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Aanvullende manuele therapie bij patiënten met schouderklachten

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2005

Manipulative Therapy in Addition to Usual Medical Care for Patients with Shoulder Dysfunction and Pain

A Randomized, Controlled Trial

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Background: Dysfunction of the cervicothoracic spine and the adjacent ribs (also called the shoulder girdle) is considered to predict occurrence and poor outcome of shoulder symptoms. It can be treated with manipulative therapy, but scientific evidence for the effectiveness of such therapy is lacking.

Objective: To study the effectiveness of manipulative therapy for the shoulder girdle in addition to usual medical care for relief of shoulder pain and dysfunction.

Design: Randomized, controlled trial.

Setting: General practices in Groningen, the Netherlands.

Patients: 150 patients with shoulder symptoms and dysfunction of the shoulder girdle.

Interventions: All patients received usual medical care from their general practitioners. Only the intervention group received additional manipulative therapy, up to 6 treatment sessions in a 12-week period.

Measurements: Patient-perceived recovery, severity of the main complaint, shoulder pain, shoulder disability, and general health.

Data were collected during and at the end of the treatment period (at 6 and 12 weeks) and during the follow-up period (at 26 and 52 weeks).

Results: During treatment (6 weeks), no significant differences were found between study groups. After completion of treatment (12 weeks), 43% of the intervention group and 21% of the control group reported full recovery. After 52 weeks, approximately the same difference in recovery rate (17 percentage points) was seen between groups. During the intervention and follow-up periods, a consistent between-group difference in severity of the main complaint, shoulder pain and disability, and general health favored additional manipulative therapy.

Limitations: The sample size was small, and assessment of end points was subjective.

Conclusion: Manipulative therapy for the shoulder girdle in addition to usual medical care accelerates recovery of shoulder symptoms.

Shoulder disorders are a widely recognized medical, social, and economic problem (1). They are characterized by functional disability due to pain in the shoulder at rest or during movement or by functional disability due to restricted range of motion. The annual incidence of shoulder symptoms in Dutch general medical practices is estimated to be 10 to 25 per 1000 enrolled patients (2–4).

In the Netherlands, shoulder disorders are treated according to the Guidelines for Shoulder Complaints of the Dutch College of General Practitioners (5, 6). Initial treatment during the first 2 weeks includes informing patients about the nature and course of shoulder symptoms and advising them on how to use the affected shoulder during daily living. Patients can also be prescribed analgesics or nonsteroidal anti-inflammatory drugs if necessary. If this initial treatment is not effective, up to 3 corticosteroid injections (in the subacromial space or glenohumeral joint) can be given. Referral for physiotherapy is considered only for patients whose symptoms persist for 6 weeks or more. This treatment regimen, according to the guidelines, provides short-term benefit for many patients but cannot prevent the often unfavorable long-term course of the symptoms. Indeed, only 50% of all new episodes of shoulder disorders resolve within 6 months, while at 12 months more than 40% of all patients are still disabled during work and leisure time (4, 7).

Pain or dysfunction of the cervicothoracic spine and the adjacent ribs (also called the shoulder girdle) often accompanies shoulder symptoms (8). A considerable proportion of patients with shoulder symptoms (approximately 20%) but no shoulder joint disorders may be found to have dysfunction of the shoulder girdle on further physical examination (9). Moreover, dysfunction of the shoulder girdle triples the risk for shoulder complications (10) and also predicts poor outcome of shoulder disorders (10–12). In clinical practice, dysfunction of the shoulder girdle can be treated with manipulative therapy, which aims to restore normal function. Winters and colleagues (13) found that manipulative therapy accelerated recovery and improved symptoms compared with physiotherapy in a relatively small subgroup of patients with both shoulder symptoms and shoulder girdle dysfunction. These effects were not sustained on long-term follow-up, possibly because of high attrition rates (14).

Evidence showing that manipulative therapy for the shoulder girdle effectively treats shoulder symptoms is scarce; Winters and colleagues have performed the only randomized trial (13, 14) to date. Our objective was to study the effectiveness of manipulative therapy for the shoulder girdle in addition to usual medical care by a general practitioner. The study design has been described elsewhere (15), and the trial was designed and reported accord-

ing to the Consolidated Standards of Reporting Trials (CONSORT) statement (16). We report the effects of the use of additional manipulative therapy for the shoulder girdle to treat shoulder symptoms.

