Adjuvant Physical Therapy Versus Occupational Therapy in Patients With Reflex Sympathetic Dystrophy/Complex Regional Pain Syndrome Type I

H. Margreet Oerlemans, PhD, PT, Rob A. B. Oostendorp, PhD, PT, Theo de Boo, MSc, Lyckle van der Laan, MD, Johan L. Severens, MSc, R. Jan A. Goris, MD, PhD

ABSTRACT. Oerlemans HM, Oostendorp RAB, de Boo T, van der Laan L, Severens JL, Goris RJA. Adjuvant physical therapy versus occupational therapy in patients with reflex sympathetic dystrophy/complex regional pain syndrome type I. Arch Phys Med Rehabil 2000;81:49-56.

Objective: To investigate the effectiveness and cost of physical therapy (PT) or occupational therapy (OT) in patients with reflex sympathetic dystrophy (RSD).

Design: Prospective randomized controlled trial, with 1 year follow-up.

Setting: Two university hospitals.

Patients: One hundred thirty-five patients who had been suffering from RSD of one upper extremity for less than 1 year.

Interventions: Patients were assigned to PT, OT, or a control group (social work).

Main Outcome Measures: Improvement in impairment level sumscore (ISS) over 1 year (Student's *t* test). A difference of 5 ISS points between the groups was defined as being clinically relevant. Furthermore, severity of disability and handicap was measured and tested exploratively (Wilcoxon; a = .05), and cost-effectiveness of the groups was calculated.

Results: PT and, to a lesser extent, OT resulted in a significant and also more rapid improvement in the ISS as compared with controls (6 and 4 ISS points, respectively). On a disability level, a positive trend was found in favor of OT. On a handicap level, no differences were found between the groups. PT had an advantage over OT regarding the cost-effectiveness ratio.

Conclusion: In different ways PT and OT each contribute to the recovery from RSD of the upper extremity.

Key Words: Physical therapy; Occupational therapy; Reflex sympathetic dystrophy; Rehabilitation.

REFLEX SYMPATHETIC dystrophy (RSD), also called complex regional pain syndrome I (CRPS I),' is a syndrome characterized by a triad of sensory, motor, and autonomic disturbances.[2,3] It may occur in one extremity (arm or leg) after an-often minor-injury or operation to that extremity.[4] In the Netherlands, the incidence of RSD is about 8,000 new cases per year. In some patients, RSD may occur spontaneously. In most patients the affected extremity is primarily warmer, ie, at the onset of RSD, although in 5% it is primarily colder than the unaffected extremity.[5,6] Early signs and symptoms are diffuse pain, edema, temperature changes, and reduced range of motion. These signs and symptoms occur in an area much larger than the area of primary injury or operation and include the area distal to the primary injury[5-8]; they are also aggravated by using the affected extremity.[5,6,8] Signs and symptoms may persist in some patients.[6,9,10] After severe RSD, only 1 out of 5 patients is fully capable of resuming previous activities." Therefore, RSD is not only physically incapacitating, but is also psychically and socially incapacitating.

A variety of medical treatments have been described, though none is uniformly successful. Adjuvant treatment with physical therapy (PT) has often been recommended.[3,12-26] At many institutes, not only PT is given but also occupational therapy (OT).[14,20,27] OT is rarely mentioned as an adjuvant treatment in research reports on RSD. However, Nielsen[20] has stated that cooperation among physical and occupational therapists is worthwhile because therapists are trained in the practice of physical instruction and in observing that it is really understood and followed by the patient.

Unfortunately, there are no adequate comparative studies on PT or OT in RSD.[17] Fialka and colleagues[15] investigated the effectiveness of two physical therapeutic regimens in the treatment of patients with RSD, without a control group. Gobelet and associates[26] researched the efficacy of intranasal salmon calcitonin: 66 patients were randomly assigned to a group with and one without calcitonin, while both groups received PT. Although both studies concluded that PT is effective as a treatment for RSD, these conclusions should be tested against a control group that does not receive PT. In a study on 70 children with RSD, Wilder and colleagues[22] concluded that PT is the mainstay of treatment, but the lack of a control group weakens this statement.

Besides the lack of randomized controlled studies (RCTs) concerning the additional value of PT and/or OT in patients with RSD, it is also not clear which form (PT or OT) is the most effective or cost-effective.

Therefore, the objectives of our prospective RCT were to investigate the effectiveness and cost of PT versus OT in a large population of RSD patients.

METHODS

Patients

All the participants had been treated and evaluated at the outpatient clinic of the Department of Surgery, University Hospital Nijmegen or the Department of Anaesthesiology, Free

From Allied Health Services (Dr. Oerlemans) and Department of Surgery (Drs. van der Laan, Goris), University Hospital Nijmegen: the Department of Medical Statistics (Mr. de Boo) and Department of Medical Technology Assessment (Mr. Severens), University of Nijmegen; and the Dutch National Institute of Allied Health Professions, Amersfoort (Dr. Oostendorp). The Netherlands; and Free University of Brussels, Brussels, Belgium (Dr. Oostendorp).

Submitted for publication January 20.1999. Accepted in revised form June IO. 1999.

Supported by a research grant from the National Insurance Board (Ziekenfondsraad), The Netherlands.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Reprint requests to Margreet Oerlemans, I I I Allied Health Services. University Hospital Nijmegen. PO Box 9101, 6500 HB Nijmegen. The Netherlands.

0003-9993/00/8101-5433$3.00/0

University Hospital Amsterdam. Criteria for inclusion were: RSD of one upper extremity, with duration shorter than 1 year; complete treatment could be given in Nijmegen or Amsterdam; and age of 18 years old or older. Criteria for exclusion were: impairment in the contralateral extremity, (for example because of rheumatoid arthritis); relapse of RSD; pregnancy; lactation; and prior sympathectomy of the affected extremity.

The diagnosis of RSD was made according to the criteria formulated by Veldman and associates? (1) presence of four of the five following signs and symptoms: pain, altered skin color, altered skin temperature, edema, reduced range of motion; (2) presence of the symptoms in an area much larger than and also distal to the primary injury; and (3) aggravation of the symptoms by physical activity of the affected extremity. None of the patients had a peripheral nerve lesion, so all were classified as CRPS I.

