Examination of a Clinical Prediction Rule to Identify Patients With Neck Pain Likely to Benefit From Thoracic Spine Thrust Manipulation and a General Cervical Range of Motion Exercise: Multi-Center Randomized Clinical Trial

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Background. A clinical prediction rule (CPR) purported to identify patients with neck pain who are likely to respond to thoracic spine thrust manipulation has recently been developed, but has yet to be validated.

Objective. The purpose of this study was to examine the validity of this CPR.

Design. This was a multi-center randomized clinical trial.

Methods. One hundred forty patients with a primary report of neck pain were randomly assigned to receive either 5 sessions of stretching and strengthening exercise (exercise-only group) or 2 sessions of thoracic spine manipulation and cervical range of motion exercise followed by 3 sessions of stretching and strengthening exercise (manipulation + exercise group). Data on disability and pain were collected at baseline, 1 week, 4 weeks, and 6 months. The primary aim (treatment group × time × status on the prediction rule) was examined using a linear mixed model with repeated measures. Time, treatment group, and status on the rule, as well as all possible 2-way and 3-way interactions, were modeled as fixed effects, with disability (and pain) as the dependent variable. Effect sizes were calculated for both pain and disability at each follow-up period.

Results. There was no 3-way interaction for either disability or pain. A 2-way (group × time) interaction existed for both disability and pain. Pair-wise comparisons of disability demonstrated that significant differences existed at each follow-up period between the manipulation + exercise group and the exercise-only group. The patients who received manipulation exhibited lower pain scores at the 1-week follow-up period. The effect sizes were moderate for disability at each follow-up period and were moderate for pain at the 1-week follow-up.

Limitations. Different exercise approaches may have resulted in a different outcome.

Conclusions. The results of the current study did not support the validity of the previously developed CPR. However, the results demonstrated that patients with mechanical neck pain who received thoracic spine manipulation and exercise exhibited significantly greater improvements in disability at both the short- and long-term follow-up periods and in pain at the 1-week follow-up compared with patients who received exercise only.

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More than 50% of individuals typically will experience neck pain[1] at some point in their life, and the incidence of neck pain appears to be increasing.[2] The economic burden associated with the treatment of patients with neck pain is high, second only to low back pain (LBP) in annual workers' compensation costs in the United States.[3] Patients with neck pain frequently are encountered in outpatient physical therapist practice.[4] Recent evidence has begun to support the effectiveness of many interventions used by physical therapists for the management of neck pain.[5–11]

One intervention often used by physical therapists in the management of neck pain is thoracic spine manipulation. Based on low-quality evidence, a recent Cochrane review suggested that thoracic spine manipulation may be beneficial for reducing pain and improving function in patients with neck pain.[12] A recently published guideline for the management of patients with neck pain has recommended the use of thoracic spine thrust manipulation in the management of this population.[13] Finally, a recent meta-analysis reported that thoracic spine manipulation has been shown to be effective in reducing pain and improving function in subgroups of patients, but the included studies examined only short-term outcomes.[14]

Recently, a derivation study was conducted with a primary goal of developing a clinical prediction rule (CPR)[15] to identify the subgroup of patients with neck pain likely to benefit from thoracic spine thrust manipulation. In this derivation study, the researchers treated all patients with thoracic manipulation and a general range of motion (ROM) exercise and identified characteristics of patients who improved most while receiving treatment. These characteristics were used to define a preliminary prediction rule for identifying patients with neck pain most likely to benefit from thoracic spine thrust manipulation. A shortcoming of a derivation study with a single treatment arm is the inability to determine whether the subgroup identified in the study includes patients who will preferentially benefit from the treatment provided or patients who have a favorable prognosis regardless of treatment.[16] A controlled trial, therefore, is required to evaluate whether the subgroup identified by the CPR derived in the previous single-arm study included patients who preferentially benefited from thoracic manipulation or simply those with a favorable prognosis regardless of treatment.[17,18] The purpose of this randomized clinical trial was to examine the validity of the previously derived CPR.

Method

Patients with a primary report of neck pain seen in 1 of 5 physical therapy clinics across the United States (Concord Hospital, Concord, New Hampshire; Bellin Health, Green Bay, Wisconsin; University of Colorado, Aurora, Colorado; Wardenburg Health Center at the University of Colorado at Boulder, Boulder, Colorado; and Newton-Wellesley Hospital, Newton, Massachusetts) between July 2007 and December 2008 were screened for eligibility. The exact inclusion and exclusion criteria from the derivation study[15] were used to determine participant eligibility for this trial. For patients to be eligible to participate, they had to have a primary report of neck pain with or without unilateral upper-extremity symptoms, be between 18 and 60 years of age, and have a Neck Disability Index (NDI) score of at least 20%. Exclusion criteria included serious pathologies, diagnosis of cervical spinal stenosis (as identified in the patients' medical intake form) or bilateral upper-extremity symptoms, evidence of central nervous system involvement, 2 or more positive neurologic signs consistent with nerve root compression, pending legal action regarding their neck pain, or inability to adhere to the treatment and follow-up schedule. All patients provided informed consent prior to their enrollment in the study.

Examination Procedures

Prior to randomization, patients underwent a standardized history and physical examination that were identical to those of the derivation study.[15] Demographic information collected included age, sex, mechanism of injury, location and nature of the patient's symptoms, and the number of days since onset of symptoms. Specific details regarding the physical examination are published elsewhere[15] and included measures of muscle length and strength (force-generating capacity), ROM, and vertebral mobility and a thorough screening examination designed to identify any contraindications to thoracic spine manipulation (hyperreflexia, unsteadiness during walking, nystagmus, loss of visual acuity, impaired sensation of the face, altered taste, the presence of pathological reflexes).[15] Additionally, any serious pathologies or conditions (tumor, fracture, metabolic diseases, rheumatoid arthritis, osteoporosis, history of prolonged steroid use) identified on the patient's medical screening questionnaire were considered contraindications to treatment.