METHODS
Participants

Potential eligible participants with shoulder symptoms (pain and dysfunction) were recruited in 50 general practices in Groningen, the Netherlands. General practitioners started initial treatment (usual medical care) at presentation, assessed eligibility criteria, and told the conducting researcher about each eligible patient. The general practitioner used a standardized eligibility checklist and a physical examination as recommended by the Dutch College of General Practitioners (5, 6). A baseline assessment at the research center was scheduled within 2 weeks of presentation. Shoulder symptoms were defined as pain between the neck and the elbow at rest or during movement of the upper arm (**Figure 1**). Pain radiating to the neck region or to the lower part of the arm was not used as an exclusion criterion. The physical examination established the presence of both shoulder symptoms and dysfunction of the cervicothoracic spine and the adjacent ribs with accompanying pain or restricted movement. Eligible patients were 18 years of age or older and had had no consultation or treatment for shoulder symptoms in the past 3 months. No limits were placed on duration of symptoms before the first consultation.

Reasons for exclusion were acute severe trauma, such as fractures, ruptures, or dislocation in the shoulder region; previous orthopedic surgery; clear treatment preference deviating from the study protocol; contraindications to manipulative therapy (for example, hypermobility, instability, or severe arthrosis of the cervicothoracic spine); signs of cervical nerve root compression; presence of specific rheumatic disorders; presence of dementia or other severe psychiatric, emotional, or behavioral disorders; shoulder disorders due to general internal disease of thoracic and abdominal organs; and inability to complete Dutch-language written questionnaires. Eligibility and exclusion criteria were verified before randomization by using a structured medical history and physical assessment.

Randomization

Patients were evenly allocated to receive manipulative therapy plus usual medical care or usual medical care alone. An independent statistician not involved in recruitment of patients generated a random list that was stratified for general practitioner by permutation of randomized blocks, with a block size of 6. After eligibility was verified, written informed consent was obtained. A researcher opened preprepared numbered, opaque sealed envelopes containing the treatment allocation codes and made appointments with manual therapists when applicable.

Context

Shoulder pain in the absence of trauma, fracture, rupture, or dislocation can lead to substantial functional limitations and can be a difficult condition to treat.

Contribution

In this randomized, controlled trial, patients with shoulder pain and shoulder girdle dysfunction assigned to receive manipulative therapy in addition to usual general practitioner care had more rapid improvement in symptoms and fewer shoulder symptoms at 12 weeks than patients assigned to usual care alone.

Implications

Manipulative therapy appears to be an effective treatment option for patients with shoulder pain and shoulder girdle dysfunction that are not due to trauma, fracture, rupture, or dislocation.

–The Editors

Interventions
Usual Medical Care

All patients received usual medical care from their general practitioners. Usual medical care was similar to that outlined by the Dutch College of General Practitioners (5, 6) and included information, advice, and therapy. During the first 2 weeks, patients were given information about the nature and course of shoulder symptoms, along with advice on daily use of the affected shoulder. Patients were prescribed oral analgesics or nonsteroidal anti-inflammatory drugs if necessary. The Dutch College of General Practitioners recommends 2 weeks of treatment with paracetamol, 4 times daily (maximum dosage, 4000 mg/d), or nonsteroidal anti-inflammatory drugs such as ibuprofen, 3 times daily (maximum dosage, 2400 mg/d); diclofenac, 3 times daily (maximum dosage, 150 mg/d); or naproxen, twice daily (maximum dosage, 1000 mg/d) (5, 6). If patients did improve, drug treatment could be extended for another 2 weeks. If this approach was ineffective, up to 3

