

# Focal Muscle Vibration in the Treatment of Upper Limb Spasticity: A Pilot Randomized Controlled Trial in Patients With Chronic Stroke

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**ABSTRACT.** Caliendo P, Celletti C, Padua L, Minciotti I, Russo G, Granata G, La Torre G, Granieri E, Camerota F. Focal muscle vibration in the treatment of upper limb spasticity: a pilot randomized controlled trial in patients with chronic stroke. *Arch Phys Med Rehabil* 2012;93:1656-61.

**Objective:** To examine the clinical effect of repetitive focal muscle vibration (rMV) on the motor function of the upper extremity 1 month after treatment in patients with chronic stroke.

**Design:** We performed a pilot randomized controlled trial using a double-blind, parallel-group study design.

**Setting:** Medical center.

**Participants:** Patients with chronic stroke (N=49).

**Interventions:** Patients randomly assigned to the study group (SG) received rMV, while patients in the control group (CG) received a placebo vibratory treatment. The patients and the clinical examiner were blind to the intervention.

**Main Outcome Measures:** The primary endpoint was an improvement of more than .37 points on the Functional Ability Scale of the Wolf Motor Function Test (WMFT FAS). The Modified Ashworth Scale and the visual analog scale were the secondary outcome measures. All measures were administered before the treatment (t0) and 1 week (t1) and 1 month (t2) after the treatment.

**Results:** Twenty-eight patients were allocated to the SG and 21 to the CG. The analysis of variance for repeated measurements revealed a significant difference in the expression of the WMFT FAS score over time only in the SG ( $P=.006$ ). The treatment was successful for 7 (33%) of 21 patients recruited in the SG and for 2 (13%) of 15 patients recruited in the CG. The relative risk was 2.5 (95% confidence interval, .60–10.39), and the number needed to treat was 5. The Wilcoxon test showed a statistically significant difference between t0 and t2 in the SG ( $P=.02$ ). No adverse event was observed in the 2 groups.

**Conclusions:** Our results suggest that rMV treatment of the upper limb may improve the functional ability of chronic stroke

patients, but a larger, multicenter, randomized controlled study is needed.

**Key Words:** Outcomes assessment; Rehabilitation; Spasticity; Stroke; Vibration.

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STROKE IS A LEADING cause of long-term disability and is often associated with persistent involvement of the upper limbs.<sup>1</sup> Six months after stroke, 30% of survivors require assistance to walk, and 25% need help to perform daily living activities.<sup>2</sup> The “best practice” for the rehabilitation of the paretic upper limb is still not clear. Motor recovery is a complex, confusing, and multifaceted process.<sup>3-5</sup> The underlying mechanisms for brain reorganization are likely to be related to increases in the numbers of synapses on dendrites and to the unmasking of neural latent networks.<sup>6</sup> It is also clear that after focal injury, some adaptive changes that are functionally relevant take place in the human brain.<sup>5</sup>

Among the different approaches to improve motor function, 1 strategy is to increase somatosensory input from the paretic hand by using somatosensory stimulation to enhance the human brain response to injury.<sup>5,6</sup> Muscle vibration is a strong proprioceptive stimulus, which, at low amplitude, preferentially produces Ia afferent input<sup>7</sup> able to reach the somatosensory and motor cortices.<sup>8-11</sup> In particular, some evidence demonstrated that a repetitive focal muscle vibration (rMV) with low amplitude repeated for 90 minutes over 3 consecutive days at a fixed frequency of 100Hz induces long-term changes of motor performance in healthy subjects and in stroke patients.<sup>12,13</sup> Recently, a study<sup>14</sup> using transcranial magnetic stimulation showed that rMV therapy, combined with physiotherapy, may help to reduce abnormalities of the corticospinal excitability and of the intracortical inhibitory systems in the damaged hemisphere of poststroke patients. To our knowledge, however, no evidence is available on the clinical efficacy of rMV in the treatment of upper limb spasticity in poststroke

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## List of Abbreviations

|                   |                                    |
|-------------------|------------------------------------|
| ANOVA             | analysis of variance               |
| CG                | control group                      |
| CID               | clinically important difference    |
| FAS               | Functional Ability Scale           |
| MAS               | Modified Ashworth Scale            |
| MDC               | minimal detectable change          |
| MDC <sub>90</sub> | MDC at the 90% confidence interval |
| rMV               | repetitive focal muscle vibration  |
| SG                | study group                        |
| VAS               | visual analog scale                |
| WMFT              | Wolf Motor Function Test           |

patients. We focused on patients with chronic stroke because the stable clinical picture may facilitate the evaluation of the effectiveness of rMV. In this study, our aim was to verify whether rMV treatment may improve the upper limb function of patients with chronic stroke.

