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Treatment of Pain Attributed to Plantar Fasciitis with Botulinum Toxin A: A Short-Term, Randomized, Placebo-Controlled, Double-Blind Study

ABSTRACT


Objective: To investigate the effect of botulinum toxin A on associated pain and functional impairment of refractory plantar fasciitis.

Design: This is a randomized, double-blind, placebo-controlled study of 27 patients (43 feet) with plantar fasciitis. Block randomization was performed using computer software. In patients with bilateral symptoms of comparable severity, botulinum toxin A was injected in one foot and saline in the other foot. The treatment group received a total of 70 units of botulinum toxin A divided into two sites per foot. One of the two sites was the tender area in the medial aspect of the heel close to the calcaneal tuberosity (40 units), and the other was in the arch of the foot between an inch anterior to the heel and middle of the foot (30 units). The placebo group received the same volume of normal saline. Main outcome measures included: Pain Visual Analog Scale, Maryland Foot Score, Pain Relief Visual Analog Scale, and pressure algometry response. Patients were assessed before injection, at 3 wks, and at 8 wks.

Results: The study revealed statistically significant changes in the treatment group. Compared with placebo injections, the botulinum toxin A group improved in all measures: Pain Visual Analog Scale (P < 0.005), Maryland Foot Score (P = 0.001), Pain Relief Visual Analog Scale (P < 0.0005), and pressure algometry response (P = 0.003). No side effects were noted.

Conclusions: Botulinum toxin A injection for plantar fasciitis yields significant improvements in pain relief and overall foot function at both 3 and 8 wks after treatment.

Key Words: Botulinum Toxin A, Botox, Plantar Fasciitis, Sports Injuries, Pain, Foot
Plantar fasciitis is the most common cause of chronic heel pain, observed in up to 10% of the general population. Approximately 10% of all cases are considered refractory to medical treatment. The condition is a major health issue in long-distance walkers, possibly caused by overuse injury, leading to repetitive microtears of the plantar fascia near the calcaneus. It is usually precipitated by a change in the individual’s activity level or training program. Biomechanical factors also play an important role. The mainstay of all treatment strategies for plantar fasciitis first includes simple measures such as application of ice and heel cups, orthosis, activity modification, and a stretching/strengthening exercise program. Further measures include deep-tissue massage therapy, night splints, and periods of immobilization. Persistent cases may respond to treatment with posterior night splints, ultrasound, iontophoresis, phonophoresis, extracorporeal shock therapy, or even local corticosteroid injections. In cases of medical failures, surgery is advocated, with modest results. There is a need for new treatment avenues, especially for refractory cases.

Over the last several years, botulinum toxin A (BTX-A) has been increasingly used in the treatment of various medical conditions. Increasing literature supports the role of BTX-A in the treatment of chronic pain syndromes such as myofascial pain and refractory headaches. Although blockade of acetylcholine release from presynaptic vesicles plays an important role in relief of muscle spasms and pain in myofascial syndromes, a number of animal studies, some of them recent, suggest alternative mechanisms for analgesic effects of this agent. Some of these mechanisms, antinflammatory action and action against locally accumulated stimulant neurotransmitters (glutamate, substance P), pertain to the pathophysiology of plantar fasciitis.

Encouraged by this literature, we conducted a prospective, randomized, double-blinded, placebo-controlled study examining the use of BTX-A in the treatment of refractory plantar fasciitis. To our knowledge, this is the first report on the use of BTX-A for this condition.

**METHODS AND DESIGN**

A prospective, randomized, double-blinded, placebo-controlled study was conducted comparing the effects of BTX-A injection with placebo (saline) in patients with plantar fasciitis. The inclusion criteria consisted of being an adult, a diagnosis of plantar fasciitis, duration of symptoms beyond 6 mos, and failure of conventional treatment strategies. Exclusion criteria consisted of an age of <18 yrs, any disease of the neuromuscular junction, and a history of hypersensitivity to BTX-A. Other exclusions consisted of an open wound of the foot or heel, history of foot surgery or fracture, or history of chronic narcotic use for any reason. In addition, patients with a physical examination consistent with fibromyalgia, nerve entrapment, radiculopathy, peripheral vascular disease, or decreased sensation of the foot or ankle were also excluded from the study. All women of childbearing age were required to have a negative pregnancy examination.

Plantar fasciitis was clinically defined as heel tenderness of gradual onset, localized to the medial process of the calcaneal tuberosity and exacerbated by weightbearing. The patients had almost all of the aforementioned therapeutic measures, with the exception of extracorporeal shock or surgery. The study was designed to recruit 60 patients. Due to the somewhat painful nature of the study, our institutional review board recommended an interim analysis to be performed if we see notable (more than double) response differences between the two groups. Our statistician recommended this to be performed after enrolling 25–30 patients (i.e., close to or at the midpoint of enrollment). Male and female participants were recruited, between the ages of 18 and 75 yrs, who met both inclusion and exclusion criteria. Patients with bilateral symptoms were included in the study and were randomly assigned BTX-A in one foot and placebo in the other. Participants and physicians were blinded to the agent that was injected. All randomization, data collection, and syringe preparation was performed by the same clinical research nurse, who maintained complete confidentiality and was not involved in patient rating. Block randomization was performed using computer-generated software provided by the Department of Clinical Investigation.

After receiving informed consent, each affected foot was randomized into either the BTX-A treatment group A or the placebo group B. The solution of BTX-A (BOTOX, Allergan, Irvine, CA) was prepared by mixing 100 units with 1 ml of normal saline. We injected the patients of group A with 70 units of BTX-A (0.7 ml) in two divided doses: 40 units (0.4 ml) in the tender region of the heel medial to the base of the plantar fascia insertion and 30 units (0.3 ml) in the most tender point of the arch of the foot (between an inch anterior to the heel to the middle of the foot) (Fig. 1). A 27-gauge, 0.75-inch needle was used for injections. Group B received normal saline at the same locations and of similar volume. In patients with bilateral plantar fasciitis of comparable severity, BTX-A was injected in one and saline in the other foot. All patients were also given a handout reviewing a home stretching program targeting the plantar fascia and gastroc/soleus muscle complex. No medication changes were recommended; however, patients were informed that receiving another injection or surgery on their foot would terminate their participation in the study.
Outcome Variables Included

The Pain Visual Analog Scale consists of a 10-cm line with the ends labeled “no pain” or “worst pain ever.” Retest reliability with literate patients has been found to be 0.94. Regarding validity, correlations between vertical and horizontal Visual Analog Scales were approximately 0.89–0.91. This study incorporated the horizontal scale.21 Patients were asked to rate each affected foot preinjection and at 3 and 8 wks postinjection.

The pressure algometry response quantitatively assesses muscle tenderness at the site of the plantar fascial insertion. The device was positioned directly perpendicular to the sole of the foot, and incremental cutaneous pressures were slowly applied over the described areas. The average pressure of three serial measurements at which the subject first reported pain was recorded in kilograms.22 All correlations of within-experimenter reliability and between-experimenter reliability were highly significant ($P < 0.01$).23 Measurements were obtained preinjection and at 3 and 8 wks postinjection.

The Maryland Foot Score, developed by the Painful Foot Center at the University of Maryland, is based on a 100-point scale (excellent, 90–100; good, 75–89; fair, 51–74; failure, <50) that assesses foot pain and function in relation to pain, gait, stability, support, limp, motion, and ability to climb stairs.24 Although clinometric studies have not been conducted, the Maryland Foot Score has been found to be a valid test for pain and physical function.25 The questionnaire for the Maryland Foot Score was administered by the physician preinjection and at 3 and 8 wks postinjection.

The Pain Relief Visual Analog Scale consists of a 10-cm line with the ends labeled “no relief” or “complete relief” of symptoms. According to the literature, because the initial and subsequent pain ratings tend to be correlated (coefficients of 0.62 and 0.63), a Pain Relief Visual Analog Scale is more advantageous than just comparing Pain Visual Analog Scale scores before and after treatment.26,27 Patients were asked to rate each affected foot at 3 and 8 wks postinjection.

The first three measures were considered our primary outcome measures. An improvement of ≥30% is considered for Visual Analog Scale and pressure algometry response, and an advancement to the next category (for example, fair to good, good to excellent) was considered significant for the Maryland Foot Score.

Statistical Analysis

The statistician assigned to the study indicated that to detect a difference of 35% response to pain between the BTX-A group (assumed 50%) and placebo group (assumed 15%) with an 85% confidence interval, 60 patients needed to be studied. Assuming an anticipated drop-out rate of 15%, we therefore set
out to recruit patients. Change over time within a group was analyzed using Wilcoxon’s signed-ranks test, and differences between groups were analyzed using Wilcoxon’s rank-sum test. Statistical significance was set at $P < 0.025$ for the interim analysis and $P < 0.05$ for the final analysis. The statistical software package utilized was SPSS vs. 12 (SPSS, Chicago, IL).

RESULTS

At the time of interim analysis (8 wks after treatment), a total of 43 feet were studied from 27 subjects. Initial and 3-wk data existed on all feet. Seven patients did not report at 8 wks. Patients lost to follow-up (seven patients) were included in 8-wk statistical analyses as nonresponders. There were 22 feet in group A (BTX-A) and 21 feet in group B (placebo). The age of participants ranged from 21 to 65 yrs, with a median age of 44 yrs. The majority of patients were white, followed by African American, and then Asian or Hispanic. Subjects with both unilateral and bilateral symptoms were included in the study. There were a total of 18 women (12 bilateral, six unilateral) and nine men (four bilateral, five unilateral) enrolled in the study. Group A consisted of 15 feet from female subjects and six feet from male subjects. Group B consisted of 15 feet from female subjects and seven feet from male subjects (Table 1). Bilateral symptoms were noted in 16 and unilateral symptoms in 11 patients. Of 16 bilateral patients, 12 improved on all outcome measures in the BTX-A–treated foot, and only one patient improved in the placebo-treated foot.

Compared with placebo, the BTX-A group manifested statistically significant results at 3 wks, with a 39% decrease on the Pain Visual Analog Scale, a 34% improvement of the Maryland Foot Score, and a 40% increase in pressure algometry response, with $P$ values of $< 0.005$, $0.001$, and $0.003$, respectively (Figs. 2–4). The Pain Relief Visual Analog Scale was also significant, with a $P$ value of $< 0.005$. The placebo group had a 2.7% worsening on the Pain Visual Analog Scale, $< 0.01$% improvement on the Maryland Foot Score, and $< 0.01$% improvement on pressure algometry response.

At 8 wks, a total of 30 feet from 20 subjects were analyzed. A total of 13 feet from seven subjects were lost to follow-up because of changes in geographic location but were included in the analyses as nonresponders. The BTX-A group, consisting of 15 feet,

<table>
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<tr>
<th>Group</th>
<th>Mean group scores (range) for main outcome measures at the three different time points</th>
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<tr>
<td></td>
<td>P-VAS</td>
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<tr>
<td>A (BTX-A)</td>
<td>5.1 (2.0–9.7)</td>
</tr>
<tr>
<td>B (placebo)</td>
<td>2.7 (0–7.9)</td>
</tr>
<tr>
<td></td>
<td>3 wks</td>
</tr>
<tr>
<td>Initial</td>
<td>1.6 (0–7.9)</td>
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FIGURE 2 Pain Visual Analog Scale scores for the botulinum toxin A (BTX-A) and placebo groups.
continued to show significant improvement in all variables, with a 56% decrease on the Pain Visual Analog Scale, a 47% increase on the Maryland Foot Score, and a 56% increase in pressure algometry response, with \( P \) values of <0.005, 0.001, and 0.003, respectively. The improvement on the Pain Relief Visual Analog Scale was also significant when compared with the placebo group (\( P \) value of <0.005). No known complications were noted in persons who maintained follow-up.

**DISCUSSION**

Plantar fascia is composed of dense collagen fibers that extend longitudinally from the calcaneus to the base of each proximal phalanx. The fascia has a medial, central, and lateral part, under which lies the abductor hallucis, flexor digitorum brevis, and flexor digiti minimi muscles, respectively. It holds down muscles and tendons in the concave surface of the sole and digits, facilitates excursion of the tendons, prevents excessive compression of digital vessels and nerves, and possibly aids in venous return.28

A number of anatomic changes have been described in plantar fasciitis. These include marked thickening of the plantar fascia as demonstrated by several sonographic studies,29 microtears related to repeated trauma, and secondary inflammatory changes. The pain in plantar fasciitis may be due to one or more of the following mechanisms: irritation of pain fibers by repeated trauma or chronic pressure from a thickened plantar fascia,30 ischemic pain from chronic pressure of thickened fascia against digital vessels, enhanced effect of local pain neurotransmitters/chemicals such as substance P or glutamate (which are shown to accumulate at the site of local trauma),31 and increased noxious sensitivity secondary to inflammation. Furthermore, in any chronic painful condition, a cascade of events typically occurs, leading to a vicious cycle of pain maintenance.32 These may include central sensitization after peripheral injury in which non-nociceptive spinal cord neurons perceive non-nociceptive peripheral stimuli as painful31 and sympathetically maintained pain in which an overgrowth of sympathetic nerve fibers occurs in the dorsal root ganglia, resulting in persistent pain transmission.14

The work from animal and human data demonstrates that BTX-A can affect each of the aforementioned mechanisms. First, both clinical and experimental data have shown that the introduction of BTX-A into a muscle results in transient loss of muscle volume via induction of muscle atrophy.33 Considering our injection methodology, it is possible that the subsequent reduction of the size of the intrinsic foot muscles resulted in the relief of pressure on the neurovascular structures trapped under a tight and enlarged plantar fascia. Second, BTX-A has been shown to inhibit the release of substance P from dorsal root ganglia and to block the release of gluta-mate from synaptosomes.12,13 Third, pretreatment with BTX-A in rats results in a decreased local inflammatory response after the administration of formalin.14 Fourth, intramuscular injection of BTX-A reduces the discharge of intrafusal muscle fibers, which normally convey large non-nociceptive input (reporting muscle length) to the spinal cord.15 In chronic pain conditions (which may be the case in our subjects, who all complained of symptoms for >6 mos), reduction of this input theoretically can reduce the level of central sensitization. In animals, administration of BTX-A reduces the discharge of sympathetic neurons16 and thus can reduce the role of the sympathetic system in pain maintenance.

Our injection technique aimed to treat both the plantar fascia and the underlying muscles (adductor hallucis, flexor digitorum brevis) in case both fascia and muscle contributed to the patients’ pain. In the fascia, we hoped BTX-A would reduce inflammation, and in the underlying muscles, we hoped to see a positive effect on heel pain via muscle relaxation and loss of muscle volume. However, other suggested BTX-A actions (decreased central sensitization, decreased sympathetic activity, and reduced accumulation of substance P and glutamate) could have worked at the level of both structures. We believe our method of injection introduced BTX-A not only to the fascia but also into underlying muscles (flexor digitorum and abductor hallucis). In clinical practice, BTX-A injection into the arch of the foot with a 27-gauge, 0.75-inch needle often relieves painful flexor toe spasms in patients with stroke, head injury, cerebral palsy, and multiple sclerosis (our observations and others). We choose to treat preferentially the tender points in our patients because previous reports in myofascial pain syndromes have linked success in pain relief to this approach.9,10
Our study provided short-term results and, as in any short-term study, has limitations. Although most of our responders visited us at 6 mos, only a few could be followed for 12 mos. This is due to the moving nature of our studied population (mostly young military soldiers) and the fact that the study was conducted at the time of a major military mobilization (2002–2004). Those who visited at 6 mos and a few who were seen at 12 mos had no recurrence of symptoms. Several subjects were able to return to full duty as military police or to return to activities such as bowling, tennis, and running. One patient was able to mow the lawn after an inability to conduct this chore for 10 yrs. A few subjects with bilateral plantar fasciitis requested that their placebo foot be injected with BTX-A. They also had similar results. These limited long-term results are encouraging but need to be reproduced in a prospective study with a larger number of patients. Due to the small number of patients at 6 and 12 mos, we could not conduct a valid statistical analysis for the long-term effect.

**CONCLUSION**

The results of our study demonstrate that the injection of BTX-A into the plantar region significantly improves the pain of recalcitrant plantar fasciitis at both 3 and 8 wks after treatment. Although the exact mechanism of action has not been elucidated, several theories have been presented in this article to explain the positive effect. Furthermore, blinded studies are necessary to confirm these results, which bear significant implications in caring for patients with this disorder. Long-term prospective studies are also necessary to show if these positive effects can be sustained with repeated treatments. Due to the high cost of BTX-A, the fiscal issues need to be evaluated in each patient individually. At the present time, treatment of plantar fasciitis with BTX-A should be considered for those patients in whom standard modes of treatment (many of them simple and inexpensive) have failed to provide pain relief.

**REFERENCES**

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Disclosures:
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Low Ejection Fraction
Effect on the Rehabilitation Progress and Outcome of Stroke Patients

ABSTRACT

Objective: To determine the effect of low ejection fraction (≤35%) on the rehabilitation progress and outcome of stroke patients and compare these variables with patients with high ejection fraction (>35%).

Design: A retrospective chart review of the 332 stroke patients admitted to the inpatient rehabilitation unit of an acute tertiary general hospital during a 36-mo period. A total of 262 (79%) of these patients (126 men and 136 women) had an ejection fraction study performed and are the subjects of this analysis. They were classified into two groups: low ejection fraction (n = 36) and high ejection fraction (n = 226). The main outcome measures included discharge total FIM score, FIM gain, FIM efficiency, length of stay, and discharge disposition.

Results: Patients with low ejection fraction had lower discharge FIM scores (82.9 vs. 89.1, t = 2.09, P < 0.04), lower FIM gain (15.9 vs. 19.3, t = 1.99, P < 0.05), and lower FIM efficiency (1.2 vs. 1.7, t = 232, P < 0.03), and they were less likely to return home (69% vs. 85%, χ² = 5.25, P < 0.04) as compared with patients with high ejection fraction. Lengths of stay were not significantly different between the two groups.

Conclusion: Compared with patients in the high ejection fraction cohort, the low ejection fraction subjects had lower discharge FIM scores, FIM gains, and FIM efficiency. However, almost 70% progressed well enough to be discharged to home. Low ejection fraction in stroke patients may well serve as an indicator of a patient population with greater medical and social needs.

Key Words: Ejection Fraction, Stroke, Rehabilitation
In recent years in the United States, approximately 700,000 people annually experience a stroke, with about 30% of these being recurrent. Cardiac disease of some sort is suggested to occur in about 75% of acute stroke survivors, such as those admitted to an inpatient rehabilitation unit. Cardiac morbidity can obviously inhibit or delay participation or performance in a therapeutic exercise program and a comprehensive rehabilitation program. No single, individual indicator of the magnitude of heart disease has been found that can be equated to progress and functional outcome of stroke patients on a rehabilitation unit. Several scattered reports have mentioned the possible utility of ejection fraction (EF) as a predictor of rehabilitation outcome. The EF is the fraction or percentage of left ventricular diastolic volume that is ejected during systole (mean normal range, 55–75%) and is a measure of global left ventricular systolic function.

The purpose of this study was to examine the progress and outcomes on a rehabilitation unit of stroke patients with low EF (LEF, ≤35%) and compare these variables with those patients with high EF (HEF, >35%).

METHODS

In a retrospective chart review, the records of 332 stroke patients admitted to the 24-bed rehabilitation unit of a private tertiary acute general hospital during a 36-mo period were reviewed. A total of 262 (79%) of these patients had an EF study performed during their acute hospitalization, and these individuals are the subjects of this study. All of the EF studies were done by two-dimensional echocardiography and interpreted by a cardiologist. The 262 patients consisted of 126 men and 136 women and were divided into two groups based on their EF (≤35% [LEF] vs. >35% [HEF]). Thirty-six patients were categorized as LEF and the remaining 226 patients as HEF. The EF value of 35% as a threshold follows the methodology of the echocardiography laboratory at our institution and the reports of others. Due to the small sample of patients at the lower range of EF, it was decided not to further fractionate the overall cohort into smaller groups (e.g., quartiles or quintiles). The ischemic stroke etiologic subtype classification used by Adams et al. and developed for TOAST (Trial of Org 10172 in Acute Stroke Treatment) was employed to categorize the ischemic strokes. A separate category for hemorrhagic strokes was added. Thus, the etiologic subtypes of stroke were classified as: large artery atherosclerosis, cardioembolism, lacune/small vessel occlusion, hemorrhagic, stroke of other determined cause, and stroke of undetermined cause.

All of the subjects of this study were diagnosed by an attending neurologist as having had a stroke and were further assessed for suitability for admission to the rehabilitation unit by a consulting physiatrist. All patients with a stroke who did not have a documented EF study on their acute stay before admission to the rehabilitation unit (NO EF) were excluded from this study, but their characteristics and outcomes were compared with the EF patients (Table 1). Criteria for admission to the rehabilitation unit (which were similar for all stroke patients) included: medical stability, the ability to tolerate ≥3 hrs of therapy daily, and realistic rehabilitation goals.

If the patient was stable medically, a low EF was therefore not an exclusion criterion for admission. All patients received twice-daily physical and occupational therapy. In addition, the services of speech pathology and neuropsychology were employed as appropriate. Patients were discharged from the rehabilitation unit when the treating team (physicians, nurses, and therapists) deemed that they had neared or reached a plateau point in their progress or had improved sufficiently to be safely discharged. Transfers back to an acute medical unit were based on medical necessity. The functional status of each patient was assessed, at a minimum, at both admission and discharge by using the FIM instrument, an 18-item measurement tool with a 7-point ordinal scale. Admission and discharge FIM total scores were calculated by summing item scores. Respective FIM gains were tabulated by subtracting admission from discharge scores. FIM efficiency was derived by dividing FIM gains by length of stay (LOS) in days. Patient demographic features, length of rehabilitation stay, side of body involved, discharge disposition, EF, FIM scores, FIM efficiency, and FIM gain were included in the analysis. The FIM scores of the two patients who died (both in the LEF group) were the most recent available (in both cases, calculated within 48 hrs of death).

Data Analysis

Descriptive statistics were obtained for all study variables, including values, standard deviations, and ranges for continuous variables and number and percentage for categorical variables. These statistics were obtained for the entire sample, separately for the groups with and without EF data available and separately for the LEF and HEF groups. Comparisons between those with and without EF data were assessed with t tests for continuous variables and χ² analyses for categorical variables. Similarly, comparisons between those with low and high EF were assessed with t tests and χ² analyses. To avoid small cell sizes, all analyses...
involving side of body affected by stroke were restricted to left and right unilateral strokes, all analyses involving stroke cause combined strokes of other determined cause with strokes of other undetermined cause, and all analyses involving discharge disposition combined all patients who were not discharged to home.

Separate multiple regression analyses were conducted that included only those with EF data to determine whether EF group (low vs. high) was significantly related to FIM outcome scores (discharge FIM score, FIM gain, and FIM efficiency) and LOS in the context of other potential predictors. Similarly, a logistic regression analysis was conducted to determine whether EF group was significantly related to discharge disposition (home or other).

RESULTS

Displayed in Table 1 are descriptive statistics for the entire sample and the groups with and without EF data. Most of the patients in both groups were discharged to home (No EF, 93%; EF, 83%). The results of statistical comparisons of the groups with and without EF are also displayed. The two groups differed significantly on age and discharge disposition. Those without EF data were younger than those with EF data by nearly 5 yrs (P ≤ 0.011), and they were more likely to be discharged to home (P = 0.039). The with and without EF groups did not differ significantly on LOS, any FIM variable (admission, discharge, gain, efficiency), sex, side of body affected by stroke, or stroke cause.

Presented in Table 2 are comparisons between the LEF and HEF groups. Compared with the LEF group, the HEF group had significantly higher scores on discharge FIM (6 points, P = 0.037), FIM gain (9 points, P = 0.047), and FIM efficiency (0.5 points, P = 0.021). The HEF group was also more likely to be discharged to home (85% vs. 69%, P = 0.031). A complete display of all discharge disposi-

<table>
<thead>
<tr>
<th>TABLE 1 Sample characteristics and comparisons of patients with and without ejection fraction data</th>
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<td><strong>Entire Sample</strong></td>
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<tr>
<td><strong>Number</strong></td>
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<td><strong>Age, yrs</strong></td>
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<tr>
<td>66.3</td>
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<tr>
<td><strong>Length of stay, days</strong></td>
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<td><strong>Admission FIM™ score</strong></td>
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<td><strong>Discharge FIM score</strong></td>
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<td>Stroke of other determined cause</td>
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<td>Stroke of undetermined cause</td>
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<tr>
<td><strong>Discharge disposition</strong></td>
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<tr>
<td>Home</td>
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<td>Other</td>
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</table>

Fisher’s exact test was used for all 2 × 2 χ² analyses.

P ≤ 0.05.

χ² analysis included only left and right side strokes to avoid small cell sizes (n = 305).

Stroke of other determined cause and stroke of undetermined cause categories were combined for the χ² analysis.
tions for each group can be seen in Figure 1. There were no significant differences between the LEF and HEF groups for age, LOS, admission FIM score, sex, side of body affected by stroke, or stroke cause.

Displayed in Tables 3 and 4 are the relationships of discharge FIM score, FIM gain, FIM efficiency, LOS, and discharge disposition with EF group (low vs. high) in the context of other study variables.