Figure 1. **Location of shoulder symptoms.**
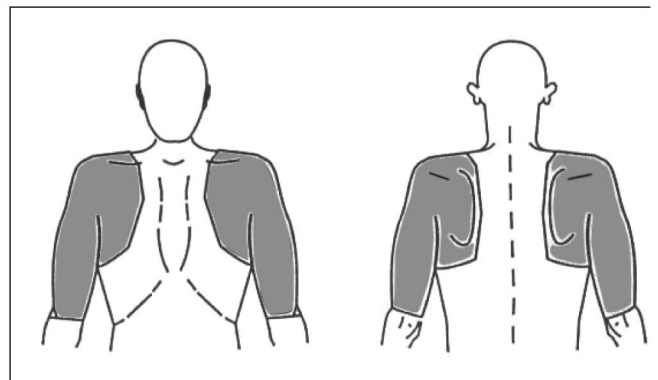
corticosteroid injections could be given in either the subacromial space or the glenohumeral joint. For injections in either location, physicians used triamcinolone acetonide, 40 mg suspended in a 1-mL vehicle, if necessary, combined with lidocaine, 10 mg suspended in a 5- to 10-mL vehicle. If improvement remained insufficient 2 weeks after injections were given, injections could be repeated. Further corticosteroid treatment was not considered appropriate if patients did not improve after the second series of injections. For symptoms persisting at least 6 weeks, physiotherapy consisting of shoulder exercises, massage, and physical applications was considered. Other referrals during the intervention and follow-up periods (for example, to a rheumatology consultant or orthopedic surgeon) were discouraged but were documented if they occurred.

Manipulative Therapy

According to the International Federation of Orthopedic Manipulative Therapists, "orthopedic manipulative (manual) therapy is a specialization within physical therapy and provides comprehensive conservative management for pain and other symptoms of neuro-musculo-articular dysfunction in the spine and extremities." Our approach to manipulative therapy focused on manual manipulation and mobilization techniques used in western Europe, North America, and Australia, including those described by Cyriax (17), Greenman (18), and Lewit (19). In our trial, manipulative therapy included specific manipulations (low-amplitude, high-velocity thrust techniques) and specific mobilizations (high-amplitude, low-velocity thrust techniques) to improve overall joint function and decrease any restrictions in movement at single or multiple segmental levels in the cervical spine and upper thoracic spine and adjacent ribs. The manual therapist chose the applied techniques on the basis of the location of the dysfunction and the therapist's technique preferences. Within the boundaries of the protocol, treatment could be reassessed and adapted to the patient's condition.

A maximum of 6 treatment sessions could be given over a 12-week period. Eight experienced physiotherapists who were members of the Dutch Association of Manual Therapy and registered by the Royal Dutch Society for Physical Therapy (a member of the International Federation of Orthopedic Manipulative Therapists) provided the manual therapy. To minimize variations in manipulative therapy, therapists received a special training session to familiarize them with the protocol's mobilization and manipulation techniques for treatment of the cervicothoracic spine and the adjacent ribs. Other interventions (for example, exercises, massage, advice about posture, and treatment of the shoulder joint) were considered deviations from the treatment protocol and were therefore discouraged throughout the trial. Specific treatment characteristics and protocol deviations were recorded at each visit.

Outcomes

Outcome measures were recorded at baseline, at 6 weeks (during the intervention period), and at 12 weeks (at completion of the intervention period). The primary outcome measure was patient-perceived recovery. Patients were considered recovered if they reported being "completely recovered" or "very much improved" on a 7-point ordinal scale. In addition, patients were asked whether they felt "cured" according to the following definition: "You are considered cured if your shoulder symptoms are improved to such an extent that you no longer perceive them as inconvenient." Secondary outcomes included the severity of 3 individual main complaints (20), shoulder pain (21), functional disability (22), general health (23), and costs (costs data not yet available) (24). The main complaint is defined as an unavoidable painful or limited functional activity during daily life in which the shoulder is involved. It is a patient-specific or individualized approach for measuring limitation of shoulder function during daily activities. During each session, manual therapists and general practitioners documented the treatment content on a standardized registration form.

Sample Size

Sample size was calculated on the basis of an assumed proportion of 50% of patients without shoulder symptoms in the control group at 6 months, a 2-sided α value of 0.05, a statistical power of 0.80, and an attrition rate of 10%. According to these assumptions, a sample size of 250 patients (125 in each treatment group) would be needed to detect a between-group difference of 20 percentage points (15).

Blinding

Manipulative therapy is an open-label treatment for which patients, general practitioners, and manual therapists cannot be blinded. The research assistants responsible for the follow-up measurements were blinded to the allocated treatment. General practitioners were not informed about patients' treatment allocation until completion of the intervention period. Each manual therapist received a letter containing information about the participating patient and a schedule for treatments and for assessments during the follow-up period. Patients were instructed not to inform the research assistants or the general practitioners about the received treatment.

