis of MG at the bedside in patients with clear-cut ptosis or extraocular muscle weakness. RNS has the advantage of being widely available and relatively simple to perform but is normal in many MG patients. In LEMS, RNS is both sensitive and specific. RNS studies also provide useful information in botulism and in the congenital myasthenic syndromes. SFEMG is the most sensitive technique in the diagnosis of NMJ disease, but it requires special equipment and training and is time and labor intensive. It is also abnormal in nerve and muscle disease, and these must be excluded before a diagnosis of a primary NMJ disorder is made. SFEMG is particularly valuable in excluding a disorder of neuromuscular transmission because normal jitter in a weak muscle indicates the weakness is not due to a defect in neuromuscular transmission.

The following are practice recommendations of the American Association of Electrodiagnostic Medicine regarding the use of electrodiagnostic tests in MG.68

- RNS of a nerve supplying a symptomatic muscle should be performed. Abnormality in MG is considered to be a reproducible 10% decrement in amplitude when comparing the first stimulus with the fourth or fifth, which is found in at least one muscle. Anticholinesterase medications should be withheld 12 hrs before testing, if this can be done safely.

### Table 4. Selection of diagnostic tests based on clinical features

<table>
<thead>
<tr>
<th>Distribution of Weakness</th>
<th>Bedside Test</th>
<th>Sensitivity, %</th>
<th>Edx Test (muscle)</th>
<th>Sensitivity, %</th>
<th>Immunologic</th>
<th>Sensitivity, %</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular</td>
<td>Edrophonium</td>
<td>60–95</td>
<td>SFEMG (muscle)</td>
<td>90</td>
<td>AChR-Ab</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ice pack</td>
<td>89</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>None</td>
<td></td>
<td>RNS (limb/cranial)</td>
<td>60</td>
<td>AChR-Ab</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SFEMG (limb/facial)</td>
<td>99</td>
<td>MuSK-Ab (if above negative)</td>
<td>40–50</td>
<td></td>
</tr>
<tr>
<td>Generalized (norm, no autonomic signs), suspect MG</td>
<td>None</td>
<td></td>
<td>RNS (limb/cranial)</td>
<td>60</td>
<td>AChR-Ab</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SFEMG (limb/facial)</td>
<td>99</td>
<td>MuSK-Ab (if above negative)</td>
<td>40–50</td>
<td></td>
</tr>
<tr>
<td>Generalized (hyporeflexia, autonomic signs), suspect LEMS</td>
<td>None</td>
<td></td>
<td>RNS (hand)</td>
<td>98</td>
<td>VGCC-Ab</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>SFEMG (limb)</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspect botulism</td>
<td>None</td>
<td></td>
<td>RNS (limb)</td>
<td>?</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspect CMS</td>
<td>None</td>
<td></td>
<td>RNS (limb)</td>
<td>?</td>
<td>None</td>
<td>Muscle biopsy</td>
<td></td>
</tr>
</tbody>
</table>

Edx, electrodiagnostic; SFEMG, single-fiber electromyography; AChR-Ab, acetylcholine receptor antibody; RNS, repetitive nerve stimulation; MuSK-Ab, muscle-specific receptor tyrosine kinase antibody; MG, myasthenia gravis; LEMS, Lambert-Eaton myasthenic syndrome; VGCC-Ab, voltage-gated calcium channel antibody; CMS, congenital myasthenic syndrome.

68 Only if ptosis is present.
If RNS is normal and there is a high suspicion for an NMJ disorder, SFEMG of at least one symptomatic muscle should be performed. If SFEMG of one muscle is normal and clinical suspicion for an NMJ disorder is high, a second muscle should be studied.

As an option, if the patient has very mild or solely ocular symptoms and it is believed the RNS will be normal, or if the discomfort associated with RNS prevents completion of RNS, SFEMG testing may be performed in place of RNS as the initial NMJ test. In laboratories with SFEMG capability, SFEMG may be performed as the initial test for disorders of neuromuscular transmission because it is more sensitive than RNS. Routine needle EMG and nerve conduction studies may be necessary to exclude disorders other than MG or LEMS.

Immunologic tests provide the most specific diagnostic confirmation of the diagnosis of MG. Anti-AChR binding antibodies, however, may be normal in up to 20% of patients with MG. Anti-AChR-negative MG patients with generalized disease should undergo MuSK antibody testing, particularly if their clinical presentation is atypical. Striated muscle antibody assays (striational, titin, and ryanodine) may be useful in predicting the presence of thymoma in certain cases, but the added yield compared with chest computed tomography is questionable. In LEMS, antibodies to the voltage-gated calcium channel provide a useful adjunct to electrophysiologic testing and may confirm the diagnosis in patients who do not have >100% postexercise facilitation on RNS.