Patients were given written and oral information about the study; written informed consent was obtained from all. The protocol received approval by the Independent Ethics Committees of the University Hospital Nijmegen and the University Hospital Amsterdam.

Design

The study was designed as a prospective randomized, controlled, single-blinded, clinical trial.

The outcome variables were evaluated five times during the 12-month study period (t0 to t4). After the baseline measurements (t0), patients were randomly assigned to one of three groups; group I, PT; group II. OT; group III, control therapy (social work [SW]). Assignment to groups was performed according to allocation lists established by the Department of Medical Statistics of the University of Nijmegen, with stratification to the duration of illness (two categories: 0 to 6 months, and 7 to 12 months) and to the temperature of the skin of the affected extremity at intake (two categories: warm and cold). Randomization was restricted to blocks of 6.

All three groups received medical treatment according to a fixed pre-established protocol, consisting of free-radical scavengers, peripheral vasodilators in the case of primarily cold RSD, and treatment of trigger points. Prescribed scavengers were dimethylsulfoxide (DMSO) 50% locally applied and *N*-acetylcysteine. DMSO was medication of first choice and was applied five times a day at the affected location; when the skin could not bear DMSO or as maintenance medication after DMSO treatment has stopped, *N*-acetylcysteine was prescribed (600mg three times a day). For vasodilatation, the calcium entry blocker verapamil, sustained-release 240mg one time a day, was given; second and third choices were, respectively, ketanserine 20mg two times a day (eventually increased to 40mg) and pentoxifylline 400mg two times a day. The effectiveness of the scavenger treatment has previously been reported.[28-30] The patients also received general information regarding RSD; notably, it was stressed to patients that they should rest the extremity and not provoke pain. They were seen by the physician at every test-moment, and as often as needed otherwise.

Depending on the group, patients received PT, OT, or SW. Therapy was given according to a standardized protocol, with outcomes of tests guiding the therapist to the accompanying treatments. The content of the adjuvant therapies is described in general terms in the appendix. Eleven therapists participated in the research, 6 physical therapists and 5 occupational therapists; 4 social workers participated for the benefit of the control condition. Reassessment was performed 6 weeks (t 1), 3 months (t2), 6 months (t3). and 12 months (t4) after inclusion in the study.

Cost parameters were measured prospectively during the I2 months of follow-up. If the patient explicitly requested a switch to another adjuvant therapy during the period of the trial, this was allowed. Using a coin. with heads or tails, it was decided which adjuvant therapy was next.

Patients were treated until no further progress could be measured, or until treatment could be stopped without recurrence of complaints.

Outcome Measures

The results of treatment were documented on three levels: impairment, disability, and handicap. On the level of impairment, the impairment level sumscore (ISS) was computed.[31] This multicomponent test has been constructed to map alterations in impairment in RSD patients. The ISS is formed by outcomes obtained with four measurement parameters and five instruments. The outcomes for each instrument are converted into a score, from which the compounded ISS is derived (table 1). The ISS is reliable and seems to have both content and concurrent validity, as was established in 45 patients with RSD

Table 1: Construction of the Impairment Level Sumscore (ISS)

Measurement Variables	Score 1	2	3	4	5	6	7	8	9	10
Visual analogue scale										
Pain resulting from effort (mm)	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-I 00
McGill Pain Questionnaire (Dutch language version)										
Total number of words chosen	0-2	3-4	5-6	7-8	9-10	11-12	13-14	15-16	17-18	19-20
Active range of motion										
Points awarded for 5 joints*	5-6	7-8	9-10	11-12	13-14	15-16	17-18	19-20	21-22	23-25
Temperature difference										
Hands (dorsal aspects; °C)	0-0.3	0.4-0.5	0.6-0.7	0.8-0.9	1.0-I .1	1.2-I .3	1.4-1.5	1.6-1.7	1.8-I .9	≥2.0
Volume difference hands (mL)†	≤16	17-23	24-29	30-36	37-43	44-50	51-56	57-63	64-70	≥71

A converted score of between 1 and 10 is given for the outcomes of each of five measurement variables. Adding these 5 scores results in a sumscore ranging between 5 and 50. A higher score indicates more severe impairment.

* For active range of motion, each joint was given points for the percentage of normal mobility: 1 point for ≥95%; 2 points for 94% to 85%; 3 points for 84% to 65%; 4 points for 64% to 25% and 5 points for <25% normal mobility. Active rnages of motion of dorsal/palmar flexion in the wrist and flexion/extension in the metacarpophalangeal and proximal interphalangeal joints of the two most restricted digits were used.

† Volume classes are defined (for example, volume class 401-500 mL), and percentages of these classes are expressed as categories of milliliters and assigned a score. The unaffected hand is fitted to a volume class. Then, the difference in volume is matched to a category and given a score.

of one upper extremity.[31] Intraobserver reliability and test-retest reliability of the instruments building the ISS are mostly >.80. Also, the responsiveness of the ISS has been found to be adequate.[31] A difference in amount of decrease of 5 ISS points between groups over the 12-month study period was considered to be clinically relevant.

On the level of disability, three measurement instruments were used. The Radboud Skills Questionnaire[32] was used to determine the perceived degree of deviation from normal use of both hands in activities of daily living. The questionnaire has been found reliable in RSD patients, with good agreement between the outcomes for the test-retest and the interobserver reliability studies as established with the method of Bland and Altman.[32,33] The modified Greentest[34] measured differences in the degree both hands could move light objects (eg, small pins, discs) within 15 seconds using different grips. The test is described as reliable; no prior studies are known using this test with RSD patients. The Radboud Dexterity Test[35] made qualitative assessments of seven skills associated with daily activities (eg, closing a zip fastener, washing hands). This reliable test was specifically developed for RSD patients.[35]

On the level of handicap no specific test was performed. Instead the evaluation incorporated elements from all three levels, using the Sickness Impact Profile (SIP).[36] The SIP is a generic clinimetric index for well-being and consists of 136 assertions. The total score was computed as well as the subscores for the degree of physical dysfunction and the degree of psychosocial dysfunction. Test-retest reliability and interobserver reliability are high (r = .97 and r = .73 to .96, respectively)." These data are derived from a large population of patients, not a specific population of patients suffering from RSD.