Statistical Analysis

All data analyses based on treatment assignment (the intention-to-treat principle) were performed according to a predetermined protocol. The baseline status of the study groups was compared with respect to the distribution of all independent prognostic variables and the baseline values of the outcome variables. Differences between groups and 95% CIs were calculated for each outcome measure according to the intention-to-treat principle. Mean changes between study groups were compared by using an independent-samples t-test (for continuous outcome variables) and

Figure 2. **Flow of patients through the study.**
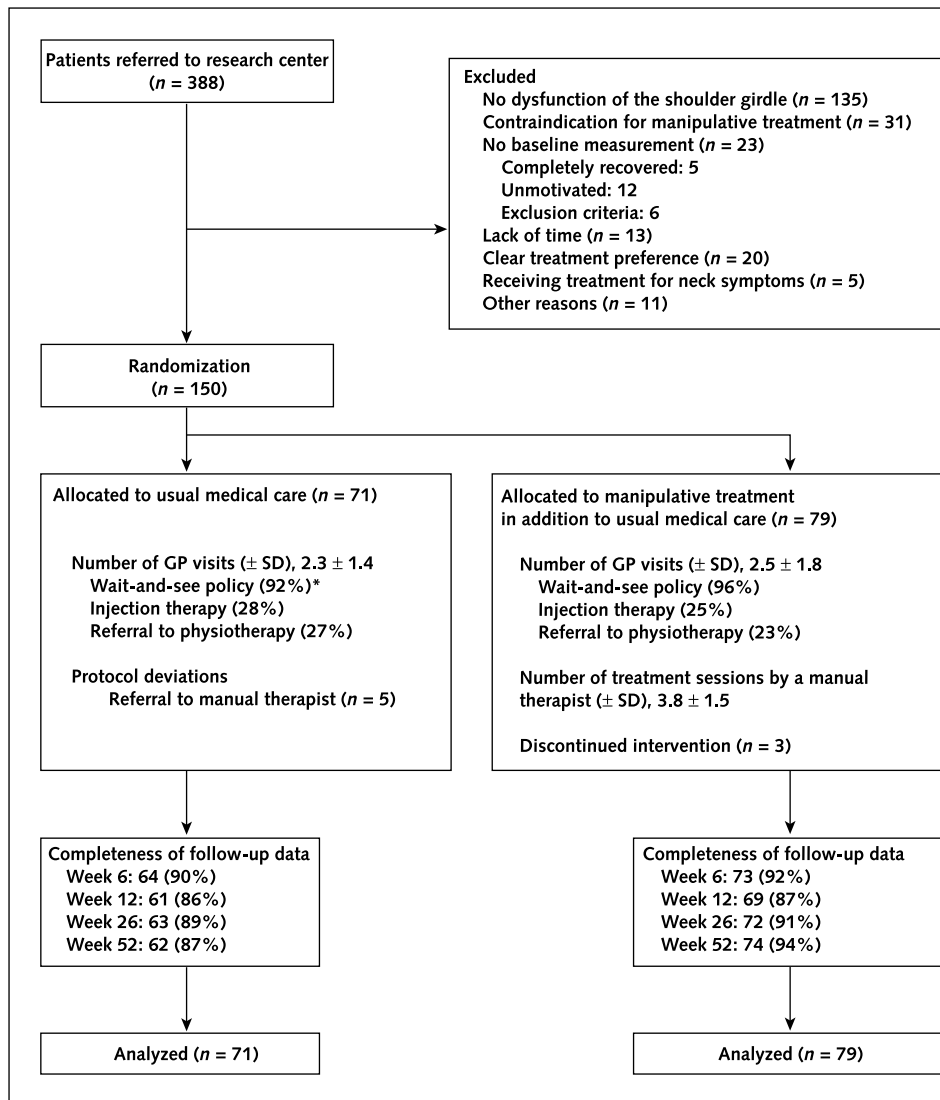
*Percentage of patients who received the intervention (wait-and-see policy along with injection therapy and physiotherapy). GP = general practitioner.

the chi-square test (for categorical outcome variables). Influences of prognostic indicators on outcomes of manipulative therapy were assessed in a multivariate logistic regression analysis. Only a 2-sided significance test was used ($\alpha = 0.05$). All analyses were done by using SPSS statistical software, version 11.0 (SPSS, Inc., Chicago, Illinois).

We used unconditional mean single imputation to replace missing data for covariates. Prognostic status at baseline for patients with and without missing values for the outcome variables was compared for the study sample and by treatment group. We present results with missing values for outcome variables replaced by the previous available value (last value carried forward) and report on the analysis in which missing values were replaced by the baseline value (baseline value carried forward).