REFERENCES
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Estimate of Daily Calorie Needs for a Neuromuscular Disease Patient Receiving Noninvasive Ventilation

ABSTRACT


The purpose of this report is to estimate the daily caloric intake needed by a person with substantial muscle wasting due to neuromuscular disease and who also uses a ventilator for substantial amounts of time. Although this study was done for a particular individual, its methodology is generalized to any nonambulatory neuromuscular disease patient. The author, the person chosen for this analysis, is a male, limb girdle muscular dystrophy patient, who uses noninvasive ventilation approximately 20 hrs/day. An experimental technique gave a range of energy requirements for the study individual of total energy expenditure (TEE) of 788 kcal/day ≤ TEE (experimental) ≤ 876 kcal/day, or an average of 832 kcal/day, and the model developed here gave a range of 801 kcal/day ≤ TEE (model) ≤ 871 kcal/day, or an average of 836 kcal/day. This article examines and then generalizes these results to develop a simple equation that clinicians and nutritionists may use to estimate daily energy needs for ventilated neuromuscular disease patients. Because severe muscle wasting—which we define for the purposes of this article to be <30% of normal—is assumed, this analysis represents a near minimum daily energy need.

Key Words: Muscular Dystrophy, Nonambulatory, Nutrition, Energy Requirements, Ventilation

Standard methods for calculating daily energy requirements for a physically able person can substantially overestimate those requirements for a person with neuromuscular disease (NMD)—especially for nonambulatory patients. The significant wasting of muscle, in this case, dystrophy-produced cachexia, in these patients substantially reduces the amount of energy that can be utilized. Further, many dystrophy patients are very sedentary and unable to expend significant amounts of energy through exercise. If the person also uses mechanical ventilation, then much of the work of breathing—though a small percentage of the total—is provided by the machine and not by energy expended in the respiratory muscles.

For those dystrophy patients who can still eat normally and have no dysphagia or related difficulties, weight maintenance—prevention of uncontrolled weight gain—is a serious issue. Although they remain ambulatory to
some extent, excess weight leads to increasing frequency of falls and difficulty rising and ambulating. After they are nonambulatory, excess weight can become an issue for their caregivers in transfers and other required physical movements of the patient. As in the general population, excess weight also exacerbates respiratory difficulties (e.g., obstructive sleep apnea) and cardiac and vascular function—all amplified by the sedentary lifestyle.

Bach1 discusses the reduced energy needs of Duchenne muscular dystrophy (DMD) patients. He provides an equation for easy estimation of these needs that is valid up to an age of 20 yrs. Many dystrophy patients live to much older ages than 20, and some even live a normal life span. For these, and for people with other types of dystrophy than Duchenne, there are no easy-to-use expressions for clinical estimation of their daily caloric needs. The addition of ventilation is a further complication that reduces their daily caloric needs. A survey of the literature failed to uncover the existence of simple equations for the daily energy needs of these patients. Some useful background information is found in Faisy et al.2 and Pessolano et al.3 An excellent review article of a number of methods for prediction of basal energy expenditure (BEE) is given in Wang et al.4 McCrory et al.5 examined total energy expenditure (TEE) for ambulatory, high-functioning, NMD patients. They found, for the NMD patients in their study, that TEE was lower by approximately 26% for women and 20% for men as compared with an able-bodied control group. They give no method by which nutritionists might estimate TEE for ambulatory or nonambulatory patients. An excellent popularized article giving many practical, weight-related issues for NMD patients is an article by Medvescek.6

The specific objectives of this study are, therefore, to (a) determine daily energy needs for the study patient and to (b) develop and validate a simple equation that clinicians can use to estimate daily energy requirements for ventilated (or nonventilated) NMD patients of extremely limited ambulation or who are nonambulatory.

**METHOD**

Two approaches are taken to estimate daily energy needs. The first is to model energy requirements based on a synthesis of the standard Harris-Benedict7 equation and an equation Bach1 uses for DMD patients. The second approach is an experimental one. The experiment was performed, by the author on himself, to determine if a reasonable estimate could be obtained with the calculation. Dietary intake was carefully controlled over a 2-mo period. With knowledge of energy inputs and weight change over that period, then one can calculate the zero weight change, equilibrium level of energy required.