Cost-Effectiveness Analysis

A societal viewpoint formed the basis of the cost-effectiveness analysis.[38] Health care resources were measured prospectively and an approximation of the true cost was made. A distinction was made between medical, nonmedical, and productivity costs. The effectiveness measures for the cost-effectiveness analysis were the ISS, the modified Greentest, and the SIP. On the basis of the difference in the mean total medical cost (up to and including t4) between the three study groups and the mean difference in effectiveness (from t0 to t4), incremental cost-effectiveness ratios were calculated for each effectiveness measure.

Sample Size and Interpretation of Results

The trial was planned to include 1.50 patients. With 50 patients per group after 1 year of treatment, differences of 6 to 7 points in mean ISS between the groups would have 80% power of being detected. Thus, with the inclusion of 135 patients, the power to recognize significant differences was somewhat smaller: the power to detect a significant treatment effect within each group was 72%, whereas differences between the three groups could be established with a power of 79%.

Assessment of the results of treatment was performed using the ISS and an analysis of its constituents. Two analyses were done: an intention-to-treat (ITT) analysis and a per-protocol (PP) analysis. For the ITT analysis, outcomes of all patients were used for the group they were assigned to. For the PP analysis, outcomes of dropouts or patients who switched to another adjuvant therapy (protocol violators) were ignored.

Apart from the analysis of the effect sizes, differences in the course of time were studied between the three groups for each of the measurement instruments.

Statistical Analysis

A repeated measurements model was used to examine center effects and possible differences over the course of time.

The primary end points were the difference in ISS between t0 and t4 and the individual components of the ISS, as tested with Student's t test. The method of Hochberg and Benjamini[39] was applied to correct for multiplicity of tests. In this study, this method yielded the following decision procedure: three t tests were done to test possible differences between treatments. Then the three p values were ordered. When the largest p value was smaller than .05, all three null hypotheses were rejected. If not, when the second largest p value was smaller than .05/2, then the null hypotheses corresponding with the two smallest p values were rejected. If not, when the smallest p value was smaller than .05/3, the corresponding null hypothesis was rejected.

On the level of disability and handicap, explorative tests were performed (Wilcoxon; $\alpha = .05$), using the difference between baseline and 1-year measurements as effect variables. Cost differences were nonparametrically tested (Mann Whitney U). Extensive sensitivity analyses were performed to judge the robustness of the findings.

RESULTS

Patients

From June 1, 1994 to February 28, 1998, 135 patients (95 women and 40 men) with RSD of one upper extremity were included in our study (fig 1). A further 10 patients fulfilled the inclusion and exclusion criteria; they were approached but refused to take part because of the travelling distance and/or lack of time, or because they were unwilling to leave their physiotherapist or participate in a research project.

The total group comprised 39 patients from the Free University Hospital Amsterdam (30 women and 9 men) and 96 from the University Hospital Nijmegen (65 women and 3 1 men). The mean age of the whole group was 53 $\pm$ 17 (SD) years. In 45% of the patients RSD was located in the right upper extremity; in 55%, it was in the left upper extremity. In half the patients, RSD occurred on the dominant side. At inclusion, the mean duration of complaints was 3.6 $\pm$ 3.4 months. The characteristics of the patient sample are described in table 2. No relevant differences in patient characteristics were present between the two treatment centers. The patients in the three research groups had similar characteristics at enrollment.

On entering the study, 62% of the patients were experiencing warm RSD, which had existed for less than half a year; in 7%, warm RSD had existed for more than half a year. In 20% of the patients, cold RSD was present, which had existed for less than half a year; in 1 1%, cold RSD had existed for more than half a year.

The primary trauma was a fracture in 53% of the patients and a contusion in 11%. In 13% of the patients, RSD occurred spontaneously. Other initiating events included mallet finger, carpal tunnel syndrome (without a nerve lesion), or some type of operative intervention to the limb and sprains. Before the first visit to the outpatient clinic, one patient had received a guanethidine block and another a sympathetic block per injection; in both cases the result was unsatisfactory.

After inclusion in the study, 44 patients were referred to PT, 44 patients to OT, and 47 patients to SW (fig 1). In the course of the 1-year study period, 7, 4, and 4 patients in each group, respectively, abandoned the trial. Another three patients from the PT group could not complete the treatment protocol (so they were protocol violators) but had test continuity. Fourteen

patients switched therapies: 12 from SW to PT (9 patients) or OT (3 patients), and 2 from OT to PT.

Center Effects and Differences Over Time

No significant center effect was present, nor was there an interaction between center and treatment. Consequently, these factors were omitted from the analyses. All the main outcome variables appeared to differ significantly over time. These patterns differed between treatments.

Impairment

The differences between t0 and t4 for the three groups. as well as the p values from the t tests for differences in effect size between the three groups, are reported in tables 3 and 4.

PT and, to a lesser extent, OT resulted in more improvement in the ISS than the control condition (SW). For the PP analysis and after ordering the three p values, both PT and OT scored significantly better than SW (p = .006 and p = .024, respectively) (table 4). For the ITT analysis, PT but not OT scored nearly significantly better than SW (p = .023 and p = .07, respectively) (table 3). The supplementary improvement was 6 ISS points for PT, which was clinically relevant. and approximately 4 points for OT. In percentages, improvements on the ISS were approximately 53% and 57% for PT (ITT and PP analysis, respectively), 48% and 48% for OT, and 38% and 37% for SW. Both PT and OT had a significantly more positive effect