The Medical Ethics Committee of the University Hospital of Groningen, Groningen, the Netherlands, approved the study protocol.

Role of the Funding Sources

The funding sources approved the study design but played no part in conducting or reporting the study.

RESULTS
Recruitment and Follow-up

Three hundred eighty-eight patients were referred to the research center, and 150 participated in the trial. Reasons for exclusion are given in **Figure 2.** Seventy-one patients were assigned to the control group, and 79 were assigned to the intervention group. Because 1 patient in the control group did not return the baseline questionnaire, the prognosis for this patient was not available for some variables. In total, 32 patients (16 per treatment

Table 1. Baseline Characteristics and Outcome Measures according to Treatment Group

Variable	Patients Receiving Usual Medical Care (n = 71)*	Patients Receiving Usual Medical Care plus Additional Manipulative Therapy (n = 79)
Mean age ± SD, y	47.8 ± 11.8	48.4 ± 12.4
Women, n (%)	37 (52)	42 (53)
Dominant side affected, n (%)	45 (63)	58 (73)
Acute onset of symptoms, n (%)	19 (27)	27 (34)
Mean duration of symptoms before consultation, n (%)		
<6 wk	28 (39)	28 (35)
6–12 wk	22 (31)	25 (32)
12–26 wk	11 (15)	10 (13)
>26 wk	10 (14)	16 (20)
Previous episodes of shoulder pain, n (%)		
None	18 (25)	18 (23)
1 episode	14 (20)	18 (23)
2–5 episodes	27 (38)	27 (34)
>5 episodes	12 (17)	16 (20)
Previous neck symptoms, n (%)	43 (61)	50 (63)
Treatment preference regarding manual therapy, n (%)		
Negative	4 (6)	4 (5)
No preference	42 (59)	57 (72)
Positive	25 (35)	18 (23)
Mean severity of main complaint ± SD†	6.4 ± 2.1	6.9 ± 1.9
Mean severity of shoulder pain‡	17.9 ± 4.3	17.8 ± 4.7
Mean severity of shoulder disability§	60.7 ± 29.0	58.6 ± 28.0
General health rating‖	0.68 ± 0.18	0.69 ± 0.19

* One patient did not return his baseline questionnaire; missing data were replaced by group means.
† Patient rating of the severity of the main complaint during the preceding week on an 11-point scale (0 = best; 10 = worst).
‡ Patient rating of pain at rest, pain in motion, nightly pain, sleeping problems caused by pain, inability to lie on the painful side, degree of radiation, and general pain on 4-point ordinal scales (1 = no pain; 4 = severe pain. Total range: 7 = best; 28 = worst).
§ Patient rating on Shoulder Disability Questionnaire for the functional status of the shoulder in the preceding 24 hours (16 items with possible responses of not applicable, yes, and no). The presented score is the percentage of positive items in the total applicable items (total range: 0 = best; 100 = worst).
‖ EuroQol health-related quality-of-life instrument (5 items on a 3-point ordinal scale; total range: −1 = worst; 1 = best).

group) had data missing for at least 1 outcome variable. In the control group, 55 patients (78%) had data available for all outcome measures, 8 patients (11%) had missing data for fewer than 25% of outcome measures, and 8 patients (11%) had missing data for more than 25% of outcome measures. In the intervention group, the corresponding numbers were 63 patients (80%), 10 patients (13%), and 6 patients (8%), respectively. Patients who missed appointments for outcome assessments had many missing values for outcome variables. In the control group, 5 patients discontinued treatment because of lack of motivation (n = 3), lack of time (n = 1), and a car accident (n = 1), and 1 patient dropped out during the follow-up period because of lack of motivation. In the intervention group, 3 patients discontinued treatment because of lack of motivation (n = 2) and family circumstances (n = 1), and 1

patient withdrew from follow-up because of lack of motivation.

In general, patients with 1 or more missing value for outcome variables had shorter pain episodes and more previous pain episodes and rated their main complaint as more severe at baseline. Among patients who had complete data for outcome variables, we compared patients whose prognoses were similar to those of patients with missing data and those who prognoses were different. Main outcome measures were similar in both groups.

Baseline Characteristics

Baseline status (patient characteristics and baseline values of the outcome measures) is given in **Table 1**. Both groups were highly similar in demographic and prognostic variables and baseline values of outcome measures.