All patients completed several commonly used instruments to assess

pain and function. The NDI is the most widely used condition-specific disability scale for patients with neck pain and consists of 10 items addressing different aspects of function, each scored from 0 to 5, with a maximum score of 50 points.[19,20] The score then is doubled and interpreted as a percentage of the patient-perceived disability. Higher scores represent increased levels of disability. The NDI has been reported to be a reliable and valid outcome measure for patients with neck pain.[19,21–23]

An 11-point numeric pain rating scale (NPRS) was used to measure pain intensity. The scale is anchored on the left (score of 0) with the phrase "no pain" and on the right (score of 10) with the phrase "worst imaginable pain." Numeric pain rating scales have been shown to yield reliable and valid data.[24–29] Patients rated their current level of pain, as well as their worst and least amount of pain in the previous 24 hours. The average of the 3 ratings was used to represent the patient's level of pain.

The Fear-Avoidance Beliefs Questionnaire (FABQ) is a 16-item questionnaire designed to quantify fear and avoidance beliefs in patients with LBP.[30] The FABQ has 2 subscales: a 7-item scale to measure fear-avoidance beliefs about work (FABQW) and a 4-item scale to measure fear-avoidance beliefs about physical activity (FABQPA). Each item is scored from 0 to 6, with possible scores ranging from 0 to 24 for the FABQPA and from 0 to 42 for the FABQW and with higher scores representing increased fear-avoidance beliefs. For this study, the FABQ was modified by replacing the word "back" with the word "neck." Both the FABQPA and FABQW, also modified in this way, were originally identified in the derivation study as potential predictors associated with a positive response to thoracic spine thrust manipulation in a patient population with neck pain.[15]

Additionally, at each follow-up period, patients completed the 15-point Global Rating of Change (GROC) described by Jaeschke et al.[31] The scale ranges from −7 ("a very great deal worse") to 0 ("about the same") to +7 ("a very great deal better"). It has been reported that scores of +4 and +5 are indicative of moderate changes in patient-perceived status and that scores of +6 and +7 indicate large changes in patient status.[31] Similar to the study that originally derived the CPR,[15] patients who rated their perceived recovery on the GROC as "a very great deal better," "a great deal better," or "quite a bit better" (ie, a score of +5 or greater) at any of the follow-up periods were categorized as a success.

Randomization

Once the examination was complete, patients were randomly assigned to 1 of 2 groups: (1) patients who received thoracic spine manipulation and an exercise program (manipulation + exercise group) or (2) patients who received a stretching and strengthening exercise program (exercise-only group). Concealed allocation was performed by an individual not involved in data collection using a computer-generated randomized table of numbers created for each participating site prior to the beginning of the study. Individual, sequentially numbered index cards with the random assignment were prepared. The index cards were folded and placed in sealed, opaque envelopes.

Treating Therapists

Ten physical therapists with a mean of 8.7 years (SD=6.9, range=1–21) of clinical experience participated in the recruitment, examination, and treatment of all patients in this study. All therapists underwent a standardized training regimen, which included studying a manual of standard procedures with the operational definitions of each examination and treatment procedure. Participating therapists underwent a 3-hour training session provided by one of the

The Bottom Line

What do we already know about this topic?

Thoracic spine manipulation appears to be beneficial in the short term for reducing pain and improving function in patients with mechanical neck pain. The authors have attempted to identify a subgroup of patients with neck pain most likely to benefit from thoracic spine manipulation.

What new information does this study offer?

The results suggest that, regardless of the patient's clinical presentation, those who received thoracic spine manipulation in addition to exercise had superior outcomes to those who received exercise only. This suggests that patients with mechanical neck pain and no contraindications to manual therapy may benefit from thoracic spine manipulation.

If you're a patient, what might these findings mean for you?

If you are experiencing neck pain, thoracic spine manipulation provided by a physical therapist may help in decreasing your level of disability.

investigators. Due to the nature of the interventions used in this study, therapists could not be blinded. However, individuals who collected all outcome measures were blinded to group assignment. Both treating clinicians and outcome assessors were unaware of patients' status on the CPR.

Treatment Procedures

Patients in both groups attended physical therapy sessions twice weekly during the first week and then once weekly for the next 3 weeks, for a total of 5 sessions over a 4-week period.

Exercise-only group. This group was treated with a stretching and strengthening program. Recent guidelines and reviews have supported the use of exercise to decrease pain, improve function, and reduce disability in a patient population with neck pain.[32,33] At each session, the physical therapist manually stretched the patient's upper trapezius, scalene, sternocleidomastoid, levator scapulae, and pectoralis major and minor muscles. Each stretch was held for 30 seconds and repeated twice.

Strengthening exercises included deep neck flexor training, cervical isometrics, and middle and lower trapezius and serratus anterior muscle exercises. Each exercise was performed for 10 repetitions, with a goal of a 10-second hold. A detailed description of the strengthening and flexibility program used in this study is available elsewhere.[34] Patients in the exercise group were instructed to perform the strengthening and flexibility exercises as a home program once daily. Patients also were advised to maintain their usual activity level within the limits of pain. Advice to maintain usual activity has been found to assist in the recovery from neck pain.[32,33] Patients were instructed to perform all activities that did not increase symptoms and to avoid activities that aggravated symptoms.

Manipulation + exercise group. The treatment received by the manipulation + exercise group differed from that of the exercise-only group for the first week only (2 treatment sessions). Beginning in the third session, these patients received the same treatment program outlined above for the exercise group (visits 3–5).