Both methods were applied to the study individual. He has a diagnosis of limb girdle muscular dystrophy. He has experienced symptoms of dystrophy since the age of 13 and was diagnosed with limb girdle muscular dystrophy at the age of 24. He maintained limited ambulation of up to 20 feet with a walker until the age of 58 and used a power wheelchair for all other mobility. During those years, he experienced many falls and injuries requiring hospitalization. These included a number of concussions, a broken tibia, and cracked pelvic bones on both right and left. All major muscle groups, by use of manual muscle testing, rate between 0 and 2 on the 6-point muscle strength scale. At the age of 57, he began bi-level positive airway pressure ventilatory assistance at night. Midway in his 58th year, he began daytime and night time, noninvasive, volume ventilation. His respiratory measurements showed significantly low maximal inspiratory pressure of 31 cm H2O (28% of normal) and low maximum voluntary ventilation of 49 liters/min (33% of normal). He experienced severe symptoms of hypercapnia during the day due to rapid shallow breathing rates of 20 breaths/min, automatically triggered by his low ventilatory capability, before initiation of daytime ventilation. His height is 182.88 cm and weight is 68.95 kg.

**MODEL SYNTHESIS**

The synthesized model allows prediction of daily energy needs for a dystrophic ventilated or nonventilated patient. It is derived by using an energy prediction model for able-bodied people and then by developing a “muscle-wasting scaling factor” that is a simple multiplier for the first, able-bodied, model. The Harris-Benedict equation has been selected for the baseline, able-bodied model. The muscle-wasting scaling factor is found by comparing predictions of this model with predictions of the Bach model (e.g., by taking a simple ratio of the Bach equation and the Harris-Benedict equation).

For a normal, healthy, male subject, the expression for BEE (in kilocalories) given by the Harris-Benedict (HB) equation is:

\[
\text{BEE (male subject, HB)} = 66.47 + 13.75 \times (\text{weight in kilograms}) + 5.00 \times (\text{height in centimeters}) - 6.76 \times (\text{age in years}) \ [7]
\]

For completeness, the same reference gives the Harris-Benedict equation for female subjects as:

\[
\text{BEE (female subject, HB)} = 665.0 + 9.56 \times (\text{weight in kilograms}) + 1.85 \times (\text{height in centimeters}) - 4.68 \times (\text{age in years}) \ [7]
\]
BEE (female subject, HB) = 655.10 + 9.60
× (weight in kilograms) + 1.85
× (height in centimeters) − 4.68
× (age in years) [2]

After calculating basal energy requirements, one multiplies Equation 1 by an activity factor to estimate the TEE. The activity factors are: 1.10 for patients receiving ventilatory support, 1.15 for bedridden or sedate patients, and 1.25 for able-bodied patients. By differencing the first and second activity factors, it is apparent that the work of breathing, for the accuracy needed here, is approximately 5% of TEE. Equation 1 is simply multiplied by the activity factor as,

TEE (HB) = BEE (HB) × Activity factor [3]

It is assumed that a possible, multiplicative stress factor caused by injury or surgery is unity. Equation 3 is the appropriate equation for use if no muscle wasting is present. The Bach equation, which accounts for muscle wasting, for children and young adults who have DMD is:

TEE (DMD/Bach) = 2000 − 50
× (age in years) [4]

where we have used the notation (DMD/Bach) to indicate that this is for DMD patients and is the Bach equation. The correct BEE and TEE for dystrophic adults can be found by multiplying Equation 3 by an additional factor, the NMD muscle wasting factor (MWF). This is obtained by finding the ratio of the Bach equation to the Harris-Benedict equation (for a normal but sedate person). The age of 20 yrs has been chosen as the reference age because it is within the validity range of both the Bach and Harris-Benedict models.

The complete TEE expression is, therefore:

TEE (NMD) = BEE (HB) ×
Activity factor × MWF [5]

MODEL RESULTS

Two methods were used to determine the MWF. The first was to calculate TEE (HB) for the study individual for his height and weight at age 20. The second was to calculate TEE (HB) for a male subject of average height and weight at age 20. To find the scaling factor, we determine the ratio of these values to the Bach equation. These two calculations, then, establish a range of possible values for the scaling factor.

For the study person, these variables are: age = 20 yrs, height = 182.88 cm, and weight = 61.24 kg. See earlier for present time descriptors of the study individual. For the average white man, these values are: age = 20 yrs, height = 177 cm, and weight = 74 kg.

Utilizing Equations 1, 3, and 4 and the variables in the preceding paragraph, yielded a range for MWF of

0.47 ≤ MWF ≤ 0.52 [6]

where the upper limit was derived from the patient's variables at age 20 and the lower limit from the average white man's variables at age 20. It is important to recall that the Bach equation is for a sedate person. Therefore, the scaling factors of Equation 6 must be derived from the Harris-Benedict equation multiplied by the factor of 1.15 corresponding to a sedate person. The range in TEE, from Equation 5, corresponding to the range in MWF shown in Equation 6, for the patient's variables at age 58, including an activity factor of 1.1, is:

801 kcal/day ≤ TEE (model)

≤ 871 kcal/day [7]

For the study patient, the average value, 836 kcal/day, is the starting point for dietary planning. At this low level of energy input, careful monitoring is required after initiating the regimen.