### TABLE 2 Comparisons of groups with low and high ejection fraction

<table>
<thead>
<tr>
<th></th>
<th>Low Ejection Fraction</th>
<th>High Ejection Fraction</th>
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<tbody>
<tr>
<td></td>
<td>EF ≤ 35%</td>
<td>EF &gt; 35%</td>
</tr>
<tr>
<td>Number</td>
<td>36</td>
<td>226</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>Mean 70.3 ± 13.6</td>
<td>Mean 66.9 ± 14.1</td>
</tr>
<tr>
<td></td>
<td>Range 38 to 91</td>
<td>Range 69 to 14.8</td>
</tr>
<tr>
<td></td>
<td>t 1.327</td>
<td>t 0.190</td>
</tr>
<tr>
<td>Length of stay, days</td>
<td>Mean 13.6 ± 7.1</td>
<td>Mean 13.9 ± 7.4</td>
</tr>
<tr>
<td></td>
<td>Range 6 to 42</td>
<td>Range 16.0 ± 40</td>
</tr>
<tr>
<td></td>
<td>t 1.048</td>
<td>t 2.093</td>
</tr>
<tr>
<td>Admission FIM™ score</td>
<td>Mean 67.0 ± 12.1</td>
<td>Mean 69.8 ± 14.8</td>
</tr>
<tr>
<td></td>
<td>Range 28 to 84</td>
<td>Range 9.4 ± 28 to 43</td>
</tr>
<tr>
<td>Discharge FIM score</td>
<td>Mean 82.9 ± 18.1</td>
<td>Mean 89.1 ± 16.0</td>
</tr>
<tr>
<td></td>
<td>Range 27 to 114</td>
<td>Range 16.0 ± 22 to 118</td>
</tr>
<tr>
<td>FIM gain</td>
<td>Mean 15.9 ± 10.4</td>
<td>Mean 19.3 ± 9.4</td>
</tr>
<tr>
<td></td>
<td>Range −17 to 33</td>
<td>Range 28 to 43</td>
</tr>
<tr>
<td>FIM efficiency</td>
<td>Mean 1.2 ± 1.0</td>
<td>Mean 1.7 ± 1.1</td>
</tr>
<tr>
<td></td>
<td>Range −2.4 to 2.6</td>
<td>Range −2.8 to 6.3</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>17 (47.2%)</td>
<td>119 (52.7%)</td>
</tr>
<tr>
<td>Male</td>
<td>19 (52.8%)</td>
<td>107 (47.3%)</td>
</tr>
<tr>
<td>Side of body affected by stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>19 (52.8%)</td>
<td>98 (43.4%)</td>
</tr>
<tr>
<td>Right</td>
<td>15 (41.7%)</td>
<td>114 (50.4%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>2 (5.6%)</td>
<td>7 (3.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0.0%)</td>
<td>7 (3.1%)</td>
</tr>
<tr>
<td>No pareses</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Stroke cause</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>8 (22.2%)</td>
<td>60 (26.5%)</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>15 (41.7%)</td>
<td>71 (31.4%)</td>
</tr>
<tr>
<td>Lacune/small vessel occlusion</td>
<td>5 (13.9%)</td>
<td>38 (16.8%)</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>4 (11.1%)</td>
<td>29 (12.8%)</td>
</tr>
<tr>
<td>Stroke of other determined cause</td>
<td>1 (2.8%)</td>
<td>5 (2.2%)</td>
</tr>
<tr>
<td>Stroke of undetermined cause</td>
<td>3 (8.3%)</td>
<td>23 (10.2%)</td>
</tr>
<tr>
<td>Discharge disposition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>25 (69.4%)</td>
<td>192 (85.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (30.6%)</td>
<td>34 (15.0%)</td>
</tr>
</tbody>
</table>

* EF, ejection fraction.
* P < 0.05.
* χ² analysis included only left and right side strokes to avoid small cell sizes (n = 246).
* Stroke of other determined cause and stroke of undetermined cause categories were combined for the χ² analysis.

FIGURE 1 Discharge dispositions of the low and high ejection fraction groups. SNF, skilled nursing facility; ASST, assisted.
For discharge FIM score, the overall model was significant at the 0.001 level. The model accounted for approximately 70% of the variance in discharge FIM score. Significant predictors included age (P < 0.001), admission FIM score (P = 0.001), and sex (P = 0.046). EF group (high vs. low) approached significance (P = 0.086). Persons with higher discharge FIM scores were men, younger, and in the HEF group, and they had higher admission FIM scores. Side of body affected by stroke and stroke cause were not significant predictors.

**FIM Gain**

The same variables were significant predictors of FIM gain, but the model only accounted for 14%
of the variance ($P < 0.001$). Significant predictors included age ($P = 0.001$), admission FIM score ($P = 0.011$), and sex ($P = 0.046$). EF group approached significance ($P = 0.086$). Persons with higher FIM gain scores were men, younger, and in the HEF group, and they had lower admission FIM scores. Side of body affected by stroke and cause of stroke were not significant predictors.

**FIM Efficiency**

The model accounted for 24% of the variance in FIM efficiency ($P < 0.001$). Age ($P = 0.015$), admission FIM score ($P = 0.001$), and sex ($P = 0.014$) were significant predictors of FIM efficiency. EF group approached significance ($P = 0.062$). Persons with higher FIM efficiency scores were men, younger, and in the HEF group, and they had higher admission FIM scores. Side of body affected by stroke and cause of stroke were not significant predictors.

**LOS**

The model accounted for approximately 57% of the variance in LOS ($P < 0.001$). Significant predictors were age ($P = 0.002$) and admission FIM score ($P = 0.001$). Persons with shorter lengths of stay were older and had higher admission FIM scores. Sex, side of body affected by stroke, stroke cause, and EF group were not significant predictors.

**Discharge Disposition**

Displayed in Table 4 are the results of a binary logistic regression analysis performed to identify the best predictors for discharge disposition (home or other). Age ($P = 0.001$), admission FIM score ($P = 0.001$), sex ($P < 0.045$), and EF group ($P = 0.008$) were significant predictors. Persons discharged to home were more likely to be men, younger, and in the HEF group and to have higher admission FIM scores. Side of body affected by stroke and cause of stroke were not significant predictors of discharge disposition.

**DISCUSSION**

Study patients in the LEF group had lower discharge FIM scores, lower FIM gain, and lower FIM efficiency, and they were less likely to go home compared with patients in the HEF group. These differences between the EF groups remain evident after accounting for other study variables in multiple and logistic regression analyses (Tables 3 and 4). Patients in the LEF group were also more likely to have a transfer to an acute medical unit (Fig. 1), although the small numbers, especially in the LEF group ($n = 2$), preclude performing formal analyses. Lengths of stay were not significantly different between the two groups. Despite the identified differences between the LEF and HEF groups, almost 70% of the LEF group progressed well enough to be discharged to the community, thus suggesting that these patients should not necessarily be excluded from an inpatient rehabilitation program if they are otherwise suitable. Other authors have commented that a low EF, or cardiac disease in general, might serve more as a "marker" of a patient with extra medical and rehabilitation needs and as an alert for extra caution to medical and rehabilitation staff.

| TABLE 4 Logistic regression analysis predicting discharge to home or elsewhere |
|--------------------------------|------------------|-----------------|-----------------|------------------|
| Discharge disposition home vs. other | $\chi^2$ | Percentage Correctly Predicted | Coefficient ($B$) | SE | Wald | Odds Ratio EXP ($B$) | 95% CI for EXP ($B$) |
| Age | 0.059 | 0.019 | 10.155 | 1.061<sup>a</sup> | 1.023–1.100 |
| Admission FIM score | -0.080 | 0.016 | 0.923<sup>a</sup> | 25.633 | 0.895–0.952 |
| Sex | 0.890 | 0.444 | 4.021 | 2.434<sup>a</sup> | 1.020–5.807 |
| Side of body affected by stroke | -0.277 | 0.435 | 0.758 | 3.250 | 0.323–1.778 |
| Stroke cause | | | | | |
| Large artery atherosclerosis | 0.112 | 0.679 | 0.027 | 1.118 | 0.295–4.233 |
| Cardioembolism | -0.704 | 0.712 | 0.978 | 0.493 | 0.123–1.996 |
| Lacune/small vessel occlusion | -0.312 | 0.850 | 0.134 | 0.732 | 0.138–3.878 |
| Hemorrhagic | 0.305 | 0.785 | 0.151 | 1.357 | 0.291–6.325 |
| Ejection fraction group | 1.376 | 0.522 | 6.939 | 3.960<sup>a</sup> | 1.422–11.026 |

<sup>a</sup> $P < 0.001$.

<sup>b</sup> $P < 0.05$.

<sup>c</sup> $P < 0.01$.
indicate that EF group, in the context of other study variables, was a significant predictor for discharge disposition but only approached significance for the FIM outcome scores (discharge FIM score, FIM gain, and FIM efficiency).

There are obvious limitations to this study. First, a bias may have existed as to who underwent an EF study in acute care. Echocardiograms were performed during the acute hospitalization on 79% of the 332 stroke patients admitted to the rehabilitation unit during the 36-mo study period. A total of 27 different physicians (cardiologists, neurologists, and internists) ordered the EF studies on the 262 patients for a variety of reasons (e.g., to rule out a cardioembolic cause of stroke, to study the overall health and integrity of the heart). The NO EF patients were significantly younger and more likely to return home but did not differ from the EF groups in any of the measured FIM variables, LOS, sex, side of body affected, or stroke etiologic subtype. It could be speculated that this more youthful group was also “healthier;” thus, an EF study was deemed to be unnecessary.

Second, all of the patients with EF data received a two-dimensional echocardiogram for determining the EF. Other methods of determining the EF, such as magnetic resonance imaging, gaited single-photon emission tomography, and radionuclide ventriculography, were not performed. It is uncertain if this had any effect on study findings.

Third, no other cardiac variables were available for all patients with EF data, thus electrocardiographic findings and the presence or absence of atrial fibrillation, among other variables, were not included as study variables. It must be remembered that EF is a numerical variable that does not necessarily indicate congestive heart failure or equate to any other specific cardiac malady. Some studies have indicated that up to half of all patients with congestive heart failure have a normal EF.15,16 An EF of 35% was chosen in this study as the determining value as to whether to put a patient into the LEF or HEF group.11,12 Other authors, however, have used differing values in formulating a definition.9,16,17

CONCLUSION

Our study and the works of others show that LEF patients may safely participate in an inpatient rehabilitation therapy program, although they may not achieve as good a result as HEF individuals.9 A low EF should serve as an indicator to medical, nursing, and therapy staff that a patient has special needs. His or her initial inpatient rehabilitation program may need to be modified (e.g., lighter exercise) to take the heart disease into account. Nonetheless, a rehabilitation program can serve as the beginning of a long-term therapeutic conditioning program.4

REFERENCES

ABSTRACT

Objective: To evaluate the accuracy for three methods for needle insertion into the subscapularis muscle for electromyography, botulinum toxin injection, and phenol nerve block.

Design: Three needle insertion methods were evaluated by cadaver injection by an American Board of Electrodiagnostic Medicine certified physician. An anatomist, blinded to the method used, served as the dissector to evaluate the effectiveness of the methods tested.

Results: A posterior axillary approach was most effective for needle insertion into the subscapular muscle compared with a medial scapular or a superior scapular approach. No approach was ideal for subscapular nerve injection.

Conclusions: A posterior axillary approach is best for needle insertion of the subscapularis muscle for electromyography or botulinum toxin injection. Subscapular nerve injection is difficult from all of the three approaches tested.

Key Words: Subscapularis Muscle, Spasticity, Needle Electromyography

The subscapularis muscle is one of the rotator cuff muscles. Its origin is the entire subscapular fossa, and it inserts on the lesser tuberosity of the humerus. The subscapularis muscle is the strongest of the internal rotators of the shoulder. It is assisted in this task by the latissimus dorsi, pectoralis major and minor, teres major, and minimally by the anterior deltoid. It also functions to adduct and extend the shoulder. To the scapula, it serves as an abductor when the humerus is stabilized, counteracting the force of the rhomboid.1 Spasticity in this muscle overwhelms the weakness of the rotator cuff muscles, resulting in shoulder adduction and internal rotation with anterior subluxation of the humeral head. Similarly, spasticity of the subscapularis overwhelms the weakness of the rhomboid, resulting in abduction and rotation of the scapula. This may be important in shoulder pain and positioning management in spastic
hemiplegia due to stroke and traumatic brain injury and in upper cervical quadriplegia due to spinal cord injury.

This is a multipennate muscle with five to seven tendons that converge on its humeral attachment. It is subserved by the posterior divisions of C5 and C6 by the upper and lower subscapular nerves. These nerves come off the posterior cord proximally, extending posteriorly to the midpoint of the scapula and descending between the scapula and rib cage to innervate the muscle.1

Methods have been discussed to achieve local spasticity control of the subscapularis. Awad2 describes a subscapular approach by accessing the nerves to the subscapularis from a medial scapular approach at the level of the spine of the scapula while the scapula is in a winged position. Phenol, 5%, is then utilized to block the intramuscular while the scapula is in a winged position. Phenol, 5%, is then utilized to block the intramuscular branches to the muscle.

Chironna and Hecht3 use a similar technique in their clinical series of hemiplegic patients with shoulder spasticity. In their series, they noted an improvement in shoulder range of motion, with no shoulder subluxation. No other complications were noted. This series was expanded to include 13 patients with spastic hemiplegia by Hecht.4 He noted shoulder range-of-motion improvements of 21 degrees of abduction, 40 degrees of flexion, and 38 degrees of external rotation after subscapular phenol nerve block using this technique. In his study, he recommended two injections to ensure blockade of the upper and lower subscapular nerves.

This study is the first study to use anatomic dissection with cadavers after needle placement to evaluate the efficacy of the injection techniques for the subscapularis muscle. The clinical relevance is noted, as internal rotation and adduction spasticity and shoulder pain is common in hemiplegia, quadriplegia, and other upper motor neuron paralysis syndromes that affect the upper limbs. This study is essential in evaluating a muscle that, due to its depth and location, is technically difficult to reach clinically for treatment. In addition, as no previous cadaver study was completed with these methods, the risks or pitfalls of each technique are not known.

METHODS

A total of 14 cadavers were used to complete bilateral subscapular muscle injections. Five were female and nine were male cadavers, with a mean age of 74.4 yrs and a range of 42–86 yrs. All of the cadavers were pressure embalmed. None of the recorded causes of death were deemed to have affected the results of this study with regard to needle placement or dissection.

Needle placement was accomplished using the method of Haig and Ruan.5 A 24-gauge florist wire with a bend at the insertion end was placed through an 18-gauge, 4.5-inch, sharpened and beveled cannula. The needle was placed in the assigned location by an American Board of Electrodiagnostic Medicine certified physician. The physician in this study was fellowship trained in electromyography and neuromuscular disease, with 15 yrs experience in spasticity management with phenol blocks and botulinum toxin. He has extensive clinical experience in the use of subscapular nerve blocks in the management of shoulder spasticity. The cannula with the wire was inserted into the skin at the appropriate place by the palpator, at which point the cannula was withdrawn, allowing the wire to hook into the tissue. The wire was bent externally, where a numbered label was placed that was also placed on the dissection sheet. The anatomist would later dissect the needles and record his observations on the dissection sheet. The dissector would record hits and misses, dangers (defined as a wire that passed through a significant nerve or blood vessel), and cautions (defined as a wire that passed within 0.5 cm of a nerve or blood vessel). This method is detailed elsewhere. Standard χ² analyses were completed. P values were deemed significant when ≤0.05.

Three methods were attempted for subscapular injection (Fig. 1). Nine needle placements were attempted with each approach. A lateral or axillary approach was used by accessing the posterior axillary fold. Palpating the brachial pulse anteriorly ensures that the injection is clear of the axillary sheath. The needle is entered posteriorly and medially toward the subscapular fossa. Once bone is contacted, the needle is withdrawn slightly.

The apical approach starts anterior to the suprascapular fossa, directing the needle behind the scapula to contact the subscapular nerves and the muscle beyond. The trapezius will be traversed before the subscapular fossa is reached. The suprascapular nerve and artery could be traversed if the injection site is too medial.

The medial or vertebral approach starts medial to the scapula at the level of the spine of the scapula. The lower trapezius and rhomboid are traversed before the needle is directed behind the scapula to the subscapular fossa and the muscle and nerves located there. Too much medial angle can result in the needle entering a rib space.

RESULTS

The lateral or axillary approach achieved an accuracy of placement of 78%, with no cautions or dangers. The misses were in two different cadavers, with one needle placement in the supraspinatus and the other in the teres minor. The medial and superior approach had an accuracy of placement of 33% and 0%, respectively, both significant at a P
value of 0.05. The successful medial approaches were in two different cadavers. Eighty percent of the superior approaches ended in the supraspinatus, and the rest were in the trapezius or levator scapulae. The misses with the axillary approach were either too lateral or inferior, resulting in latissimus dorsi or teres major injection. The successful medial approaches rested between 2 and 3 cm from the branches of the upper and lower subscapular nerves, too far away for effective phenol nerve blockade. The lateral approaches brought the wires to within 1 and 2 cm from the subscapular nerve branches (Fig. 2). In the dissections, between three and five branches from the brachial plexus were noted, rather than just a distinct upper and lower subscapular nerve. There was no detected pattern of improved success with needle placement with the number of trials.

**DISCUSSION**

Previous studies have pointed to the medial or vertebral approach as the approach of choice in achieving blockade of the subscapularis muscle. This study refutes that finding and notes that the axillary approach is superior in targeting the muscle and in achieving proximity to the nerves to this muscle. These results are despite the difficulty with stretching the shoulder in abduction and external rotation in the cadaver. This would be the same difficulty seen in patients with upper motor neuron weakness and spasticity of the upper limbs. This would indicate that with similar difficulties, the same

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**FIGURE 1** Approaches and cautions for each method used in the subscapularis study. Each description is accompanied by a photo showing the site and angle of insertion. Left, subscapular placement A: lateral (axillary) approach. From the anterior position, access the posterior axillary fold. Palpate a high brachial pulse to ensure that you are clear of the axillary sheath and its contents. Insert the needle posteriorly toward the subscapular fossa’s lateral edge and withdraw slightly. The line marks the lateral edge of the scapula. This is a superficial placement, but if the needle is inserted too inferiorly or too laterally, there may be early contact with the latissimus dorsi or teres major. Middle, subscapularis placement B: superior (apical) approach. Mark the vertebral border of the scapula. Below the root of the spine of the scapula, insert the needle as if you were heading toward the serratus anterior. Angle along the subscapular fossa laterally. This is a deep placement and involves traversing first the rhomboid major and the serratus anterior before contact with the subscapularis. Too much anterior angle on the needle may cause it to enter the rib space. Right, subscapularis placement C: medial (vertebral) approach. Palpate and mark the edges of the scapula. From the superior angle, go medially and begin insertion to the superior border. Ensure that the needle slides along the anterior side of the superior border and into the subscapularis. This is a deep placement and involves traversing the trapezius. If the needle is too posterior or inferior, the supraspinatus will be entered. If the needle is too lateral, there is a chance of encountering the suprascapular nerve and artery.
improved success with subscapularis injection using the axillary approach should be obtained.

A limit to this study is that despite needle entry into the muscle, this study does not measure the success in spasticity management with these techniques. It has already been noted that the subscapularis is multipennate. If botulinum toxin injections were going to be accomplished by any technique, one would have to be sure that enough of the muscle could be reached with the technique to achieve the desired clinical result. If phenol were to be used, proximity to the nerve fibers is critical. Although this was best seen with the axillary approach, the question would need to be made about whether proximity to nerve included all of the nerve branches to the penna of the muscle or whether the main nerve branch was in proximity. This was not answered by this study. This may account for why studies looking at spasticity and function changes with botulinum toxin A injections noted improvement with distal arm treatment but not with treatment of shoulder adduction spasticity in hemiplegic stroke patients.6 Other studies did not even attempt to block this muscle.7–11

CONCLUSION

Subscapularis injection is best accomplished by the lateral axillary approach. This was associated with little concern for cautions or dangers in the case of needle electrodiagnostic evaluation. For spasticity management, two unique limitations exist. First, this muscle is multipennate, requiring injection in multiple locations to achieve maximal effect with botulinum toxin A. Second, phenol nerve blockade requires the identification of more than two nerve branches off of the brachial plexus. Further study would include evaluation of spasticity reduction, range of motion improvement, and pain control with different doses and number of injections of botulinum toxin A in the subscapularis. Additional study could look at alternative methods of achieving subscapular nerve blockade. In addition, the use of radiologic or ultrasound guidance could be studied in patients to achieve improved muscle targeting.

REFERENCES

Sleep-Disordered Breathing in Spinal Muscular Atrophy Types 1 and 2

ABSTRACT


Objective: Our aim was to assess the respiratory pattern during sleep in patients affected by spinal muscular atrophy types 1 and 2 and to compare their apnea-hypopnea indices with those of controls.

Design: All consecutively referred patients underwent polysomnography. Sleep stages were defined as either wake, quiet sleep (QS), or active sleep (AS). As measures of thoracoabdominal coordination, we measured: phase angle during QS and AS (Ph Angle QS and AS), phase relation during inspiration and expiration during QS and AS: (Ph RIB QS, Ph RIB AS, Ph REB QS; Ph REB AS) and the apnea-hypopnea index.

Results: The 14 consecutively referred infants and small children (age, 11.7 ± 11.4 mos) showed a higher apnea-hypopnea index (P < 0.001), Ph Angle QS (P < 0.001), Ph Angle AS (P < 0.001), Ph RIB QS (P < 0.001), Ph RIB AS (P < 0.001), Ph REB QS (P < 0.001), and Ph REB AS (P < 0.001) compared with 28 healthy controls (age, 10.1 ± 8.9 mos).

Conclusions: Patients affected by types 1 and 2 spinal muscular atrophy had significantly higher apnea-hypopnea indices than controls. Thoracoabdominal asynchrony was present during the inspiratory and expiratory phases in both quiet and active sleep. Measures of thoracoabdominal coordination may be useful for the evaluation and monitoring of therapeutic interventions for these patients.

Key Words: Spinal Muscular Atrophy, Respiratory Inductive Plethysmography, Thoracoabdominal Coordination, Sleep-Disordered Breathing, Polysomnography
Spinal muscular atrophy (SMA) is an autosomal recessive disorder characterized by degeneration of the anterior horn cells in the spinal cord and motor nuclei in the lower brainstem. It has a rate of approximately 1 per 5000 births. The gene responsible for SMA has been located within the complex genomic region at chromosome 5q11.2–q13.3, which contains a 500-Kb inverted duplication. Within this inverted duplication lies the SMA-determining gene, the survival motor neuron (SMN) gene. Gene deletions are detectable in 98% of patients. The survival motor neuron gene is present in two copies, designated the survival motor neuron centromeric and survival motor neuron telomeric genes. Mutations in the survival motor neuron telomeric gene are thought to be responsible for the SMA phenotype. Severity, which is inversely proportional to the amount of complete survival motor neuron 1 protein, ranges from severe generalized paralysis and need for ventilatory support from birth to relatively mild conditions presenting in young adults. This disorder is an important cause of morbidity in the neonate and the leading hereditary cause of infant mortality.

SMA is classified into five types based on severity of muscle weakness. The SMA type 1 infant never attains the ability to sit independently, acute respiratory failure occurs during chest infections usually in the first 2 yrs of life, and unless treated with recently described respiratory muscle aids or tracheostomies, 90% of these children die before their second birthdays. Children with SMA type 2 can temporarily sit independently but can never walk, and they, too, usually have periods of respiratory failure during early childhood. Other SMA types have milder courses.

All SMA patients have diffuse, symmetric muscle weakness and decreased or absent deep tendon reflexes. Because the upper cranial nerves are spared, patients with SMA type 1 typically have an alert expression, furrowed brow, and normal eye movements early on. However, weakness of the respiratory and bulbar-innervated muscles results in a weak cry, underdevelopment of the chest wall and lungs, and a weak cough. Weakness of bulbar-innervated muscles also results in poor suck and swallow reflexes, pooling of secretions, and aspiration, which along with a weak cough, predispose the patient to pneumonia and acute respiratory failure.

The intercostal muscles are typically more affected than the diaphragm, resulting in paradoxical breathing (inspiratory efforts cause the rib cage to move inward as the abdomen moves outward), the development of a characteristic bell-shaped chest deformity and pectus excavatum, and often greater vital capacity with the patient in the supine rather than sitting position. Respiratory muscle discoordination increases the work of breathing and reduces tidal volume. Hypercapnia only occurs during acute respiratory failure, when patients are treated with home oxygen therapy, or much later during childhood when obesity or scoliosis develops. Mechanical ventilation to rest inspiratory muscles and better expand the lungs and chest wall can improve both growth and development of lung parenchyma and the chest wall, slow or reverse the progression of chest wall deformity, and increase the duration and quality of life.

The aim of our study was to assess the thoracoabdominal pattern of spontaneous breathing during sleep and the apnea-hypopnea indices (AHI) in patients affected by types 1 and 2 SMA.

METHODS

Sample

We studied 14 consecutively referred infants and children with DNA-deletion confirmed SMA types 1 or 2 (aged 11.7 ± 11.4 mos) who had not had any signs of respiratory tract infection for ≥2 wks and 28 age matched controls (aged 10.1 ± 8.9 mos). Controls were recruited among infants and children followed in our hospital for apparent apnea episodes, cyanosis, pallor, flushing, plethora, marked changes in muscle tone (usually limppness), choking, or gagging. Evidence-based protocols on evaluating and managing such episodes are lacking. Our approach includes performing sleep studies for the assessment of these subjects. Exclusion criteria for controls included: (1) genetic disorder or craniofacial anomaly, (2) abnormal growth or development, (3) previous adenoidectomy or tonsillectomy, (4) history of seizure, (5) and preexisting lung disease. Informed consent was obtained from the parents of each child. This study was approved by the ethics committee of our hospital.