During the first 2 sessions, patients in the manipulation + exercise group received thoracic spine thrust manipulations and a ROM exercise only. All patients received 3 different thoracic spine thrust manipulations that were identical to those used in the derivation study.[15] We will use the model for describing thrust manipulations as recently proposed by Mintken et al[35]:

1. A high-velocity, midrange, distraction force to the midthoracic spine on the lower thoracic spine in a sitting position. The therapist placed his or her upper chest at the level of the patient's middle thoracic spine and grasped the patient's elbows. A high-velocity distraction thrust was performed in an upward direction.

2. A high-velocity, end-range, anterior-posterior force applied through the elbows to the upper thoracic spine on the midthoracic spine in cervicothoracic flexion. This technique was performed with the patient positioned supine. The therapist used his or her manipulative hand to stabilize the inferior vertebra of the motion segment targeted and used his or her body to push down through the patient's arms to perform a high-velocity, low-amplitude thrust.

3. A high-velocity, end-range, anterior-posterior force applied through the elbows to the middle thoracic spine on the lower thoracic spine in cervicothoracic flexion. This technique was performed with the patient positioned supine. The therapist used his or her manipulative hand to stabilize the inferior vertebra of the motion segment targeted and used his or her body to push down through the patient's arms to perform a high-velocity, low-amplitude thrust.

Following the manipulations, patients were given the same general cervical mobility exercise as in the derivation study. The following exercise was originally described by Erhard[36] as a general mobility exercise for patients with neck pain. To perform this exercise, each patient was instructed to place the fingers over the manubrium. The patient started with the chin on the fingers, then rotated to one side as far as possible and returned to neutral. This exercise was performed alternately to both sides within pain tolerance. The patient started using 5 fingers, then progressed to 4, 3, 2, and finally 1 finger as mobility improved. The patient was asked to perform this exercise for 10 repetitions to each side, 3 to 4 times per day, within pain tolerance, each day during participation in the study. Patients in this group also were advised to maintain usual activities that did not increase symptoms and to avoid all activities that exacerbated their symptoms.

At the third treatment session, patients in the manipulation + exercise group began the exercise program listed above for the exercise-only group. Patients were treated twice a week for the first week and then once a week for the next 3 weeks, for a total of 5 therapy sessions.

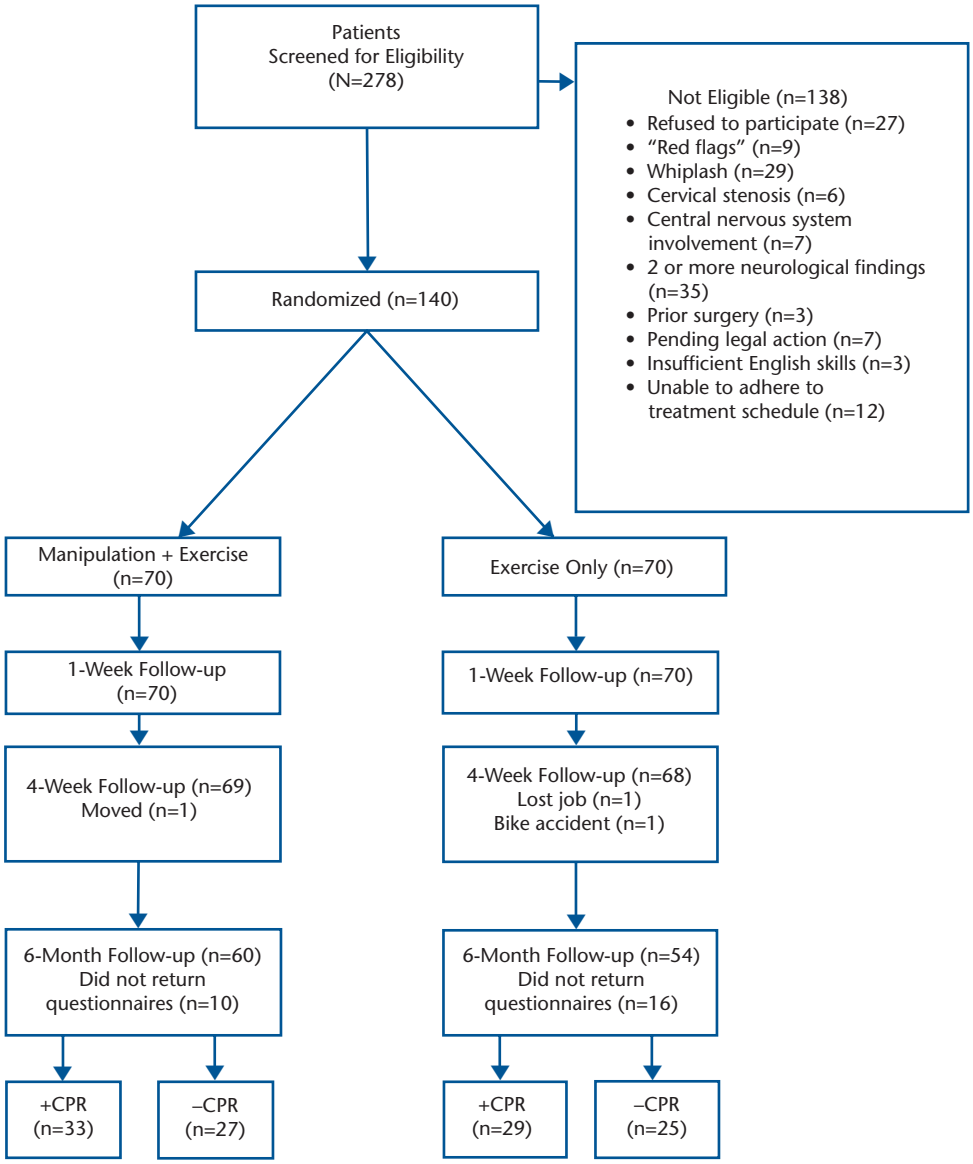

Figure 1.
Flow diagram of participant recruitment and retention. +CPR=positive on the clinical prediction rule, –CPR=negative on the clinical prediction rule.