The equation for use by clinicians and nutritionists to estimate energy requirements for ventilated dystrophy patients who are nonambulatory or have limited ambulation, which yields this average value, is

TEE = 0.54 [66.47 + 13.75 ×
(weight in kilograms) + 5.00 ×
(height in centimeters) − 6.76 ×
(age in years)] [8]

where we have explicitly used the average value of the lower and upper MWF limits of Equation 6 multiplied by 1.1 for the ventilation activity factor. This is the leading coefficient in Equation 8. For a person who is not ventilated, the leading coefficient would be approximately 5% higher, or 0.57. Equation 8 is approximately 50% of the energy requirements of an able-bodied person as compared with the 74% for women and 80% for men found by McCrory et al.5 for high-functioning, ambulatory, NMD patients.

An alternate method, as a cross check, was used to obtain MWF using an expression for BEE given in Gallagher et al.12 In their article, they give

After calculating basal energy requirements, one multiplies Equation 1 by an activity factor to estimate the TEE. The activity factors are: 1.10 for patients receiving ventilatory support, 1.15 for bedridden or sedate patients, and 1.25 for able-bodied patients. By differencing the first and second activity factors, it is apparent that the work of breathing, for the accuracy needed here, is approximately 5% of TEE. Equation 1 is simply multiplied by the activity factor as,

TEE (HB) = BEE (HB) × Activity factor [3]

It is assumed that a possible, multiplicative stress factor caused by injury or surgery is unity. Equation 3 is the appropriate equation for use if no muscle wasting is present. The Bach equation, which accounts for muscle wasting, for children and young adults who have DMD is:

TEE (DMD/Bach) = 2000 − 50
× (age in years) [4]

where we have used the notation (DMD/Bach) to indicate that this is for DMD patients and is the Bach equation. The correct BEE and TEE for dystrophic adults can be found by multiplying Equation 3 by an additional factor, the NMD muscle wasting factor (MWF). This is obtained by finding the ratio of the Bach equation to the Harris-Benedict equation (for a normal but sedate person). The age of 20 yrs has been chosen as the reference age because it is within the validity range of both the Bach and Harris-Benedict models.

The complete TEE expression is, therefore:

TEE (NMD) = BEE (HB) ×
Activity factor × MWF [5]

MODEL RESULTS

Two methods were used to determine the MWF. The first was to calculate TEE (HB) for the study individual for his height and weight at age 20. The second was to calculate TEE (HB) for a male subject of average height and weight at age 20. To find the scaling factor, we determine the ratio of these values to the Bach equation. These two calculations, then, establish a range of possible values for the scaling factor.

For the study person, these variables are: age = 20 yrs, height = 182.88 cm, and weight = 61.24 kg. See earlier for present time descriptors of the study individual. For the average white man, these values are: age = 20 yrs, height = 177 cm, and weight = 74 kg.

Utilizing Equations 1, 3, and 4 and the variables in the preceding paragraph, yielded a range for MWF of

0.47 ≤ MWF ≤ 0.52 [6]

where the upper limit was derived from the patient's variables at age 20 and the lower limit from the average white man's variables at age 20. It is important to recall that the Bach equation is for a sedate person. Therefore, the scaling factors of Equation 6 must be derived from the Harris-Benedict equation multiplied by the factor of 1.15 corresponding to a sedate person. The range in TEE, from Equation 5, corresponding to the range in MWF shown in Equation 6, for the patient's variables at age 58, including an activity factor of 1.1, is:

801 kcal/day ≤ TEE (model)

≤ 871 kcal/day [7]

For the study patient, the average value, 836 kcal/day, is the starting point for dietary planning. At this low level of energy input, careful monitoring is required after initiating the regimen.

The equation for use by clinicians and nutritionists to estimate energy requirements for ventilated dystrophy patients who are nonambulatory or have limited ambulation, which yields this average value, is

TEE = 0.54 [66.47 + 13.75 ×
(weight in kilograms) + 5.00 ×
(height in centimeters) − 6.76 ×
(age in years)] [8]

where we have explicitly used the average value of the lower and upper MWF limits of Equation 6 multiplied by 1.1 for the ventilation activity factor. This is the leading coefficient in Equation 8. For a person who is not ventilated, the leading coefficient would be approximately 5% higher, or 0.57. Equation 8 is approximately 50% of the energy requirements of an able-bodied person as compared with the 74% for women and 80% for men found by McCrory et al.5 for high-functioning, ambulatory, NMD patients.