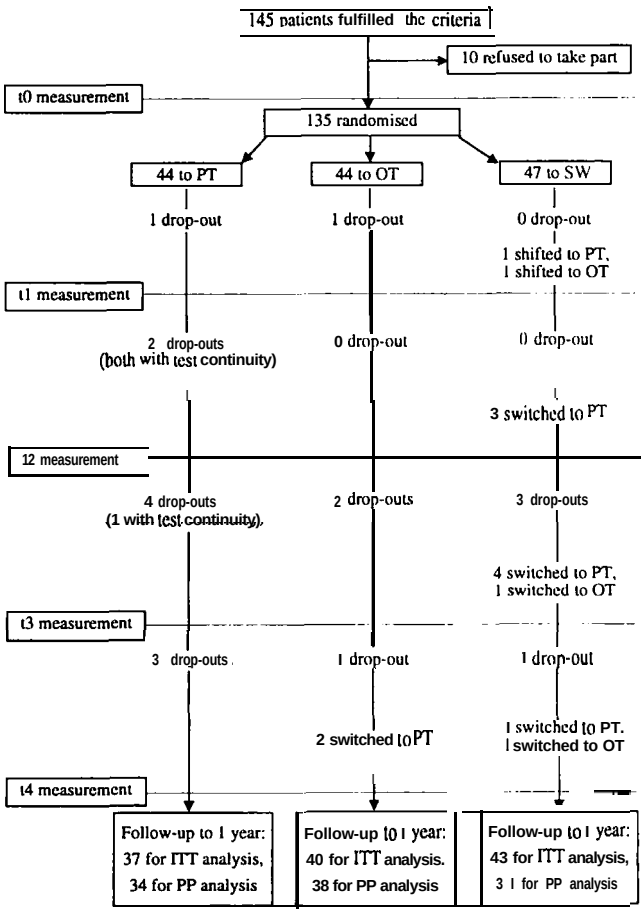

Fig 1. Trial profile. PT, physical therapy; OT, occupational therapy; SW, social work (control therapy); ITT analysis, intention-to-treat analysis; PP analysis, per protocol analysis.

Table 2: Characteristics of the Patient Sample

	PT n = 44	OT n = 44	S W n = 47	Total n = 135
Age (yrs)				
Mean	50.4	56.3	51.5	52.7
SD	15.6	17.0	16.9	16.6
Duration of symptoms (mo)				
Mean	3.1	2.9	2.9	3.0
SD	3.4	2.5	3.1	3.0
Time since primary trauma (mo)				
Mean	3.7	3.6	3.5	3.6
SD	3.5	2.6	3.9	3.4
	n %	n %	n %	%
Gender				
Male	15 (34%)	13 (30%)	12 (26%)	3 0 %
Female	29 (66%)	31 (70%)	35 (74%)	70%
Stratification*				
Warm-short	28 (64%)	28 (64%)	28 (60%)	62%
Warm-long	3 (7%)	3 (7%)	3 (6%)	7%
Cold-short	9 (20%)	8 (18%)	10 (21%)	20%
Cold-long	4 (9%)	5 (11%)	6 (13%)	11%
RSD side				
Left	26 (59%)	25 (57%)	23 (49%)	55%
Right	18 (41%)	19 (43%)	24 (51%)	4 5 %
RSD on				
Dominant side	21 (48%)	22 (50%)	23 (49%)	49%
Nondominant side	23 (52%)	22 (50%)	24151%)	51%

*** Stratification: warm, warm RSD; cold, cold RSD; short, RSD less than 6 months; long, RSD 6 months or longer.**

on the absolute difference in skin temperature than the control condition (an improvement of 0.6°C to 0.7°C). Furthermore. the effects of PT and, to a lesser extent, OT on the McGill Pain Questionnaire were larger than that of SW.

The different values (based on the computed means) of the ISS over time are shown in figure 2 (ITT analysis) and figure 3 (PP analysis). PT and. to a lesser extent, OT resulted in more rapid improvement in the ISS than SW. especially at tl and t2. This finding also applied to the individual components of the ISS, except for the absolute differences in swelling.

Disability

The Radboud Skills Questionnaire did not reveal any significant differences between the three treatment groups in the ITT and the PP analyses of the total score and the subscores for the categories of personal care. domestic activities. and other activities. Thus. the improvement in the perceived use of both hands did not differ between the three groups. Also, the improvement over time in mean skill levels was similar in all three groups.

The Greentest could not identify any significant differences in the overall results between groups: the improvement in the ratio of moving objects with the RSD hand versus the non-RSD hand was about the same in the three groups. When the individual components of the Greentest were analyzed, however. both the ITT and PP analyses revealed significant differences in favor of OT in 3 of the 7 components (moving pins with the pinch grip. and moving small sticks and somewhat larger sticks with the three-point grip). Furthermore, improvement in skills over time was more rapid for OT.

OT had a significantly better effect on the overall score on the

Table 3: Differences in Effect Between Baseline and 12-Month Impairment-Level Sumscores and Components (Intention-to-Treat Analysis), and t Test *p* Values

Variable	PT	OT	SW	PT-OT	PT-SW	OT-SW
ISS	15.8 (1.6)	14.2 (1.2)	10.7 (0.5)	1.6 (2.0)	5.1 (2.2)	3.5 (1.9)
				—	p = .023	p = .07
Temperature	0.5 (0.1)	0.6 (0.1)	-0.1 (0.1)	-0.1 (0.2)	0.6 (0.2)	0.6 (0.2)
				—	p = .003	p = .001
VAS	46.4 (4.5)	41.2 (4.2)	41 .9 (4.5)	5.2 (6.1)	4.5 (6.4)	-0.7 (6.2)
				—	—	—
MPQ-DLV	9.2 (1.0)	6.4 (0.8)	5.6 (0.9)	2.8 (1.3)	3.6 (1.3)	0.8 (1.3)
				p = .04	p = .01	—
Volume	14.4 (4.4)	18.5 (4.5)	10.5 (3.2)	-4.1 (6.2)	3.9 (5.3)	8.0 (5.3)
				—	—	—
AROM	5.5 (0.8)	5.8 (0.6)	5.1 (0.7)	-0.3 (1.0)	0.5 (1.0)	0.7 (0.9)
				—	—	—

Values reported as mean (standard error). The p values are for the t test for differences in effects between the three groups. Only p values $<.10$ are reported.
Abbreviations: PT, physical therapy; OT, occupational therapy; SW, social work (control therapy); ISS, impairment-level sumscore; VAS, visual analogue scale; MPQ-DLV, McGill Pain Questionnaire (Dutch language version); AROM, active range of motion.

Radboud Dexterity Test than SW (both ITT and PP analyses); patients in the OT group showed greater improvement in performing specific skills of daily living. This better effect mainly arose from closing a zipper, closing a buckle, and carrying a tray (the PP analysis also included putting on a shirt). Improvement over time was more rapid with OT in both analyses (and for PT in the PP analysis) than with SW.