Treatment during the Intervention Period

Patients consulted their general practitioners a mean of 2.4 times. There was a small difference between the control group and the intervention group in mean number of visits (2.3 vs. 2.5 visits). Ninety-two percent of controls were treated with a wait-and-see policy, 28% were treated with corticosteroid injections (mean, 1.6 injections), and 27% were referred to a physical therapist for a maximum of 9 treatment sessions. In the intervention group, these percentages were 96%, 25% (mean, 2.1 injections), and 23%, respectively (**Figure 2**).

Patients in the intervention group received a mean (±SD) of 3.8 ± 1.5 treatment sessions from a manual therapist. In each treatment session, different manipulation techniques (mean [±SD], 1.9 ± 1.1) and mobilization techniques (mean [±SD], 1.1 ± 0.9) were performed. The mean duration (±SD) of a manipulative therapy session was 23 ± 13 minutes. In 16% of all sessions of manipulative therapy, a manipulative technique was applied on a joint or vertebral segment outside the shoulder girdle.

Effectiveness of the Interventions
Outcomes after Randomization at 6 and 12 Weeks

Consistently, for all outcome variables, the 6-week outcomes for the intervention group were similar to the 12-week outcomes for controls (**Table 2**). Measurements at 6 and 12 weeks showed a consistent difference in favor of additional manipulative therapy, but none of the differences at 6 weeks reached statistical significance. At 12 weeks after randomization, statistically significantly more patients in the intervention group reported full recovery or very large improvement than did patients in the control group (difference, 22 percentage points [95% CI, 6.9 to 35.4 percentage points]). In addition, a significant between-group difference was seen at 12 weeks for mean improvement in severity of the main complaint (difference, 1.5 points [CI, 0.5 to 2.5 points] on an 11-point scale) and shoulder pain (difference, 2.0 points [CI, 0.3 to 3.7 points] on a 21-point scale). The outcomes of shoulder disability and general health favored additional manipulative ther-

Table 2. **Mean Improvement and Differences between Groups in Primary and Secondary Outcome Measures**

Outcome Measure	Patients Receiving Usual Medical Care (*n* = 71)	Patients Receiving Usual Medical Care plus Additional Manipulative Therapy (*n* = 79)	Between-Group Difference (95% CI)*
Patient-perceived recovery, *n/n* (%)†			
Patients "recovered" at 6 wk	10/71 (14)	16/79 (20)	6 (−6.2 to 18.1)
Patients "recovered" at 12 wk	15/71 (21)	34/79 (43)	22 (6.9 to 35.4)
Patients "recovered" at 26 wk	25/71 (35)	32/79 (41)	5 (−10.1 to 20.2)
Patients "recovered" at 52 wk	25/71 (35)	41/79 (52)	17 (0 to 31.4)
Patients "cured" at 6 wk	13/71 (18)	19/79 (24)	6 (−7.5 to 18.5)
Patients "cured" at 12 wk	24/71 (34)	36/79 (46)	12 (−3.9 to 26.5)
Patients "cured" at 26 wk	29/71 (41)	41/79 (52)	11 (−4.8 to 26.2)
Patients "cured" at 52 wk	30/71 (42)	47/79 (59)	17 (1.2 to 32.1)
Mean improvement ± SD in severity of main complaint‡			
6 wk	2.2 ± 3.2	3.1 ± 3.0	0.9 (−0.1 to 1.9)
12 wk	2.9 ± 3.4	4.4 ± 3.0	1.5 (0.5 to 2.5)
26 wk	3.5 ± 3.3	4.7 ± 3.1	1.2 (0.2 to 2.2)
52 wk	3.6 ± 3.4	5.0 ± 2.9	1.4 (0.4 to 2.4)
Mean improvement ± SD in severity of shoulder pain§			
6 wk	2.8 ± 4.4	3.6 ± 4.5	0.8 (−0.6 to 2.3)
12 wk	3.7 ± 5.2	5.7 ± 5.1	2.0 (0.3 to 3.7)
26 wk	5.2 ± 5.5	5.9 ± 5.3	0.7 (−1.0 to 2.5)
52 wk	5.5 ± 5.5	6.7 ± 5.4	1.2 (−0.5 to 3.0)
Mean improvement ± SD in shoulder disability‖			
6 wk	11.3 ± 30.0	16.8 ± 21.3	5.5 (−2.9 to 13.8)
12 wk	18.2 ± 32.4	26.6 ± 32.3	8.5 (−2.0 to 18.9)
26 wk	20.3 ± 35.9	33.0 ± 34.6	12.7 (1.3 to 24.1)
52 wk	27.7 ± 38.9	36.3 ± 35.7	6.9 (−3.5 to 20.7)
Mean improvement ± SD in general health¶			
6 wk	0.03 ± 0.18	0.07 ± 0.18	0.04 (−0.01 to 0.10)
12 wk	0.16 ± 0.25	0.09 ± 0.28	0.06 (−0.03 to 0.15)
26 wk	0.08 ± 0.21	0.11 ± 0.19	0.03 (−0.04 to 0.09)
52 wk	0.12 ± 0.25	0.12 ± 0.19	0.00 (−0.07 to 0.08)