## METHODS

### Study Design and Participants

We performed a pilot randomized controlled trial, using a pragmatic double-blind, parallel-group study design. Patients affected by chronic spastic hemiplegia/hemiparesis resulting from ischemic or hemorrhagic stroke at least 1 year before were eligible to participate in the study. Exclusion criteria were a cardiovascular event (myocardial ischemia or infarction) occurring within 12 months, injections of antispastic drugs into the upper limb muscles, surgical treatment in the previous year, and a score of less than 24 on the Mini-Mental State Examination.

Patients were recruited by a neurologist (G.G.) who evaluated the subjects after a rehabilitation program at the Fondazione Don Gnocchi in Rome. The Fondazione Don Gnocchi is a rehabilitation center where mainly patients with subacute and chronic stroke are treated. The patients were randomly placed into study and control groups (respectively, SG and CG) using a computer-generated randomization list. The patients were allocated by sealed envelope, sequentially numbered, which were opened just before the treatment. rMV was applied by 2 trained physiatrists (F.C. and C.C.). The clinical evaluations were performed by 1 neurologist (P.C.) blinded to the intervention and different from the recruiting physician (G.G.). The neurologist who clinically evaluated the patients was always the same (P.C.). Data analysts (G.L. and E.G.) were kept blinded to the allocation. The experimental protocol was designed according to the Declaration of Helsinki and was approved by the local ethics committee. All study participants provided informed consent.

### Intervention

Vibratory stimulation was applied to the muscles using a specific device<sup>a</sup> that consisted of an electromechanical transducer, a mechanical support, and an electronic control. The support was rigidly anchored to the floor to guarantee good mechanical contact with tissue. A mechanical arm permitted the transducer to be placed on the treatment site. The soft tissues were compressed to ensure better transmission of vibrations to the muscles.

The transducer applied perpendicular to the muscle, near its distal tendon insertion, generated a sinusoidal displacement of 0.2 to 0.5mm (peak to peak). The transducer was driven to produce forces ranging between 7 and 9N. The vibration frequency was set at 100Hz, as previously described.<sup>11-15</sup>

During rMV, the participants were supine, and they were requested to contract the treated muscles. The assessors (F.C. and C.C.) monitored the muscular contraction throughout the series of applications. Figure 1 shows a typical treatment setting. In the SG, rMV was simultaneously applied to the pectoralis minor and the biceps brachii of the affected limb. During another session on the same day, 1 transducer was applied to the flexor carpi muscle. The mechanical applications were applied over 3 consecutive days. For each muscle, the applications consisted of 3 vibration sessions, each with a duration of 10 minutes. A 1-minute interval separated the sessions. During the intervals, rMV was interrupted and the subject was requested to relax the muscle. The CG participants



Fig 1. Focal vibratory device and application setting to the upper limb.

underwent false (placebo) rMV while the treated muscles were kept contracted. In this group, the vibrator was positioned close to the tendon but without touching the skin, as previously described.<sup>15</sup> In this condition, the patients were subjected only to the faint buzzing sound of the vibrator. Like the SG subjects, however, the CG participants were told that they were being treated with a vibrating electromagnetic device. The placebo rMV applications were organized over 3 days as described for the SG. All the participants continued to undergo their rehabilitation program (3d/wk for 1h/d). To verify that rMV was applied following the described protocol, all rMV sessions were videotaped, and the tapes were checked by the neurologist who recruited the patients (G.G.).

The patients allocated to the CG were treated with rMV at the end of the study.

### Outcome Measures

The patients of both groups were clinically evaluated before rMV treatment (t0) and 1 week (t1) and 1 month (t2) after treatment. During the 3 sessions, the patients were evaluated by the Wolf Motor Function Test (WMFT), the Modified Ashworth Scale (MAS), and the visual analog scale (VAS). The WMFT was our primary outcome measure; MAS and VAS were secondary outcome measures.