Identification of the Status on the Rule

After the patients completed the study, the principal investigator determined each patient's status on the rule using data collected at the initial evaluation. Using the same criteria identified in the initial study,[15] patients who met at least 3 of the following criteria were classified as likely responders (ie, positive on the rule). Patients who met 2 or fewer criteria were classified as likely nonresponders (ie,, negative on the rule):

1. FABQPA score <12 points
2. Duration of current episode <30 days (judged from the patient's self-report)
3. No symptoms extending distal to the shoulder (judged from the pain diagram)
4. Decreased cervical extension <30 degrees (measured with a bubble inclinometer)
5. Decreased T3–T5 kyphosis (identified during the postural examination)

Table 1.
Baseline Demographic and Self-Report Variables for all Treatment Groups[a]

Variable	All Patients (N=140)	Manipulation + Exercise Group (n=70)	Manipulation and +CPR (n=37)	Manipulation and −CPR (n=33)	Exercise-Only Group (n=70)	Exercise and +CPR (n=38)	Exercise and −CPR (n=32)
Age (y), mean (SD)	39.9 (11.3)	39.2 (10.5)	37.0 (10.2)	41.6 (10.4)	40.6 (12.0)	41.8 (12.8)	39.2 (11.1)
Sex (female)	97.0 (69%)	46.0 (66%)	27.0 (73%)	19 (57%)	51.0 (72.9%)	27.0 (71.1%)	24.0 (75%)
Days since onset, mean (SD)	63.5 (57.2)	62.5 (53.3)	53.1 (47.0)	73.0 (58.5)	64.4 (61.3)	47.6 (46.5)	84.4 (70.9)
Medication use for neck pain	52.0 (37%)	23.0 (33%)	13.0 (35%)	10.0 (30.3%)	29.0 (41.4%)	15.0 (39.5%)	14.0 (43.8%)
FABQPA, mean (SD)	11.1 (5.6)	11.5 (5.5)	9.4 (4.9)	13.9 (5.2)	10.6 (5.8)	8.8 (5.7)	12.8 (5.0)
FABQW, mean (SD)	10.6 (7.7)	10.97 (7.5)	9.3 (8.1)	12.8 (6.5)	10.2 (7.9)	9.8 (7.9)	10.6 (7.9)

[a] +CPR=positive on the clinical prediction rule, −CPR=negative on the clinical prediction rule, FABQPA=Fear-Avoidance Beliefs Physical Activity Subscale (range=0–24), FABQW=Fear-Avoidance Beliefs Work Subscale (range=0–42).

6. Patient reports that looking up does not aggravate his or her symptoms (identified during the historical examination)

Follow-up

Follow-up assessments were performed after 1 week (prior to treatment on the third visit), at 4 weeks (prior to treatment on the fifth visit), and at 6 months. At each follow-up assessment, patients completed the NDI, NPRS, and GROC. All patients attended the third visit, allowing for data collection. If patients did not attend the fifth visit, data were not collected for that follow-up period.

Sample Size and Power

We based sample size calculation on detecting a clinically important difference in NDI score between any of the 4 cells of the study based on the patients' status on the rule (positive or negative) and treatment group (manipulation + exercise or exercise only) at an alpha level of .05. Based on our previous research,[15] we expected a standard deviation of change scores on the NDI of 12 points. To detect a 10-point change in NDI at the 1-week follow-up with 85% power using a 2-tailed hypothesis and assuming a 50% distribution of patients[37] who do and do not meet the rule, 30 patients per cell were required. We recruited 140 patients to permit approximately a 15% dropout rate or the possibility of unequal distribution of groups.

Data Analysis

We examined the primary aim using a linear mixed model with repeated measures to account for the correlation among repeated observations from the same patient. Time, treatment group, and status on the rule, as well as all possible 2-way and 3-way interactions, were modeled as fixed effects, with the NDI score as the dependent variable. A first-order auto-regressive covariance structure was used for the repeated measures. The primary aim focused on evaluation of the 3-way interaction among time, treatment group, and status on the rule. A separate model was constructed in a similar fashion with pain (NPRS) as the dependent variable. Similarly, to investigate the secondary aim of the study, we examined the 2-way (time × group) interaction to determine whether patients who received thoracic manipulation achieved superior outcomes regardless of status on the rule. We also examined the 2-way interaction between status on the rule and time to determine whether rule status was an important prognostic factor regardless of treatment received. Treatment effects were calculated from the between-group differences in change score from baseline to the 1-week, 4-week, and 6-month follow-up periods. As a secondary analysis, we examined the effects of treatment, rule status, and the interaction between treatment and rule status at each follow-up point using separate mixed model analyses, with the NDI score at each follow-up point as the dependent variable. Treatment group, rule status, and the interaction between treatment and rule status were included as fixed effects, and the baseline NDI score was included as a fixed effect covariate. Similar analyses were performed to examine NPRS scores at each follow-up point. No patients were removed from the analysis for lack of adherence to treatment procedures. Missing data points were estimated in the mixed model analyses using restricted maximum likelihood ratio estimation with 100 iterations.