Instruments and Technique

A SomnoStar PT (SensorMedics, Yorba Linda, CA) seven-channel recorder was used to measure heart rate, pulse rate, pulse waveforms, pulse oxyhemoglobin saturation (SpO2), and calibrated respiratory inductive plethysmography (thoracic, abdominal, and sum channel) in a dark room. This technique has been previously used in infants and children, and technical details have been published elsewhere. Calibration of the rib cage and abdominal signals was performed during the first 5 mins of the quantitative diagnostic calibration procedure. Apnea and hypopnea thresholds were based on a calibrated baseline volume observed on the SomnoStar PT during the first 5 mins of operation. This baseline represented the...
average breath volume during the 5-min period normalized to an amplitude of 100%. All breaths were expressed as a percentage of the calibrated baseline volume. Sleep respiratory events and behavior were videotaped by an infrared videocamera. Sleep stages were defined as either wake, quiet sleep (QS or no rapid-eye-movement sleep), or active sleep (AS or rapid-eye-movement sleep) based on the presence of movements, heart rate variability, and by reference to the video record. No sedation or sleep deprivation was used. A parent accompanied each patient throughout the night.

Thoracoabdominal Coordination Variables

The rib cage (RC) and abdominal (AB) waveforms define the two-compartments model of respiration described by Konno and Mead. These two components can move together or independently. Among the major indices that describe the coordination of movement between RC and AB compartments is the phase angle. A phase angle of 0 degrees indicates perfect in-phase movements, whereas values of 180 degrees indicate completely out-of-phase movements between RC and AB compartments. Intermediate values indicate varying degrees of asynchronous and paradoxical motion. Phase relation was computed for each breath during the expiratory cycle, inspiratory cycle, and total cycle. The phase angle during QS and AS (Ph Angle QS and AS) represents the percentage of agreement between direction of RC and AB movements over the entire cycle of a breath. During QS and AS, the phase relation during inspiration (Ph RIB QS and Ph RIB AS) and that during expiration (Ph REB QS and Ph REB AS) represents the percentage of agreement between direction of RC and AB movements over the inspiratory and expiratory phases of a breath, respectively. The analysis of thoracoabdominal coordination was expressed as the mean of three periods of 5 mins randomly selected during QS and AS.

Respiratory Variable Definitions

Paradoxical apneas and hypopneas were defined by paradoxical chest/abdominal wall motion with amplitudes decreased by 80% and 50–80% on the respiratory inductive plethysmography summation channel, respectively. The definition of a hypopnea also necessitated a decrease in SpO2 of ≥4%. Both apneas and hypopneas had to last for at least two respiratory cycles. Central apneas were defined by unmeasurable chest/abdominal wall motion associated with an ≥80% decrease in amplitude on the respiratory inductive plethysmography summation channel for ≥10 secs or of any duration associated with desaturation of ≥4%. Mixed apneas were defined by having both central (>3 secs in duration or twice the baseline respiratory cycle length) and paradoxical (of any length) components. The AHI was defined by the number of mixed/paradoxical apnea/hypopneas per hour of sleep. Sleep-disordered breathing was defined as having an AHI of ≥1.

The oxygen desaturation index was defined as the number of desaturations of ≥4% from baseline per hour of sleep. Oximetry artifacts in the pulse waveform tracing were discarded manually after visual inspection of the traces.

Statistical Analysis

Statistical analysis was carried out using SPSS (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation. Comparison between patients and controls was done using an unpaired t test, with the level of statistical significance determined by P ≤ 0.05.

RESULTS

Ten of the 14 patients had SMA type 1. Eight of the 14 were boys. The patients weighed 7.3 ± 3.8 (3.6–16) kg and were 74.3 ± 20.8 (57–125) cm in length. There were no significant differences in the patients and controls in age, weight, or height.

The sleep study results are in Table 1. The AHI was greater than 1 in nine SMA patients but in only

<table>
<thead>
<tr>
<th>TABLE 1. Comparison of cardiorespiratory sleep study results</th>
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<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>SpO2, mean, %</td>
</tr>
<tr>
<td>SpO2 &lt; 95%, %TST</td>
</tr>
<tr>
<td>ODI, no. per hour</td>
</tr>
<tr>
<td>AHI, no. per hour</td>
</tr>
</tbody>
</table>

SMA, spinal muscular atrophy; SpO2 mean, mean pulse oxyhemoglobin saturation; SpO2 <95%, percentage of total sleep time that SpO2 was <95%; ODI, number of desaturations of ≥4% per hour; AHI, number of mixed-paradoxical apneas/hypopneas per hour.

Results are expressed as mean ± SD (range).
three controls. Controls were recruited from a population presenting for a cardiopulmonary medical evaluation and not from the general population; it is thus possible that their data could be partially confounded by underlying medical conditions. They spent 8.5% ± 9.1% of their total sleep time with an SpO2 level at <95%. These data are not surprising considering that the SpO2 values for this age group may be influenced by episodes of desaturation occurring in association with brief apneas and cycles of period breathing.23 Nevertheless, the SMA patients had significantly greater thoracoabdominal asynchrony with paradoxical motion during the inspiratory and expiratory phases of both QS and AS (Table 2).

Six patients with SMA type 1 and one patient with type 2 with severe paradoxical breathing used nocturnal bilevel positive airway pressure ventilation. All 14 patients had one or more episodes of respiratory failure before their second birthdays.

DISCUSSION

The SMA children had more asynchronous (paradoxical) breathing during AS and QS than healthy controls, as was also true when they were awake. Paradoxical movements of the rib cage and abdomen were also seen physiologically during rapid-eye-movement sleep in normal infants, decreasing within 3 yrs of life,24 and in otherwise normal children during obstructive sleep apneas.25

Thoracoabdominal paradox is mainly the result of the imbalance of muscular forces that normally concomitantly expand the thoracic and abdominal compartments during breathing. Perez et al.26 observed paradoxical breathing in 31 patients with SMA and in 19 patients with myopathies (mean age, of 9.7 ± 3 yrs) by using the percentage of thoracic contribution to tidal volume, a Labored Breath Index, and phase angles. They also found nearly full correction during intermittent positive-pressure ventilation. Diaz27 also observed chest wall motion asynchrony in five children and young adults (mean age, 15.6 yrs) with neuromuscular disease and its correction by noninvasive mechanical ventilation.

Our study was of a much younger SMA population. Although the presence of thoracoabdominal asynchrony is clinically obvious in all SMA type 1 and many type 2 patients, we were able to quantify it and found it present during both QS and AS. During AS, the normal relative hypotonia of the intercostal and accessory muscles place a burden on the diaphragm, which is ill-suited to meet this challenge in these patients.9,14,25

An interesting consideration is that both inspiratory and expiratory phases contribute to alterations of the thoracoabdominal synchrony due to muscular weakness. When intercostal muscle weakness predominates, as in these patients, there is paradoxical inward rib cage motion. When diaphragm weakness predominates, which did not occur in these patients, there is passive upward movement of the diaphragm into the chest and a paradoxical inward abdominal motion. In either case, there is failure to synchronize thoracic and diaphragmatic movements, so tidal volume is reduced because the inspiratory motion of the one compartment is opposed by the passively induced expiratory action of the other.9,11,14,25 In addition, when these mechanical limitations of the ventilatory pump are superimposed on the physiologic reduction of compensatory inspiratory mechanisms during sleep and an increased upper airway resistance, there can be serious impairment in a patient’s ability to maintain adequate respiration.25,26 This most probably explains the nocturnal periods of perspiration and flushing and frequent arousals that have been reported to be relieved by the use of nocturnal noninvasive ventilation.1,7

Thoracoabdominal asynchrony is usually present during obstructive sleep apneas/hypopneas but is not specific for them. It also results from intercostal muscle weakness. Respiratory inductive

<table>
<thead>
<tr>
<th>Variables</th>
<th>SMA Types 1 and 2</th>
<th>Controls</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Ph Angle QS</td>
<td>116.4 ± 30.7 (68.7–163.3)</td>
<td>13.2 ± 6.8 (5.3–85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ph Angle AS</td>
<td>135.7 ± 17.0 (110.3–164.0)</td>
<td>81.3 ± 35.1 (19.6–138.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ph RIB QS</td>
<td>67.4 ± 20.0 (31.9–90.2)</td>
<td>11.0 ± 9.2 (2.6–48.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ph RIB AS</td>
<td>80.6 ± 8.5 (64.4–91.9)</td>
<td>48.7 ± 22.6 (10.1–94.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ph REB QS</td>
<td>45.6 ± 17.5 (33.1–87.9)</td>
<td>15.7 ± 9.4 (4.9–39.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ph REB AS</td>
<td>59.2 ± 14.8 (39.8–86.0)</td>
<td>39.9 ± 14.4 (12.1–67.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SMA, spinal muscular atrophy; Ph Angle QS, phase angle during quiet sleep; Ph Angle AS, phase angle during active sleep; Ph RIB QS, phase relation during inspiration for a breath during quiet sleep; Ph RIB AS, phase relation during inspiration for a breath during active sleep; Ph REB QS, phase relation during expiration for a breath during quiet sleep; Ph REB AS, phase relation during expiration for a breath during active sleep.

Results are expressed as mean ± SD (range).
plethysmographic data cannot be used to distinguish between paradox caused by upper airway obstruction or inspiratory muscle weakness. Although the infants and children with SMA types 1 and 2 had severe paradox and significantly more sleep apneas and hypopneas than controls, in adults, an AHI of 1.9 would not be considered as an indication for treatment.20–22 Indeed, the primary problem of these patients is inspiratory muscle weakness. Nevertheless, collapse of the upper airway (obstructive apneas) may be a contributing factor. Thus, nocturnal high-span bilevel positive airway pressure is indicated for all infants and small children who manifest paradoxical breathing to ease paradox, rest labored inspiratory muscles, relieve diaphoresis and flushing, to eliminate or reverse pectus excavatum and promote more normal lung and chest wall growth,14 and relieve airway obstruction, if present.28 The extent, if any, that upper airway obstruction plays a role and the possible benefit, if any, of the expiratory positive airway pressure await to be determined by future studies.

Serial sleep studies permit the quantification of changes in breathing patterns, ongoing evaluation of the efficacy of nocturnal noninvasive ventilation, and can be performed for research and for outcome measures in medical treatment trials. They are not required to indicate the need for noninvasive ventilation, for which the clinical observation of paradoxical breathing in the growing lungs and chest walls of these small children suffices. Our data demonstrate that nocturnal nasal ventilation is indicated for infants, despite relatively low AHI values by adult sleep-disordered breathing standards. This is important because third-party payors often apply AHI standards established for the diagnosis of sleep-disordered breathing in adults as a rationale for refusing such vital treatment for children.

REFERENCES

Psychometric Properties and Developmental Differences in Children’s ADL Item Hierarchy: A Study of the WeeFIM® Instrument

ABSTRACT


Objective: To investigate the measurement properties of the WeeFIM® instrument and examine the developmental differences in motor item difficulty in a pediatric inpatient rehabilitation sample.

Design: Database approach, retrospective study, using 814 WeeFIM records from 12 facilities. Rasch rating scale analysis was used for all analyses. Data for the complete sample were used to evaluate the dimensionality and item fit of the WeeFIM instrument. Patients were then divided into three age groups, <3 yrs of age (toddlers), 3–7 yrs of age (preschoolers and kindergartners), and >7 yrs of age (school-age children), and their data were used to compare the order of motor items by level of difficulty within and across different age groups.

Results: Principal component analysis of the WeeFIM suggests distinct motor and cognitive scales. Within the motor scale, bowel and bladder items misfit, suggesting they measure a distinct aspect of function. The order of motor item difficulty, an indicator of construct validity, varies across age groups, suggesting that motor tasks present different challenges to children at different developmental stages: toileting is the most difficult, whereas locomotion is the easiest motor item for toddlers. For children >3 yrs of age, eating is easiest and stair climbing is most difficult, followed by tub transfer and bathing.

Conclusions: Similar to the adult FIM™ instrument, the WeeFIM instrument has two distinct dimensions. The motor items form a unidimensional construct with acceptable measurement properties. Developmental differences in motor task mastery among children with disabilities are assumed but rarely tested. As evidenced by the age-specific item hierarchies found in this study, developmental differences among children with disabilities mimic that of children without disabilities.

Key Words: Functional Assessment, Disability Evaluation, Rasch Analysis

Measurement of functional status in children with disabilities is inextricably tied to developmental attainment. However, the purpose of developmental testing is to systematically detect the rate and pattern of what is “different” from “typical,” comparing what is observed with what is expected as behavior within a particular age span. Early developmental psychologists such as Gesell and Piaget used observational methods to document children’s motor and mental development, and they later developed theories of neuromotor maturation and
cognitive development. Others built on these early theories, identified salient developmental skills, and operationalized them as developmental milestones.1,2

In the past decade, another type of measure has become available and widely used (i.e., pediatric functional assessments). These tests are used with children who have congenital or acquired disabilities. The test items tap developmentally appropriate “functional skills,” and the goal of functional assessment is to document the outcomes of rehabilitation services.3,4 Unlike developmental testing, functional assessments emphasize independence rather than typical performance. They are usually developed by clinical researchers to fulfill a pragmatic need (i.e., to measure treatment outcomes). Typically, these tests encompass several functional domains and can be administered by multiple team members, including physicians, nurses, and physical, occupational, and speech-language therapists. Often, a Likert scale is used to rate a child’s ability or the extent to which the child can perform everyday tasks, rather than assigning a pass or fail score.

The Pediatric Evaluation of Disabilities Inventory5 and the WeeFIM® instrument6 are two examples of pediatric functional assessments. Both contain items from different functional domains (self-care, mobility, and social/cognitive), and both use the average performance of age-equivalent children without disabilities as a standard of comparison.7 During the test development process, both instruments specifically targeted children without disabilities from 6 mos to 7.5 yrs of age, and both were administered to small samples of children with disabilities. For example, they were administered to children with cerebral palsy, who were born pre-term, or had other types of developmental disabilities. The items of the Pediatric Evaluation of Disabilities Inventory were developed to fit the Rasch model.3,5,8 This type of analysis simultaneously estimates item difficulty and personal ability while placing measures of each on a common scale and a dual continuum from “easy” to “difficult” and from “less able” to “more able.” It also uses fit statistics to indicate the extent to which the items measure a unidimensional construct.

In contrast, the WeeFIM instrument was adapted from the adult FIM™ instrument, and the developers used traditional testing methods to develop its scoring method (i.e., total score and developmental quotients). They examined its concurrent validity with other developmental assessments such as the Vineland Adaptive Behavior Scales,7 the Battelle Developmental Inventory,10 and the Clinical Linguistic Auditory Milestone Scale.1 When compared with norms for peers without disabilities, they found clinical populations invariably performed less independently.4,11–15

Liu et al.16 examined the correlations between WeeFIM scores (total score and motor and cognitive composite scores) and chronological age in 110 children without disabilities between the ages of 6 and 100 mos. They found a linear relationship between overall function and development (i.e., total scores and motor and cognitive composite scores increased progressively with age). However, when examining distributions of motor and cognitive item ratings at each age, the relationships between age and mastery of functional skills were not always linear. Specific motor tasks showed a gradual change from dependence to independence as age increased, whereas other tasks were mastered rapidly at an early age. That is, the rates of changes were not equal across items. In the case of locomotion and transfers, children were dependent as infants and toddlers but achieved independence around 3 yrs of age, and young children achieved independence in walking before eating, upper and lower body dressing, bathing, and grooming. In a subsequent article, Tsuji et al.17 used Rasch rating scale analysis (RSA) to examine WeeFIM motor and cognitive item difficulty. They concluded that walking, bed/chair transfer, stair climbing, and eating were the easiest items, whereas grooming and bathing were the hardest items for Japanese children without disabilities. The item difficulty pattern was similar across age groups (6–21 mos, 22–45 mos, 46–62 mos, 63–100 mos), except for toilet transfer, which was easier for older children (i.e., children 63–100 mos of age) than children <63 mos old.

To date, no published research has been reported using Rasch analyses on WeeFIM ratings for children with disabilities. Because WeeFIM items were not developed with Rasch RSA, it is important to use this methodology to examine its scale properties and provide evidence of its validity from a contemporary perspective.18 Questions like these have been investigated by researchers for its adult counterpart FIM instrument using Rasch RSA.19,20

The first objective of this study was, therefore, to examine the overall quality of the WeeFIM scale by assessing its dimensionality and linearity: that is, whether items of WeeFIM constitute a unidimensional interval-level scale or have separate motor and cognitive scales. A second objective was to compare the order of motor item difficulty across age groups to understand the developmental differences in children’s motor performance.

**METHOD**

**Data Sources**

Data for this study came from a national database that contains WeeFIM ratings of children who...
received inpatient rehabilitation services including physical, occupational, and speech therapies. The database is maintained by the Uniform Data System for Medical Rehabilitation as an activity of the UB Foundation. The study was approved by the Institutional Review Board on Human Subjects Protection at SUNY-Buffalo (UB) and the Feinberg School of Medicine at Northwestern University, and it was approved by institutional review board committees of the participating institutions where required.

**WeeFIM® Instrument**

The WeeFIM Instrument is an 18-item functional assessment for children. Clinicians rate the assistance needed while performing functional tasks. It has a seven-level rating scale with response categories ranging from “total dependence” to “complete independence.” The items are categorized in specific functional domains: self-care (eating, grooming, bathing, dressing upper-body, dressing lower-body, toileting), sphincter control (bowel management, bladder management), mobility (chair/bed transfer, toilet transfer, tub transfer), locomotion (crawling/walking/wheelchair, stair climbing), communication (comprehension, expression), and social cognition (social interaction, problem solving, memory). The item descriptions and rating definitions are similar to the adult FIM instrument, with slight modifications, so that they can be used for a pediatric population.

**Data Acquisition and Description**

WeeFIM subscribers from 1996 to 1998 were contacted about participating in the study. An invitation letter was sent along with a reply fax form. Follow-up phone calls were made by the first author to enroll the interested facilities and to coordinate data acquisition. Twelve facilities agreed to participate in the study and to submit therapy billing records. Although, in recent years, Uniform Data System offers training and credentialing to WeeFIM subscribers, we do not believe the raters received training during the study period.

**Sample Composition**

The sample was formed in three phases. First, we applied inclusion criteria to identify eligible cases; then, we applied criteria regarding the use of admission or discharge ratings; finally, we formed age groups.

More than 1200 records were received from the 12 facilities; 814 patient records fulfilled the study criteria: all WeeFIM items were rated, the length of stay was >4 days (i.e., beyond initial evaluation) and <150 days (i.e., 3 SD from the mean length of stay), and the period of hospital rehabilitation therapy billing records corresponded to the rehabilitation admission only. Duplicate records were excluded, as were cases that received no rehabilitation therapies and patients who were <12 mos at discharge with a rating of “1” (i.e., “dependent”) at admission and discharge for all FIM items.

Among the 814 patients who met the inclusion criteria, 55% had brain injuries (41% traumatic and 14% nontraumatic), 11% had cerebral palsy, and 7% had major multiple trauma. The remaining 27% had a variety of diagnoses with only a small proportion in each category. Demographic and clinical information about the sample is described elsewhere.

Data for the complete sample were used for the first analysis. As in previous research on the adult FIM instrument, both admission and discharge ratings were used in the current study. To ensure that within-subjects autocorrelation was not an issue, we examined correlations between admission and discharge item ratings. Only low to moderate correlations were observed (Spearman’s rho between 0.32 and 0.62). Next, we compared the estimated difficulty levels for the motor items with the following three samples: (a) admission and discharge records of the entire sample (1628 records), (b) a discharge-only sample (814 records), and (c) an independent sample containing an equal number of admission and discharge records randomly selected from the 814 cases. We found negligible differences in Rasch statistics or differences in the motor item hierarchy across analyses. Thus, we analyzed admission and discharge records together. Including both sets of ratings not only increased sample size but also increased heterogeneity of the sample because distributions of admission ratings tended to be negatively skewed and distributions of discharge ratings tended to be positively skewed. Readers can obtain these analyses from the first author.

Next, children were grouped by age into three groups. The cut-off ages used to form the age groups, ages 3 and 7 yrs, were selected because age 3 is when preschools typically admit children; it is also the age when early intervention services terminate and children with disabilities transfer to school-based services. At age 3, the majority of children are toilet trained, can walk, and can express themselves with words. At age 7, children enter elementary schools and are usually independent in self-care and mobility tasks; it is also the upper age limit of WeeFIM standardization. The sample was unevenly distributed by age group. Among the 814 children, 75 children were <3 yrs old at discharge (12–36 mos; i.e., toddlers), 183 children were between 3 and 7 yrs (3–84 mos; i.e., preschoolers and kindergartners), and 556 children were >7 yrs (≥85 mos; i.e., school-age children). The large discrepancies in sample sizes could have
a serious effect on the results of Rasch RSA by weighting the older group. To address sample size discrepancy among groups, we selected equal-sized samples from each age group by randomly selecting 75 sets of WeeFIM admission and discharge records from the preschooler-kindergartner and school-age sample and combining them with the 75 sets of toddler records. Then, we co-calibrated the 450 records from these 225 children. To ensure that the item scale structure was the same across groups, we used step measures (distances between the steps or ratings) derived from the co-calibration to anchor subsequent age-group analyses.

Data Analyses

We conducted three sets of analyses: (1) ratings of all 18 WeeFIM items and (2) motor items only, with and without the bowel and bladder items for the complete sample, and (3) motor ratings without bowel and bladder items, separately for each age group.

In all these analyses, we examined indicators of separation (indicating the extent to which the measure distinguished distinct levels [high, average, and low] of motor ability), fit of the individual items to the model and correlation with the total score, and a principal component analysis of the residual variation, all of which were produced by the Winsteps software.23 The specific criteria used to evaluate measure quality as recommended by Wright and Linacre24 and others25,26 were: person reliability estimates of ≥0.80 that distinguish three distinct functional status levels, fit statistics (in this case, infit mean square values) within a 0.60–1.40 range, item-measure correlations of >0.30, and secondary measures from principal components analyses that explained <10% of the residual variance.26 We also compared the empirical item difficulty order with clinical judgment. The estimated item difficulty values are reported in log-odd units, also called logits; in this scale, negative values represent easier tasks and positive values represent harder tasks.

Examining Overall Quality of the WeeFIM Scale

To determine if the WeeFIM items formed a unidimensional measure, we first conducted Rasch RSA using Winsteps23 Version 3.3 on all 18 WeeFIM items. Of particular interest were the results of the principal components analysis. We subsequently conducted Rasch RSA on the motor items only, with and without bowel and bladder items (13 and 11 items respectively). The fit statistics were of particular interest.

Examining Developmental Differences in Motor Item Difficulty

In the third set of analyses, we investigated how difficult motor tasks were for children at different developmental stages. We first examined distributions of WeeFIM item ratings categorized as needing more assistance (1–3) vs. less assistance (4–7) for each age group, and we then conducted separate RSAs. Of particular interest were the motor item hierarchies for each age group. In these initial RSAs, we specified locomotion modality (bi-pedal walking vs. walking with alternative modes) to understand better the level of difficulty in these different modes of locomotion in relation to other motor tasks. We compared item difficulty estimates derived from these (separate age groups) analyses between pairs of age groups using differential item functioning procedures.23 We compared the difference between the estimates of item difficulty in relation to twice their errors of measurement (comparable with computing a Student’s t statistic and using a critical value of 2.0) to identify common items (i.e., items that function essentially the same across age groups) and age-specific differential item functioning items (i.e., items whose age-adjusted values were significantly different across age groups). We recoded the original data to treat the age-specific differential item functioning items as separate items for each age group, dropped the locomotion modalities, and recalibrated the data using the common items as “anchors.”

RESULTS

Measurement Characteristics of the WeeFIM Instrument

The first set of analyses examined the overall measurement quality of the WeeFIM instrument. Two dimensions (i.e., motor and cognitive) were identified by the principal component analysis of the item residuals.

Subsequent RSAs of motor items showed that bowel and bladder items had the largest misfits (1.95 and 2.0). With all children included, the motor items without bowel and bladder yielded a person separation reliability of 3.88 (reliability, 0.94). The distribution of ratings was reasonable for this inpatient sample: 61% needed minimal or more assistance, 19% needed supervision or setup, 7% had modified independence, and 13% were totally independent. Table 1 presents the item hierarchy, fit statistics, and item-measure correlations for the entire sample.

Developmental Influence on Motor Performance

The distribution of item ratings varied across the three age groups, suggesting that developmen-
tal differences exist in motor task performance. For example, at discharge, 47% of toddlers required minimal to no assistance (WeeFIM ratings, 4–7) for locomotion and 40% of toddlers required minimal to no assistance for eating, whereas only 9% of toddlers required minimal to no assistance for grooming or upper body dressing, and 1% required minimal to no assistance for toileting or bathing. At discharge, about 65% of preschoolers and kindergartners could perform eating tasks with minimal to no assistance; nearly 50% could groom, put on shirts, and walk; and about 30% could bathe or self-clean after toileting with minimal to no assistance. Among school-age children, 89% could eat, 81% could walk, 84% could groom or put on shirts, and 74% could bathe or perform toileting tasks with minimal to no assistance.