The WMFT quantifies the movement ability of the upper extremity through functional timed tasks.<sup>16</sup> It requires few tools and minimal training. The WMFT is one of the most used outcome measures in studies on stroke rehabilitation to assess upper extremity function.<sup>17</sup> We evaluated the 15 items (of the 17 items comprising the WFMT, 2 of the tasks are a simple measure of strength) that investigate functional ability. Those items contributed to the generation of 2 scores: the performance time (WMFT time) score and the Functional Ability Scale (FAS) (WMFT FAS) score. In the present trial, the primary endpoint with respect to the efficacy of rMV was the proportion of patients achieving a minimal detectable change (MDC) higher than .37 points on the WMFT FAS from baseline to t2. We decided to use the WMFT FAS because it is more responsive to changes than the WMFT time.<sup>18</sup> The performance was rated using a 6-point FAS ranging from 0 (inability to use the involved arm) to 5 (normal movement).<sup>19</sup> The summary score for the WMFT FAS is expressed as a mean of the item scores. To evaluate whether the change from baseline was clinically important, we considered a clinically important difference (CID) to be a variation of 0.2 to 0.4 points in the mean WMFT FAS score.<sup>18</sup>

The MAS was used to measure spasticity; the scale evaluates the resistance of a relaxed limb to a rapid passive stretch in 6 stages.<sup>20</sup> Zero indicates a normal or slightly increased muscle

tone, and 5 indicates a state in which the passive movement of the affected limb is impossible. We tested abduction and adduction of shoulder, and flexion and extension of the elbow and wrist.

The VAS was applied to evaluate pain severity during passive mobilization of the shoulder, elbow, and wrist of the affected upper limb (VAS, 0–10cm: 0, no pain; 10, severe pain).<sup>21</sup>

### Statistical Analysis

The statistical analysis was conducted with the SPSS software package for Windows, release 19.0.<sup>b</sup> The Kolmogorov-Smirnov probability test was used to assess the normality of the distributions. The analysis of variance (ANOVA) for repeated measures (Pillai's trace F test) was used to verify differences in the expression of the variables over time (from t0 to t2) in the 2 groups.

Moreover, to evaluate the changes of the WMFT FAS score between the t0 to t1 and t0 to t2 conditions, we used the Wilcoxon test for paired samples. In the SG and CG, we evaluated the incidence of subjects with a change from baseline on the WMFT FAS score exceeding the values .37 (MDC at the 90% confidence interval [MDC<sub>90</sub>]), 0.2 (lower CID value), and 0.4 (higher CID value). To assess the difference between SG and CG, we calculated the relative risk to have a clinical improvement when the patient is treated with rMV (a patient was considered improved when the MDC<sub>90</sub> of the WMFT FAS score was higher than .37 at t2). Moreover, we calculated the number needed to treat. We used the Mann-Whitney *U* test to compare the central tendency measures (medians) of the MAS and VAS scores in the 2 groups. The significance level was set at *P* < .05. The presentation of the results is made according to the CONSORT statement.<sup>22-24</sup>

## RESULTS

Forty-nine consecutive patients affected by chronic stroke were recruited between September 2009 and June 2010. The recruitment was stopped because all the chronic patients who were treated at the rehabilitation center had been evaluated to participate in the study. The patients enrolled in the 2 groups showed a functionally important impairment at t0, with a minimum ability to perform active upper limb movements using the shoulder and/or the elbow and/or the wrist joints. Table 1 shows the clinical and demographic characteristics of participants at baseline (including WMFT, MAS, and VAS scores for both groups). Figure 2 shows the flow of participants. The primary analysis was intention to treat and involved 21 of 28 patients in the SG and 15 of 21 in the CG for all the outcome measures. Three patients in the SG were lost at t1 (1 patient moved to a different city, and 2 did not participate in the study because of practical or personal reasons; these 2 patients were evaluated at t2). At t2, 7 patients were lost to follow-up (the patient who moved away and 6 patients who did not participate because of practical or personal reasons). One patient in the CG was lost to follow-up at t1 because of personal reasons, but he was evaluated at t2. At t2, 6 patients were lost to follow-up because of practical or personal reasons.