An alternate method, as a cross check, was used to obtain MWF using an expression for BEE given in Gallagher et al.12 In their article, they give
a regression equation for BEE in terms of only brain mass and skeletal muscle mass for able-bodied people. For DMD patients, Franciotta et al. give an average skeletal muscle mass of 5.4 kg. If we assume an average skeletal muscle mass of 30 kg for an able-bodied person, then we find an approximate value for MWF of 0.55 by determining the ratio of the two values of BEE from Gallagher et al.—in reasonable agreement with Equation 6.

EXPERIMENTAL RESULTS

To validate the results of the synthesized model, actual weight loss for the study individual was used to determine TEE. Experimentally, TEE can be found by consuming less energy than required and measuring the weight loss over a suitable period of time. Because the input energy in kilocalories is known, and the equivalent kilocalorie loss can be calculated from the weight loss, TEE is found simply by taking the sum of these two numbers, or:

\[
\text{TEE (experimental)} = \text{Weight lost per day} \times 3500 \text{ kcal} + \text{Average kilo calories consumed per day} [9]
\]

where 3500 is the conversion factor from pounds of weight to kilocalories.

The critical data needed for this analysis is actual weight on a daily basis and the energy consumed in food each day. Weight was measured each morning after toileting and bathing and without clothing. Measurements were taken on a calibrated Health-O-Meter balance-beam scale. All food (and drink) items consumed were recorded, their protein, carbohydrate, and fat content determined, and total daily caloric input calculated. The daily average energy input was 513 kcal/day, with only 6 days being 100 kcal above or below this value. In this and in other diets for NMD patients, it is important to provide adequate protein intake to minimize diet-induced muscle wasting.

The most difficult task is to determine a value for daily weight loss from data that clearly includes substantial components due to water variations (Fig. 1). Two methods were used to determine first a minimum value of the daily solid mass loss and, second, a maximum value for that loss. The maximum value of TEE was determined from a linear regression fit to the first and 14th through 21st days of the study to avoid larger, systematic fluctuations in water loss that occurred in the early days of the study. The minimum daily solid mass loss was found from fitting a linear regression to the beginning weight and the peaks of the weight-loss curve. Both of these linear, least-squares fits are shown and labeled with the complete data set in Figure 1.

The first minimum in the weight curve is clearly water loss. All data sequences that included loss or gain of >0.3 pounds/day were considered to be water fluctuations. The long slope toward the center of the curve followed switching to a low carbohydrate diet of about 20 g of carbohydrates per day and is primarily water loss. The peak toward the end of the study was produced by water gain on switching back to a high carbohydrate diet and its fall-off by returning to the low carbohydrate diet.

The regression equations are as follows. For the minimum solid mass loss (upper line in Fig. 1), the equation is

\[
W_{\text{min}}(d) = -0.0786 \text{ days} + 151.84 \left[10\right]
\]

with a correlation coefficient of 0.9999. For the maximum solid mass loss (lower line in Fig. 1), the equation is

\[
W_{\text{max}}(d) = -0.1152 \text{ days} + 152.01 \left[11\right]
\]

with a correlation coefficient of 0.9618.

For both, W is the weight in pounds and d is the number of days. The coefficient of d is the weight loss in pounds per day (i.e., the first term on the right in Equation 9). From Equations 9, 10, and 11, we find for the experimental value of TEE that,

\[
788 \text{ kcal/day} \leq \text{TEE (experimental)} \leq 876 \text{ kcal/day} [12]
\]

which closely overlaps the range found from the synthesized model as shown in Equation 8 and validates the model results for this patient. The average value from the two data analysis techniques, applied to the experimental data, is 832 kcal/day.
kcal/day, which is virtually identical to the model average result of 836 kcal/day.

CONCLUSIONS

We have shown that a simple model, for an NMD patient with severe muscle wasting, can be used to predict daily energy needs based on the patient’s age, weight, and height. Two methods, one experimental and one a model, yielded a range of TEE values for a specific NMD patient who is noninvasively ventilated of 788 kcal/day ≤ TEE (experimental) ≤ 876 kcal/day and 801 kcal/day ≤ TEE (calculated) ≤ 871 kcal/day. The average values are, respectively, 832 kcal/day and 836 kcal/day. The experimental determination verifies that the model calculation can be used to obtain an approximate value for energy needs. A generalized, simple equation is given that can be used by nutritionists and clinicians to estimate daily energy requirements for any NMD patient—of nonambulatory status or with limited ambulation—with or without ventilation. Values derived from this equation represent a very different paradigm for weight control and assessment than for a physically normal person. The very small amount of energy required for equilibrium implies that weight management is extremely difficult for these patients. Within this energy budget, it is also necessary to ensure adequate nutrition in terms of essential amino acids and other nutritional elements. Dietary-induced muscle wasting is an important consideration and must also be accommodated in the diet. The predictive model developed in this article is limited to individuals with quite severe muscle wasting and, therefore, represents a minimum value for daily energy needs. From the work of McCrory et al., it is evident that ambulatory NMD patients have energy needs that are considerably higher than those shown in this article. Even in that case, the energy requirements are considerably lower than those for control subjects without NMD. In a future article, a more general model is developed that applies to patients with any degree of muscle wasting. There, the single-valued MWF is replaced with a simple function based on the extent of muscle wasting.