Handicap

The results and improvement over time of the SIP scores were similar in all three groups. This applied to both the ITT and PP analyses of the total score and the subscores for physical and psychosocial dysfunctioning.

Cost-Effectiveness Analysis

The treatment cost and travelling expenses in the control group were significantly lower than those in the PT and OT groups. For the other medical, nonmedical, and productivity costs there were no differences. The difference in increase in effectiveness was not significant in the modified Greentest and the SIP. According to the ISS, PT was superior to OT. Compared with SW, the incremental cost-effectiveness ratio of PT appeared to be modest (Netherlands guilders [NLG] 1861 ISS point), whereas it was higher for OT (NLG 1467/ISS point). The total medical cost per group is given in figure 4 (ITT analysis). Sensitivity analysis showed a modest influence of the cost parameters on the cost-effectiveness findings of the study.

DISCUSSION

This study showed that in patients with RSD of less than 1 year's duration, localized in one upper extremity, adjuvant PT and, to a lesser extent, OT had a clinically relevant therapeutic effect on impairment. This effect was additional to that of the medical treatment. These results support previous recommendations regarding PT in the treatment of RSD, as mentioned earlier.

PT makes a valuable contribution to the relief and cure of signs and symptoms of RSD and plays an important role in the adjuvant treatment. The additional value of OT was somewhat smaller. Nevertheless, on the level of disability there was a positive trend in favor of OT: for 1 of 3 instruments (the Radboud Dexterity Test), the overall score was better for OT than for SW. Furthermore, 3 of the 7 subscores from the Greentest were better for OT. The additional value of PT and OT seemed to be located on different levels: impairment and disability, respectively. Therefore, it might be advisable to offer both therapies in a well-organized protocol to RSD patients. At many hand clinics and rehabilitation centers, both treatments are already being offered to RSD patients, sometimes with one

Table 4: Differences in Effect Between Baseline and 12-Month Impairment-Level Sumscores and Components (Per Protocol Analysis), and *t* Test *p* Values

Variable	PT	OT	SW	PT-OT	PT-SW	OT-SW
ISS	16.4 (1.7)	14.4 (1.3)	9.6 (1.7)	2.0 (2.1)	6.8 (2.4)	4.8 (2.1)
				—	p = .006	p = .024
Temperature	0.5 (0.1)	0.6 (0.1)	-0.2 (0.2)	-0.1 (0.2)	0.6 (0.2)	0.7 (0.2)
				—	p = .004	p = .002
VAS	47.9 (4.6)	42.2 (4.3)	41.2 (5.2)	5.7 (6.3)	6.7 (6.9)	-1 .0 (6.7)
				—	—	—
MPQ-DLV	9.6 (1.0)	6.5 (0.9)	5.3 (1.1)	3.1 (1.4)	4.3 (1.5)	1.2 (1.4)
				p = .025	p = .005	—
Volume	15.3 (4.8)	18.8 (4.7)	7.7 (3.5)	-3.5 (6.7)	7.6 (6.0)	11.1 (6.0)
				—		p = .07
AROM	6.1 (0.8)	6.1 (0.6)	4.7 (0.8)	0.0 (1.0)	1.4 (1.2)	1.3 (1.0)
				—	—	—

Values reported as mean (standard error). The p values are for the t test for differences in effects between the therapies (a dash indicates $p > .10$).
Abbreviations: PT, physical therapy; OT, occupational therapy; SW, social work; ISS, impairment-level sumscore; VAS, visual analogue scale; MPQ-DLV, McGill Pain Questionnaire (Dutch language version); AROM, active range of motion.

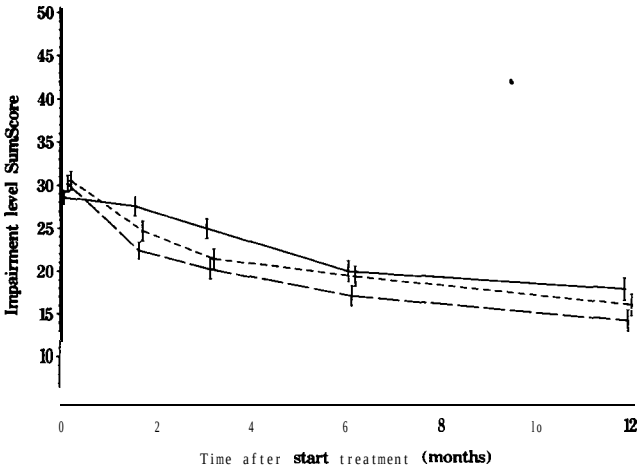

Fig 2. Impairment level sumscore (ISS) outcomes over time (based on the mean outcomes and their standard error; intention-to-treat analysis):-, social work (control therapy); ---, occupational therapy; - -, physical therapy.

(hand) therapist giving both treatment modalities.[16,18] It would be worthwhile to study the efficacy of a protocol that combines PT and OT, as compared to monodisciplinary adjuvant treatment.

In the light of the cost-effectiveness ratio, PT can be highly recommended. The better outcome after PT did not cost much more than SW. OT was more expensive. The major part of the additional cost resulted from "shopping," ie, consulting other medical specialists or bringing in other helpers. In a multidisciplinary setting, this shopping might be prevented.

The decrease in the severity of the signs and symptoms over time in all three groups was to be expected, given that the effectiveness of the medical treatments has previously been demonstrated in different research studies.[29,40] As control therapy, patients were treated by social workers. Therefore, all three groups received a form of attention and support from professionals within the hospital. Furthermore, all the patients received general information concerning RSD. Therefore, the additional recovery measured in the PT and OT groups relative

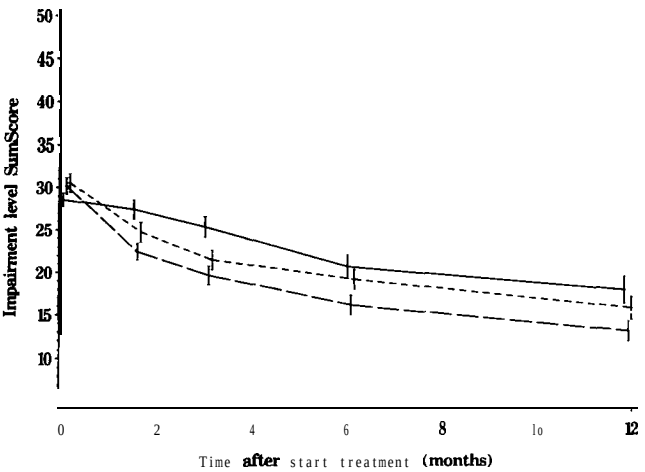

Fig 3. Impairment level sumscore (ISS) outcomes over time (based on the mean outcomes and their standard error; per protocol analysis): —, social work (control therapy); ---, occupational therapy; - -, physical therapy.