When we calibrated motor items separately for each age group, the results supported our speculation that order of motor item difficulty varies across ages. These results are presented in Table 2, in which motor item measures are organized from highest (most difficult item) to the lowest (easiest item) for school-age children. Among toddlers, locomotion was the easiest item and toileting was the hardest. Among preschoolers and kindergartners, eating was the easiest and tub transfer and stair climbing were the hardest.

### Differential Item Functioning

The comparison of item difficulty estimates across age groups distinguished common from age-specific items. Plots of item-difficulty estimates between pairs of age groups are presented in Figures 1–4. Items that fall outside the control lines suggest age-specific items. Items that fall within the control lines suggest common items.

Significant differences were found between pairs of the difficulty estimates for all but four items. The difficulty levels for grooming, toileting, upper and lower body dressing, and walking for toddlers were substantially different from those for preschoolers and kindergartners and for school-age children (differences, >2 SE) but not between the latter two age groups. In contrast, the between-group differences for stair climbing were significant across all groups. The item difficulty estimates for eating, chair transfer, bathing, and tub transfer were not significantly different across age groups; thus, they were used as common items for the final calibration.

In the final calibration, the common items (eating, chair transfer, bathing, and tub transfer) were calibrated along with the age-specific items on the entire sample. This analysis produced a person separation of 3.98 (reliability, 0.94), suggesting that the items covered a wide range of motor task difficulties, adequately targeted the sample, and reliably separated the sample into multiple levels of motor abilities. Table 3 presents a summary of the calibration. Item hierarchy is presented in order of difficulty, with motor difficulty aligned on the same continuum, regardless of developmental stage. Only eating and stair climbing for school-age children had large fit statistics (1.65 and 1.80, respectively). These items are near the extremes of the continuum; it is not unusual for extreme items to misfit.

### DISCUSSION

Previous research has established the psychometric properties of the adult FIM using Rasch analysis. The objective of this study was to apply these procedures to the WeeFIM Instrument. Our analyses showed that the WeeFIM has distinct motor and cognitive domains, and bowel and bladder items misfit the motor domain. These findings are consistent with the research on the adult FIM. Heinemann et al. and Linacre et al. analyzed a large national data set and reported that the FIM is composed of two domains; they suggested that motor and cognitive items should be
treated as separate scales. Noting the bowel and bladder misfits of the researchers speculated that this might be because both physiologic (i.e., continence) and performance aspects are rated. When FIM motor items are calibrated separately, two other items tend to misfit: eating and stair climbing.19,20,22 Our results support this conclusion, although stair climbing only misfit for the school-age sample.

The item hierarchy for school-age children was almost identical to adults who received inpatient rehabilitation services.19,20,22 This suggests that the construct of motor function becomes stable by age 7. Both school-age children and adults require considerable assistance in self-care and mobility in an inpatient setting; ambulation, stair climbing, and transfers are the most difficult tasks to perform independently. In contrast, locomotion and stair climbing are easier for younger children. This finding may be explained by differences in body stature between younger and older children, or it may reflect primary learning by younger children rather than relearning motor tasks by older children and adults. The fact that locomotion is easier than eating for toddlers may also reflect safety concerns: choking may be life threatening, whereas falling and stumbling occur often without severe consequences.

Our second objective was to investigate developmental differences of children receiving rehabilitation services. Two recent studies used Rasch methods to examine the construct validity and developmental sensitivity of the WeeFIM instrument in a sample of children without disabilities.16,17 Our intent was not to change the structure or the scoring of the instrument. Rather, we were interested in knowing if clinical data yield reliable measures taking into account children’s ages. To that end, we conducted two analyses on the motor items, first separately by age group and then combined by age group with age-specific items. The results from both analyses showed that the WeeFIM instrument had adequate scale properties. Although recoding does not substantially improve its psychometric quality, the order of item difficulty using age-specific items is consistent with clinical experience. Lack of dramatic changes in the results is reassuring because it suggests that the WeeFIM instrument with its current scoring is ade-

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### TABLE 2 Item measures (in logits) for each age group measured on the same metric

<table>
<thead>
<tr>
<th>Item</th>
<th>Age 1</th>
<th>Age 2</th>
<th>Age 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stair climbing</td>
<td>-0.14</td>
<td>0.92</td>
<td>1.41</td>
</tr>
<tr>
<td>Tub transfer</td>
<td>0.32</td>
<td>0.67</td>
<td>0.58</td>
</tr>
<tr>
<td>Bathing</td>
<td>0.39</td>
<td>0.43</td>
<td>0.37</td>
</tr>
<tr>
<td>Bipedal walking</td>
<td>-1.47</td>
<td>-0.09</td>
<td>0.28</td>
</tr>
<tr>
<td>Lower body dressing</td>
<td>0.53</td>
<td>0.17</td>
<td>0.17</td>
</tr>
<tr>
<td>Toileting</td>
<td>2.01</td>
<td>0.43</td>
<td>0.11</td>
</tr>
<tr>
<td>Toilet transfer</td>
<td>0.55</td>
<td>0.41</td>
<td>0.00</td>
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<td>-0.38</td>
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<tr>
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<tr>
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<td>0.76</td>
<td>-0.26</td>
<td>-0.60</td>
</tr>
<tr>
<td>Eating</td>
<td>-1.24</td>
<td>-1.17</td>
<td>-1.15</td>
</tr>
</tbody>
</table>

Age 1, toddlers (12–36 mos); Age 2, preschoolers and kindergartners (37–84 mos); Age 3, school-age children (85–216 mos).

---

**FIGURE 1** Scatter plot of items between age-group 1 and age-group 2.
Clinicians tacitly recognize the developmental patterns in children by taking into consideration children's age and developmental level. Our study also demonstrated that motor tasks present different challenges to children at different ages. Toileting was most difficult for toddlers but was relatively easier for older children; walking was the easiest for toddlers but was relatively harder for older children; grooming was difficult for toddlers but was easier for older children. Although parents and clinicians tacitly recognize that less assistance is needed for locomotion than self-care by younger children, this phenomenon is studied infrequently. Our study, along with a study by Tsuji et al., supports parents' and clinicians' impressions about children with and without disabilities. The orders of motor items differ between our study and that of Tsuji et al. For example, our rehabilitation sample found lower body dressing more difficult than upper body dressing in all three age groups, whereas Tsuji et al. found equivalent difficulty in every age group in their sample of children without disabilities. These differences may be explained by the composition of the samples: our sample covers...
a wider age span and received inpatient rehabilitation services. Sociocultural (or environmental/architectural) differences may also explain why certain tasks are more difficult for Japanese children than American children (e.g., eating with chopsticks or toilet transfer).

This study is not without limitations. First, the data came from 12 self-selected facilities, which may have created a selection bias. Moreover, motor task mastery is not only influenced by age and development, it may also reflect the nature of the impairment. A large proportion of this sample sustained brain injuries; the proportion of children with other impairments was much smaller, which precluded us from examining the effect of impairment on motor task performance. Third, it is not clear if the clinicians completed WeeFIM training or credentialing. Finally, changes have been made in the WeeFIM instrument in recent versions. It is not clear if we would reach the same conclusions with newer ratings.

CONCLUSION

Functional outcome measures should be valid, reliable, and practical. The WeeFIM Instrument, with only 18 items and a seven-level ordinal rating scheme, is easy to use and practical. Adding to the previous reliability and validity evidence, this study

<table>
<thead>
<tr>
<th>Item</th>
<th>Item Measure</th>
<th>Error</th>
<th>Infit</th>
<th>Score</th>
<th>Correlation</th>
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<tbody>
<tr>
<td>Toileting (1)</td>
<td>1.98</td>
<td>0.27</td>
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<td>0.06</td>
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<td>Toilet (2,3)</td>
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<td>0.99</td>
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<td>Lower body dressing (2,3)</td>
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<tr>
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<td>0.90</td>
<td>0.76</td>
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<tr>
<td>Stair (1)</td>
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<td>0.11</td>
<td>0.93</td>
<td>0.88</td>
<td></td>
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</tbody>
</table>

Tub transfer, bathing, chair transfer, and eating were used as common linking items, each with an "A" to denote "anchor." Age-specific items are indicated by the number(s) following the item: 1, 12–36 mos; 2, 37–84 mos; 3, 85–216 mos; 1 and 2, <7 yrs; 2 and 3, >3 yrs.

FIGURE 4 Comparison of item hierarchies across age groups with item anchoring.
provides empirical support to the WeeFIM® Instrument's measurement properties and construct validity. Similar to the adult FIM instrument, it consists of distinct motor and cognitive dimensions; the bowel and bladder items, although important aspects of function, measure separate aspects of daily activities. This study demonstrated developmental differences in motor task difficulty; these differences may be related to children's ability, task complexity, and the sociocultural context. Finally, the results suggest that clinicians attend to the differences in WeeFIM item definitions and are able to use it accurately and effectively.

REFERENCES

Anatomic Localization of Motor Points in Gastrocnemius and Soleus Muscles

ABSTRACT

Objective: To identify the range of the terminal motor points of the triceps surae muscles in relation to bony landmarks.

Design: Eight limbs of four male cadavers were anatomically dissected. The range of terminal motor points from the tibial nerve to each triceps surae muscle was identified related to the bony landmarks. Bony landmarks were medial and lateral epicondyles of the femur and medial and lateral malleoli of the tibia. The length of the lower leg was defined as the distance from the intercondylar line of the femur to the intermalleolar line of the tibia. The locations of the motor points were expressed as the percentage of the length of the lower leg.

Results: The motor points of the medial gastrocnemius, lateral gastrocnemius, and soleus muscles were diffusely distributed along the muscle longitudinal bulk. The highest motor points of the medial gastrocnemius, lateral gastrocnemius, and soleus were located in 9.6% ± 3.5%, 12.0% ± 3.4%, and 20.5% ± 3.9%, respectively, of the length of the lower leg. The lowest motor points were located in 37.5% ± 5.5%, 37.9% ± 2.3%, and 46.7% ± 3.6%, respectively, of the length of the lower leg.

Conclusions: The present study defined the longitudinal distribution pattern of terminal motor points in the triceps surae muscles. This concept can be helpful for further studies evaluating the effectiveness of the botulinum toxin injection method.

Key Words: Triceps Surae Muscle, Motor Point, Botulinum Toxin, Injection
For chemodenervation with botulinum toxin, with the precise localization of the motor endplate, maximum paralysis effects can be achieved safely. An electromyographic guidebook is generally used as a reference for botulinum injection sites. However, there has been some inconsistency in the botulinum injection site. Cosgrove described four points for the botulinum injection of the gastrocnemius. The motor point is defined as the point over a muscle where a contraction of a muscle may be elicited by a minimal-intensity, short-duration electric stimulus. The motor point corresponds anatomically to the location of the terminal portion of the motor nerve fibers (endplate zone). Previous anatomic studies defined the motor point as the location where the motor branch entered the muscle belly. However, the motor endplate is not located where the motor branch entered the muscle belly.

We investigated the anatomic distribution of individual motor points to the triceps surae musculature as deep as we could dissect along the motor nerve branches into the muscle belly. Localization of motor points by this method may facilitate the efficacy and efficiency of botulinum toxin injections.

METHODS

Eight limbs from four male cadavers were dissected for the study. All limbs were able to be positioned to neutral anatomic alignment and did not have evidence of posterior thigh or calf trauma.

Each cadaver was placed prone, with the hip and knee extended in the anatomic position. The posterior tibial nerve was exposed, and the location of motor points were recorded. All measurements were done with one investigator. A motor point was defined as the location where the terminal motor branch entered the muscle belly, rather than the location where the motor branch entered the muscle belly. The dissections were made as deep as we could go.

For each limb, four bony landmarks were identified as reference points: the medial and lateral epicondyles of the femur and the medial and lateral malleoli of the tibia. The lower leg length was defined as the distance from the intercondylar line to the intermalleolar line. The shortest distances between the intercondylar line and the highest and lowest motor points to the medial gastrocnemius, lateral gastrocnemius, and soleus muscles were measured and recorded as a percentage of the total lower leg length. The position relative to the leg width was not measured because the dissection procedure to the terminal motor branches distorted the width relationship of this position.

RESULTS

Eight limbs from four male cadavers were dissected for the study. The mean lower leg length was 37.2 ± 1.4 cm. About 6 to 12 motor points for each of the triceps surae were identified in all limbs. The motor branches of each muscle branched out several times like a tree branches out (Fig. 1). The terminal motor points of the medial gastrocnemius, lateral gastrocnemius, and soleus muscles were diffusely distributed along the muscle longitudinal bulk. The range of motor points of the medial gastrocnemius was from 9.6% ± 3.5% to 37.5% ± 5.5% of the lower leg length distal to the intercondylar line. In the lateral gastrocnemius muscle, the highest was at 12.0% ± 3.4% and the lowest was at 37.9% ± 2.3%. In the soleus muscle, the highest was at 20.5% ± 3.9% and the lowest was at 46.7% ± 3.6% (Table 1).

DISCUSSION

The motor points of medial gastrocnemius, lateral gastrocnemius, and soleus muscles are diffusely distributed along the muscle longitudinal bulk. Defining the motor point as the location where the motor branch entered the muscle belly, 90% of the limbs had one or two motor points in the medial and lateral gastrocnemius and 100% of the limbs had one or two motor points in the soleus muscle. However, according to the anatomic correspondence of the motor points (the end plate area), we dissected the motor branches into muscle bulks as deep as we could. Just one or two motor branches near the entering point branched out several times along the muscle longitudinal bulk. The motor branches were distributed across the whole muscle bulk, except the tendon area.

The position of motor terminals is usually found in a narrow band across the central zone of the muscle fiber. Each terminal branch attaches to a single muscle fiber at a specific region approximately at its midpoint, referred to as the endplate or neuromuscular junction. Classically, we could think the motor points are near the middle of the muscle bulk. However, we have to consider the muscle morphology. All of the muscles do not have the fusiform morphology. The morphologic type of the gastrocnemius muscle is the bipennate type, and the morphological type of the soleus muscle is the unipennate type, in which fascicles pass obliquely between deep and superficial aponeuroses. Usually, muscle fibers traverse only part...
of a muscle, ending in tendinous extensions or intersections within it.\textsuperscript{8}

Once we consider the muscle morphology type, we can imagine that the motor points will be longitudinal along the muscle bulk rather than just in the middle of the muscle bulk.

For the botulinum toxin injection for a specific muscle, we have to consider the specific morphology and know the location of motor points of the muscle. Shaari and Sanders\textsuperscript{1} stressed the injections near the endplate zone and multiple injections in one muscle for botulinum toxin. It may be better to inject botulinum toxin into several terminal motor points rather than just into a middle motor point of the muscle bulk. However, further detailed clinical study is needed to reveal the effectiveness of the multiple injection method.

There were no significant differences noted between sex or left vs. right side in terms of the number and the location of motor points\textsuperscript{7} in a study of 36 limbs. We thought a study with eight limbs would be fine to investigate the anatomic distribution. One limitation of this study was that horizontal measurement was not done because horizontal dimension was disorganized during dissection, although the

<table>
<thead>
<tr>
<th>TABLE 1. Mean distance from intercondylar line to motor points originating from the medial gastrocnemius, lateral gastrocnemius and soleus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>The highest motor point</td>
</tr>
<tr>
<td>The lowest motor point</td>
</tr>
</tbody>
</table>

\textbf{FIGURE 1} Motor points were dissected as far as possible at the medial gastrocnemius (top left), the lateral gastrocnemius (top right), and the soleus (bottom left). Nerve branches detached from the muscles look like a tree branching out (bottom right).
center can be the appropriate motor point inferred from morphologic consideration.

REFERENCES
Cardiovascular Adaptations to Exercise Training After Uncomplicated Acute Myocardial Infarction

ABSTRACT


Objective: This study examined the cardiovascular adaptations of an exercise training program and evaluated the role of peripheral vasodilator capacity in contributing to these adaptations after myocardial infarction.

Design: A total of 44 consecutive patients with uncomplicated myocardial infarction underwent 3 wks of exercise training. Controls (n = 12) with comparable myocardial infarction were selected from our database and were restricted to a program with minimal activity. All patients performed cardiopulmonary exercise testing with hemodynamic measurements. Forearm and calf reactive hyperemic flow were measured by venous occlusive plethysmography as indices of peripheral vasodilator capacity.

Results: Despite no change in arteriovenous oxygen difference at peak exercise after training, training resulted in significant increases in oxygen consumption, cardiac output, and stroke volume and a significant decrease in systemic vascular resistance at peak exercise (overall, P < 0.05). Calf reactive hyperemic flow increased significantly after training (P < 0.001), but forearm reactive hyperemic flow did not. Furthermore, increase in calf reactive hyperemic flow after training had a positive correlation with increases in peak cardiac output, stroke volume, and oxygen consumption after training and an inverse correlation with peak systemic vascular resistance.

Conclusions: Exercise training improved exercise tolerance by improving hemodynamic responses to exercise after myocardial infarction. This improved exercise performance was linked to a training-induced increase in calf vasodilator capacity.

Key Words: Exercise Training, Reactive Hyperemia, Myocardial Infarction, Cardiopulmonary Exercise Test
Exercise intolerance is one of the most common problems experienced by patients with cardiac disease.1–5 These patients exhibit reductions not only in central circulation but also in peripheral circulation during exercise because the increase in peripheral vascular conductance is tightly linked to the cardiac output.3–5 Physical training produces a broad range of central and peripheral adaptations and an increase in exercise tolerance in subjects who have experienced heart failure7–9 and in normal subjects.10–14 Previous studies indicated that exercise training after acute myocardial infarction (MI) also resulted in an increase in exercise tolerance accompanied with that in cardiac output.10,15 Recent randomized studies16–18 observed that exercise training soon after anterior wall MI did not cause further deterioration of left ventricular function but improved peak oxygen consumption. These observations indicate that carefully selected patients with MI can be safely entered into exercise training programs and achieve an increase in exercise performance. In contrast, several investigators12,14,19 demonstrated that exercise training enhances maximal limb vasodilator capacity as a peripheral adaptation, which may facilitate central hemodynamic performance. However, the relative contributions of central and peripheral mechanisms to these adaptations have not been completely defined.

Accordingly, the present study was designed to investigate the cardiovascular adaptations of a supervised, short-term, in-hospital exercise training program and to evaluate the role of peripheral vasodilator capacity in contributing to these adaptations in clinically stable patients 2–3 wks after acute MI.

**METHODS**

**Patient Population**

A controlled study was a predefined choice to minimize, in a limited number of patients, any possible difference in the level of ventricular dysfunction between trained and untrained postinfarction patients. The subjects were 44 consecutive postinfarction patients who underwent emergency coronary arteriography in the acute phase for the purpose of revascularization and revealed single-vessel disease. The subjects agreed to participate in the study. All patients included in this study had had their first acute Q-wave MI 2–3 wks before the study, and none had postinfarction angina, critical arrhythmia, or uncontrolled congestive heart failure in the acute phase of the disease. The patients participated in a 2- to 3-wk in-hospital exercise program immediately after the acute stage of their infarct. A total of 18 were in New York Heart Association functional class I, 19 were functional class II, and seven were functional class III. Before entry into the study, each patient underwent complete physical examination. All the patients in the exercise program were free of exercise-induced myocardial ischemia, ventricular tachyarrhythmia (higher than Lown classification IVa), atrial fibrillation, flutter, significant valvular heart disease by Doppler echocardiography, uncontrolled hypertension, chronic obstructive lung disease, peripheral vascular disease, severe exercise intolerance (peak oxygen consumption [VO2] of <12 ml/min/kg), pulmonary rales, or orthopedic conditions precluding regular exercise. A total of 12 patients selected from those enrolled in the acute MI database of Kansai Medical University (n = 140) were retrospectively matched with the postinfarction patients. The following clinical and hemodynamic baseline matching criteria were used: age ± 3 yrs, same New York Heart Association class, left ventricular ejection fraction of ≥30%, cardiac index of ≥0.3 liters/min/m², pulmonary arterial occlusion pressure of ≤3 mm Hg, peak VO2 of ≥3 ml/min/kg. Cardiac medications were not altered throughout the study period. The risks of the study were fully explained, and informed consent was obtained from each patient before the study.

**Study Protocol**

All studies were performed according to a research protocol approved by the Kansai Medical University Ethics Committee. Before entrance into the study, patients were required to be in clinically stable conditions. The functional evaluations both at entry (2–3 wks after the onset of MI) and 3 wks later included Doppler and two-dimensional echocardiographic study, limb blood flow measurements, and symptom-limited cardiopulmonary exercise testing with measurements of expired gas analysis and central hemodynamic responses. All medications were discontinued for ≥48 hrs before the baseline and the final evaluations.

**Exercise Testing**

Patients were studied in the upright position at rest and during bicycle ergometric exercise. Upright bicycle exercise was performed to familiarize the patients with a bicycle ergometer (Cat-eye Ergociser EC-1200, Osaka, Japan) 2 or 3 days before the study. On the day of the study, a Swan-Ganz catheter was inserted through the internal jugular vein and advanced to the pulmonary artery. An arterial catheter was inserted in the radial artery. After 30 mins of resting, bicycle exercise testing was performed with expired gas analysis. The electrocardiogram and pulmonary and systemic arterial pressures were monitored continuously. Exercise began at a work load of 25 W with the pedal
speed maintained at 60 rpm and increased by 25 W every 3 mins until a symptom-limited maximum load.

**Expired Gas Analysis**

Expired gases were analyzed with an Oxycon-4 (Mijnhardt Company, Bunnik, Holland). Instruments were calibrated at the beginning of each study and before all measurements. From these data, VO₂ and carbon dioxide production were measured at rest on the bicycle and continuously during exercise. Averaged measurements during the last 30 secs of each exercise stage were used for analysis.

**Hemodynamic Measurements**

Right atrial, pulmonary arterial, and systemic arterial blood pressures were recorded continuously, and pulmonary arterial occlusion pressure was recorded intermittently at rest and at each exercise stage with the DS-3000 system (Fukuda Denshi, Tokyo, Japan). Blood samples were drawn simultaneously from the radial and pulmonary artery at rest and within the last 30 secs of each exercise stage. The blood samples were used for the immediate measurements of pH, partial pressure of oxygen, partial pressure of carbon dioxide (ABL2, Radiometer Company, Copenhagen, Denmark), oxygen saturation, and hemoglobin concentration (OSM2, Radiometer Company, Copenhagen, Denmark). From these data, cardiac output was determined by the Fick principle for oxygen consumption. Mean arterial blood pressure was calculated as the diastolic pressure plus one third of the pulse pressure. Stroke volume was obtained by dividing cardiac output by heart rate. Systemic vascular resistance was calculated using the standard formula.

**Radionuclide Angiography**

Radionuclide angiography was performed at rest by use of a multcrystal gamma camera (Baird Atomic System 77) in the anterior projection 2 or 3 days before the study. Left ventricular ejection fraction was determined from the background-corrected representative cardiac cycle as follows: (end-diastolic counts − end-systolic counts)/end-diastolic counts × 100 (%). Regional wall motion was assessed semiquantitatively by an experienced echocardiographer who had no knowledge of the clinical information. Wall motion at rest in each of 16 segments was scored 1 through 5. The wall motion score index was determined at rest as the sum of the segmental scores divided by the number of visualized segments as previously described.²⁰

**Limb Blood Flow Measurements**

Before exercise testing, limb blood flow was measured in the forearm and the calf with the subject in supine position. Limb blood flows were measured at rest and during reactive hyperemia using mercury-in-silastic strain gauges placed around the upper forearm or the upper calf and connected to an electronically calibrated plethysmograph (SPG16, MedaSonics, California). Limb reactive hyperemic flows were measured by inflating cuffs placed around the upper arm or the upper thigh to 40 mm Hg greater than the systolic pressure to occlude arterial flow for 5 mins. To avoid the variation of limb blood flow values at various time points after the release of arterial occlusion, we measured limb blood flows initially at 5 and 15 secs after release of arterial occlusion and averaged these two flow measurements to estimate limb reactive hyperemic flow as previously described.⁴–⁶

**Training Program**

After the baseline studies, patients were enrolled in the 3-wk in-hospital exercise program. Patients exercised for 1 hr five times each week at a heart rate corresponding to 70% of the peak VO₂ determined from the baseline exercise testing. Exercise consisted of supervised ergometer cycling (30 mins) and walking (30 mins). Training was monitored daily by heart rate and blood pressure recordings before and after each training session.

Patients in the control group avoided any strenuous physical activity during their hospital stay. They were restricted to daily walking in the hospital.

**Statistical Analysis**

For statistical evaluation, nonparametric tests (Mann-Whitney U test, Wilcoxon’s signed-rank test) were used to avoid the potential errors from nonnormal distribution of the data. Linear regression analysis was used to determine the relation between baseline calf reactive hyperemic flow and hemodynamic variables and the percentage of change in calf reactive hyperemic flow with training and percentage of change of hemodynamic variables. Probability values of <0.05 were considered statistically significant. All data are presented as mean ± standard deviation.
RESULTS

All patients in the training and control groups completed the study without cardiac events and change in drug therapy. There were no adverse training-related side effects reported by the subjects other than mild fatigue after exercise. Clinical and hemodynamic characteristics of the 44 trained patients and of the 12 control patients at baseline are reported in Table 1. The two groups were almost identical in terms of level of ventricular dysfunction after MI. Echocardiographic variables are shown in Table 2. There were no intergroup differences in these variables in the baseline study. Furthermore, there were no significant changes in these variables after 3 wks in either group.