* Values for differences between percentages are expressed as percentage points.
† Patient-perceived recovery. Possible responses for recovery were "recovered," "completely recovered (yes or no)," or "very large improvement" on a 7-point ordinal scale ranging from very much improved to very much deteriorated. "Cured" was determined as follows: "You are considered cured if your shoulder symptoms are improved to such an extent that you no longer perceive them as inconvenient (yes/no)."
‡ Patient rating of the severity of the main complaint during the preceding week on an 11-point scale (0 = best; 10 = worst).
§ Patient rating of pain at rest, pain in motion, nightly pain, sleeping problems caused by pain, inability to lie on the painful side, degree of radiation, and general pain on 4-point ordinal scales (1 = no pain; 4 = severe pain. Total range: 7 = best; 28 = worst).
‖ Patient rating on Shoulder Disability Questionnaire for the functional status of the shoulder in the preceding 24 hours (16 items with possible responses of not applicable, yes, and no). The presented score is the percentage of positive items in the total applicable items (total range: 0 = best; 100 = worst).
¶ EuroQol health-related quality-of-life instrument (5 items on a 3-point ordinal scale; total range: −1 = worst; 1 = best).

apy, but the difference did not reach statistical significance at 6 or 12 weeks.

Outcomes at 26 and 52 Weeks after Randomization

During follow-up, more patients from the intervention group reported full recovery or very large improvement. The intervention and control groups differed significantly in perceived recovery (difference, 17 percentage points [CI, 0.0 to 31.4 percentage points]) and patients who reported feeling cured (17 percentage points [CI, 1.2 to 32.1 percentage points]) at 52 weeks. The main complaint was significantly less severe in patients treated with manipulative therapy at 26 weeks and at 52 weeks after randomization (between-group difference, 1.2 points [CI, 0.2 to 2.2 points] and 1.4 points [CI, 0.4 to 2.4 points], respectively, on an 11-point scale). The outcomes of shoul-

der pain and disability consistently favored additional manipulative therapy; however, only shoulder disability reached a statistically significant difference at 26 weeks (difference, 12.7 points [CI, 1.3 to 24.1 points] on a 100-point scale).

Adjustment of the analysis for age, sex, treatment preference, duration of symptoms before consultation, onset of symptoms, previous shoulder symptoms, and previous neck symptoms did not change any of the outcomes. However, there appeared to be a differential effect across manual therapists. Regardless of prognostic status, patient recovery rates for individual therapists ranged from 14% to 67% at the end of the intervention period (12 weeks) and from 14% to 83% at the end of the follow-up period (52 weeks). However, a chi-square test showed no significant effects across therapists.

Alternative Analysis

We performed an alternative analysis that replaced missing data according to the baseline-value-carried-forward method. In general, the results (magnitude and SE of between-group differences) were very similar to those of the analysis performed according to the last-value-carried-forward method. However, for patients who reported feeling cured, the between-group difference at 12 weeks reached statistical significance (16 percentage points [CI, 0.4 to 30.4 percentage points]), although the between-group difference at 52 weeks for the proportion of patients reporting full recovery or very large improvement did not (15 percentage points [CI, −0.0 to 30.2 percentage points]).

DISCUSSION

In our study, manipulative therapy for the cervicothoracic spine and the adjacent ribs in addition to usual medical care by a general practitioner accelerated recovery of shoulder symptoms. At 12 weeks after randomization, we found a statistically significant difference in recovery rate (43% vs. 21%; difference, 22 percentage points [CI, 6.9 to 35.4 percentage points]) in favor of additional manipulative therapy. Other outcome measures, such as shoulder pain and shoulder disability, consistently favored additional manipulative therapy, supporting our main finding.