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REFERENCES

Migraines Linked to Interferon-β Treatment of Multiple Sclerosis

ABSTRACT

Migraine headache is now emerging as a previously under-recognized side effect of interferon-β, the most commonly used therapy for relapsing multiple sclerosis (MS). We describe an MS patient who developed migraine headaches, which followed a specific pattern coincident with interferon-β administration. The frequency and severity of these migraines escalated and seemed to culminate in an MS exacerbation. Since initiation of migraine prophylaxis with daily amitriptyline, our patient reported a significant decrease in the frequency and severity of her migraines on interferon. It has been postulated that migraine headaches may trigger MS relapse. If so, migraine prophylaxis in MS patients, especially those treated with interferon-β, is of paramount importance. Migraine headaches can be a significant source of disability. Identifying and treating migraines in MS patients serves to enhance their function and reduce disability.

Key Words: Interferon-β, Migraine, Multiple Sclerosis

It is known that migraines are more prevalent in multiple sclerosis (MS) patients. Rolak and Brown¹ report a 52% prevalence of headache in MS patients compared with 18% in matched general neurology patients. Pollman et al.² report a lifetime prevalence of headache in MS at 54%, the most common type being migraine without aura. The underlying pathophysiology connecting these two conditions has not yet been elucidated.

Clinically, MS and migraine often have similar presentations. Reports have described migraines “masquerading” as MS, demonstrating that migraine is an important part of the differential diagnosis of MS.¹,³,⁴ Conversely, MS has been considered in the differential diagnosis of migraine.⁴ Heredity plays a part in both migraines and MS. A recent study by Zorzon et al.⁵ has shown that migraine and even family history of migraine are both independent risk factors for MS. In addition, migraine has also been reported as a presenting symptom of MS.⁶ Both migraine and MS occur more commonly in women between the ages of 20 and 45 yrs old. Symptoms of MS and migraine improve during pregnancy and increase during the postpartum period.⁷ Both conditions may be exacerbated by stress, temperature changes, and sunlight exposure. Migraine is associated with systemic disturbances in serotonin (5-hydroxytryptamine) metabolism.⁸ Serotonergic disturbances are also implicated in MS relapse.⁷ The similarities between these two conditions suggest a link in their pathophysio-
logic mechanisms. In fact, migraine has been observed to coincide with exacerbations of MS, and may even be a harbinger of MS relapse.7

The most widely prescribed medication for the prevention of MS relapse is interferon (IFN)-β. Flu-like symptoms such as fatigue, myalgias, chills, and fever are well recognized side effects of IFN-β. Prophylaxis with acetaminophen or ibuprofen has been recommended for the patient who experiences these symptoms. Migraine has recently emerged as an under-recognized side effect of IFN-β therapy.1 If not appropriately addressed, migraine may contribute to the burden of disability that MS patients incur.

**CASE DESCRIPTION**

A 36-yr-old Puerto Rican woman was diagnosed with MS in 2003. Her symptoms, however, had emerged 3 yrs earlier and initially consisted of episodes of sudden bilateral lower limb weakness lasting a few hours. These episodes remitted, but over the next year, she had occasional bouts of fatigue, generalized weakness, and paresthesias of the distal lower limbs. In 2003, she experienced an extended bout of lower limb weakness, which affected her ability to ambulate and finally prompted her to seek medical care. At this time, the diagnosis of MS was made based on clinical and magnetic resonance imaging findings and on the presence of oligoclonal bands in the cerebrospinal fluid.