We calculated the effect size using the Cohen *d* coefficient between the manipulation + exercise and

Table 2.
Disability and Pain Scores for All Groups at Each Follow-up Period[a]

Group	Baseline (95% CI)	1 Week (95% CI)	4 Weeks (95% CI)	6 Months (95% CI)
Neck Disability Index				
Manipulation + exercise	29.5 (27.7, 31.3)	14.8 (13.1, 16.5)	10.1 (8.6, 11.5)	7.1 (5.4, 8.7)
Manipulation and +CPR	28.0 (25.5, 30.5)	12.5 (10.2, 14.9)	8.2 (6.2, 10.2)	6.3 (4.1, 8.5)
Manipulation and −CPR	31.0 (28.4, 33.7)	17.0 (14.5, 19.4)	11.9 (9.8, 14.0)	7.9 (5.4, 10.3)
Exercise only	28.6 (26.7, 30.4)	18.4 (16.7, 20.1)	13.5 (12.0, 15.0)	11.7 (10.0, 13.4)
Exercise and +CPR	27.7 (25.2, 30.1)	18.2 (15.9, 20.5)	13.6 (11.5, 15.7)	11.8 (9.8, 14.1)
Exercise and −CPR	29.4 (26.8, 32.1)	18.6 (16.1, 21.1)	13.4 (11.3, 15.6)	11.6 (9.1, 14.1)
Numeric Pain Rating Scale				
Manipulation + exercise	4.4 (4.0, 4.7)	2.3 (2.0, 2.5)	1.7 (1.4, 1.9)	1.4 (1.1, 1.7)
Manipulation and +CPR	4.3 (3.8, 4.8)	1.9 (1.6, 2.3)	1.6 (1.3, 2.0)	1.5 (1.1, 1.8)
Manipulation and −CPR	4.5 (4.0, 5.0)	2.6 (2.2, 3.0)	1.7 (1.4, 2.1)	1.3 (0.9, 1.7)
Exercise only	3.9 (3.6, 4.3)	3.0 (2.7, 3.2)	1.9 (1.6, 2.1)	1.8 (1.5, 2.0)
Exercise and +CPR	4.4 (3.9, 4.8)	3.1 (2.7, 3.4)	2.0 (1.7, 2.3)	1.8 (1.4, 2.2)
Exercise and −CPR	3.5 (3.0, 4.0)	2.9 (2.5, 3.3)	1.7 (1.4, 2.1)	1.7 (1.3, 2.2)

[a] 95% CI=95% confidence interval, +CPR=positive on the clinical prediction rule, −CPR=negative on the clinical prediction rule.

exercise-only groups at each follow-up period.[38] An effect size of 0.2 was considered small, 0.5 moderate, and 0.8 large.[38] We also compared the number of successful outcomes between groups. Patients who rated their perceived recovery on the GROC as "a very great deal better," "a great deal better," or "quite a bit better" (ie, a score of +5 or greater) at each follow-up period were classified as having a successful outcome, based on the initial study.[15] The percentage of patients experiencing a successful outcome at each time period between groups was examined using a chi-square test of independence. We then calculated the numbers needed to treat (NNT) and 95% confidence intervals (CI) at the 1-week, 4-week, and 6-month follow-up periods. We used an intention-to-treat analysis, with patients analyzed in the group to which they were allocated for the GROC analysis. Missing data were replaced with the mean score of the respective group for each missing GROC value. Data analysis was performed using SPSS version 15.*

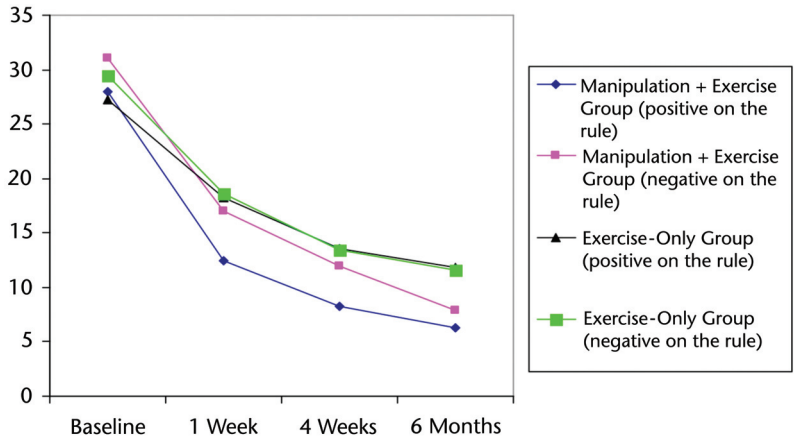

Figure 2.
Mean scores for the Neck Disability Index for each treatment group relative to status on the clinical prediction rule.

Role of the Funding Source

Funding was provided by the Foundation for Physical Therapy and the Orthopaedic Section of the American Physical Therapy Association. The funding agency had no role in the study design, writing of the manuscript, or the decision to submit the manuscript for publication.

Results

Two hundred seventy-eight consecutive patients with neck pain were screened for possible eligibility. One hundred forty patients, mean age 39.9 years (SD=11.3) (69% female), satisfied the eligibility criteria and agreed to participate. Seventy patients were randomly assigned to receive manipulation and exercise, and 70 patients were randomly as-

* SPSS Inc, 233 S Wacker Dr, Chicago, IL 60606.