The Kolmogorov-Smirnov probability test showed that the WMFT FAS score was normally distributed in both the SG and the CG at the t0 and t1 evaluations. At the t2 evaluation, the WMFT FAS scores of the SG were normally distributed, but the WMFT FAS scores of the CG were not normally distributed. The change in the WMFT FAS scores from baseline was normally distributed at t1 and t2 for both groups. The MAS and VAS scores showed a distribution that was not normal for both

**Table 1: Demographic and Clinical Characteristics of Participants at Baseline**

| Characteristics                       | SG<br>(n=28) | CG<br>(n=21) |
|---------------------------------------|--------------|--------------|
| Age (y)                               | 57.42±12.79  | 61.85±15.74  |
| Men/women                             | 20/8         | 14/7         |
| Months since stroke                   | 100.71±82.76 | 96.4±66.84   |
| Hypertension                          | 15/28        | 14/21        |
| Diabetes mellitus                     | 11/28        | 12/20        |
| Stroke type: ischemic/<br>hemorrhagic | 18/10        | 15/7         |
| Affected side: right/left             | 14/14        | 9/12         |
| Baseline WMFT FAS<br>score            | 1.7±1.23     | 1.53±1.36    |
| Baseline WMFT time<br>score           | 24.9±13      | 27.05±11.4   |
| Baseline MAS at<br>shoulder           | 1 (0–5)      | 1 (0–3)      |
| Baseline MAS at elbow                 | 2 (0–4)      | 1 (0–3)      |
| Baseline MAS at wrist                 | 1 (0–5)      | 2 (0–4)      |
| Baseline VAS at<br>shoulder           | 4 (0–10)     | 6 (0–10)     |
| Baseline VAS at elbow                 | 0 (0–9)      | 0 (0–9)      |
| Baseline VAS at wrist                 | 0 (0–8)      | 0 (0–10)     |

NOTE. Values are mean ± SD, n, or median (minimum–maximum). WMFT time refers to performance time of WMFT.

groups at t0, t1, and t2. We found no statistically significant difference between the SG and the CG at t0.

The ANOVA for repeated measurements revealed a significant difference in the expression of the WMFT FAS score over time only in the SG (*P* = .006); no difference was found in the CG. The MAS and VAS scores showed no difference over time in the 2 groups. The Wilcoxon test showed a statistically significant difference in the WMFT FAS score between t0 and t2 in the SG (*P* = .02); no difference was found between t0 and t1. In the CG, we found a statistically significant difference between t0 and t1 (*P* = .04); no difference was found between t0 and t2. When we consider the change in WMFT FAS scores from baseline, in the SG we found a mean value ± SD of .15±0.5 and .27±.49, respectively, for the t1 and t2 evaluations. In the CG, the mean change from baseline was .19±.43 and .13±.40, respectively, at t1 and t2.

Table 2 shows the incidence of patients who showed a change from baseline on the WMFT FAS score greater than .37 (MDC<sub>90</sub>), 0.2 (lower CID value), and 0.4 (higher CID value) at t1 and t2 in both groups. At t2, the proportion of patients achieving an MDC<sub>90</sub> higher than .37 points on the WMFT FAS was more than 2 times greater in the SG than in the CG, although this difference was not statistically significant. The number needed to treat was 5. We found no difference between the SG and the CG in the VAS and MAS scores at t0, t1, and t2.

Table 3 shows summary results for each group and for each outcome at 1 month after treatment. No adverse event was observed in the 2 groups.

## DISCUSSION

In this study, we evaluated the possible application of rMV therapy in the functional recovery of the upper limb after stroke. Because no evidence is available on the clinical effectiveness of rMV, and because soon after the acute event the clinical picture may evolve consistently,<sup>25</sup> we decided to perform a pragmatic pilot study in a group of poststroke patients