两个月后 MS 被诊断，治疗 IFN-β 被启动。她被指示注意可能的流感样症状与 IFN-β 治疗相关的。病人抱怨有寒战和肌肉疼痛在每次注射和使用扑热息痛后，作为指示，30 分钟前注射以减少这些症状。她还报告说，在启动治疗后，她开始经历头痛。在启动 IFN-β 治疗前，她从未有过慢性头痛和没有家族病史的偏头痛。

起初，头痛是可以管理的，并且只持续了几个小时。它们通常被定位到一侧的头部并被描述为在眼和与光敏。在持续的头痛恶化，强度的头痛恶化。头痛在大约 24 小时后发作。在启动 IFN-β 治疗后，在 IFN-β 治疗时，她没有头痛。

当她的头痛与睡眠，病人被指示在夜间尝试 IFN-β 的 IFN-β 治疗的早晨。头痛变得更加明显在白天，并且她的睡眠在早晨而不是晚上。头痛在大约 2–3 天后，干扰了日常活动。大量使用扑热息痛和吲哚美辛提供了最小的缓解。避免所有接触，与休息在一个黑暗的房间，成为了一件日常事件。

在四月 2004 年，她被送往医院与突然的右侧下肢无力。她不能走或负重在她的右脚。她还抱怨了一个电击的麻痹在右脚，最突出的颈部屈曲。一个 MS 发作被诊断，并且在静脉内有严重的烧灼性的麻木，组件以突起的脖子。她抱怨了光敏和严重的跳动的头痛，然后拒绝了任何变化在视力。反射是粗的，但等同在任何方面。感觉是不完整的在任何尺度到轻轻地触摸和疼痛，虽然过敏性麻痹阻止了完整的检查的右下肢。她抱怨了光敏和严重的跳动的头痛在 IFN-β 注射一天后。头痛阻止了她完全参与在物理和职业治疗。

病人被治疗与麻醉症，和偏头痛预防治疗被启动与 25 mg 的氨氯地平每晚。病人在我们的服务在的另一次与去甲替林和，在那个时间，保持头痛-free 而继续她的 IFN-β 治疗。在 1 mo 的 IFN-β 与 prophylactic 去甲替林，病人报告了 5 倍下降在偏头痛频率。偏头痛的持续时间从 2–3 天到 <1 天。病人也报告了偏头痛的强度的下降和能功能独立。

**DISCUSSION**

A recent study conducted by Pollman et al.2 looked prospectively at 65 patients with MS who had undergone treatment with IFN-β and found that headache frequency and duration increased significantly in the first 6 mos of treatment. In addition, two retrospective groups were studied, one treated with IFN-β (n = 53) and one with glatiramer acetate (Rebif) (n = 49). Compared with the patients receiving glatiramer acetate therapy, a significantly higher percentage of patients receiving IFN-β reported increased headache frequency.1 The most common headache reported in this study was migraine. Many studies, which initially dis-
migraine. This phenomenon may have been overlooked because headache, not considered a severe side effect, may have been underreported, attributed to MS itself, or grouped with the flu-like category of side effects.

A migraine patient is defined as one who has had at least two attacks with aura or at least five attacks without aura. An isolated migraine does not label a patient as a migraine patient, whereas the occurrence of repeated attacks does. Migraine attacks recur when either a genetically predetermined threshold is reduced or when the triggers are strong or frequent enough to overcome this threshold. Goadsby et al. describe "the basic biological problem in migraine to be the dysfunction of an ion channel in the aminergic brain stem nuclei that normally modulates sensory input and exerts neural influences on cranial vessels." The aminergic neurotransmitter 5-hydroxytryptamine is now known to play a major role in migraine pathology and is, in fact, the therapeutic target for many migraine-abortive drugs. The serotonergic decrease that is observed in migraine may serve to disrupt the blood–brain barrier, the breakdown of which is believed to be a crucial element in the initial phase of MS exacerbation. One may therefore extrapolate that preventing migraine promotes the integrity of the blood–brain barrier and may serve to reduce the rate of MS relapse. Freeman and Gray performed a retrospective study of 1113 patients and found 44 patients (4%) with a herald migraine before MS onset or relapse.

Several other mediators are involved in migraine, including nitric oxide, magnesium, and several immune molecules such as complement and various cytokines, including interleukin (IL)-1, IL-2, IL-4, IL-6, and IFN-γ. IFN-β, a cytokine and an immunomodulating drug, is the most widely prescribed therapy for the long-term treatment of relapsing remitting MS. An acute increase in the release of proinflammatory cytokines in response to an IFN-β injection may represent the mechanism by which IFN-β triggers migraine in these patients. MS patients, who have a higher prevalence of migraine, may be more susceptible to the above effect. In our case, it was apparent that the IFN-β injections were acting as migraine triggers because of the direct cause-and-effect relationship observed. In patients receiving IFN-β therapy, this known migraine trigger is repeated on a regular, continuous basis.