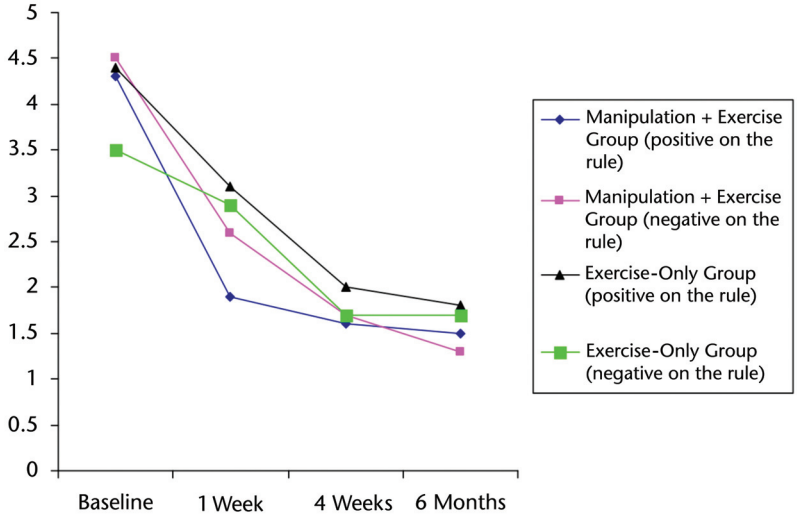

Figure 3.
Mean scores for pain for each treatment group relative to status on the clinical prediction rule.

signed to receive exercise only. Figure 1 shows a flow diagram of patient recruitment and retention. Baseline variables for all groups are shown in Table 1. Recruitment of patients was not equally distributed among the participating clinics, with rates of 34%, 26%, 19%, 16%, and 5% across sites. The overall long-term response rate was 81.0%. The dropout rates were 14% (n=10) for the manipulation + exercise group and 23% (n=16) for the exercise-only group. No reasons were provided for the long-term follow-up dropouts. No adverse events were reported for either group during the trial. Disability and pain scores for each follow-up period are shown in Table 2.

Repeated-measures analyses failed to reveal a significant 3-way interaction for either NDI scores (P=.79) or NPRS scores (P=.22). This finding indicates that outcomes over time were not dependent upon the combination of a patient's treatment group and status on the rule (Figs. 2 and 3). Mean scores for the NDI and pain for each treatment group relative to status on the rule are reported in Table 2.

There was a significant 2-way interaction between group and time for both the NDI (P=.01) and the NPRS (P=.003). Regardless of their status on the rule, patients who received manipulation and exercise experienced greater improvements in disability and pain across time than patients who received exercise alone. Estimated marginal means for the NDI by group at each time period are graphed in Figure 4. There were no significant 2-way interactions between rule status and time for either disability (P=.71) or pain (P=.26) (Fig. 5).

Results of the secondary analyses examining the effects of treatment, rule status, and the interaction between treatment and rule status at each follow-up period demonstrated that the manipulation + exercise group experienced significantly lower scores for disability at 1 week (P=.003), 4 weeks (P=.001), and 6 months (P<.001) and for pain at 1 week (P<.001) than patients who received exercise alone (Tab. 3). There was a significant interaction between status on the rule and treatment received for disability at 1 week (P=.011) and 4 weeks (P=.05) and the NPRS score after 1 week (P=.014); however, the differences were similar when compared with the manipulation + exercise intervention versus the exercise-only intervention, a finding that does not support the value of the prediction rule (Fig. 3).

Effect sizes for disability at the 1-week, 4-week, and 6-month

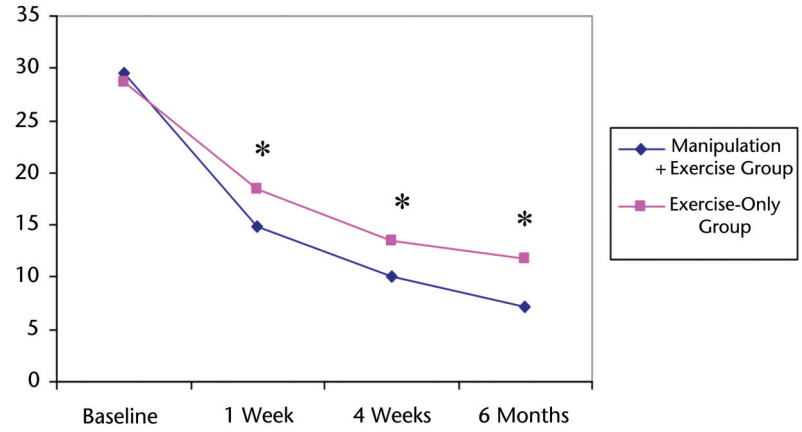

Figure 4.
Mean scores for the Neck Disability Index by group at each time period. Asterisk indicates statistically significant difference between groups.

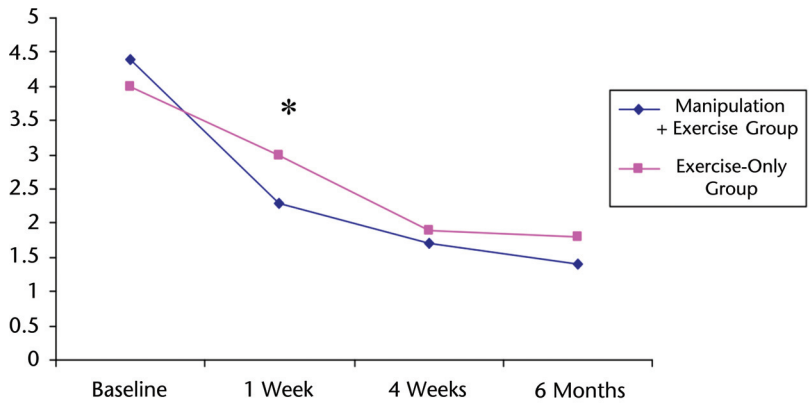

Figure 5.
Mean scores for pain by group at each time period. Asterisk indicates statistically significant difference between groups.