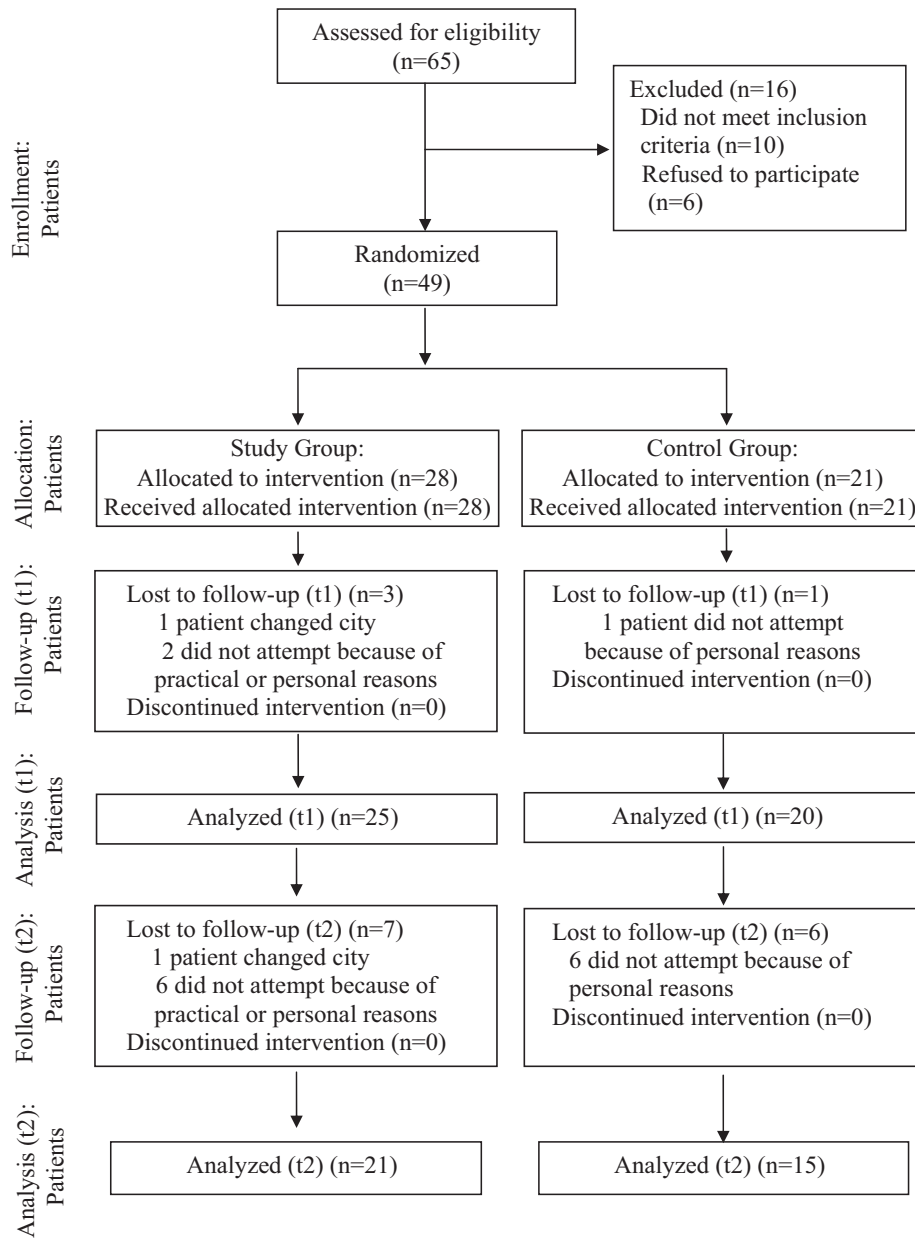


Fig 2. Diagram showing the flow of participants.

with a stable clinical picture. Indeed, in a stable sample of patients, the confounding factor resulting from spontaneous changes, occurring in subacute patients, is minimized.<sup>25</sup> Because clinically significant improvement after therapy does not necessarily coincide with statistically significant change, we

used as the outcome measure the WMFT scale. Indeed, for the 2 scores of the WMFT scale (WMFT time and WMFT FAS), a cutoff value is available for MDC<sub>90</sub> and CID, and this allows for the interpretation of the trial results, giving them clinical significance, if present.<sup>18</sup> Previous evidence suggests that

Table 2: Proportions of Patients Who Exceeded the Cutoff Values for MDC<sub>90</sub> and CID in the WMFT FAS Score at t2 Evaluation

| Scale          | Patients Exceeding the MDC <sub>90</sub> |           | Patients Exceeding the CID Value of 0.2 |            | Patients Exceeding the CID Value of 0.4 |           |
|----------------|--|-----------|---|------------|---|-----------|
|                | SG                                       | CG        | SG                                      | CG         | SG                                      | CG        |
| WMFT FAS at t1 | 40 (10/25)                               | 35 (7/20) | 56 (14/25)                              | 55 (11/20) | 40 (10/25)                              | 35 (7/20) |
| WMFT FAS at t2 | 33 (7/21)                                | 13 (2/15) | 52 (11/21)                              | 53 (8/15)  | 29 (6/21)                               | 13 (2/15) |

NOTE. Values are % (number of subjects exceeding MDC<sub>90</sub> or CID).