Pharmacologic therapy for migraine is divided into abortive and preventative therapy. The abortive agents can be further divided into nonspecific, such as aspirin, acetaminophen, opiates, or nonsteroids, and migraine-specific agents, such as ergotamine, dihydroergotamine, and triptan medications. The decision to begin preventative treatment is made based on several factors and must be taken in context. The frequency, duration, severity, and tractability of attacks, and the preference of the patient, must be taken into account. As IFN-β has become a mainstay of MS treatment, its potential for triggering migraine attacks must be anticipated and addressed. Migraine can be a source of substantial disability, as it was in the case of our patient, and in such instances, preventative therapy should be considered. A trend toward increasing frequency of attacks, also exhibited by our patient, is a strong indication for prophylactic treatment. Although it is not clear how preventative therapy works, it is thought to increase the threshold for migraine. The most widely prescribed prophylactic agents are beta-blockers, such as propranolol and metoprolol, and amitriptyline, a tricyclic antidepressant. Less commonly prescribed agents with proven efficacy include valproate, flunarizine, pizotyline, and methysergide. Approximately two thirds of patients treated with one of these agents will have a 50% reduction in headaches. Verapamil and selective serotonin reuptake inhibitors have also been used without proven benefit. The choice of prophylactic agent is usually guided by the patient’s preexisting conditions and the medication side effects. The patient in this case exhibited consistently low heart rate, usually ranging from 50 to 60 beats/min, making beta-blockers an unfavorable option. This was the main reason why we chose amitriptyline, whose main side effect is drowsiness, a problem easily overcome with evening dosing. Our patient exhibited a significant decrease in headache frequency, intensity, and duration while receiving 25 mg of amitriptyline. The recommended dose of amitriptyline for migraine prophylaxis is 25–75 mg, or 1 mg/kg body weight, given at bedtime. This is considerably lower than the recommended dose for depression (up to 300 mg). Some patients have responded to doses as low as 10 mg.

This patient’s history demonstrated a direct cause-and-effect relationship between IFN-β administration and migraine. This is a phenomenon that has been overlooked until recently. Because IFN-β is so widely prescribed, cases such as this one are likely to be common, and clinicians should maintain vigilance. Furthermore, the possibility that migraine may play a role in MS relapse gives further incentive to identify, treat, and prevent this side effect.

**REFERENCES**

A 57-yr-old, right-handed woman with known diabetes mellitus, obesity, and a recent right below-knee amputation presented with a 3-mo history of right shoulder discomfort. Her specific symptoms included weakness with overhead activities and aching shoulder pain that worsened after her below-knee amputation, as she then relied on the shoulder joint for weightbearing with her rolling walker and for transfers. Physical examination of the right shoulder revealed diffuse anterior shoulder tenderness and crepitus on palpation, with limited range of motion at 45 degrees of abduction with the scapula stabilized. Mild weakness was noted during external rotation with applied resistance. The upper limb was otherwise neurologically intact.

The decision was made to further investigate the shoulder joint, and hence, magnetic resonance imaging without contrast was chosen. Arthrography is specific for rotator cuff tears but has a low sensitivity because it does not pick up partial tears well and therefore has been largely replaced by magnetic resonance imaging. A review of the magnetic resonance image clearly revealed acromial impingement, with a resultant tear on the supraspinatus tendon (Fig. 1 and Fig. 2).

The supraspinatus muscle is the largest component of the rotator cuff. Its primary function is abduction of the arm, particularly the first 20–30 degrees. Due to its size and position, it is the most likely to be impinged between the humeral head and lateral edge of the acromion. Three types of acromia are described: type I, flat with the least amount of degenerative changes; type II, curved with increasing wear changes prevalent; and type III, hooked with highest rate of tears and degenerative joint disease (the subject of this vignette has a type I acromion). The acromion can best be visualized with the outlet Y-view radiograph, which is typically included in the impingement series with the anteroposterior, external rotation, and West Point (modified axillary) views.

Key history points in a patient with supraspinatus tendinopathy usually include worsening of pain with reaching overhead, along with more severe pain at night. Physical examination may review tenderness with direct pressure over the acromioclavicular joint and weakness with initial abduction. Treatment varies based on the severity and time from onset. Initial treatment consists of conservative measures, including initial relative rest, ice, compression, and elevation (RICE) and nonsteroidal antiinflammatory medications (NSAIDs) for 1–2 wks. After pain and inflammation have been managed, physical therapy can be initiated, first focusing on flexibility, followed by isometric and then isotonic exercises as tolerated. More specifically, wand and pendulum exercises are especially helpful, along with continued modalities such as ice, heat, and massage therapies. Difficult cases warrant an injection of an anesthetic agent such as lidocaine with or without steroid. If these approaches fail after a period of 3–6 mos, an orthopedic surgical consultation may be indicated.

REFERENCES