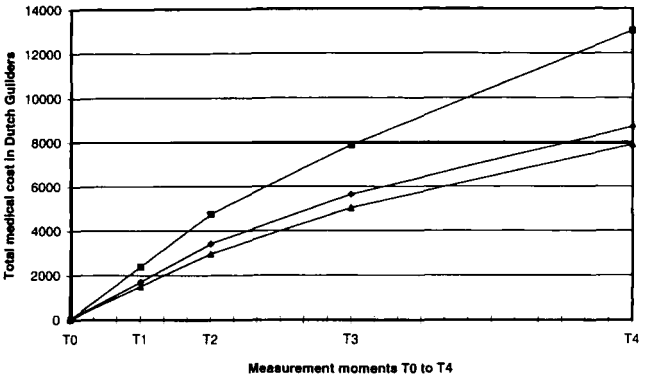

Fig 4. Total medical cost at t0 to t4 (mean outcomes; intention-to-treat analysis): ■ , occupational therapy; ● , physical therapy; A, social work (control therapy).

to the recovery in the SW group can be fully attributed to these therapies.

Although the study was set up with a single-blinded design. it turned out that blinding easily was disrupted after the baseline measurement. For example, patients wore splints or had partially tanned skin because of splints, or used transcutaneous electrical nerve stimulation (TENS) or showed evidence of having used plasters to connect TENS electrodes to the skin. Also, patients were seen on their way to the treatment departments. Therefore, the internal validity of the study was not optimal. We endeavoured to overcome this problem by using reliable and validated measurement instruments, by having four independent researchers/research assistants do the measurements, by holding mutual training and control sessions concerning the measurement methods, and by not doing any data analysis before the end of the study. In our opinion, it will be very difficult to maintain blinding in clinical studies of this type, with patients participating in physiotherapy or OT for several months at the hospital in which the research is being conducted.

Veldman and colleagues[6] reported that 322 of 489 patients (66%) who were receiving PT perceived temporary increase in complaints for a few hours following treatment. We did not measure such short-term complaints. As PT not only yielded significantly better results than SW, but also led to more rapid improvement over time, the probable temporary increase mentioned by Veldman did not influence the process of recovery of our PT patients. Furthermore, our positive results may be due to the specific content of the therapies. The increase in complaints reported by Veldman might have been the result of, for example, more demanding exercise therapy and is in keeping with one of the diagnostic criteria for RSD: "aggravation of the symptoms by physical activity of the affected extremity."

It has been demonstrated that the oxygen extraction in RSD of the upper extremity-as opposed to the unaffected contralateral extremity-is severely impaired.[5] Also abnormal phosphate energy metabolism has been found in the calf muscles of lower extremities affected by RSD. This finding may be caused by cellular hypoxia or diminished oxygen utilization.[41,42]

Furthermore, the venous refill times of healthy legs and RSD legs differ significantly.[43] Microcirculatory abnormalities have also been demonstrated in RSD extremities.[44] Therefore, a stress rehabilitation program that includes aggressive exercise therapy is not a treatment modality to be recommended, at least not in early RSD. In our study, a sort of "with pain, no gain protocol" was used, in which patients were taught to gain control of the pain, to observe their own reactions following activities, and to only execute activities that did not (yet)

exacerbate the pain or after which the pain decreased within a reasonable time. Within these margins, patients were instructed to practice often, in accordance with an individually set schedule.

Part of the OT comprised various forms of splinting. Some authors warn against immobilization,[45,46] and most articles published on RSD emphasize the importance of early restoration of normal function.[17,47,48] As nutritional flow to the RSD extremity is significantly disturbed, there is much to say for, for example, a resting splint or a cock-up splint that reduces oxygen utilization of the affected extremity while the patient is performing activities. Naturally, the use of these splints must be well instructed and reduced as soon as possible.

The physical and occupational therapeutic treatment protocols were specially constructed for this research. The protocols were based on current opinion and practice concerning the treatment of RSD patients in The Netherlands. Although the protocols received careful consideration, they probably still can be improved. This study forms the first step. We agree with Charlton,[17] who stated that future studies must pay attention to the type of physiotherapy (and OT) being applied and to identifying measures that are most appropriate to judge treatment progress and outcome.

CONCLUSION

On the basis of our randomized controlled clinical study of 135 patients with RSD of the upper extremity, we conclude that adjuvant PT, and to a lesser extent OT, makes a valuable contribution to the relief and cure of signs and symptoms of RSD. Although patients of all three groups improved by the applied medical treatment, improvement was significant and clinically relevant larger in PT (and, to a lesser extent, in OT) and was seen in a much earlier stage. Related to SW, both PT and OT did not raise additional costs much, with PT being the least expensive.

Acknowledgments: The authors are grateful to the staff at the Departments of Physiotherapy, Occupational Therapy, and Social Work for their enthusiastic cooperation, and to Mrs. M. Graff, Mr. R. Perez, and Mrs. J. Dijkstra for their assistance with data collection and organization of the study. Furthermore, the authors thank Mr. A. Reintjes, Department of Medical Statistics, for data management and Mr. P. Krabbe. Department of Medical Technology Assessment, for support with the SIP analysis.