**Table 3: Summary Results for SG and CG and for Primary and Secondary Endpoints**

| Endpoint                  | Percentage (n) |           | RR (95% CI)     |
|---------------------------|----------------|-----------|-----------------|
|                           | SG (n=21)      | CG (n=15) |                 |
| <b>Primary endpoint</b>   |                |           |                 |
| WMFT FAS >.37 at 1mo      | 33 (7)         | 13 (2)    | 2.5 (.60–10.39) |
| <b>Secondary endpoint</b> |                |           |                 |
|                           | Median (Range) |           | Mann-Whitney    |
|                           | SG (n=21)      | CG (n=15) |                 |
| MAS at shoulder (0–5)     | 0 (0–5)        | 1 (0–3)   | NS              |
| MAS at elbow (0–5)        | 1 (0–4)        | 1.5 (0–3) | NS              |
| MAS at wrist (0–5)        | 1 (0–5)        | 1.5 (0–3) | NS              |
| VAS at shoulder (0–10)    | 0 (0–9)        | 5 (0–10)  | NS              |
| VAS at elbow (0–10)       | 0 (0–8)        | 0 (0–9)   | NS              |
| VAS at wrist (0–10)       | 0 (0–8)        | 0 (0–9)   | NS              |

Abbreviations: CI, confidence interval; NS, not significant; RR, relative risk.

WMFT FAS is a more reliable parameter than WMFT time in measuring modifications of the clinical picture,<sup>18</sup> and for this reason we used WMFT FAS as a primary outcome measure. The concept of CID, applicable to a group of subjects, means that if the mean change score is higher than a cutoff value, the change is clinically important. Because different methods are available to calculate the CID value,<sup>18</sup> we used 2 cutoff values (0.2 and 0.4) to interpret the results. Looking at the CID value, we found that in the SG, the statistically significant difference between t0 and t2 indicates a clinically important improvement, while in the CG, the statistically significant variation between t0 and t1 has no clinically important meaning.

The concept of MDC<sub>90</sub> is quite different from that of CID. The MDC<sub>90</sub> refers to the smallest change in a single subject that likely reflects a true change<sup>26</sup> rather than a measurement error. Looking at the MDC<sub>90</sub> for WMFT FAS, we may observe that the value of .37 is similar to the CID value (0.2–0.4). Therefore, we can assume that when the MDC<sub>90</sub> is higher than .37, the statistical significance expresses a clinically important change.<sup>18,27,28</sup> This kind of evaluation showed that the probability of showing clinical improvement is 2 times higher in the SG than in the CG, despite the absence of statistical significance because of the small sample size.

We think that a very interesting finding of our work is the absence of variation of MAS and VAS scores in the 2 groups at the ANOVA for repeated measurements, associated with a variation over time of the WMFT FAS score only in the SG. A possible explanation is that the stable contractures of tendons and the reduced joint range of motion determine strong functional limitations in the chronic patients of the 2 groups, and consequently this clinical picture prevents a significant improvement of the passive mobilization and of pain when patients are to undergo rehabilitation. The focal vibratory stimulation determines an improving trend in the SG probably because it acts on functional but not structural limitations caused by the muscular spasticity. Of course, the improvement observed in the SG, despite the presence of joint limitations, is encouraging. Probably, more details on the efficacy of the focal vibratory stimulation could be obtained in acute or subacute patients when anatomic alterations of the joints are not yet present. In this case, a larger sample of patients should be studied, and our findings justify this effort.

## Study Limitations

A limitation of our study is the absence of a sample size calculation. We did not calculate the sample size because, for economic reasons, we had a target group composed of patients followed up in our center (approximately 70 patients). Although our study was limited by the low number of randomized subjects, we believe that our results suggest that in the studied group, rMV treatment of the upper limb may improve functional ability in patients with chronic stroke. The results assume more relevance if we consider that, despite the possible presence of soft tissue contractures and joint limitations in the studied samples, the SG showed a clinical improvement at t2.

## CONCLUSIONS

To our knowledge, this is the first pragmatic randomized controlled trial that evaluates the clinical effectiveness of rMV therapy applied to the upper limbs of patients with chronic stroke. Currently, we do not think that our results can be generalized to patients with chronic stroke, but considering the lack of evidence on the effects of rMV, the reported data justify a larger, multicenter, randomized controlled study.

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#### Suppliers

- a. CroSystem; NEMOCO srl, Via Francesco Siacci 3, 00197 Rome, Italy.
- b. SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.