follow-up periods were 0.51, 0.48, and 0.65, respectively. Effect sizes for pain were 0.54 for the 1-week follow-up, 0.18 for the 4-week follow-up, and 0.25 at the 6-month follow-up. Using an intention-to-treat analysis, after 1 week, 18.5% (13/70) of the patients in the manipulation + exercise group achieved success, which was defined as having scores of +5 or greater on the GROC, compared with 11.4% (8/70) of the patients in the exercise-only group. There was no statistically significant difference between groups (P=.17). After 4 weeks, a significant difference existed between groups, with 51.4% (36/70) of the patients in the manipulation + exercise group and 31.4% (22/70) of the patients in the exercise-only group achieving success (P=.01). There also was a significant difference between groups at the 6-month follow-up period, with 80% (56/70) of patients in the manipulation + exercise group achieving success and 35.7% (25/70) of the patients in the exercise-only group achieving success. Figure 6 demonstrates the success rates across time for each group. The NNT for the manipulation + exercise group was 15 (95% CI=−4.6, 18.9) at the 1-week-follow-up, 6 (95% CI=1.9, 34.8) at the 4-week follow-up, and 4 (95% CI=2.1, 7.5) at the 6-month follow-up.

Discussion

It is essential to validate a CPR prior to incorporating it into widespread clinical practice.[17,18] Therefore, we sought to examine whether a previously derived CPR[15] exhibited validity for identifying a subgroup of patients with neck pain who responded favorably to thoracic manipulation. The derived CPR was based on the identification of clinical findings that predicted a good outcome in a cohort of patients with neck pain who received thoracic manipulation. Validation of a previously derived CPR needs to be performed using a study that includes randomization to different treatments to determine whether the clinical findings can be used to describe a subgroup of patients who preferentially respond to thoracic manipulation. The

Table 3.
Secondary Analyses Examining the Effects of Treatment, Rule Status, and the Interaction Between Treatment and Rule Status at Each Follow-up[a]

Group	Disability Score (95% CI)	*P*	Pain Score (95% CI)	*P*
1 week				
Manipulation + exercise vs exercise only	−3.6 (−6.0, −1.2)	.003	−0.70 (−1.1, −0.32)	<.001
+CPR vs −CPR	−2.4 (−4.9, 0.17)	.07	−0.26 (−0.64, 0.12)	.18
Manipulation × status on the rule	−4.4 (−7.8, −1.0)	.011	−0.68 (−1.2, −0.14)	.014
4 weeks				
Manipulation + exercise vs exercise only	−3.5 (−5.6, −1.3)	.001	−0.19 (−0.53, 0.16)	.29
+CPR vs −CPR	−1.8 (−4.0, 0.30)	.05	0.08 (−0.26, 0.43)	.63
Manipulation × status on the rule	−3.9 (−6.7, −0.85)	.012	−0.08 (−0.56, 0.40)	.74
6 months				
Manipulation + exercise vs exercise only	−4.6 (−7.0, −2.2)	<.001	−0.35 (−0.75, 0.04)	.08
+CPR vs −CPR	−0.68 (−3.1, 1.7)	.09	0.09 (−0.30, 0.49)	.64
Manipulation × status on the rule	−1.6 (−4.8, 1.7)	.35	0.14 (−0.40, 0.69)	.61

[a] 95% CI=95% confidence interval, +CPR=positive on the clinical prediction rule, −CPR=negative on the clinical prediction rule. For both pain and disability, negative values represent better outcomes.

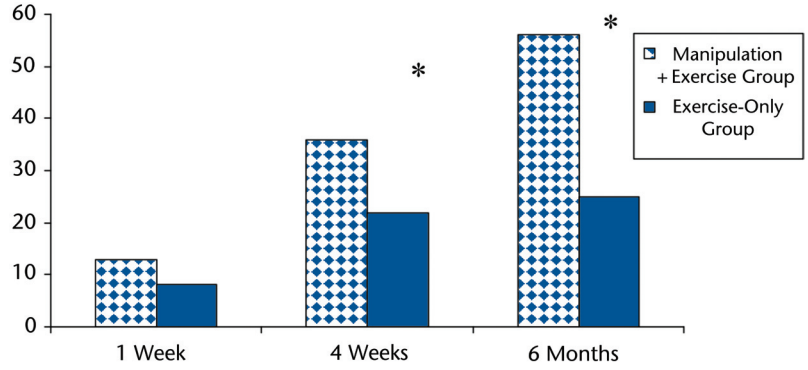

Figure 6.
Success rates across time for each group. Success was defined as scoring +5 or greater on the Global Rating of Change scale. Asterisk indicates statistically significant difference between groups.

current study sought to broadly validate the CPR in a multi-site trial using a sound methodological design.[39] The results of this study generally failed to validate the CPR. The results of our study indicated that regardless of a patient's status on the CPR, those who received thoracic spine manipulation exhibited reductions in pain at 1 week and improvements in disability at 1 week, 4 weeks, and 6 months that were statistically significant. The effect sizes for disability were moderate at each follow-up period and were moderate for pain at the 1-week follow-up. The benefits of targeting manipulation to patients who were positive on the CPR were marginal and were evident only at the short-term (1- and 4-week) follow-ups. It does not appear that clinical decision making based on the CPR is likely to improve clinical outcomes; therefore, the CPR cannot be advocated for adoption into clinical practice. The results of this study suggest that short- and long-term outcomes would be improved by providing thoracic manipulation regardless of status on the CPR.