References

1. Stanton-Hicks M, Jlnig W, Hassenbusch S, Haddox JD, Boas R. Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. Pain 1995;63:127-33.
2. Jlnig W, Blumberg H, Boas RA, Campbell JN. The reflex sympathetic dystrophy syndrome: consensus statement and general recommendations for diagnosis and clinical research. In: Bond MR, Charlton JE, Woolf CJ, editors. Pain research and clinical management vol. 4. Amsterdam: Elsevier Science Publishers BV; 1991. p. 373-6.
3. Blumberg H, Griesser H-J, Homyak M. Neurologic aspects of clinical manifestations, pathophysiology, and therapy of reflex sympathetic dystrophy (causalgia, Sudeck disease) [Dutch]. Nervenarzt 1991;62:205-11.
4. Sudeck P. Die sogen. akute Knochenatrophie als entzündungsvorgang. Der Chirurg 1942;15:449-58.
5. Goris RJA. Kolkman WFA. Leenen LPH. von Bebber IPT. Corstens FHM, Heerschap A. Symptomatologie van posttraumatische dystrofie. In: van Es JC, Joossens JV, editors. Het Medisch Jaar [Dutch]. Utrecht/Antwerpen: Bohn Scheltema en Holkema; 1988. p. 164-77.
6. Veldman PHJM, Reynen HM, Amtz IE, Goris RJA. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. Lancet 1993;342:1012-6.
7. Goris RJA, Reynen JAM, Veldman PHJM. De posttraumatische dystrofie. In: van Mourik JB, Patka P, editors. Letsels van de enkel en de voet. Epidemiologie, diagnostiek, therapie en revalidatie [Dutch]. Haren, The Netherlands: Symposiumcommissie Chirurgie Nederland; 1990. p. 435-46.
8. Goris RJA, Reynen JAM, Veldman P. The clinical symptoms in posttraumatic dystrophy [Dutch]. Ned Tijdschr Geneeskd 1990; 134: 2138-41.
9. Fialka V, Zifko I, Bochdansky T, Schneider B, Schimmerl S. Late sequelae of reflex sympathetic dystrophy: results of clinical, scintigraphic and dynamometric investigations. Eur J Phys Med Rehabil 1991;3:59-64.
10. Stanton-Hicks M, Jänig W, Boas RA, editors. Reflex sympathetic dystrophy. Dordrecht: Kluwer Academic Publishers; 1990.
11. Subarrao J, Stillwell GK. Reflex sympathetic dystrophy syndrome of the upper extremity: analysis of total outcome of management of 125 cases. Arch Phys Med Rehabil 1981;62:549-54.
12. Hardy MA, Hardy SGP. Reflex sympathetic dystrophy: the clinician's perspective. J Hand Ther 1997;10:137-50.
13. Fialka V. What kinds of physical therapy in reflex sympathetic dystrophy? [Dutch] Fortschr Med 1994;112:21 l-2.
14. Oostendorp RAB. Bemards ATM, Hagenaars LHA, Bemards JA, Schoot MA. Sympatische reflexdystrofie, een fysiotherapeutische benadering. In: van Es JC, Joossens JV, editors. Het medisch jaar 1990 [Dutch]. Utrecht/Antwerpen: Bohn Scheltema en Holkema; 1990. p. l-20.
15. Fialka V, Wickenhauser J, Engel A, Schneider B. Reflex sympathetic dystrophy. Effectiveness of physical therapy treatment of Sudeck's Reflexdystrophie. Wirksamkeit physiotherapeutischer disease [German]. Fortschr Med 1992;9:146-8.
16. Raj P, Cannella J, Kelly J, McConn K, Lowry I? Multi-disciplinary management of reflex sympathetic dystrophy. In: Stanton-Hicks M, Jänig W, Boas RA, editors. Reflex sympathetic dystrophy. Boston/Dordrecht/London: Kluwer Academic Publishers; 1990. p. 165-72.
17. Charlton JE. Reflex sympathetic dystrophy; noninvasive methods of treatment. In: Stanton-Hicks M, Jänig W, Boas RA, editors. Reflex sympathetic dystrophy. Boston/Dordrecht/London: Kluwer Academic Publishers; 1990. p. 151-64.
18. Bengtson K. Physical modalities for complex regional pain syndrome. Hand Clin 1997;13:443-54.
19. Hareau J. What makes treatment for reflex sympathetic dystrophy successful? J Hand Ther 1996;9:367-70.
20. Nielsen SR. Reflex sympathetic dystrophy and the role of active exercise. Acta Anaesthesiol Scand 1997;41: 1087.
21. Borg AA. Reflex sympathetic dystrophy syndrome: diagnosis and treatment. Disabil Rehabil 1996; 18: 174-80.
22. Wilder RT, Berde CB, Wolohan M, Vierga MA, Masek BJ, Micheli LJ. Reflex sympathetic dystrophy in children. J Bone Joint Surg Am 1992;74:910-9.
23. Husslage P. Physiotherapy and its regimen in the treatment of reflex sympathetic dystrophy. Pain Clin 1995;8:77-9.
24. Blumberg H, Griesser H-J, Homyak M, Specks C. Krankheitsbild un krankengymnastische Therapie der sympatischen Reflexdystrophie (Morbus Sudeck). Krankengymn 1991;43:128-36.
25. Lindenfeld TN, Bach BR, Wojtys EM. Reflex sympathetic dystrophy and pain dysfunction in the lower extremity. J Bone Joint Surg Am 1996;78:1936-44.
26. Gobelet C, Waldburger M, Meier JL. The effect of adding calcitonin to physical treatment in reflex sympathetic dystrophy. Pain 1992;48:171-5.
27. Abspoel M, Bernards ATM, Oostendorp RAB. Fysiotherapie bij sympatische reflexdystrofie: inventarisatie van hypothesen, rationales en behandelvormen [Dutch]. Amersfoort, The Netherlands: Stichting Wetenschap en Scholing Fysiotherapie; 1994.
28. Zuurmond WWA, Langendijk PNJ, Bezemer PD, Brink HEJ, Lange JJd, Loenen ACv. Treatment of acute reflex sympathetic dystrophy with DMSO 50% in a fatty cream. Acta Anaesthesiol Scand 1996;40:354-67.
29. van der Laan L, Goris RJA. Sudeck's syndrome. Was Sudeck right? [Dutch] Unfallchimrg 1997;100:90-9.