Effects of Training on Exercise Tolerance and Exercise Hemodynamics

In all patients, bicycle exercise was limited by exercising muscle fatigue and not by dyspnea. No patient had chest pain or significant ST changes suggestive of myocardial ischemia during exercise. The peak exercise respiratory gas exchange ratios indicated a comparable maximal or near-maximal exercise effort in both groups. Peak VO2, peak exercise workload, and exercise time of the baseline study were similar in the two groups, and the variables increased significantly after 3 wks in the training group but not in the control group (Table 3). There were no significant differences in any of the resting hemodynamic variables between the two groups in the baseline study. Furthermore, both training and control groups showed no significant changes in these resting variables after 3 wks. In the training group, cardiac output and stroke volume at peak exercise increased significantly after training. Systemic vascular resistance at peak exercise decreased significantly after training. Heart rate, systolic arterial pressure, pulmonary arterial occlusion pressure, and arteriovenous oxygen difference did not change significantly at peak exercise after training (Table 3). The control group showed no significant changes in any of these variables at peak exercise from the baseline to 3 wks into the study.

TABLE 1 Baseline clinical and hemodynamic characteristics

<table>
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<th>Control Group (n=12)</th>
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<td>mean ± SD</td>
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<td>Age, yrs</td>
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<td>CI, liters/min/m²</td>
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<tr>
<td>PAOP, mm Hg</td>
<td>6.3 ± 1.9</td>
<td>6.1 ± 1.3</td>
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<tr>
<td>Peak VO2</td>
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<td>21.5 ± 3.5</td>
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<tr>
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<td>Men</td>
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<td>Inferior</td>
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<tr>
<td>Antiplatelet agents</td>
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</table>

NYHA, New York Heart Association on Functional Class; LVEF, left ventricular ejection fraction; CI, cardiac index; PAOP, pulmonary arterial occlusion pressure; VO2, oxygen consumption; MI, myocardial infarction; ACE, angiotensin converting enzyme.

Relationship Between Initial Limb Reactive Hyperemic Flow and Exercise Tolerance and Exercise Hemodynamics

At the baseline evaluation, forearm and calf reactive hyperemic flows did not correlate with any of the resting hemodynamic measurements. However, calf reactive hyperemic flow correlated positively with VO2 (r = 0.62, P < 0.001), cardiac output (r = 0.50, P < 0.001), and stroke volume (r = 0.46, P < 0.01) and correlated inversely with systemic vascular resistance (r = −0.48, P < 0.001) at peak exercise (Fig. 1), whereas forearm reactive hyperemic flow did not.

Effects of Training on Reactive Hyperemic Flow

There was no significant difference in the baseline reactive hyperemic flow between the two groups. There was no significant difference in reactive hyperemic flow in the forearm (26.6 ± 7.9 vs. 26.5 ± 8.0 ml/min/100 ml tissue) and the calf (18.0 ± 4.3 vs. 18.4 ± 4.4 ml/min/100 ml tissue) after 3 wks in the control group. However, training resulted in a significant increase in calf reactive hyperemic flow (17.8 ± 5.8 vs. 20.3 ± 6.3 ml/min/100 ml tissue, P < 0.001) but not in the forearm (25.6 ± 9.0 vs. 26.7 ± 8.2 ml/min/100 ml tissue) (Fig. 2). Percentage of increase in calf reactive hyperemic flow after training had a positive correlation with percentage of increase in peak VO2 (r = 0.60, P < 0.001), peak cardiac output (r = 0.51, P < 0.001), and peak stroke volume (r = 0.55, P < 0.001) and had an inverse correlation with percentage reduction in peak systemic vascular resistance (r = −0.40, P < 0.01) (Fig. 3).

DISCUSSION

Two important findings emerged by short-term exercise training early after the onset of acute

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Exercise Training After Myocardial Infarction

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MI. First, exercise tolerance, hemodynamic responses to exercise, and peripheral vasodilator capacity of the trained calf muscle improved. Second, the improvement of hemodynamic responses to exercise and exercise tolerance after exercise training was strongly related to the training-induced increase in calf vasodilator capacity. These results suggest that the effects of exercise training after acute MI were related to changes in the peripheral vasodilator capacity.

Previous studies1–6 observed that distribution of skeletal muscle perfusion during exercise is an important factor determining exercise capacity and is markedly impaired in patients with cardiac disease. Wilson et al.2 and Sullivan et al.3 indicated that increments in cardiac output during exercise are directed primarily to working skeletal muscle. A recent study from our laboratory5 demonstrated that intrinsic calf reactive hyperemic flow as maximal peripheral vasodilator capacity was also an important determinant of skeletal muscle perfusion during exercise in patients with left ventricular dysfunction. In the present study, baseline calf reactive hyperemic flow correlated with peak cardiac output and peak VO2. These observations suggest that skeletal muscle perfusion during exercise...
seems to be determined by a functional interaction of exercise cardiac output response and limb vasodilator capacity. Moreover, the maximal peripheral vasodilator capacity seemed to be linked to central hemodynamic response to peak exercise and reflected exercise tolerance.

Exercise training has been reported to increase exercise tolerance, manifest as increased peak VO\textsubscript{2}, in cardiac patients and in normal subjects.\textsuperscript{7,10–12,15} This increase in peak VO\textsubscript{2} after training is attributed to the increase in cardiac output or arteriovenous oxygen difference.\textsuperscript{11} Sullivan et al.\textsuperscript{7} demonstrated that long-term exercise training resulted in increases in peak VO\textsubscript{2}, cardiac output, arteriovenous oxygen difference, and leg blood flow at peak exercise. The training-induced increase in peak cardiac output accompanied with increased leg blood flow rather than that in peripheral oxygen extraction plays an important role in the improvement of exercise tolerance after training. Because of the short-term training period, our patients did not demonstrate improvement of arteriovenous oxygen difference, but peak stroke volume, cardiac output, and VO\textsubscript{2} increased significantly and systemic vascular resistance decreased significantly after training. These findings indicated that central hemodynamic adaptations, but not peripheral oxygen extraction, can contribute to improved exercise tolerance after training. Furthermore, our results are consistent with previous observations\textsuperscript{12,14,19} that exercise training enhances reactive hyperemic flow only in the trained limb. We extend these observations by demonstrating that a training-induced increase in calf reactive hyperemic flow had positive correlation with training-induced increase in cardiac output, stroke volume, and peak VO\textsubscript{2}. These findings provide the first evidence that the peripheral vasodilator adaptation to training after acute MI is tightly linked to central hemodynamic adaptations to training and therefore contributes to the improvement in exercise tolerance.

Our data did not define the primary factor responsible for the increase in calf reactive hyperemic response after training. One possible explanation is the improvement in endothelial function. Vascular abnormalities of the lower limbs may be in part secondary to a chronic reduction in limb blood flow that in turn may depress vascular endothelium function, which involves both resistance and conductance vessels.\textsuperscript{26} Currently, limb reactive hyperemic response has been reported to represent maximal vasodilator capacity\textsuperscript{1} and to be an index of endothelial vasodilation.\textsuperscript{27} Other studies\textsuperscript{28,29} have indicated that physical training restored peripheral vascular resistance and endothelial function of the lower limb skeletal muscle microvasculature in patients with heart failure. Although we did not directly measure endothelial function before and after training, this probably occurred because we observed improvements in exercise systemic vascular resistance and reactive hyperemic flow after training and a significant relation of these variables. Furthermore, it is possible that the changes seen in vascular fluid retention and autonomic control of the circulation during early recovery phase of MI may affect those seen in calf vasomotor tone and vasodilator capacity.

Our data did not define the primary factor responsible for the increase in calf reactive hyperemic response after training. One possible explanation is the improvement in physical deconditioning. Sinoway\textsuperscript{19} observed that reactive hyperemic response was impaired with deconditioning and enhanced with training stimuli. In addition, previous studies reported that physical training regimens improved muscle and vascular abnormalities by increasing skeletal muscle bulk,\textsuperscript{8,21} capillary density,\textsuperscript{13,22} and oxidative metabolic capacity,\textsuperscript{23–25} and thereby increased the limb vasodilator capacity. In patients with MI, a rapid deconditioning due to bed rest during acute phase of the disease is probably observed, which could be improved with exercise rehabilitation. Another possible explanation is the improvement in endothelial function.

Figure 2: Effect of training on reactive hyperemic flow. Training resulted in a marked increase in reactive hyperemic flow in the calf but not in the forearm. NS, not significant.

Figure 3: Relations of percentage of change ($\Delta$) in calf reactive hyperemic flow after training to change in peak exercise oxygen consumption ($\Delta$Peak VO\textsubscript{2}), cardiac output ($\Delta$Peak CO), stroke volume ($\Delta$Peak SV), and systemic vascular resistance ($\Delta$Peak SVR) after training.
The clinical implication of this study is that noninvasive measurement of calf reactive hyperemic flow after training can lead to improvements in clinical care such as identification of good responders to cardiac rehabilitation or application of resistance training in patients after acute MI. A potential limitation of our study should be addressed. First, the present study was not designed as a randomized, controlled trial; the patients assigned to the control group led their hospital life avoiding any strenuous physical activity during hospitalization. The well established various benefits of a postinfarct exercise training program could not ethically allow us to design the study in such a fashion. Although the training group and control group were well matched for all of the baseline variables and none of the variables changed significantly in the control group after 3 wks, this potential selection bias should be noted. The small number of patients in this control group should be recognized as one limitation of the study. Second, in this study, the improvement in peak reactive hyperemic flow was a local effect. There is evidence that regulation of peripheral vascular function differs in the upper and lower limbs,

perhaps because of the smaller muscle mass in the arms or because of evolutionary adaptations to upright posture in the human race. It is possible that this difference in regulation of peripheral vascular function in the upper and lower limbs also contributed to the disparity between forearm and calf reactive hyperemic blood flow.

In conclusion, there are improvements in cardiac and exercise performance and peripheral vasodilator capacity with short-term training, but the majority of the training effect is likely to be seen in the periphery after uncomplicated acute MI.

REFERENCES


Objectives:
On completion of this article, the reader should be able to (1) recognize that negative myoglobin staining in hemiplegic muscle of acute stroke patients occurs in poststroke hemiplegia, (2) understand potential mechanisms of negative myoglobin staining after stroke, and (3) explain how negative myoglobin staining correlates with functional recovery.

Level: Advanced.

Accreditation: The Association of Academic Physiatrists is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians. The Association of Academic Physiatrists designates this continuing medical education activity for a maximum of 1.5 credit hours in Category 1 of Physician’s Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he or she actually spent in the education activity.

Disclosure: Disclosure statements have been obtained regarding the authors’ relationships with financial supporters of this activity. There is no apparent conflict of interests related to the context of participation of the authors of this article.

Negative Myoglobin Staining in Hemiplegic Muscle of Acute Stroke Patients Predicts Functional Recovery

ABSTRACT

Objective: There is little information on skeletal muscle changes in patients with acute stroke, despite the repeated observation that levels of serum creatine kinase (CK) and myoglobin (Mb) increase in the initial phase of strokes. It is also not clearly known whether the CK and Mb are derived from skeletal muscle or myocardium.

Design: Biceps muscle biopsies of the hemiplegic side were obtained from 157 ischemic stroke patients on the second day of stroke onset and were examined for immunoreactivity to Mb, and measurements of Mb, total CK, troponin T, epinephrine, and norepinephrine were made on the same day. The degree of disability of patients was assessed at 7 days and at 12 mos after stroke using the Barthel index and the Scandinavian Stroke Scale. The control group consisted of 159 healthy volunteers matched in age and sex.

Results: Lack of Mb immunoreactivity was observed in 109 patients. The prevalence of negatively stained muscle fibers ranged from 0.0% to 22.0%, with a mean of 5.9% ± 6.0%. The mean values of serum Mb, CK, troponin T, and norepinephrine were higher in patients than those in the control group (P < 0.0001 for all indices; percentage differences were 658% for Mb, 529% for CK, and 258% for norepinephrine). A positive correlation was observed between the prevalence of negative Mb immunostaining in fibers and the Mb (r² = 0.968, P < 0.0001), CK (r² = 0.910, P < 0.0001), and norepinephrine levels (r² = 0.835, P < 0.0001). During the 12-mo study period, Barthel index and Scandinavian Stroke Scale values improved. The percentage change of the Barthel index and Scandinavian Stroke Scale correlated positively with the prevalence of negative Mb immunostaining in fibers.

Conclusions: It was speculated that ischemia, resulting from vasoconstriction induced by an increase in norepinephrine, may be responsible for the occurrence of fibers with negative immunoreactivity for Mb. Patients with higher negative immunostaining for Mb fibers had poor functional recovery of hemiplegia 12 mos after stroke onset. This implies that these muscular alterations may hamper functional recovery.

Key Words: Norepinephrine, Myoglobin, Hemiplegia, Skeletal Muscle, Stroke Outcome
Elevated levels of serum creatine kinase (CK) have been reported during the initial phase of stroke. However, there has been controversy as to the origin of serum CK. We have demonstrated that serum myoglobin (Mb) concentrations were elevated in patients with all types of acute stroke and that serum Mb concentrations correlated positively with serum CK concentrations. In acute severe stroke, in patients who had concomitant acute respiratory failure requiring tracheostomy due to seriously impaired consciousness, a biopsy of sternothyroid muscle from the nonhemiplegic side obtained during tracheostomy showed hypoxic changes such as degenerating and regenerating fibers, ragged red fibers, and increases in acid phosphatase activity. In these patients, there was elevated serum levels of Mb or CK, suggesting Mb and CK were from skeletal muscle origin. On the contrary, myocardial muscle CK isoenzyme (CK-MB) activity has been shown to increase in certain patients with ischemic stroke and with subarachnoid hemorrhage in the absence of any clinically evident acute coronary syndrome. A continuing low-grade myocardial necrosis suggestive of myocyte loss, the pathologic hallmark of stroke-related cardiac damage distinguished by foci of swollen myocytes, intestinal bleeding, and mononuclear infiltration in the vicinity of cardiac nerves have all been implicated as possible cause of CK-MB elevation. To further investigate the clinical significance of Mb, we examined whether immunohistochemical staining for Mb of the biceps muscle of the hemiplegic side could predict functional recovery in acute stroke patients. We estimated a study size of 157 stroke patients and 159 control subjects was appropriate due to our previous experience in studies on serum Mb and CK in stroke patients.

MATERIALS AND METHODS
All patients and volunteers were informed of the nature of the study. Consent was obtained from each participant or from family members when patients were unable to understand because of disturbed consciousness. The study protocol was approved by the local ethics committee.

Study subjects were 157 hemiplegic patients with acute ischemic stroke who were admitted to our hospital between 6 and 24 hrs after the stroke onset. Patients were excluded if they had severely disturbed consciousness (stupor and coma) or impairment of renal function (serum creatinine of >1.2 mg/dl). Those with signs of myocardial ischemia at admission were also excluded by electrocardiogram. We also serially determined cardiac enzymes before enrollment to make sure that non-ST wave myocardial infarction had not occurred.

Diagnosis of the type of the ischemic stroke was made on the basis of the results of mode of onset, clinical examination, electrocardiogram, and magnetic resonance imaging and magnetic resonance angiography. According to the Classification of Cerebrovascular Diseases III of the National Institute of Neurological Disorders and Stroke, strokes were classified as lacunar infarction (n = 39), atherothrombotic infarction (n = 61), or cardioembolic stroke (n = 57).

On the second day of stroke, serum levels of Mb, CK, and troponin T and plasma levels of epinephrine and norepinephrine were determined after the administration of oxygen if the patients were hypoxic. The control group for Mb, CK, troponin T, epinephrine, and norepinephrine included 159 age- and sex-matched healthy volunteers who did not have a history of stroke, other vascular or muscular diseases, or vascular risk factors such as diabetes mellitus, hypertension, and hyperlipidemia.

Thirty minutes before the removal of blood samples for serum Mb, CK, and troponin T and plasma epinephrine and norepinephrine, an indwelling heparin lock device was inserted into a forearm vein, and the patients and control subjects were maintained in a supine position in quiet surroundings. Mb was determined by radioimmunoassay with iodine-125–labeled and unlabeled Mb preparations (Daichi Radioisotope, Tokyo, Japan). CK was assayed by ultraviolet method (Nittobo, Tokyo, Japan). Troponin T was measured by electrochemiluminescent immunoassay (Roche Diagnostics, Tokyo, Japan). Analysis of epinephrine and norepinephrine was based on high-pressure liquid chromatography separation of radioenzymatically methylated catecholamines obtained by extraction of plasma with catecholamine-O-methyltransferase and tritiated S-adenosyl-L-methionine (Toso, Tokyo, Japan).
kyo, Japan). On the same day, arterial blood oxygen was measured.

We previously found absence of Mb immunoreactivity in fibers in the biopsied sternothyroid muscle on the nonhemiplegic side of patients with acute stroke, we hypothesized a similar change may occur on the hemiplegic side and affect the functional prognosis of stroke. Thus, biceps muscle specimens of the hemiplegic side were obtained on the second day of stroke onset in all 157 patients. Serial thin sections (10 μm) were prepared from samples fixed in formalin and embedded in paraffin. These sections were stained with hematoxylin and eosin and assessed for immunoreactivity for Mb as described below. The avidin-biotinylated peroxidase complex method was used with the OmniTag System (Lipshaw, Detroit, Michigan). In brief, sections were washed with phosphate-buffered saline, incubated sequentially with rabbit anti-human Mb serum for 10 mins at 37°C, then biotinylated with goat anti-rabbit immunoglobulin G for 10 mins at 37°C. After washing, each preparation was incubated with the biotinylated peroxidase complex for a further 10 mins. For each sample, the number of fibers negatively or weakly stained for Mb was determined in randomly selected fields by two physicians who were blind to the patients’ information. The values were reported as a percentage of negatively stained fibers in total muscle fiber surface area. For each sample, the number of negatively or weakly immunostained fibers was determined as a percentage of the total fibers counted (322–698). There was no artifact in Mb immunostaining. Then, the loss of Mb immunoreactivity was observed by comparing specimens stained with hematoxylin and eosin. We previously demonstrated that the negatively or weakly-stained fibers for Mb were consistently associated with hyaline degeneration on hematoxylin and eosin staining in biopsy specimens of the sternothyroid muscle obtained during tracheostomy from patients with severe acute stroke manifesting respiratory failure. In the present study, we examined this correlation in ten patients and confirmed the validity of the staining for Mb.

The degree of disability and functional status of patients were assessed at day 7 and at 12 mos after stroke using the Barthel index (BI). Clinical severity of hemiplegia was evaluated using the initial prognostic and long-term score of the Scandinavian Stroke Scale (SSS) on the first day and at 12 mos after stroke onset (i.e., point total for motor power of the hand, arm, and leg was calculated, in which a score of 0 is defined as complete hemiplegia and a score of 18 represents normal power). During the first 7 days, 27 patients were excluded from the study due to death (n = 7), artificial respiration (n = 9), or complications such as gastrointestinal bleeding or pneumonia (n = 11). Thus, 157 patients were enrolled in the study. All patients received intense physical rehabilitation for ≥3 mos after the onset of stroke. A total of 20 patients were excluded or withdrew from the study due to death, loss to follow-up, or intercurrent illness. Thus, a total of 137 patients completed the trial.

All statistical procedures were performed using Statview J 5.0 and software packages (Abacus Concepts, Berkeley, CA). The results are expressed as mean ± standard deviation. The χ² test was used to analyze differences between patients and controls concerning categorical data. The unpaired t test was used for comparing mean values of continuous variables between the two groups. Pearson’s correlation coefficients were calculated to examine correlations among serum Mb, serum CK, serum troponin T, PaO₂, plasma epinephrine and norepinephrine, and the percentages of negative staining for Mb levels at baseline. Multivariate linear regression analysis was used to estimate independent effects of predictor variables for BI and SSS after 12 mos. P values of <0.05 were considered as statistically significant.

**RESULTS**

**Baseline Characteristics of Study Subjects**

Clinical information for the patient and for control groups is summarized in Table 1. No differences were observed between the patient group and the control group for age and sex. The mean Mb, CK, and norepinephrine values were higher in the patient group than for control subjects. The mean plasma epinephrine concentration in the patient group was significantly higher than in control subjects. PaO₂ in the patient group was significantly lower than in the control subjects. However, no significant difference was seen in the serum troponin T concentration between the two groups.

Clinical information for the three patient groups (alertness, confusion, and somnolence) defined by level of consciousness is summarized in Table 2. No differences in such variables as age, sex, degree of hemiplegia, troponin T levels, and epinephrine levels were found among the three groups. Serum levels of Mb, CK, and norepinephrine and the frequency of the fibers negative for Mb were significantly higher in the confusion and somnolence groups than in the alertness group. The mean PaO₂ was significantly lower in the confusion and somnolence groups than in the alertness group.

A positive correlation was observed between the serum Mb level and the serum CK level (r² = 0.910, P < 0.0001) and norepinephrine (r² = 0.860, P < 0.0001), although there was not a correlation between the serum Mb level and troponin T (r² = 0.010, P = 0.22), epinephrine (r² = 0.002, P = 0.63), and PaO₂ (r² = 0.001, P = 0.71).
Prevalence of Negative Mb Immunostaining of Fibers

Immunostaining (Fig. 1) for Mb was negative in the muscle fibers of 109 of 157 stroke patients (i.e., no fiber negative for Mb was seen in 48 of the stroke subjects). Among patients, the prevalence of negatively stained muscle fibers ranged from 0.0% to 22.0%, with a mean of 5.9% (95% confidence interval, 4.9–6.8%). Two patterns of negative staining for Mb were observed; the first pattern of fibers was adjacent to each other on microscopic examination (Fig. 1, left) and the second was a pattern of scattered foci of negative Mb-immunostained fibers (Fig. 1, right).

A positive correlation was observed between the prevalence of negatively immunostained fibers and serum Mb levels ($r^2 = 0.968$, $P < 0.0001$), serum CK ($r^2 = 0.910$, $P < 0.0001$), or norepinephrine ($r^2 = 0.835$, $P < 0.0001$), whereas negative correlation was observed between the negative fiber prevalence and $\text{Pao}_2$ ($r^2 = −0.047$, $P = 0.0067$). There was not a correlation between the prevalence of negative Mb immunostaining in fibers and troponin T ($r^2 = 0.005$, BL = 0.39), epinephrine ($r^2 = 0.02$, $P = 0.59$, BL = 0.001, $P = 0.71$), and SSS ($r^2 = 0.0002$, $P = 0.99$).

When patients were divided into two groups according to the severity of hemiplegia, there was no significant difference in the percentage of fibers with negative Mb immunostaining between the patients with SSS of <6.8 (mean baseline SSS of all

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Demographic and baseline clinical characteristics of the stroke patients at study entry</th>
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<tbody>
<tr>
<td>Variables</td>
<td>Control Subjects $(n = 159)$</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>$62.2 \pm 12.7$</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>89/70</td>
</tr>
<tr>
<td>Barthel index$^b$</td>
<td>54.0 ± 20.1</td>
</tr>
<tr>
<td>Degree of hemiplegia$^c$</td>
<td>6.8 ± 4.4</td>
</tr>
<tr>
<td>Serum myoglobin, ng/mL</td>
<td>$21.3 \pm 11.1$</td>
</tr>
<tr>
<td>Serum creatine kinase, IU/liter</td>
<td>25.0 ± 6.1</td>
</tr>
<tr>
<td>Serum troponin T, ng/mL</td>
<td>0.068 ± 0.037</td>
</tr>
<tr>
<td>Plasma epinephrine, ng/mL</td>
<td>0.064 ± 0.018</td>
</tr>
<tr>
<td>Plasma norepinephrine, ng/mL</td>
<td>0.327 ± 0.139</td>
</tr>
<tr>
<td>$\text{Pao}_2$, Torr</td>
<td>97.0 ± 4.5</td>
</tr>
</tbody>
</table>

NS, not significant. Values are mean ± standard deviation.

$^a$ Unpaired t test.
$^b$ Barthel index was evaluated 7 days after stroke, and serum indices were measured on the second day after stroke onset.
$^c$ Degree of hemiplegia was evaluated on the first day using the initial prognostic and long-term score of the Scandinavian Stroke Scale.$^{12}$

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Demographic and baseline clinical characteristics of the stroke patients at study entry according to level of consciousness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of Consciousness</td>
<td>Alertness $(n = 90)$</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>$61.7 \pm 12.4$</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>49/41</td>
</tr>
<tr>
<td>Barthel index</td>
<td>61.0 ± 22.8</td>
</tr>
<tr>
<td>Degree of hemiplegia$^b$</td>
<td>6.7 ± 4.4</td>
</tr>
<tr>
<td>Serum Mb, ng/mL</td>
<td>115.7 ± 114.8</td>
</tr>
<tr>
<td>Serum creatine kinase, IU/liter</td>
<td>113.6 ± 109.8</td>
</tr>
<tr>
<td>Serum troponin T, ng/mL</td>
<td>0.076 ± 0.039</td>
</tr>
<tr>
<td>Plasma adrenaline, ng/mL</td>
<td>0.133 ± 0.042</td>
</tr>
<tr>
<td>Plasma noradrenaline, ng/mL</td>
<td>0.526 ± 0.698</td>
</tr>
<tr>
<td>$\text{Pao}_2$, Torr</td>
<td>94.4 ± 4.6</td>
</tr>
<tr>
<td>Negative staining for Mb, %</td>
<td>3.7 ± 5.8</td>
</tr>
</tbody>
</table>

Mb, myoglobin. Values are mean ± standard deviation.

$^a$ Differences between the three groups by analysis of variance.

$^b$ Degree of hemiplegia was evaluated using the initial prognostic and long-term score of the Scandinavian Stroke Scale.$^{12}$

$^c P < 0.0001$ rs. alertness.

$^d P < 0.0001$ rs. confusion.

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patients) and those with SSS of >6.8 (5.8% ± 6.1% vs. 6.0% ± 6.0%, P = 0.85).

**Multiple Regression Analysis**

During the 12-mo study period, BI (from 59.7 ± 23.4 to 81.4 ± 20.1, P < 0.0001) and SSS scores (from 6.8 ± 4.4 to 10.8 ± 6.3, P < 0.0001) increased significantly as compared with baseline values. Table 3 shows the results of multiple regression analysis in which age, BI, SSS, and prevalence of Mb-negative fibers at baseline were selected as independent variables, with BI and degree of hemiplegia (SSS) after 12 mos as the dependent variables. Age, SSS, and prevalence of negative fibers correlated significantly with BI after 12 mos, and age, BI, and prevalence of negative fibers correlated significantly with SSS after 12 mos.

**DISCUSSION**

We found a lack of immunoreactive Mb in fibers in the biceps muscle of the hemiplegic side in patients with acute ischemic stroke. Age, initial BI, degree of hemiplegia (SSS), and prevalence of Mb-negative fibers were independent determinants of recovery of hemiplegia and immobility 12 mos after the onset of stroke. The extent of skeletal muscles lacking Mb may provide valuable information for predicting functional prognosis.

The serum concentrations of troponin T (a more specific biochemical marker of myocardial injury), CK-MB, and Mb were studied in 32 patients with acute large hemispheric infarction. According to this study, serum troponin T levels were normal, and serum CK-MB, Mb, and total CK levels were elevated, indicating CK-MB elevation in acute ischemic stroke is of noncardiac origin. Similarly, troponin T levels were not elevated in the present study. This implies that Mb and CK elevations observed in patients with stroke do not reflect stroke-related myocardial scattered foci of microlesions. The prevalence of negative immunostaining for Mb in fibers varied from 7.8% to 1.2%.

**FIGURE 1** Upper Panel, myoglobin staining (biceps muscle biopsy; avidin-biotinylated peroxidase complex method, 200×) in a 64-yr-old woman with lacunar stroke manifesting alertness. The serum myoglobin and total creatine kinase were 287 ng/ml and 221 IU/liter, respectively. A group of fibers lacking myoglobin immunostaining is visible. The percentage of negatively immunostained fibers is 7.8%. Lower Panel, myoglobin staining (biceps muscle biopsy; avidin-biotinylated peroxidase complex method, 200×) in a 68-yr-old man with atherothrombotic infarction manifesting confusion. Serum myoglobin and total creatine kinase were 42 ng/ml and 51 IU/liter, respectively. Small numbers of scattered foci lacking immunoreactivity or with weak staining (arrows) for myoglobin in fibers are visible. Two foci lacking immunoreactivity are arterioles (arrowheads). The percentage of negatively immunostained fibers is 1.2%.
case to case, and no apparent correlation was demonstrated between this prevalence and epinephrine levels. On the contrary, there were correlations between prevalence of non–Mb-immunoreactive fibers and Mb, CK, and norepinephrine levels.

Two patterns of negative Mb-immunostained fibers were observed; the first pattern was of negative Mb-immunostained fibers adjacent to each other on microscopic examination, and the second pattern was a scattered foci of negative Mb-immunostained fibers. It seems, however, that grouped fibers that lacked immunoreactivity for Mb exist in the areas corresponding to the territory of an artery or arteriole. These regions of negative Mb immunoreactivity corresponding to the territory of an artery have been shown experimentally and clinically in ischemic myocardium after occlusion of the coronary artery.18,19

Accordingly, Mb release in acute stroke is thought to be a consequence of a more sensitive response of muscle fibers to ischemia on both the hemiplegic and nonhemiplegic sides. It is speculated that ischemia produced by enhanced catecholamine release, with consequent vasoconstriction in acute stroke,20–23 is the cause of the negative Mb-immunostained fibers. The vasoconstriction may occur in the territory of a poorly collateralized artery or arteriole, although the muscles are provided with a rich collateral circulation.24 Norepinephrine produces vasoconstriction in skeletal muscle via α1 receptors, but epinephrine dilates the blood vessels in skeletal muscle via β2 receptors.25,26 In the present study, the prevalence of negative Mb immunoreactivity correlated negatively with norepinephrine but not with epinephrine. Also, norepinephrine levels in stroke patients were significantly higher than in control subjects, whereas epinephrine did not differ between the stroke group and control subjects. Therefore, norepinephrine-induced vasoconstriction overshadowed epinephrine-induced vasodilatation. On the other hand, hypoxemia resulted in a high prevalence of fibers with negative Mb immunoreactivity. This may have caused scattered foci of negative fibers. If norepinephrine-induced vasoconstriction and hypoxemia are responsible for lack of immunoreactivity in hemiplegic muscles, their effect may present on the nonhemiplegic side. Indeed, in our previous study of acute stroke, similar observation of negative Mb immunostaining was observed in the sternothyroid muscle on the nonhemiplegic side.11 Also, two patients showed negative Mb staining of the muscle fiber obtained during tracheostomy in the chronic stage.11 Although we did not measure the muscle strength on the nonhemiplegic side, it is probable that nonhemiplegic muscles are weaker at baseline. It is unlikely that recovery of Mb-negative muscles takes place on both hemiplegic and nonhemiplegic sides in longstanding stroke.

The correlation between muscle findings and the functional outcomes might be due to the fact that both of these two measurements reflect the severity of hemiplegia. However, this explanation may be unlikely because there was no significant change in the percentage of Mb-negative fibers between the patients with an SSS of <6.8 and those with an SSS of >6.8.

Because negative Mb immunoreactivity was observed in muscle specimens that were obtained 2 days after stroke onset and because patients with a high prevalence of negative Mb immunoreactivity had poor functional recovery after 12 mos, the muscle changes may have occurred very early and persisted longer, until the chronic stage. Although the consciousness level and degree of pyramidal tract disorder due to stroke are mainly responsible for the severity of hemiplegia and functional recovery, these muscular alterations (i.e., hyaline degeneration) may serve as one of the factors that hamper functional recovery because we found that prevalence of Mb-negative fibers, in addition to age, initial BI, and degree of hemiplegia (SSS), was an independent determinant of recovery of hemiplegia and immobility 12 mos after the onset of stroke. It is noteworthy that patients with disturbed consciousness had a higher prevalence of Mb-negative fibers and higher serum levels of Mb, CK, and

| TABLE 3 Multiple regression analysis of Barthel index (BI) and Scandinavian Stroke Scale (SSS) after 12 mos with age, BI, SSS, and prevalence negative myoglobin (Mb) staining fiber at baseline selected as independent variables |
|-----------------------------------------------|----------------|----------------|
| BI After 12 mos                               | SC  | P   |
| Age                                           | 0.029 | 0.40  |
| BI                                            | 0.722 | <0.0001 |
| SSS                                           | 0.272 | 0.0156 |
| Negative Mb staining fiber                    | -0.707 | <0.0001 |
| Multiple R                                    | 0.851 | 0.892  |
| Adjusted R²                                   | 0.846 | 0.796  |
| F                                             | 188.3 | 128.6  |
| SSS After 12 mos                              | SC  | P   |
| Age                                           | 0.026 | 0.51  |
| BI                                            | 0.844 | <0.0001 |
| SSS                                           | 0.260 | 0.0264 |
| Negative Mb staining fiber                    | -0.232 | <0.0001 |
| Multiple R                                    | 0.851 | 0.892  |
| Adjusted R²                                   | 0.846 | 0.796  |
| F                                             | 188.3 | 128.6  |
norepinephrine. In addition, the mean PaO_2 was significantly lower in the confusion and somnolence groups than in the alertness group. These findings imply that hypoxemia in severe stroke contributed to the occurrence of Mb-negative fibers. The above fact is important clinically in that the degree of biopsied muscle fibers lacking immunoreactivity for Mb may provide valuable information regarding functional prognosis. Estimation of Mb immunoreactivity in skeletal muscles and serum concentrations of Mb in a large number of patients with acute stroke will further disclose the functional prognostic value of assessing the loss of immunoreactivity for Mb in muscle fibers.

This study has several limitations. Muscle perfusion was not actually examined in the acute stage. Regardless, Mb is present in fiber type 1 and 2A and is absent in fiber 2B; we could not analyze this in reference to Mb tissue distribution and immunohistochemistry of fast and slow myosin heavy chains. In addition, Mb immunoreactivity on the nonhemiplegic side may provide more useful information regarding its relation to the functional outcome; we examined Mb staining only on the hemiplegic side. We also did not assess serial BI and SSS to better track functional status.

In conclusion, based on a statistical approach, we found that stroke patients with more fibers negative for immunoreactive Mb at onset had a poor functional status 12 mos after stroke onset.

REFERENCES

How to Obtain CME Category 1 Credits
To obtain CME Category 1 credit, this educational activity must be completed and postmarked by December 31, 2006. Participants may read the article and take the exam issue by issue or wait to study several issues together. After reading the CME Article in this issue, participants may complete the Self-Assessment Exam by answering the questions on the CME Answering Sheet and the Evaluation pages, which appear later in this section. Send the completed forms to: Bradley R. Johns, Managing Editor, CME Department-AAP, American Journal of Physical Medicine & Rehabilitation, 7240 Fishback Hill Lane, Indianapolis, IN 46278. Documentation can be received at the AAP National Office at any time throughout the year, and accurate records will be maintained for each participant. CME certificates are issued only once a year in January for the total number of credits earned during the prior year.

10. Special report from the National Institute of Neurological Disorders and Stroke: Classification of cerebrovascular diseases III. Stroke 1990;21:637–76
CME Self-Assessment Exam Questions

CME Article Number 5: Y. Sato, et al.

1. In this study, negative immunostaining of myoglobin on Hematoxylin and Eosin (HE) staining in acute stroke patients was associated with:
   A. Fiber necrosis.
   B. Hyaline degeneration.
   C. Fiber splitting.
   D. Opaque fiber.

2. In acute stroke, the incidence of negative myoglobin staining on the hemiplegic side was:
   A. 10%.
   B. 30%.
   C. 50%.
   D. 70%.

3. Based on this study, a determinant of the lack of myoglobin immunoreactivity on the hemiplegic side in acute phase of stroke may be:
   A. Norepinephrine.
   B. Epinephrine.
   C. Serum creatine kinase.
   D. High levels of tissue oxygenation following stroke.

4. Among acute stroke patients, the increased serum creatine kinase is likely derived from:
   A. Brain.
   B. Myocardium.
   C. Skeletal muscle.
   D. Myocardium and skeletal muscle.

5. In this study which of the following were independent determinants of recovery of hemiplegia and immobility 12 months after the onset of stroke:
   A. Presence of myoglobin negative fibers.
   B. Serum epinephrine level.
   C. Serum creatine kinase level.
   D. Serum myoglobin.

INSTRUCTIONS TO OBTAIN CATEGORY 1 CME CREDITS:

1. Read the Designated CME Articles in this issue.

2. Read the following CME Self-Assessment Exam Questions.

3. Photocopy and complete the CME Self-Assessment Exam Answering Sheet and CME Evaluation.

4. Send the completed Answering Sheet and Evaluation to: Bradley R. Johns, Managing Editor, CME Department-AAP, American Journal of Physical Medicine & Rehabilitation, 7240 Fishback Hill Lane, Indianapolis, IN 46278

This is an adult learning experience and there is no requirement for obtaining a certain score. The objective is to have each participant learn from the total experience of studying the article, taking the exam, and being able to immediately receive feedback with the correct answers. For complete information, please see “Instructions for Obtaining Continuing Medical Education Credit” at the front of this issue.

Every question must be completed on the exam answering sheet to be eligible for CME credit. Leaving any item unanswered will make void the participant’s response. This CME activity must be completed and postmarked by December 31, 2006. The documentation received will be compiled throughout the calendar year, and once a year in January, participants will receive a certificate indicating CME credits earned for the prior year of work. This CME activity was planned and produced in accordance with the ACCME Essentials.
Access to Healthcare Services Among Persons with Osteoarthritis and Rheumatoid Arthritis

ABSTRACT


Objective: Persons with osteoarthritis and rheumatoid arthritis frequently require access to a broad range of healthcare services. The purpose of the current study was to examine the healthcare access experiences of these two populations.

Design: Mail surveys were completed by 409 adults with self-reported osteoarthritis or rheumatoid arthritis who were recruited through a variety of recruitment strategies such as advertisements placed in arthritis publications, internet sources, and physician referrals.

Results: Participants self-reported not obtaining needed health care at high rates for several service domains, including mental health services (42%) and rehabilitation therapies (39%). The most frequent reasons for not obtaining services included lack of service coverage by the health plan and high costs. Type of arthritis was predictive of the ability to obtain primary doctor services.

Conclusions: The United States healthcare system continues to focus on treating acute disorders and has yet to adapt to the growing prevalence of chronic illness and disability. Changes will be needed in both healthcare financing and delivery structures to promote access to specialized services such as mental health services and rehabilitation therapies for persons with osteoarthritis and rheumatoid arthritis.

Key Words: Osteoarthritis, Rheumatoid Arthritis, Health Care, Access, Utilization
Persons with osteoarthritis and rheumatoid arthritis require access to a broad range of healthcare services, including rheumatologic care, prescription medications, rehabilitative therapies, mental health services, and inpatient hospitalization. The healthcare costs for these two populations are substantial. For example, annual healthcare and work-loss costs per employee can be twice as high for individuals with rheumatoid arthritis than for individuals without rheumatoid arthritis.1

Despite the high costs of health care for persons with osteoarthritis and rheumatoid arthritis, there is little evidence about whether these populations are obtaining needed health care. Access to services is a substantive policy issue when considering the cost savings that occur when consumers are able to obtain preventive care and early medical intervention. For example, access to rheumatologists is associated with improved function and decreased disability.2 If persons with osteoarthritis or rheumatoid arthritis are not able to obtain needed health care in a timely manner, decreased community integration, lower quality of life, and increased healthcare costs may result. The extant literature has not adequately documented whether these consumers are able to obtain needed health care nor has it described the sociodemographic, insurance, and other factors related to access to care.

Research by the Centers for Disease Control and Prevention revealed that, among the general population, nearly 21% of respondents aged 18–64 yrs reported an unmet healthcare need.3 The same study revealed that 11% of individuals aged 65 yrs and older reported an unmet medical need, despite the fact that this population has near universal coverage through Medicare.4 A national study among the general population revealed that >16% of consumers were unable to obtain at least one needed healthcare service.5 Variables that were associated with difficulty obtaining services included minority status, low income, fair or poor health, receiving public insurance, being uninsured, and cost barriers.3–6

Although numerous research studies have examined the effect of health insurance on access to services among the general population,3–6 few studies have been conducted among persons with chronic illness. The existing literature indicates that access to health care for persons with chronic illnesses or disabilities is poor.7 For example, 25% of persons with disabilities report difficulty finding a doctor that understands their disability.8 Women with disabilities have lower utilization rates for Pap smears, mammograms, and breast examinations than those without disabilities.9,10 Persons with disabilities report having difficulty obtaining prescription drugs (32%), dental care (29%), assistive equipment (21%), and mental health services (17%). Among persons receiving Medicare, individuals who report having a disability are more likely to report problems with access to care than persons without a disability.11,12

Beatty et al.13 conducted a large survey of individuals with chronic illnesses and disabilities, including the current sample of persons with arthritis but also individuals with other disabilities. Whereas the research by Beatty et al.13 examined the ability of a large group of persons with illnesses and disabilities, the current study identified the reasons for and the factors related to not obtaining needed services for persons with osteoarthritis or rheumatoid arthritis only. The results of the Beatty et al.13 study revealed that 45% of the respondents reported not obtaining rehabilitation therapy when needed, and 30% reported not obtaining needed assistive equipment. Respondents with the poorest health and the lowest incomes were the least able to obtain needed healthcare services. Consequences associated with not accessing services include the development of secondary conditions such as pressure sores, general and functional decline, psychological distress, and social and economic decline.14,15

Research is just beginning to provide more information on access to services for persons with arthritis. For example, elderly persons with rheumatoid arthritis have had difficulty accessing rehabilitative and mental health services.16 Elderly persons with arthritis who had more comprehensive insurance coverage were more likely to utilize arthritis-related services. Individuals in fair health, those who did not receive care at a particular place, and those with diabetes or a mental health disorder were less likely to utilize arthritis-related services.17 Minorities, specifically African Americans, Hispanics, and Asians, were less likely than white people to receive total joint replacement for osteoarthritis.18 Conversely, persons who were employed, had more education and social support, those who were younger at the onset of symptoms, and those with more joint swelling/tenderness were less likely to experience delays accessing rheumatologists.19

In addition, there is limited evidence that individuals enrolled in managed care programs have more difficulty accessing services than those in fee-for-service programs.11,13 A study of Medicare beneficiaries found that those who dropped out of a health maintenance organization obtained hip arthroplasty nearly four times more often as those in Medicare fee-for-service. The rates for osteoarthritis-related knee replacement were over three times higher among persons who dropped out of a health maintenance organization, compared with those receiving fee-for-service Medicare.20 These results
suggested that consumers with arthritis might have had difficulty obtaining these high-cost services within managed care settings. Therefore, they disenrolled into a fee-for-service system to obtain these surgeries. In contrast, a series of studies by Yelin et al.2,21,22 revealed few differences in utilization of healthcare services across fee-for-service and managed care systems.

More research is needed to determine the level of access to needed healthcare services among persons with arthritis and to identify the factors associated with access to services.23 The aim of the current study was to examine the healthcare experiences among persons with osteoarthritis and rheumatoid arthritis in both public and privately funded insurance programs.

Research Questions

1. Do persons with osteoarthritis and rheumatoid arthritis report obtaining commonly needed health services?
2. What are the reasons for not obtaining a needed service?
3. What sociodemographic, health, and insurance-related variables predict access to healthcare services?

PATIENTS AND METHODS

Recruitment

Data for this research came from the first year of a 4-yr longitudinal survey of adults with osteoarthritis of the hip or knee or with rheumatoid arthritis. To be included in the study, individuals had to report being diagnosed with rheumatoid arthritis or osteoarthritis of the hip or knee by a physician, be 18 yrs of age or older, and have Medicare, Medicaid, or private insurance coverage. Individuals with more than one type of insurance were placed in the category corresponding to the first payer. At the time the survey was completed, all participants resided in the United States.

A variety of recruitment strategies yielded a convenience sample. Mailing lists of Arthritis Foundation chapters provided 33% of the participants. The following methods resulted in the recruitment of additional individuals: advertisements in national and arthritis-specific publications, including the Arthritis Today magazine (22%), the Washington Post (0.2%), and Arthritis Foundation chapter newsletters (4.2%); arthritis/disability-related educational groups (9%); internet sources, including disability and disease-specific listservs (11%) and project Web sites (3%); physician referrals (8%); participant referrals (3%); recruitment fliers posted in libraries (0.5%) and centers for independent living in major metropolitan areas throughout the United States (1.2%); and 4.9% from sources not identified.

Interested individuals completed a brief recruitment questionnaire indicating diagnosis and type of insurance coverage. Individuals provided written consent to participate through the recruitment materials, following a protocol approved by a university institutional review board. Due to open recruitment methods, data were not available on persons who were eligible but did not inquire about participating.

Data Collection

Participants received the survey via United States Postal Service. Participants who failed to return the questionnaire in the specified time received a series of reminders in the mail. If study participants were not physically able to complete the questionnaire, the protocol allowed them to have assistance from a friend, family member, or member of the research staff via telephone.

Data collection occurred between January and November of 1999. During this time period, a total of 488 surveys were mailed to potential participants. A total of 415 individuals returned surveys for a response rate of 85%. Six individuals were subsequently not eligible to participate in the study because they indicated being younger than 18 yrs of age, were uninsured at the time they completed the survey, or did not meet diagnostic criteria.

Participants

Of the 409 adults in this study, 44% had osteoarthritis of the hip or knee, 47% had rheumatoid arthritis, and 9% had both conditions. The sample was predominately women (84%) and white (94%), with an average age of 55 yrs (SD = 14). Nearly half (45%) of the respondents reported an annual income of >$40,000. Fifty-four percent were enrolled in fee-for-service programs and 46% were enrolled in managed care programs for their primary healthcare insurance (four respondents did not answer this question). Fifty-nine percent of the respondents reported having private insurance, and 35% reported Medicare coverage, and 6% had Medicaid coverage. Forty-one percent of the respondents were employed, and 59% were not employed. One third of the respondents (33%) described their health status as either fair or poor, and nearly one third (31%) reported feeling depressed at least some of the time. The average reported time since receiving a diagnosis of osteoarthritis or rheumatoid arthritis was 15 yrs (SD = 12). Additional sociodemographic and health-related information is included in Tables 1 and 2.

Healthcare Survey

The 120-item paper-and-pencil survey assessed respondents’ experiences across the healthcare delivery spectrum. Major areas of interest covered by
the survey include patterns of healthcare access, utilization, and satisfaction. The survey consisted of the depression and disability severity questions adapted from the National Health Interview Survey and the health status question from the SF-36. Both of these instruments are well-known, psychometrically sound survey tools that measure health status and functioning and have been used successfully among persons with a wide variety of chronic illnesses. Pretesting of the survey provided an assessment of the readability of the survey. Comments received from consumers informed revisions to the survey.

**Predictor Variables**

All data analysis included a dichotomous indicator of health plan type. Using the following broad descriptions of health plan type, survey respondents indicated the type of coverage that best described their primary health insurance plan: Fee-for-service: Traditional health insurance that allows you to choose your provider and the services you receive without limitation. Claims are filed by you or your doctor for health services received, and the insurance company covers the services after you pay a deductible amount. Managed care: An insurance plan in which all or most of the health care you receive is from doctors who are associated with the plan. Some managed care plans allow you to visit doctors not associated with the plan, but this involves an extra cost to you. Generally, you do not have to submit claims for the costs of medical services, and you may be required to visit your primary care doctor before visiting a specialist.

The primary type of insurance coverage defined source of funding (Medicare, Medicaid, or private insurance). The primary insurance coverage for individuals over the age of 65 was Medicare. Respondents reported whether they currently receive Social Security Disability Insurance or Supplemental Security Income. Type of arthritis was defined by the report of a diagnosis of osteoarthritis of the hip or knee or rheumatoid arthritis from a physician. Co-morbid conditions were defined by having any other self-reported disease or health condition in addition to the diagnosis of arthritis. Participants provided information on their health status by rating their health as excellent, very good,
good, fair, or poor. Respondents provided information on depression by answering if they feel depressed none of the time, a little of the time, some of the time, or all of the time. Disability severity was determined by 12 items measuring ability to perform activities of daily living and instrumental activities of daily living, including bathing, dressing, eating, toileting, transferring, getting around inside the home, managing money, doing housework, shopping, and preparing meals. All analyses used a summative score of the 12 activities of daily living/instrumental activities of daily living questions.

Categorical sociodemographic variables included sex, race (white, black/African American, Asian/Pacific Islander, or other), annual household income level ($<$20,000, $20,001–$40,000, $40,001–$60,000, $>$60,000), and education (less than high school diploma, high school diploma/general equivalency diploma, 1–4 yrs after high school, 5 yrs after high school). Age and time since diagnosis were continuous variables.

**Criterion Variables**

Access to healthcare services was defined as the receipt of the following services, when needed, as determined by the participant: (1) primary/personal physician care in the last 6 mos, (2) specialist(s) care in the last 6 mos, (3) prescription medications in the last 3 mos, (4) mental health care in the last 12 mos, and (5) rehabilitation therapies (i.e., physical therapy, occupational therapy, or speech therapy) in the last 3 mos. For each of these healthcare services, survey participants were asked about their need for, and use of, the service during the indicated period of time. If the participant reported not obtaining a service every time he or she needed it within the specified time frame, the response received the code corresponding to not obtaining a service and the respondent listed the primary reason(s) the service was not received. Participants were not limited to one response for each service.

**Statistical Analyses**

The base sample size for the analyses was 409 individuals. Several analyses had slightly smaller samples due to missing data. Descriptive statistics addressed the research questions regarding the perceived need for and the ability to obtain healthcare services.

Analyses included hierarchical multiple regression models for each of the five service domain areas to determine the predictors of obtaining needed services. Each of the hierarchical regressions forced in a set of variables and tested each set of variables for statistical significance. If the $P$ value for the test was $<$0.10, the variables remained in the model and the analyses introduced the next collection of variables. The collections of variables were entered in the following order: (1) sociodemographic and arthritis type, (2) health status, and (3) insurance variables. In addition, due to the large percentage of respondents reporting depression (31%), the regression model for mental health services included depression, which was entered in the third step, before the insurance variables.