These favorable effects were maintained during the follow-up period. At 52 weeks, we found a statistically significant difference in recovery rate (52% vs. 35%; difference, 17 percentage points [CI, 0 to 31.4 percentage points]) in favor of additional manipulative therapy. Adjustment for important prognostic factors (for example, age, sex, treatment preference, and duration of symptoms) did not change our results. However, we found a differential effect of individual manual therapists. The patient recovery rates for individual therapists varied from 14% to 67% at the end of the intervention period, regardless of prognostic status or the number of patients treated. Analysis of the treatment registration forms showed that all therapists treated within the boundaries of the protocol; therefore, this variation is probably due to unfavorable prognostic status among treated patients. Although such differential effects across therapists reflect daily health care practice, they probably caused us to underestimate the overall effectiveness of manipulative therapy.

To our knowledge, this is the first trial to focus on the effectiveness of adding manipulative therapy for the cervicothoracic spine and the adjacent ribs to usual medical care for treatment of shoulder symptoms. We did not deviate from the original study design, which was published independently of the study results (15). At randomization, the treatment groups were similar in demographic and patient characteristics and putative prognostic indicators. Our sample is comparable to those of other studies examining shoulder symptoms in general practice (3, 14). To improve the transparency of the contrasted treatments, we used specific protocols for both usual medical care and manipulative therapy. Protocols for manipulative therapy focused on a limited number of manipulative and mobilizing techniques that target prespecified bones and joints.

Because of the open nature of manipulative therapy, blinding of patients, general practitioners, and physical therapists was not possible. Lack of blinding among patients could have caused ascertainment bias. Patients' treatment preferences could have influenced their responses regarding subjective outcome measures (25). Therefore, patients who were a priori unwilling to adhere to allocated treatments and those who had an absolute preference for or against manipulative therapy were excluded. In addition, our analyses showed that treatment preferences did not affect patient-perceived recovery. Lack of blinding of general practitioners and manual therapists could have reduced the comparability of usual medical care. However, the number and content of general practitioner sessions were similar for both groups.

Because recruitment yield was lower than expected, we decided to extend the inclusion period by 6 months, which allowed us to include 150 patients instead of the intended 250 patients. We decided to stop recruitment because of time and budget constraints. Neither decision was supported by interim analysis. Before the start of the study, we considered a difference of 20 percentage points in favor of manipulative therapy to be clinically relevant (15); the reported difference in recovery of 22 percentage points is in line with our expectations. However, we anticipated a recovery rate of 50% in patients who received usual medical care, twice as high as the actual rate observed. In addition, although we expected that 10% of patients would be lost to follow-up, only 3 patients discontinued the allocated manipulative therapy. The amount of missing data due to attrition is limited and appears to be completely random. Because fewer patients in the control group recovered and adherence to allocated treatments and follow-up was high, we reached sufficient statistical power with a smaller-than-planned study sample.

Our trial was necessarily designed using open-label treatment. Therefore, discontinuation of treatment and attrition may have biased our results (26). However, patients with missing values were equally distributed between treatment groups, and there were no indications that treatment discontinuation and attrition were related to prognostic status or treatment allocation or outcome. Imputation of missing values according to the last-observation-carried-forward method and the baseline-value-carried-forward method yielded similar results. However, missing values for outcome measures may have made our results less precise.

Manipulative therapy for treatment of shoulder symptoms is rarely studied. Our findings corroborate the findings of the previous study by Winters and colleagues (13, 14), which found that manipulative therapy for the shoulder girdle yielded considerable benefit compared with physiotherapy. We demonstrated that manipulative therapy for the shoulder girdle in addition to usual medical

care by a general practitioner accelerated recovery of shoulder symptoms and reduced their severity. These effects were sustained at 52 weeks of follow-up. Compared with the study by Winters and colleagues (13, 14), our study included only patients with shoulder symptoms and dysfunction of the shoulder girdle. We also included more patients, had nearly complete follow-up, and restricted manipulative therapy to avoid bias due to treatment contamination.

We believe that general practitioners should include a short physical examination of the shoulder girdle in their structured medical examinations. For patients with shoulder symptoms in whom dysfunction of the cervicothoracic spine and adjacent ribs is found, referral to a manual therapist should be considered.

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