There are several reasons why a CPR that is derived in one cohort of patients with a single treatment arm may not be validated in a follow-up clinical trial. First, findings in the derivation study may have been due to chance associations or to associations idiosyncratic to the original sample and, therefore, would not be replicated in a new sample of patients.[16,40] It also is possible that the clinicians in this study did not interpret or measure the clinical factors comprising the CPR in the same manner as the clinicians in the original study. This possibility seems unlikely due to the nature of the clinical factors in the CPR and their demonstrated interrater reliability.[7] Finally, it is possible that a CPR derived from a single treatment arm study may be identifying factors that generally identify patients with a good prognosis, but not specifically related to receiving the treatment being studied.[16] This possibility does not appear to have occurred in this instance because the current study did not identify status on the CPR as related to prognosis. It seems most likely that the results of the derivation study were based on either chance associations or findings unique to the sample of patients in the original study.

The results of this study are in agreement with those of studies that examined the impact of thoracic spine manipulation in patients with acute or subacute mechanical neck pain.[5,41,42] The current study also demonstrates that patients with neck pain who received thoracic spine manipulation continued to experience greater improvements at the long-term follow-up. The minimal clinically important difference (MCID) for the NDI has been reported to range from 10% to 19%. We recognize that the differences between groups, although statistically significant, did not surpass the MCID. However, the percentage of individuals who experienced a successful outcome on the GROC was significantly greater in the manipulation + exercise group compared with the exercise-only group at 4 weeks and 6 months. Additionally, the NNT at the 4-week and 6-month follow-up periods was 6 and 4, respectively, providing further evidence for the use of thoracic spine manipulation in addition to exercise in this population. This finding suggests that perhaps individuals with neck pain who do not have any contraindications to manipulation or meet any of the exclusion criteria should receive thoracic spine thrust manipulation regardless of additional factors in the clinical presentation. It also should be recognized that a statistically significant interaction for pain occurred between manipulation and status on the rule at the 1-week follow-up period. Although the treatment effects for reductions in pain for those who satisfied the rule at 1 week were similar to those when comparing the manipulation + exercise and exercise-only groups, we feel the results of the current study do not warrant utilization of the rule. Clinical prediction rules are valuable only if they improve patient outcomes.[17] The results of the current study suggest that using the rule does not improve patient care and that patients with neck pain and no contraindications to

manipulation should receive thoracic spine manipulation regardless of clinical presentation.

A limitation of the current study is that, although the exercise regimen was based on current published guidelines, no agreement exists as to the most effective exercises for the treatment of patients with neck pain. Therefore, it is possible that different exercise approaches may have resulted in a different outcome. Additionally, although the distribution of patients who satisfied the rule was close to our expected 50% in each treatment group, future studies should consider using stratified randomization to ensure equal distribution.

Conclusion

The results of the current study did not support the validity of the previously developed CPR.[15] However, the 2-way interaction between group and time suggests that patients with mechanical neck pain who do not exhibit any contraindications to manipulation exhibit statistically significant improvements in disability in both the short- and long-term follow-up periods.

Dr Cleland, Dr Mintken, Dr Fritz, Dr Whitman, and Dr Childs provided concept/idea/research design and writing. Dr Cleland, Dr Mintken, Dr Carpenter, and Dr Glynn provided data collection and participants. Dr Cleland and Dr Fritz provided data analysis. Dr Cleland provided project management. Dr Cleland, Dr Whitman, and Dr Childs provided fund procurement. Dr Cleland, Dr Mintken, and Dr Carpenter provided facilities/equipment. Dr Cleland, Dr Mintken, Dr Carpenter, Dr Fritz, Dr Whitman, and Dr Childs provided consultation (including review of manuscript before submission). The authors thank all of the clinicians who participated in data collection and treatment of the patients in this clinical trial.

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Invited Commentary

Mark J. Hancock

The study published by Cleland et al[1] in this issue of **PTJ** is an important addition to the physical therapy literature. I believe the value of the article extends well beyond the primary findings of the study. The study is one of very few high-quality studies investigating subgroups of patients who respond to specific physical therapy interventions. The study provides a model for future research in the area and some important warnings when interpreting other lower-quality evidence.

Physical therapists have a wide range of treatment options for treating patients with musculoskeletal disorders, including neck pain. Identifying subgroups of patients who best respond to specific interventions has been suggested as a research priority[2] and has the potential to improve patient outcomes. Some subgroups are defined by a single feature such as patient's sex. However, in other conditions, clinicians and researchers argue that knowledge of a combination of findings is required to identify an important subgroup. A clinical prediction rule (CPR) is a tool that enables a combination of patient characteristics to be considered simultaneously to help in identifying a subgroup.[3] There has been debate in the physical therapy literature about appropriate study designs to develop and validate CPRs that identify subgroups of responders to specific interventions.[4–6] There is general agreement, however, that a randomized controlled trial (RCT) is required before a CPR can confidently be considered to predict response to a specific intervention. Unfortunately, to date very few CPRs that aim to identify responders to treatment have been tested in RCTs.[4]

The trial by Cleland et al is a high-quality study with the primary aim of investigating whether the subgroup of patients with neck pain who meet a CPR respond better to thoracic spine thrust manipulation than patients who do not meet the CPR. The CPR was developed in a previous single-arm trial,[7] so it was unclear whether the CPR identified response to thrust manipulation or simply favorable prognosis.[6] Cleland et al found that the CPR did not identify patients who respond best to thoracic spine thrust manipulation. Although this finding is disappointing, it is still important, as it demonstrates that subgroups identified in single-arm trials must be tested in RCTs before being considered subgroups who respond to a specific intervention. I would go a step further and say the RCT is the first true test of the subgroup (based on a CPR) as a predictor of response to an intervention and as such should not be called a validation study. I note that the current article does not include validation in the title, which I think is important. The literature on CPR development refers to a study following the derivation of a CPR as a validation study.[3] However, the assumption is that both studies used an