Based on existing literature, the following sociodemographic variables were forced into the regression models first: age, race, sex, education, income, and type of arthritis. Age and education were continuous variables. Because of the small number of minority participants, race included only two categories (white vs. other). Participants reporting an annual income of $\leq$20,000 per year were compared with participants reporting an annual income of $>$20,000. Participants with osteoarthritis were compared with persons with rheumatoid arthritis and to participants with both conditions.

Data on disability severity were collected but were not included in the regression models due to the high collinearity between health status and disability severity. Because health status is closely related to the ability to obtain services in the literature, this variable was included in the regression model instead of disability severity. The insurance variables of health plan type and source of funding entered into the regression at the final step. In doing so, the analysis accounted for variance attributable to individual characteristics before that of insurance status.

**RESULTS**

Nearly all (98%) of the respondents reported needing prescription medications. The large majority of respondents reported needing care by specialist physicians (81%) and primary care physicians (77%). Thirty-nine percent of the respondents reported needing rehabilitation therapies, including physical therapy and occupational therapy. Twenty-six percent of the respondents reported needing mental health services (Fig. 1).

Participants reported not obtaining needed mental health services and rehabilitative therapies at high rates (42% and 39%, respectively). Nearly a fifth of the respondents reported not obtaining primary care physician services when needed (19%). Participants reported not obtaining needed specialty physician services and prescriptions at lower rates (14% and 10%, respectively) (Fig. 2).

The most cited reason for not receiving a service when it was needed was, “Health plan does not cover service.” The next most frequent reason was,
“service costs too much” (16%), followed by “thought problem would go away” (15%). Other reasons for not accessing services included “appointment not immediately available” (10%), “could not get referral” (9%), and “health plan has limits on number of visits allowed” (9%) (Table 3).

With the exception of prescription medications, “Thought problem would go away” was a frequent response for not obtaining needed services. Thirty-three percent of the participants who did not obtain primary care physician services when needed gave this response, followed by 30% for specialist services, 24% for mental health services, and 22% for rehabilitation therapies.

The services participants reported having the most difficulty obtaining were mental health services and rehabilitation therapies. The most frequent reasons given for not obtaining mental health services when needed were: “service costs too much” (43%), “plan does not cover service” (33%), “limits on number of visits” (26%), and “thought problem would go away” (24%). The most common reasons given for not obtaining rehabilitation therapies when needed were: “plan does not cover service” (31%), “limits on number of visits allowed” (24%), “service costs too much” (22%), “thought problem would go away” (22%), and “no transportation” (21%).
Relationship Among Access to Services, Health Plan, and Sociodemographic Variables

Primary Care Physician

Hierarchical regression revealed that type of arthritis predicted access to primary physician services (Table 4). The odds of obtaining primary care physician services were lower for respondents reporting both osteoarthritis and rheumatoid arthritis compared with persons with osteoarthritis only (odds ratio 0.204, \( P = 0.0012 \)).

Prescription Medications

Age was predictive of obtaining prescription medications when needed. Despite the fact that age was statistically significant in predicting access to prescription medications (\( P < 0.0279 \)), the differences across age groups were so minor that they were of little consequence. The odds of accessing prescription medications for older individuals were 4% greater than the odds of accessing prescriptions medications for younger individuals.

The hierarchical regressions were not statistically significant for rehabilitation therapies (\( P < 0.2416 \)), specialist services (\( P < 0.3424 \)), or mental health services (\( P < 0.8929 \)).

DISCUSSION

This study revealed that a sample of highly educated, largely white individuals with self-reported osteoarthritis and rheumatoid arthritis described not obtaining needed healthcare services at high rates. More than one-third of the sample did not obtain mental health services and rehabilitation therapies that participants perceived needing. It is important to note that these percentages include both access problems due to barriers related to providers and health plans in addition to individual consumer barriers (i.e., thought problem would go away). These percentages are higher than those reported in the Centers for Disease Control and Prevention general population study\(^3\,4\) but similar to other studies conducted among persons with disabilities and chronic conditions.\(^7\,8\,13\,29\) For example, individuals with disabilities frequently report being unable to obtain physical therapy, mental health services, and assistive equipment.\(^5\,29\) The high rates of described inability to obtain needed healthcare services suggest that persons with self-reported osteoarthritis and rheumatoid arthritis and others with chronic conditions are not receiving comprehensive services and perhaps even adequate health care.

Respondents clearly attributed the inability to obtain needed services for insurance-related reasons. For example, “plan does not cover service” was the most common reason given for not obtaining needed healthcare services overall. Healthcare costs have increased at double-digit rates for four consecutive years, and both state Medicaid plans and private insurers have reduced health service benefits and increased out-of-pocket costs. Therefore, it is likely that these barriers to healthcare services will persist for some time. A considerable

### Table 3: Reasons for not being able to access services when needed \(^a\)

<table>
<thead>
<tr>
<th>Service</th>
<th>Plan Does Not Cover Service (%)</th>
<th>Service Costs Too Much (%)</th>
<th>Thought Problem Would Go Away (%)</th>
<th>Appointment Not Immediately Available (%)</th>
<th>Could Not Get Referral (%)</th>
<th>Limits on Number of Visits Allowed (%)</th>
<th>No Transportation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary doctor</td>
<td>(n = 46)</td>
<td>24</td>
<td>20</td>
<td>30</td>
<td>28</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Mental health</td>
<td>(n = 57)</td>
<td>7</td>
<td>16</td>
<td>33</td>
<td>7</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Rehabilitation therapies</td>
<td>(n = 46)</td>
<td>33</td>
<td>43</td>
<td>24</td>
<td>9</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>Prescription medication</td>
<td>(n = 58)</td>
<td>31</td>
<td>22</td>
<td>22</td>
<td>7</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>Percentage of responses given</td>
<td>18(^d)</td>
<td>16</td>
<td>15</td>
<td>10</td>
<td>9</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\)Participants were not limited to one response for each service.

\(^b\)\(n\) = number of people who did not access a service when needed (i.e., \(n = 46\) people did not access specialists when needed).

\(^c\)Twenty-four percent of people who did not access specialists when needed gave the response, “plan does not cover service.”

\(^d\)Eighteen percent of the responses given by participants who could not access a service gave the response, “plan does not cover service.”

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minority of the respondents gave the response, “Thought problem would go away,” as a reason for not obtaining healthcare services. “Best practice” guidelines among rheumatologists and other healthcare professionals should include education and encouragement to seek treatment when needed.

Income, health status, source of insurance, and type of health plan were not associated with access to health services among this sample, despite the high rates of access problems. Because 45% of the sample reported an annual income of $40,000, there may not have been enough income variance in the sample to detect a significant relationship between income and access to services. Additional research should include samples with greater socioeconomic status variability, including research among persons without health insurance.

The lack of relationship between source of funding and access may relate to the survey design. Although the study collected information on Medicare, Medicaid, and private insurance, this study did not collect data on secondary insurance coverage, which has the potential to influence access to services. Benefit restrictions and cost-containment practices are similar across both public and private sectors (source of funding) and across managed care and fee-for-service payment systems (health plan type).21,22

The absence of a relationship between type of health plan and access may also relate to the way in which the health plan questions were phrased. Self-reported data were used to determine health plan type (fee-for-service or managed care). Because this is typically a difficult distinction for the general public to make, items included broad definitions to assist participants in making the distinction. Given that there were very few missing responses to this item, nearly all of the participants were able to place themselves in one category or the other. Studying the differences between fee-for-service and managed care systems has become difficult, however, because hybrid models are now increasingly common.20 Nevertheless, future research should endeavor to study specific cost-containment practices that may reduce access to needed healthcare services.

Individuals with both osteoarthritis and rheumatoid arthritis were less likely to obtain primary care when needed. Individuals with both of these conditions are likely to need proportionately more healthcare. Therefore, the chances of not obtaining needed services increases. One might suggest that individuals with both conditions are more likely to see a rheumatologist as their primary care physician. Although 14% of the respondents reported seeing a rheumatologist as their primary care physician, few of these individuals (11%) cited not obtaining primary care when needed. A less intuitive finding involves prescription medications.

The results of this study may not generalize well to the entire population of persons with osteoarthritis and rheumatoid arthritis. A convenience sample was used for this study because the costs of securing a verifiable representative sample of the population are prohibitive. Individuals without insurance were excluded from this study, and the sample was well educated and had minimal racial and ethnic diversity. The age and sex for the current study, however, were similar to previous samples of persons with arthritis.1,22,30 Further research should involve larger and more ethnic and racially diverse samples to identify in more detail the factors related to obtaining needed healthcare services and health outcomes. Furthermore, there was no method for examining differences between those who responded to the recruitment strategies and those who did not respond. Effects of a non-response bias should be minimal given the high

TABLE 4 Prediction of access to primary doctor services

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (df)</th>
<th>Test Statistic</th>
<th>B</th>
<th>SE</th>
<th>Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Model</td>
<td>282 (10)</td>
<td>21.9987</td>
<td>0.0071</td>
<td>0.0177</td>
<td>1.007</td>
<td>0.0152</td>
</tr>
<tr>
<td>Age a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race (white)</td>
<td></td>
<td></td>
<td>-0.9124</td>
<td>0.8064</td>
<td>0.402</td>
<td>0.2579</td>
</tr>
<tr>
<td>Sex (female)</td>
<td></td>
<td></td>
<td>0.0696</td>
<td>0.4659</td>
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<td>0.8812</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
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<td>0.990</td>
<td>0.8692</td>
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<tr>
<td>Income (&lt;$20,000)</td>
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<td></td>
<td>-0.5422</td>
<td>0.4298</td>
<td>0.581</td>
<td>0.2072</td>
</tr>
<tr>
<td>Type of arthritis b</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Rheumatoid arthritis and osteoarthritis</td>
<td>-1.5877</td>
<td>0.4909</td>
<td>0.204</td>
<td></td>
<td></td>
<td>0.0012</td>
</tr>
<tr>
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<td>0.716</td>
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a The odds ratio for age is in units of 20 yrs.

b Participants with osteoarthritis were compared with persons with rheumatoid arthritis and to participants with both conditions.
survey response rate (85%). In addition, self-report is a well-accepted and valid method of data collection in studies on access to health care. It is difficult, however, to verify "need" of a healthcare service or to distinguish between medical necessities and desired medical services. Future studies should attempt to verify both diagnoses and perceived needs through the use of chart reviews or some other objective method for documenting self-report data.

Overall, refined models of health delivery are needed for individuals with arthritis and other chronic illnesses. The United States healthcare system continues to focus on treating acute disorders and has yet to adapt to the growing prevalence of chronic illness and disability. The acute care model does not provide the education and specialized supportive services needed for individuals with chronic health conditions, resulting in greater suffering and higher healthcare costs. Both healthcare financing and delivery structures need to be adapted to promote access to specialized services such as mental health services and rehabilitation therapies for persons with osteoarthritis and rheumatoid arthritis. One strategy for improving the healthcare system is the expansion of disease management programs to rheumatic diseases, especially those associated with high costs. Disease management programs focus on delivering efficient, high-quality, interdisciplinary care in a timely manner and have resulted in improved care, reduced costs, and improved patient outcomes for individuals with arthritis and other chronic conditions. The results of this study indicate that disease management programs may be helpful for persons with arthritis.

Key stakeholders, including persons with arthritis, healthcare providers, and professional and advocacy organizations, should engage in collegial discussions with state and federal lawmakers regarding needed changes in health care for persons with arthritis. For example, these discussions should include consideration of reducing the 50% co-insurance rate for mental health services for Medicare beneficiaries. Lack of health insurance can be particularly devastating to persons with chronic diseases like rheumatoid or osteoarthritis given their substantial healthcare needs. Eliminating the 24-mo waiting period for persons who receive Social Security Disability Insurance to qualify for Medicare would improve access to healthcare services. Other options include expanding insurance coverage through subsidized high-risk pools and implementing insurance reforms that decrease barriers such as refusing or limiting coverage because of preexisting conditions.

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Moving Up
Successful Negotiation for the Position of Academic Chair

ABSTRACT

This article was written for the Academic Affairs Committee to help candidates for physical medicine and rehabilitation chair positions to effectively negotiate the new position. The article summarizes negotiation strategies provided from personal interviews and other communication via e-mail and phone with experienced physical medicine and rehabilitation chairpersons.

Key Words: Negotiate, Negotiation, Physical Medicine and Rehabilitation Chairperson, Academic Position

Negotiation has a history of mystique and misunderstanding. Many have referred to it as an art, whereas others have characterized it as just common sense. Nevertheless, professionals in the business world, and in the academic community, invest large amounts of time and money in mediation and negotiation consulting.

There is a growing body of knowledge about negotiation in business, including communication skills and conflict resolution strategies. Sometimes, the information is characterized as too simplistic, but the information has proven useful over and over and should be taken seriously if one is to be a successful negotiator. This article focuses on specific strategies for negotiating a position as an academic department chair.

NEGOTIATION PERSPECTIVE

One of the first steps of successful negotiation is the right attitude. Some individuals are wary of negotiation because they view it as a struggle or confrontation to win or lose. The following describes a more positive and objective approach.

Recruitment negotiation should be viewed as a cooperative enterprise, one in which both parties work together to reach a mutual agreement. When negotiation is completed there should be two winners—not a winner and loser! At the end of negotiation, individuals should feel they reached the best arrangement possible, made appropriate, fair decisions, and feel enthusiastic about the outcome.

During the negotiation process, it is important to establish a positive relationship with the Dean or Medical Director; however, the reality is that
academic environments, especially those in medicine, are highly competitive and demanding. Resources are becoming more limited. If your “wish list” is not addressed during the recruitment negotiation, the chances of acquiring these resources once the job has begun are slim to none. Deans recognize the need to support a new department Chairperson, but this need must be well organized and articulated to be effective. The competition for space, staff, research support, curriculum time, etc. is intense and ongoing. From the Dean’s perspective, support provided to a new Chairperson, as part of a recruitment package, may have to be taken away from another department or service.

Negotiation literature suggests that an appropriate perspective is “wanting” but “not too much.” The temptation is to let the enticement and excitement of a new position diminish mature, rational analysis. As one Chair interviewee warned, “Guard against an outcome of thinking you are taking ‘one job’ and then, once there, discovering it is an entirely different position.”

PREPARATION: THE GATHERING STAGE

When negotiation begins, it is wise to resist an attitude of, “I must show how important it is for this organization to offer me the position!” A more successful beginning can be achieved by investing the time to listen, read, and learn everything possible about the new culture. After acquiring in-depth information, it will then be feasible to develop a reasonable plan for bringing effective change to the organization. Knowledge provides power and negotiating leverage. The consistent advice from current Chairs: collect detailed, in-depth information about the new position!

The information gathering stage begins by requesting and reviewing documents. An important aspect of this search is to look for areas of weakness and areas of limited performance to which you can apply your expertise. Seek areas in which money is being lost, services are lacking, financial opportunities are being missed, and academic needs are neglected.

Following are examples of potentially useful information to request. The goal is to identify patterns, trends, opportunities, disparities, and concerns to factor into the negotiation process.

University

- Medical school mission
- Budgets of the total institution and other academic departments—current (and past 2 years if possible)
- Organizational chart—lines of authority/reporting relationships
- List of faculty and salaries (proportion of professors, associate/assistant professors, instructors)
- Promotion/tenure policies
- Grants (sources, amount/duration, number of funded investigators, management of indirects, availability of intramural 'seed' money for start-up projects)
- Political structure of departments, frequency of secondary appointments in other departments, frequency/nature of interdepartmental collaboration
- Committee structure—physical medicine and rehabilitation (PM&R) faculty representation
- Medical school curriculum structure—PM&R representation

Hospital

- Hospital budget—current and previous 2 years
- Organizational chart and reporting structure
- Strategic plan—PM&R role
- Department statistics—current and previous 2 years:
  - Number of inpatient PM&R beds, occupancy percentage, number of discharges per year, patient impairment groups, relative proportions (case mix)
  - Length of stay (overall and for major impairment groups)
  - Functional outcomes data—discharge percentage to community, change in FIM™ score, discharge FIM score, comparison with regional/national peers
  - Payor mix
  - Number of outpatient physician visits per clinic/month/year, number of work relative value units (RVUs), referral sources
  - Number of electromyographies, interventional procedures, etc.
- Staffing in Physical Therapy, Occupational Therapy, Speech/Language Pathology, Rehabilitation Psychology, Social Work/Case Management, Rehabilitation Nursing, Recreation Therapy, Vocational Counseling, etc.
- History of capital equipment funding
- History of philanthropic support
- Sources of all PM&R revenue

(Note: If there are multiple hospitals, you may need data from each hospital.)

PM&R Department

- Mission/strategic plan of the department (when last updated, what process/frequency to review and update)
• Strengths and weaknesses—ask for an internal review or annual reports from previous 2 years
• External reviews
• Department budget—current and previous 2 years, budget process/degree of input, capital equipment budget
• Resident roster—previous training institutions, number of internal medicine groups
• Residency Review Committee survey report, plan of correction/progress reports
• Affiliated institutions for resident training
• Faculty roster with areas of expertise/specialization, curriculum vitae, allotted teaching and research time
• Formulas for how faculty members are paid (salary, incentive payments, fee-for-service receipts, other)
• Fringe benefits—malpractice coverage, insurances, secretarial support, etc.
• Department research funding, space, equipment
• Formula for how department earns revenue—physician practice, electromyography, interventional procedures, therapy services (professional vs. technical vs. both)
• Who are the department’s allies and opponents?
• What are obstacles to success?

Preparing for successful negotiation is difficult because the responsibility of gathering and carefully analyzing the necessary information falls on your shoulders. The hospital or academic department will provide standard information and promotional materials, but it will be your inquiries that produce the critical in-depth information to formulate an accurate perspective of the opportunities and challenges of this new position.

A relatively new chairperson lamented that, “You don’t know what you don’t know,” which makes the information gathering even more difficult. Negotiation literature suggests that the more successful negotiators asked twice the number of questions and spent over twice the amount of time acquiring and clarifying information.2

Patience is required. Approach the information gathering much like a reviewer determining the validity of a research paper, a problem solver taking on a complex question, or a detective digging up facts to solve a mystery. As you analyze the information, keep a running list of questions.

PERSONAL KNOWLEDGE

A critical aspect of preparation is to know yourself and your family needs. If driving more than 15 miles to work is a deal breaker, do not start negotiating with an institution where location is a barrier. Before any negotiation, talk to your family about lifestyle, schools, spousal needs, etc. You should have already had a “heart-to-heart” talk with your significant other about what he or she wants and about what the family needs to be happy. It is surprising how many times a chair candidate sees an opportunity and jumps into the fray without seriously including family members. The deal eventually falls apart because these diverging perspectives and expectations were never merged.

Ask yourself important questions such as: What do I want to be doing 5 to 10 years from now? Is the opportunity a short-term or long-term option? Is it an endpoint or a step in the career ladder? Financially, what do I require to be satisfied with my compensation, and how does it compare with the living standards in my current location? What are my family needs in terms of schools, cultural opportunities, ethnic considerations, recreational activities, etc.? Will my family fit in socially?

INSTITUTIONAL INTERVIEW

While in the interview phase, ask to speak with people at different levels of authority, not just the top leadership. Explore the attitudes of people already working in this culture—are they happy, bored, overworked, appropriately challenged, etc.? Make it a point to gather multiple perspectives by talking with faculty members, allied health professionals, residents, and support staff.

You cannot begin to think about negotiating until armed with knowledge covering a wide range of data—financial, human resource, formal and informal authority, chain of command, etc. Does the institution have a strategic plan in place, and if so, what are the goals for the next 5 to 10 years? What will be expected of you, and can you realistically meet these expectations?

During interviews ask questions and listen to the answers. Where is the real power and authority? Which services would be under your authority; which would not? Can any of this be changed? Are personnel changes necessary? Are additional faculty or staff members needed? These are just some of the questions with which to begin.

One very important part of negotiating is matching your “internal world” with the “real world.” Be cautious of making faulty assumptions. For example, a female student at Columbia University directed a man coming into the Department to a back room scheduled for painting because the gentleman was dressed from head to toe in white-cotton shirt, pants, and white tennis shoes. In reality, he was a faculty member who was highly allergic to fabric dyes and always dressed in white cotton; he was not the painter.

We often make hasty judgments based on
little data. The common pitfall is to make a decision or give a response based on incomplete information, which is later shown to be inaccurate. The term “inference ladder” is used to describe the process of observing, comparing that information with what we think we know, running that through our experience filters, and then acting on that inference.3

The bottom line is not to jump too quickly to make assumptions or wrong inferences. Fact is different from speculation, or rumor; figures in documents are frequently different from those supplied verbally. All individuals have agendas, and often, they are related to self-preservation and turf protection. If you are interviewing for a leadership position, there may be others in that professional community who have reason to be concerned, intimidated, or threatened. Be alert to stated and potentially hidden agendas.

During face-to-face interviews, listening is a major challenge. Research indicates that the average physician interrupts after 30 seconds of listening. Because we can think faster than we can talk, the temptation is to think about what we will say next instead of listening to what the other person is saying.4

The words someone chooses are significant, as are the tone and volume of voice and the emotional content. “Active listening” that allows you to come away with a true understanding of the intended message is a challenging task.1 Taking notes while listening can be helpful. It is sometimes useful to rephrase and repeat back the perceived content of the message to check on the accuracy of your understanding. This helps to ensure the correct understanding of the other person’s message before conveying your own thoughts. People feel respected when their messages “are heard,” and they tend to listen more carefully in return.

It is commonly known that two thirds of a message is delivered through nonverbal communication, which may be sending a different message than what is being delivered verbally. Communication experts say that “every movement has meaning.” Be sensitive to small facial, hand, and body movements of individuals with whom you interact. They will be sending you messages in many different ways. Don’t miss the valuable information. Signals are sent—interpretation occurs—learning results. By the same token, your body language and verbal messages should be congruent to ensure accurate communication delivery.

Satisfaction of needs still drives human behavior and was spelled out by Abraham Maslow in his book Motivation and Personality published in 1954.5 These needs still are regarded as the basic motivation for human behavior and move up a scale from the most basic (physical survival) to the most advanced (self-actualization).

Need theorists suggest that most people dread boredom, fear the unknown, and dislike disorder. The hiring of a new chairperson will change the status quo and cause individuals inside and outside the department to be concerned about the effect on their needs. A clear understanding of the perceptions of both sides and the existing needs is imperative to successful negotiation. Something as apparently simple as losing morning breaks to something as significant as modifying the faculty compensation schedule can create major concerns.

The more strategies and flexibility a negotiator has at his or her disposal to adapt to differing agendas and personality styles, the more successful the negotiation. Rigidity and negotiation do not fit well together.

**FOLLOW-UP TO THE INITIAL INTERVIEWS**

As follow-up to the interviewing process, write the appropriate thank you letters. When writing to the University/Hospital, clearly state your requests. The requests should be reasonable, feasible, and justifiable for what will be required to meet the needs of the PM&R department and the expectations of the institution. Put everything in writing. One successful Chair reported that he submitted an initial 20-page document to the institution. Do not be afraid to ask for what you want and need. It is a usual negotiation tactic to ask for more than it might be possible to obtain.

PM&R Chairpersons strongly cautioned, however, against building on requests—first asking for one thing, and then asking for more. The consistent advice was to present a complete wish list with a rationale to accompany each item on the list. Issues might include having enough faculty, having a full-time researcher, terminating certain employees, acquiring research laboratory space, etc. Request examples: “All therapies should report to the PM&R Chair because. . .”; “I am requesting dollars for an Electromyography lab because. . .”; “I am requesting dollars for an Electromyography lab because. . .”

Consider what you want to “sell” to the Dean. Does the institution emphasize research productivity, or maximizing patient care revenues, or is the priority to fix a therapy management problem? Ask yourself what you bring to the table for the dollars you will be making? Be sensitive to the potential for conflicting agendas between the hospital, university, and affiliates.

One Chairperson interviewee commented that being a successful department chair is all about that “vision thing” and noted that his Dean is looking for a leader who has vision and a sense of mission, not just a manager (although man-
REACHING THE GOAL

Complete the negotiation process by acknowledging the positive aspects of the institution/department. Begin with a confirmation of the items to which you have already mutually agreed. Gradually move to items that are not being offered but are important to you. Remember to link requests to how the institution will be benefited. Work your way to the smaller, more personal issues, such as meeting/travel allowance, parking space, etc.

Do not be confrontational during the process, but do maintain an objective detachment, while still displaying emotional warmth. Do not neglect to ask questions about sensitive areas, for example, “How did a particular situation happen or become structured in a certain way?” Give the other person an opportunity to put information into a context. Sometimes what seems to be a harmless question has emotional overtones of which you are unaware.

For example, an inquiry about why electromyography is in another department rather than PM&R could produce an angry response about previous battles lost or won. If a particularly sensitive area is uncovered it might be best to leave that topic and return to it at a later time. A better understanding of such issues could provide insight into denied requests.

Be careful not to speak negatively about previous professional experiences. You may share an unflattering story about someone and find out that the individual is a personal friend or relative of the Dean. It has happened! Put comments in as positive perspective as possible. No one wants to employ a “black cloud.” Remember also that it is possible to demonstrate decisiveness and confidence without appearing arrogant.

Allow appropriate time for deliberation after the initial negotiation; do not give an immediate answer. Take time to step away from the visit, discuss with significant others, and let the emotional aspects of the visit cool. If, at the end of your first round of interviews, there is pressure to make a decision, politely state that you are not quite ready to make a decision and agree to talk again in 2 to 4 weeks. It is important to send a follow-up letter that includes your understanding of items on which agreement was reached. Mention issues that are still a concern. Group Negotiating Items into Three Categories: Major items—must agree; Important items—compromise possible; Would like but not crucial—can give up if necessary.

Be aware of the potential for explicit trade-offs involving differences in preferences and relative values. For example, one of your highest priorities might be establishing a pool of seed funding for young faculty investigators, but you have no strong preference for adding curriculum time for PM&R in the medical school. On the other hand, the Dean’s agenda is for faculty to teach musculoskeletal anatomy and functional correlation. Your research revealed that the Dean has an endowment fund to support intramural research funding. A tradeoff might be to commit your faculty to teach medical students (which helps increase awareness of PM&R) in return for the Dean’s commitment of research seed funding for your faculty. The outcome is a “win–win.”

An important negotiation tactic is to make a concession in return for receiving one of comparable value. If there is an impasse, the best strategy may be to do nothing. Waiting to see how much the institution is willing to step up to meet your requests often brings the best response and provides clues as to your relative strength in negotiating. It is important, however, not to play games. For instance, do not request what you know to be unrealistic for either you or the institution.

The more time invested in negotiation, the more serious you should be about taking the position. Do not extend the negotiation process to “buy time,” use as leverage for negotiation somewhere else, or for window shopping. It raises ethical questions about you personally and places PM&R generally in a negative light. Remember that medical leadership in general and PM&R leadership in particular are relatively small worlds in which reputations become quickly known (positive and negative).
THE FINAL AGREEMENT

Once you reach an agreement—PUT EVERYTHING IN WRITING. Items promised over the phone or in a conversation frequently have a way of never getting written down on paper, and they then risk becoming a source of conflict or disappointment later. Keep a list of what has been agreed to and check off as you find in the contract.

Always have an attorney review the contract for appropriate legal language and to safeguard your best interests. This is well worth the financial investment.

Remember that you are trying to (and need to) build a relationship with the Dean and the hospital’s Vice President for Medical Affairs. If the negotiation is too contentious or laborious, you will lose in the long run.

Professional Items Typically Negotiated May Include:

- Department budget, including capital equipment funding (equipment costing more than $1000)
- Formula for department revenue
- Dean’s expectation for the program
- Research support (including seed funds for new investigators)
- Staff support (especially secretarial staffing for physicians)
- Number of faculty (ability to recruit new faculty)
- Tenure possibility
- Research laboratory, library, and conference room space
- Residency Program Coordinator
- Program payback to the Dean’s Office (“Dean’s tax,” faculty time/effort for medical school teaching)
- Departmental resources you wish to control—physical therapy, occupational therapy, electromyography, etc.
- Hospital beds—number of dedicated beds, layout/staffing/equipment for the rehabilitation unit
- Outpatient space—amount, location, staffing/equipment

Personal Items Chairpersons Have Negotiated in Contracts:

- Start date
- Allowance or direct payment for relocation expenses
- Vacation days—typically 3–4 weeks per year
- Professional meetings—support for registration, travel, etc.
- Continued medical education opportunities—seminars, workshops
- Clinical vs. administrative time
- Release time for research or teaching
- Fees for joining professional organizations
- Parking
- Office space—location, type of furniture
- Secretarial or administrative assistant support
- Book, journal allowance
- Items such as laptop computer, handheld computer, cell phone, etc.
- Service on medical school committees

IF I COULD DO IT AGAIN

Chairpersons commented that in retrospect they might have been more assertive in requesting personal benefits such as tuition breaks for children. One interviewee commented that obtaining university commitment for an internal review of the PM&R department would have been most helpful in setting expectations for the next 2 to 4 years. Others commented that making major critical changes, (e.g., modifying faculty compensation schedules) would have been easier and more effective if the decision had been made before arrival.

Chairpersons noted that mentoring by colleagues was helpful. An old Chinese proverb says, “If you want to know what to expect on the road ahead, ask someone who has just come back.” Mentors and trusting collegial relationships are invaluable; however, be careful to confide in those who you know have your best interests at heart and are trustworthy with confidential information.

An additional Chair recommendation was to attend a training course for medical administration/medical management (such as the Harvard Course for Clinical Chairs, the Physician Executive Curriculum offered by the American College of Physician Executives) or participate in an MBA (Masters in Business Administration), MHA (Masters in Healthcare Administration), or MMM (Masters in Medical Management) program.

Cliff Notes on Success

As a conclusion, Chairpersons recommended the following for success: 1. Initiate and maintain communication top to bottom. 2. Initiate strategies to gain support of faculty and staff. 3. Demonstrate moral authority/role model—live what you say. 4. Be cautious about the agendas of others. 5. Keep enemies close at hand. 6. Strive for win–win outcomes. 7. Maintain balance between work and life (professional/family/personal needs).

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How to Assess the Reliability of Measurements in Rehabilitation

ABSTRACT


To evaluate the effects of rehabilitation interventions, we need reliable measurements. The measurements should also be sufficiently sensitive to enable the detection of clinically important changes. In recent years, the assessment of reliability in clinical practice and medical research has developed from the use of correlation coefficients to a comprehensive set of statistical methods. In this review, we present methods that can be used to assess reliability and describe how data from reliability analyses can aid the interpretation of results from rehabilitation interventions.

Key Words: Reference Values, Reproducibility of Results, Research Design, Statistics

In rehabilitation, measurements are obtained for clinical practice and research purposes. To be clinically and scientifically useful, measurements must be reliable. Reliability refers to the reproducibility of measurements. Measurements are reliable if they are stable over time and show adequate levels of measurement variability. They must also be sufficiently sensitive to detect clinically important changes after rehabilitation interventions. The more sensitive your measurement, the easier it is to detect improvements after interventions or deterioration over time.

Reliability in clinical practice and medical research is most commonly determined from measurements of the same subjects on two occasions: so-called retest reliability. By applying well-defined statistical methods, physiatrists and clinical scientists can determine whether measurements are sufficiently reliable for a particular purpose. In recent years, there has been a growing interest in the statistical methods for the assessment of reliability in clinical practice and medical research. Today, there is general agreement that a comprehensive set of statistical methods is required to address the reliability of measurements.

In this review, we present the statistical methods that are part of the current approach to the assessment of retest reliability based on continuous data and illustrate them using measurements of isokinetic muscle strength. We also describe how data from reliability analyses can aid the interpretation of results from rehabilitation interventions and the detection of clinically important changes. In the Appendix, we present the equations that are used to calculate reliability. This provides physiatrists and clinical scientists with a
source of reference for the determination of the characteristics of measurements and how to interpret data obtained from rehabilitation interventions.

RETEST CORRELATION COEFFICIENTS

The most common approach in the assessment of retest reliability is to measure a group of subjects on two occasions, separated by hours or days. This is done on the same type of subjects or patients who one wants to use in an intervention. Once the data are obtained, the first step is to plot the data. In Figure 1, data on concentric ankle dorsiflexor muscle strength at 30 degrees/sec obtained from 30 healthy young men and women at two test occasions 7 days apart are presented. The data come from a larger study in which we evaluated the reliability of peak torque, work, and torque at a specific time at different angular velocities using the Biodex dynamometer.5

Clearly, the closer the values are to a straight line, the better is the reliability. The usual Pearson’s correlation coefficient (Pearson’s $r$) can be used to quantify the reliability. The value of Pearson’s $r$ is here 0.91; as a value of 1.00 represents perfect agreement and a value of 0.00 no agreement, we can already at this stage presume that our measurements are highly reliable.

The intraclass correlation coefficient (ICC) is nowadays the preferred retest correlation coefficient.9 The ICC has several advantages: for example, it can be used with small samples and with data from more than two test occasions. There are different types of ICCs available for different study designs, but in practice, their values are often very similar.5,10 The ICC2,1 (Equation 1, Appendix), which is calculated from a two-way repeated-measures analysis of variance, covers most situations and also has the advantage that it provides the basis for the calculations of some of the other reliability indices. (Reliability can also be determined for ordinal data obtained from, for example, clinical rating scales. The equivalent to a correlation coefficient is then the kappa coefficient.11)

The data plotted in Figure 1 were analyzed using a two-way analysis of variance, and the values from the analysis of variance table were substituted into Equation 1. The value of ICC2,1 is 0.915, which is very close to the Pearson’s $r$. This is often the case when measurements of the same subjects on two occasions are analyzed.5

How do we then interpret the values of ICC? As a matter of fact, no generally agreed ICC “cut-off” points exist. In their original publication from 1979, Shrout and Fleiss9 suggested that specific values of ICC could be considered to represent “acceptable,” “good,” and “fair” reliability. Fleiss12 later recommended that ICC values of $>0.75$ represent “excellent reliability” and values between 0.4 and 0.75 represent “fair to good reliability.”

It is becoming clear that the use of only ICCs for the analyses of reliability is not sufficient.3,4,7,8 The ICC can give misleading results—for example, if the sample is homogeneous, the value of ICC (and Pearson’s $r$) may be low. We should therefore avoid assessing reliability just from retest correlations and also avoid using global terms, such as “good reliability,” and instead interpret reliability from several statistical methods.

CHANGES IN THE MEAN

The next step in the reliability analysis is to calculate changes in the mean from the measurements obtained from the two test occasions. The change in the mean values between two test occasions can consist of two components: a random change and a systematic change. A random change is often referred to as the “sampling error” and comes from the variability in the actual test situation. It can be due to the variability in the equipment or method used and to the inherent biological variability. A systematic change is a nonrandom change in the mean values between the two test occasions. This occurs if the subject or patient systematically performs better (or worse) on the second test occasion as a result of, for example, a change in behavior, a learning effect, or fatigue if performance is measured.

To detect a systematic change, several indices

FIGURE 1

To illustrate the analysis of reliability, measurements of concentric ankle dorsiflexor muscle strength at 30 degrees/sec are used. The data were obtained from 30 healthy young men and women at two test occasions 7 days apart.5
can be calculated (Equations 2–4). Based on these calculations, a 95% confidence interval for the mean difference between the two test occasions can be formed (Equation 5). This will allow you to determine if there is a true systematic difference between the two test occasions. If the mean value is positive or negative, the measurements from one test occasion tend to be larger or smaller than those from the other occasion. When the 95% confidence interval does not include zero, this indicates a systematic change in the mean, for example, due to a significant learning effect. If this happens, one should choose tests or equipment that minimize this learning effect or let the subjects familiarize themselves before the real trials. This is less of a problem in a controlled study if both groups are equally affected by systematic changes in the mean.

Using the data from Figure 1, the indices representing the changes in the mean are calculated from Equations 2–5 and are presented in Table 1. The mean difference between the two test occasions is here positive (test occasion 2 minus 1), indicating that the isokinetic muscle strength at the second test occasion tended to be larger than at the first occasion. However, as zero is well within the 95% confidence interval, there is no significant change in the mean muscle strength between the two test occasions, and we can therefore conclude that there is no systematic change between the two test occasions.

The next step is then to present the data graphically in so-called Bland–Altman plots. In these plots, the differences between measurements from the two test occasions are plotted against the mean of the two test occasions for each subject, and any systematic bias or outliers can be seen. The Bland–Altman plot for the data in Figure 1 is presented in Figure 2; the mean difference in muscle strength between the two test occasions (test occasion 2 minus 1) and the 95% confidence interval are also included. It is clearly seen that the mean difference is close to zero, that zero is included in the 95% confidence interval, and that there are no apparent systematic biases or outliers in the data.

### MEASUREMENT VARIABILITY

Once we have established if there are any systematic changes in the mean, we want to quantify the actual size of the variability between the measurements obtained from the two test occasions. This is often referred to as the “within-subject variation,” “typical error,” or “typical variation” and is one of the more important reliability indices. Quite naturally, a change after any intervention will be easier to detect if we have established that the variability between measurements from two test occasions is small.

A simple index of the measurement variability is the standard deviation of the differences between the two test occasions (SD_{diff}) (Equation 3). Dividing the SD_{diff} by \sqrt{2} yields the “method error” (ME) (Equation 6). An alternative index is the “standard error of measurement” (SEM). There are different ways to calculate SEM; a preferred way is to take the square root of the mean square error term (WMS) from the analysis of variance (Equation 7). If the sample size is sufficiently large and the mean difference small, both highly likely conditions, ME and SEM take similar values. These values are, on their own, not easily interpreted because we do not know how much of the variability comes from the change in the mean and how much is due to the typical variation.

This can be overcome by expressing the measurement variability as a coefficient of variation. The ME or the SEM is then divided by the mean of

| Mean difference between two test occasions (d) | 0.03 |
| Standard deviation of the differences between two test occasions (SD_{diff}) | 2.88 |
| Standard error of d (SE) | 0.53 |
| 95% confidence interval of d (95% CI) | −1.04 to 1.10 |

**TABLE 1. Indices of changes in the mean between two test occasions**
all the measurements and multiplied by 100 to give a percentage value. These indices—the CV% (Equation 8) and the SEM% (Equation 9)—are independent of the units of measurements and are therefore more easily interpreted. The CV% and SEM% indicate the typical variation expressed as a percentage value and can be used to interpret the results of an improvement after an intervention.

Substituting the data from Figure 1 into Equations 6–9, we can calculate the values of ME, SEM, CV%, and SEM%. As can be seen in Table 2, ME and SEM and CV% and SEM% are very similar. We can then determine that with a CV% of 6.36 and a mean isokinetic muscle strength of 31.9 Nm (based on the data in Fig. 1), the average person’s muscle strength has a typical variation from one test occasion to the other of 2.03 Nm. An improvement after an intervention that is smaller than the typical variation does not, in most situations, indicate a clinically important improvement.

CLINICALLY IMPORTANT CHANGES

To evaluate more specifically if a measurement represents a clinically important change, we can use the data from the two test occasions to calculate an interval, which represents the 95% likely range for the difference between a subject’s measurements from these two test occasions. This is a form of “reference range” that can be used to determine if differences between measurements subsequently obtained before and after “real” interventions represent clinically important changes. If the difference for a subject or patient is outside (or within) this reference range, it does (or does not) represent a clinically important change. It is clear that the smaller the reference range, the more sensitive are the measurements, and also that the measurements can be considered highly reliable, but the reference range is too wide to be clinically or scientifically useful.

The “smallest real difference” (SRD), introduced by Beckerman et al. is one way to evaluate clinically important changes. The SRD is similar to the “limits of agreement” proposed by Bland and Altman. The SRD (Equation 10) is formed by taking the measurement variability, represented by the SEM, and multiplying it by \(\sqrt{2}\) and by 1.96 to include 95% of the observations of the difference between the two measurements. To obtain a reference range or “error band” around the mean difference of the measurements from the two test occasions, a 95% SRD can be calculated (Equation 11). The SRD is then divided by the mean of all the measurements and multiplied by 100 to give a percentage value, the SRD% (Equation 12). The SRD%, like the SEM% and CV%, is independent of the units of measurements and therefore more easily interpreted.

To form practically useful 95% SRD and SRD%, a fairly large sample size is required. This brings us to the question of how many subjects or patients you need to determine the reliability of a measurement. In comparison with clinical trials, sample sizes have received little attention in the reliability literature. Some scientists have recommended specific sample sizes, but these recommendations are usually based on practical experience. A sample size of 15–20 is often used in reliability studies with continuous data. Larger sample sizes, 30–50, have been suggested more recently and would be required to form practically useful 95% SRD and SRD%.

The values of SRD, 95% SRD, and SRD% are then calculated from Equations 10–12 using the data from Figure 1 and are presented in Table 3. The SRD% is 18.1, which indicates that a measurement should exceed that value to indicate a clinically important change. Taking the mean value of the isokinetic muscle strength in Figure 1 (31.9 Nm), this has to change 5.7 Nm to indicate a clinically important improvement in strength.

Having done all this, one should remember that there is an essential difference between the reliability indices described here and clinically important changes. The reliability indices describe the clinometric property of a measurement, whereas clinically important changes are more arbitrarily chosen values that physiatrists and clinical scientists judge as minimally (and clinically) important. An interesting area for future research is to explore the clinometric property of measurements and how that corresponds to what physiatrists and clinical scientists judge as clinically important. Such research will help us to define optimal outcome measures for clinical practice and research purposes.

<table>
<thead>
<tr>
<th>TABLE 2. Indices of measurement variability</th>
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<tbody>
<tr>
<td>Method error (ME)</td>
</tr>
<tr>
<td>Standard error of the measurement (SEM)</td>
</tr>
<tr>
<td>Coefficient of variation (CV)</td>
</tr>
<tr>
<td>Standard error of the measurement (SEM)</td>
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</tbody>
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<table>
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<tr>
<th>TABLE 3. Indices of clinically important changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smallest real difference (SRD)</td>
</tr>
<tr>
<td>Smallest real difference (95% SRD)</td>
</tr>
<tr>
<td>Smallest real difference (SRD%)</td>
</tr>
</tbody>
</table>
APPENDIX

Repeatability to Repeatability Coefficients

The intraclass correlation coefficient (ICC2,1) for \( n \) subjects and for two test occasions is defined by

\[
\text{ICC2,1} = \frac{(\text{BMS} - \text{EMS})}{(\text{BMS} + \text{EMS} + 2[\text{JMS} - \text{EMS}]/n)}
\]

where BMS is the between-subjects mean square, EMS is the residual mean square, JMS is the within-subjects mean square, all obtained from the two-way analysis of variance, and \( n \) is the number of subjects.

Changes in the Mean

To evaluate changes in the mean between two test occasions, \( \bar{d} \) is defined by

\[
\bar{d} = \text{the mean difference between the two test occasions}
\]

The variation about \( \bar{d} \) is assessed by

\[
\text{SD}_{\text{diff}} = \text{the standard deviation of the differences}
\]

The variation of \( \bar{d} \) is assessed by the standard error of the mean (SE)

\[
\text{SE} = \text{SD}_{\text{diff}}/\sqrt{n}
\]

where \( n \) is the number of subjects. SD_{diff} represents the variability of the differences between the two test occasions and SE represents the precision of \( \bar{d} \) as an estimate of the underlying change in the mean. An approximate 95% confidence interval (95% CI) of the mean difference \( (\bar{d}) \) between the two test occasions is defined by

\[
95\% \text{ CI} = \bar{d} \pm 2 \times \text{SE}
\]

The multiplier of SE in Equation 5 depends on the number of subjects, \( n \); 2 is a good approximation when \( n \) is \( > 20 \). For the data in Figure 1, it should be 2.045, which is obtained from the t-table with 29 \( (n - 1) \) degrees of freedom.

Measurement Variability

The method error (ME) is defined by

\[
\text{ME} = \text{SD}_{\text{diff}}/\sqrt{2}
\]

where SD_{diff} comes from Equation 3.

The standard error of measurement (SEM) is defined by

\[
\text{SEM} = \sqrt{\text{WMS}}
\]

where WMS is the mean square error term from the analysis of variance.

The coefficient of variation (CV\%) is defined by

\[
\text{CV\%} = \left( \frac{\text{ME}}{\text{mean}} \right) \times 100
\]

The SEM% is defined by

\[
\text{SEM\%} = \left( \frac{\text{SEM}}{\text{mean}} \right) \times 100
\]

where mean in Equations 8 and 9 is the mean of all the data from the two test occasions.

Clinically Important Changes

The smallest real difference (SRD) is defined by

\[
\text{SRD} = 1.96 \times \text{SEM} \times \sqrt{2}
\]

The 95% SRD is defined by

\[
95\% \text{ SRD} = \bar{d} \pm \text{SRD}
\]

The SRD% is defined by

\[
\text{SRD\%} = \left( \frac{\text{SRD}}{\text{mean}} \right) \times 100
\]

where mean in Equation 12 is the mean of all the data from the two test occasions.

References

LETTERTOTHEEDITOR

PREGABALIN ASSOCIATED ASTERIXIS

To the Editor: We read with great interest the article of Babiy et al.1 on asterixis (negative myoclonus) related to gabapentin as a cause of falls. The authors present an important observation on a presumably underestimated pharmacologic side effect of gabapentin. In addition, they succeeded splendidly in giving a comprehensive overview on the topic of falls and positive and negative myocloni. From the literature, it is well known that gabapentin can cause a number of neurological side effects, such as dizziness, ataxia, and sleepiness, which are often dose-dependent and mostly transient.2 However, pronounced positive myocloni,3,4 movement disorders such as oculogyric crisis,5 dystonia,6 chorea (our own unpublished observations), or even asterixis, as described by the authors,7 often lead to discontinuation and failure of treatment. Recently, pregabalin was introduced as a new GABA-ergic drug in clinical practice with similar indications as gabapentin for the treatment of epilepsy and neuropathic pain.7,8

We recently cared for a 89-yr-old woman who developed severe asterixis after intake of 150 mg of pregabalin twice daily for the treatment of postherpetic pain. Clinically, she showed prominent negative myoclonus in all her limbs, which was slightly stronger in the upper limbs. The asterixis severely impaired her standing and walking and also led to recurrent falls, necessitating hospitalization. Other causes for asterixis such as metabolic disorders, focal brain lesions, and inflammation were excluded by laboratory tests, cerebrospinal fluid analysis, and computerized tomography. The patient’s co-medication included 10 mg of ramipril, 10 mg of torasemid, and 20 mg of omeprazole, which were unchanged within the preceding months and prescribed for arterial hypertension and erosive gastritis. Discontinuation of pregabalin led to rapid improvement of the asterixis. Two days later, the patient was able to stand and walk without support and regained self-dependency in activities of daily life. Pain management was continued with opioids (tramadol) and metamizol.

Considering that, pharmacologically, pregabalin acts similarly to gabapentin, comparable side effects of both drugs can be expected. Thus, pregabalin-related positive myoclonus has been observed9 but hitherto not asterixis (negative myoclonus). Unfortunately, in our patient, diagnosis of asterixis was based on clinical observation only. Neither electromyographic nor electroencephalographic recording could be performed in our patient because clinical symptoms resolved rapidly after discontinuation of pregabalin. However, despite the lack of an electroencephalographic recording, it is highly unlikely that the asterixis was due to an epileptic seizure because mental function was not impaired at any time. This assumption is further supported by our observation of a rapid recovery after discontinuation of pregabalin as the single therapeutic intervention. Other frequent causes of metabolic disorders provoking myocloni were excluded with high certainty. Thus, we strongly assume an association between the asterixis and the intake of pregabalin in our patient. Recently, a similar case report describes ataxia, generalized myocloni in combination with hand dystonia, and agitation during pregabalin therapy.10 Thus, side effects of pregabalin might cover a broader spectrum of neurological signs and symptoms than previously known. Myocloni in general have been described after the intake of gabapentin, lamotrigine, carbamazepine, oxcarbazepine, and now pregabalin. We therefore speculate that a common mechanism (e.g., electrical changes at the cerebral cell membranes with dysbalance of action potentials and transmitters) might be involved in the pathogenesis of drug-related myocloni.11,12

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REFERENCES

Shoulder Mass and Pain in a Patient with C5 American Spinal Injury Association Grade A Tetraplegia

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A 25-yr-old man with a C5 American Spinal Injury Association grade A spinal cord injury secondary to a diving accident 2 yrs previously presented for evaluation of a right scapular mass that had been increasing in size for the previous 9 mos. He reported vague pain of his right shoulder initially, but he did not seek medical attention until he noticed the mass. He complained of pain on deep palpation and shooting pain from the left shoulder to the right arm. He had no other associated symptoms.

On physical examination, the patient was noted to have a 10 × 10 cm mass, which was nonfluctuant, firm, and nonmovable (Fig. 1). He had tenderness to deep palpation. Passive range of motion of the right glenohumeral joint was 0–90 degrees of abduction, 0–90 degrees of flexion, 0–45 degrees of extension, and 0–30 degrees of internal and external rotation.

Chest radiographs revealed a prominent soft-tissue density along the lateral aspect of the right side of the chest. A computed tomographic scan with intravenous contrast of his thorax revealed a right posterior chest wall mass measuring 10 cm in transverse diameter involving the transverse spinal, iliocostalis, longissimus thoracis, and the right rhomboid muscles, with no obvious bony destruction (Fig. 2).

A computed tomographically guided fine-needle aspiration biopsy revealed a spindled soft-tissue proliferation most consistent with extraabdominal fibromatosis, or desmoid tumor. The patient subsequently underwent surgical excision of the tumor, and pathologic analysis confirmed the presence of spindle cells with abundant rough endoplasmic reticulum in the cytoplasm and features consistent with myofibroblastic differentiation and desmoid tumor.

Extraabdominal fibromatosis, or desmoid tumor, is a benign fibrous proliferative tumor that characteristically grows into local surrounding structures. This tumor arises from the aponeurotic fascia of muscles and is found most commonly in adolescents and young adults. It has been reported to be associated with Gardner’s syndrome.

The tumor most commonly involves the shoulder and pelvic girdles and usually presents as a deep, firm, solitary mass. Pain is usually produced with palpation or with movement of the affected musculature or may be spontaneous with involvement of a contiguous nerve.

This visual vignette describes an extraabdominal fibromatosis in a patient with C5 American Spinal Injury Association grade A tetraplegia. Early detection might be challenging due to the patient’s baseline impairment in active motion. In the non–spinal-cord-injury population, impairment in active range of motion at the glenohumeral joint may precede the development of a perceptible mass, leading to early diagnosis and treatment. Although uncommon, it is therefore important to suspect a possible soft-tissue mass in a spinal-cord-injury patient presenting with vague shoulder pain and loss in passive range of motion.

REFERENCES


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