30. Goris RJA, Dongen LMV, Winters HAH. Are toxic oxygen radicals involved in the pathogenesis of reflex sympathetic dystrophy? Free Radic Res Comms 1987;3: 13-8.
31. Oerlemans HM, Goris RJA, Oostendorp RAB. Impairment level sumscore in reflex sympathetic dystrophy of one upper extremity. Arch Phys Med Rehabil 1998;79:979-90.
32. Oerlemans HM, Cup EHC, de Boo T, Goris RJA, Oostendorp RAB. The Radboud Skills Questionnaire: construction and reliability in patients with reflex sympathetic dystrophy of one upper extremity. Nijmegen, The Netherlands: University Hospital Nijmegen; 1998.
33. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-10.
34. Dapper MML. Een handreiking; een pilot-study naar het gebruik van de gemodificeerde Greentest na handoperaties bij patienten met reumatoïde arthritis [Dutch]. Nijmegen, The Netherlands: St. Maartenskliniek; 1988.
35. Cup EHC, van der Ven-Stevens LAW, Corstens-Mignot MAAMG. Radboud Dexterity Test (RDT). Nijmegen, The Netherlands: Department of Occupational Therapy, University Hospital Nijmegen; 1998.
36. Jacobs HM, Luttik A, Touw-Otten FWMM, de Melker RA. The Sickness Impact Profile: results of an evaluation study of the Dutch version [Dutch]. Ned Tijdschr Geneeskd 1990;134: 1950-4.
37. Damiano AM. The Sickness Impact Profile. In: Spilker B, editor. Quality of life and pharmacoeconomics in clinical trials. 2nd ed. Philadelphia: Lippincott-Raven Publishers; 1996. p. 347-5.
38. Drummond MF, O'Brien B, Stoddard GL, Torrance GW. Methods for economic evaluation of health care programmes. 2nd ed. Oxford: Oxford Medical Publications; 1997.
39. Hochberg Y, Benjamini Y. More powerful procedures for multiple significance testing. Stat Med 1990;9:8 11-8.
40. Langendijk PNJ, Zuurmond WWA, van Apeldoom HAC, van Loenen AC, de Lange JJ. Good results of treatment of reflex sympathetic dystrophy with a 50% dimethylsulfoxide cream [Dutch]. Ned Tijdschr Geneeskd 1993;137:500-3.
41. Heerschap A, de Hollander JA, Reynen H, Goris RJA. Metabolic changes in reflex sympathetic dystrophy: a ^{31}P NMR spectroscopy study. Muscle Nerve 1993;16:367-73.
42. Goris RJA. Reflex sympathetic dystrophy: model of a severe regional inflammatory response syndrome. World J Surg 1998;22: 197-202.
43. Fialka V, Saradeth T, Uher EM, Leitha T, Ernst E. Venous refill time in reflex sympathetic dystrophy (RSD)—a pilot study. Eur J Phys Med Rehabil 1996;6:82-4.
44. Kurvers HAJM, Jacobs MJHM, Beuk RJ, van der Wildenberg FAJM. Kitslaar PJEHM, Slaaf DW, et al. Reflex sympathetic dystrophy: evolution of microcirculatory disturbances in time. Pain 1995;60:333-40.
45. Wilson PR. Post-traumatic upper extremity reflex sympathetic dystrophy. Clinical course, staging, and classification of clinical forms. Hand Clin 1997;13:367-72.
46. Hood-White R, Gainor J. Reflex sympathetic dystrophy in an 8-year-old: successful treatment by physical therapy. Orthopedics 1997;20:73-4.
47. Wilson PR. Sympathetically maintained pain: principles of diagnosis and therapy. In: Stanton-Hicks M, Jänig W, Boas RA, editors. Reflex sympathetic dystrophy. Boston/Dordrecht/London: Kluwer Academic Publishers; 1990. p. 25-8.
48. Soucacos PN, Diznitsas LA, Beris AE, Xenakis TA, Malizos KN. Reflex sympathetic dystrophy of the upper extremity. Clinical features and response to multimodal management. Hand Clin 1997;13:339-54.

APPENDIX: PHYSICAL THERAPY, OCCUPATIONAL THERAPY, AND SOCIAL WORK TREATMENT PROTOCOLS FOR PATIENTS WITH RSD OF THE UPPER EXTREMITY

Physical Therapy and Occupational Therapy

After a structured assessment and according to fixed criteria, the patient was assigned to a specific treatment condition within the protocol for which the main treatment objectives were specified and adapted for intensity and method. Then, the intensity and form of treatment were adjusted for the individual patient. Measurements were taken monthly to evaluate and adjust the treatment condition. The treatment modalities and their use are described in the protocols.

Physical Therapy

Main treatment objectives:

1. Increasing control of pain and optimizing coping with RSD by talking (directed towards helping the patient gain control of the pain complaints by offering insight, practical advice, and support) or by relaxation exercises (to increase the selectivity of the patients);
2. Extinguishing the source of the ongoing pain by rest (locally), connective tissue massage, trancutaneous electric nerve stimulation (TENS), exercises for reducing the pain (directed to stimulate kinetic receptors type I and II);
3. Improving skills by practicing compensatory activities, giving instructions about the position of the body, and training skills.

Occupational Therapy

Main treatment objectives:

1. Reducing symptoms of inflammation and/or protecting and supporting the hand/wrist/forearm in the most functional and comfortable position, for example, by means of splint treatment;
2. Normalizing sensibility by means of different tactile materials, game activities, or techniques with a great deal of tactile and proprioceptive input;
3. Improving functional abilities of the arm/hand by executing various activities, while moving as normally as possible;
4. Improving independence in activities of daily living, by training, by learning how to perform activities differently, or by advising the patient regarding devices.

Social Work

In the control group, social work mostly comprised giving attention to the patient. Attention was given in a passive form, by listening to the patients and helping them in a limited form to gain insight into the social problems accompanying RSD. General information regarding RSD was also offered to the patients, concerning how not to evoke pain, while they were encouraged to take enough rest and to ask for help with executing activities that were too demanding for them.

Further information concerning the protocols can be obtained from Mr. J. Oosterhof, 355 Department of Physical Therapy or Mrs. E.H.C. Cup, 300 Department of Occupational Therapy, University Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands.