# Intermittent physical recovery has similar benefits to continuous physical recovery in patients in the acute and early sub-acute stages following a stroke

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Received August 12, 2022; Accepted December 16, 2022

DOI: 10.3892/etm.2023.11979

**Abstract.** Stroke is one of the most important causes of death and disability worldwide. The recovery of stroke survivors represents a real challenge for healthcare services. The aim of the present pilot study was to evaluate and compare the efficiency of two different approaches of physical rehabilitation in patients in the acute and early sub-acute stages following a stroke. Two groups of patients consisting of 48 and 20 patients, respectively, underwent continuous and intermittent physical recovery, and were assessed through electromyography and clinical evaluation. After 12 weeks of rehabilitation, no significant differences were identified between the outcomes obtained from the two groups. Due to the added value of intermittent physical recovery, this method of rehabilitation could be considered an approach that needs to be further studied for the treatment of patients in the acute and early sub-acute stages following a stroke.

## Introduction

According to the World Health Organization data, stroke is the second leading cause of death worldwide, and the third leading cause of death and disability combined. In recent decades, the incidence and prevalence of stroke has increased by >70% (1). In Europe only, stroke affects >1 million people every year with a mortality rate of 40% (2,3), and the prognosis is even worse in the context of population aging and exposure to risk factors, such as hypertension or other cardiovascular diseases, diabetes, low physical activity, obesity, unhealthy diet, smoking and abusive alcohol consumption (4,5). In addition, the forecast of the cost-related burden of stroke has severely increased, with an estimated increase by 27% by 2050 (6).

It is widely known that there are two major categories of stroke: Ischaemic and haemorrhagic. Ischaemic strokes are generated by interruption of the blood supply to a certain cerebral region, which leads to a sudden loss of function. Haemorrhagic strokes, also called intracerebral haemorrhages, have their origin in a burst blood vessel and the subsequent bleeding into and around the brain (7). Worldwide, ischaemic strokes are more common than haemorrhagic strokes, and account for ~80% of the total number of strokes; however, these data vary depending on the country and population (4).

Starting with symptoms that include trouble speaking, confusion, paralysis or paresis of the face and upper or lower limbs, visual impairment, headache, vomiting, dizziness, loss of coordination or altered state of consciousness, stroke can lead, in the majority of cases, to long-term effects (8). These long-lasting consequences are usually localized in the neurological (post-stroke seizures, hydrocephalus, spasticity), psychiatric (depression, anxiety, anger, frustration, personality change, post-stroke pain syndromes), cognitive (impairment in the field of communication, dysarthria, aphasia, spatial awareness, difficulties with memory, concentration, executive function and praxis, vascular dementia) and vascular (recurrent stroke, coronary artery disease, peripheral vascular disease) fields (9).

One of the most important sequelae of stroke is chronic motor deficits in the upper or lower limbs, which can lead to a severe impairment of the activities of daily living (ADL) and thus a decrease in the quality of life. Therefore, this disability represents an important target in the post-stroke rehabilitation process (10).

The assessment of motor status for stroke survivors is performed in both the acute and chronic phases through electromyography (EMG), which is the most often used and accurate study of muscle electrical activity. EMG is employed to localize the lesion and appreciate its degree of severity, to determine the nerve pathophysiology, and to evaluate the evolutionary timeline and rate of recovery (11). EMG studies have the advantage of customization in order to specifically localize the nerve lesion and offer to the clinician a clear image

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*Key words:* stroke survivors, rehabilitation, electromyography, activities of daily living, recovery

of the physiological status and the pathological processes that underlie the muscle disease or neuromuscular dysfunction. Based on these advantages, EMG is a useful tool for narrowing down differential diagnoses.

The recovery process after a stroke is strongly related to the evolutionary timeline, and currently, the most common categories of stroke stages are those proposed by the Stroke Roundtable Consortium: The first 24 h, hyperacute phase; the first 7 days, acute phase; the first 3 months, early sub-acute phase; months 4-6, late sub-acute phase; and from 6 months on, chronic phase (12). Related to this timeline, it has been reported that the most favourable period for recovery interventions is the early sub-acute phase, when the most significant improvements have been shown to occur (13). The subsequent stages are often characterized by a relative plateau in the amplitude of the recovery process, whereas the chronic phase is dominated by a deficit of rehabilitation (14). However, even though these phases are well-defined regarding their duration, in reality recovery is substantially different between affected individuals and the processes supporting the recovery for a given phase are still being studied (15). It has been reported that in the 6th month after a stroke, only 60% of survivors with hemiparesis who received rehabilitation procedures in hospital became independent in simple ADL (16).

Post-stroke rehabilitation involves a multidisciplinary approach, which needs to start in stable patients at least 48 h after the initial symptoms. The outcomes of the rehabilitation can lead to significant advantages for the patients, their families or caregivers and even for the community in which they live, in terms of reducing social and economic burden. As aforementioned, multidisciplinary effort is needed in order to solve the sequalae of strokes, and must include physicians (neurologists, neurosurgeons, rehabilitation medicine specialists) and physical, occupational and speech therapists, as well as psychological services, social support and medical equipment providers (17).

One of the main goals of the neurobiological rehabilitation strategies is represented by the restitution of neuronal activity, which can be achieved through pharmacological approaches and physical techniques. The physical techniques used include kinesiotherapy, cryotherapy, thermotherapy, electrotherapy and massage; all of these methods are currently used during the post-stroke rehabilitation process (18). The present study aimed to evaluate and to compare the efficiency of different approaches of physical rehabilitation in patients in the acute and early sub-acute stages following a stroke.

## Materials and methods

*Patients*. For the aim of the present study, which was carried out over a period of 2 years (January 1, 2019-December 31, 2021), 68 hemiparetic stroke survivors were recruited, who were admitted to the Rehabilitation Clinic, Emergency County Hospital of Craiova (Craiova, Romania), with which the University of Medicine and Pharmacy Craiova has a clinical agreement for medical services. All subjects had their diagnosis confirmed by a neurologist following a specialized examination, where the haemorrhagic aetiology of the brain injury was ruled out by a skull CT scan. At the time of recruitment, all subjects were clinically stable and within 48-72 h after the onset of a stroke.

The inclusion criteria were as follows: i) Post-stroke duration between 48 and 72 h after the onset of symptoms; ii) unilateral movement impairment of the upper limbs; iii) clinically stable; iv) without recent injury; v) without being under medication that can impact neuromuscular function; vi) without a positive history for recurrent vascular episodes. The exclusion criteria were as follows: i) Patients with aphasia, as they were not able to provide informed consent; ii) patients with cardiac implantable electronic devices where the electrotherapy could interfere with their functionality; iii) patients who did not agree to participate.

All patients were clinically evaluated by the medical recovery specialist at the beginning of the rehabilitation process by measuring the force of the brachial biceps and triceps muscles, as well as grading the spasticity of the upper limbs using the Modified Ashworth Scale (19). This assessment procedure was repeated every 2 weeks during the entire period of the study.

The motor function of the upper limbs was assessed using the Fugl-Meyer Assessment for Upper Extremity (FMA-UE) subscale, which consists of 33 items (domains: A, upper extremity; B, wrist; C, hand; D, coordination/speed), each item being scored on a 3-point ordinal scale (0, 1 or 2), with 0 generally corresponding to no function, 1 to partial function and 2 to perfect function. The general score was represented by the sum of the scores, with a maximum score (no impairment) of 66 points (20). The functional ability of the subjects was evaluated using the Barthel Index for ADL (0-100) (21), ADL (0-6) (22) and iADL (0-8) (23), scoring different activities that evaluate the patient's ability to act in activities of daily life using data related to occurrence of urinary or faecal incontinence, quantifying the ability of the patient to perform hair grooming, dressing, feeding, walking, climbing stairs, using the toilet and bathing independently. These four evaluation tools were used at the beginning and at the end of the rehabilitation program (study period). Demographic (age, sex and residency) and clinically relevant (comorbidities, health-risk behaviours and laboratory results) data were also collected.

All subjects were included in the present study on a voluntary basis and provided written informed consent. The present study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova (approval no. 167/12.06.2017; Craiova, Romania) and was in line with The Declaration of Helsinki.

*Recovery strategies*. All patients underwent complex physical therapy, consisting of kinesiotherapy, cryotherapy, thermotherapy, electrostimulation and massage, for 12 weeks. The patients were divided into two study groups that received an identical program of recovery therapies in terms of the procedures; however, the frequency of the rehabilitation sessions was different between the two groups: A total of 48 patients received continuous physical therapy, weekly for the whole study period, whereas the remaining 20 patients received intermittent rounds of physical therapy every 2 weeks (weeks 2, 4, 6, 8, 10 and 12). The two study groups were created based on the therapeutic approach decided on by the specialists from the Rehabilitation Clinic, Emergency County Hospital of Craiova.

Every patient underwent the same type of rehabilitation program as follows (Table I): i) Kinesiotherapy, consisting

Table I. Recovery therapies applied in the present study.

| Procedure | Monday | Tuesday | Wednesday | Thursday | Friday |
|---|---|---|---|---|---|
| Kinesiotherapy | 30 min | 30 min | 30 min | 30 min | 30 min |
| Cryotherapy | 20 min | 20 min | 20 min | 20 min | 20 min |
| Thermotherapy | 20 min | 20 min | 20 min | 20 min | 20 min |
| Electrotherapy | 45 min | 45 min | 45 min | 45 min | 45 min |
| Massage | Not applicable | 10 min | Not applicable | 10 min | Not applicable |

of passive and active-passive mobilizations of the affected shoulder, elbow and wrist joints, was performed twice a day for 15 min at a time, every morning and afternoon; ii) Cryotherapy was applied to the biceps brachii and triceps muscles, and consisted of ice pack applications for 10 min on each of the muscles, only if spasticity was present on the affected limb. This procedure was done daily from the onset of spasticity until its remission; iii) Thermotherapy was performed using paraffin wraps at a temperature of 55˚C placed on the affected arm, for 20 min, encompassing both the shoulder and elbow joints. This procedure was performed daily before the first kinesiotherapy session of the day. It increases ligament laxity, and thus could increase the passive and active range of motion of the affected arm; iv) A total of 10 min of upward massage of the affected upper limb was performed, targeting the reduction of swelling by stimulating fluid circulation in the arm. Massage was performed two times a week; v) Electrotherapy consisting of transcutaneous electrical nerve stimulation (TENS) and galvanization. The electrodes were applied with the negative pole placed on the proximal third of the stimulated muscle and the positive pole placed on the distal tendon of the respective muscle. Electrostimulation began with 10 min of galvanization, then TENS was applied followed by another 10 min of galvanization. TENS amplitude was raised until a 6-10 sec sustained contraction appeared, followed by a 1-min pause. The number of contractions per session was set at 20, thus accounting for ~25 min of TENS and a total of 45 min of electrotherapy. The biceps brachii and triceps were stimulated on a daily alternative basis, for example: Monday, biceps; Tuesday, triceps; Wednesday, biceps; Thursday, triceps, and so forth.

*Experimental setup and EMG recording.* For EMG recording, Participants were seated in an upright position with their arm comfortably supported. The forearm was immobilized by the examiner during the examination and was placed in full supination at 90˚ with the arm. Subjects were instructed to voluntarily produce hand-to-forearm or forearm-to-arm flexion. EMG recordings were done over the biceps brachii or flexor carpi ulnaris using Neuropack M1 MEB-9100 EMG/EP/IOM System (Nihon Kohden Corporation). In order to ensure appropriate electric contact and low baseline noise, the surface of the electrodes was placed over the skin only after it was cleaned with alcohol. The signal sampled every other 100 $\mu$sec was amplified and filtered with a bandwidth of 10 Hz to 10 kHz. Each subject was asked to perform the same protocol at the time of admission (week 1) and every 2 weeks until the end of the recovery program (weeks 2, 4, 6, 8, 10 and 12). When the setup was completed, patients were asked to perform maximal contraction of the recorded muscles. Discharge firing rate (DFR) was considered the main objective data that could provide an indication of how the rehabilitation sessions should be targeted.

Table II. Sociodemographic data of the two study groups.

| Characteristic | Continuous therapy group, n=48 (%) | Intermittent therapy group, n=20 (%) |
|---|---|---|
| Mean age, years | 57.83±1.73 | 58.05±1.64 |
| Sex | | |
| Male | 32 (66.67) | 10 (50.00) |
| Female | 16 (33.33) | 10 (50,00) |
| Environment | | |
| Urban | 20 (41.67) | 8 (40.00) |
| Rural | 28 (58.33) | 12 (60.00) |

*Statistical analysis.* All clinical and non-clinical items, and the results of the working instruments were recorded in a Microsoft Excel file (Microsoft Excel 2016; Microsoft Corporation). The descriptive analysis of the samples was realized using absolute and relative frequencies (%) or median and interquartile range (IQR). After testing, some of the data were found not to be parametrical. More complex analysis of the possible associations between recorded variables was performed using Prism 9.3.0 (GraphPad Software; Dotmatics) and SPSS version 20 (IBM Corp.). The following statistical tests were performed: Shapiro-Wilk's test for data normality analysis; Wilcoxon's rank-sum or Wilcoxon signed-rank tests followed by Bonferroni's corrections, or Friedman followed by Nemenyi's test, and mixed ANOVA followed by Sidak's test. Where the statistical tests could not be carried out due to the small number of subjects, this was noted in the tables of results as not applicable. $P<0.05$ was considered to indicate a statistically significant difference.

## Results

The socio-demographic data of the study samples revealed that the two samples had a comparable average age of the subjects, whereas in the continuous therapy group, the sex ratio was 2:1

Table III. Clinical data of the two study-samples.

| Characteristic | Continuous therapy group, n=48 (%) | Intermittent therapy group, n=20 (%) |
|---|---|---|
| Smokers | 31 (64.58) | 14 (70.00) |
| Comorbidities | | |
| Diabetes mellitus | 4 (8.33) | 1 (5.00) |
| High blood pressure | 25 (52.08) | 11 (55.00) |
| Diabetes mellitus + Hypertension | 10 (20.83) | 3 (15.00) |
| Laboratory data | | |
| Total cholesterol, mg/dl | 229.66±46.55 | 252.00±52.47 |
| Triglycerides, mg/dl | 208.60±57.94 | 222.40±54.50 |

male-to-female, while the intermittent group had a 1:1 ratio. Regarding where the patients lived, the distribution was also similar between the two groups (approximately two-thirds of the patients lived in a rural area) (Table II).

According to the study methodology, clinical and laboratory data considered to have an influence on the onset and evolution of stroke were collected. It was revealed that almost two-thirds of both groups consisted of smokers and >75% of patients had one or multiple associated medical conditions (diabetes mellitus and/or high blood pressure). Laboratory data revealed that both total cholesterol and triglyceride levels were high, which is characteristic for dyslipidaemia (Table III). All these collected data suggested that almost all patients were exposed to severe risk factors for the development of stroke.

The number of brain lesions was revealed by a CT scan. In the continuous therapy group, 33 patients (68.75%) presented with a left hemisphere injury resulting in an impairment of the right hemibody, and the remaining 15 patients (31.25%) had a lesion localized in the right hemisphere resulting in an impairment of the left hemisphere. In the intermittent therapy group, the lesion was situated on the left side for 14 subjects (70.00%), whereas it was situated on the right side for the remaining 6 subjects (30.00%).

According to the obtained results, the intermittent recovery appeared to be similar in effectiveness compared with continuous recovery for acute and sub-acute stroke. Clinical monitoring of the patients based on the scoring scales developed for patients with stroke revealed no differences between the patients enrolled in a continuous form of recovery program compared with those enrolled in an intermittent regimen (Fig. 1). The scores of the FMA-UE exhibited an improvement between weeks 1 and 12 for both continuous (n=48; P<0.0001) and intermittent (n=20; P<0.0001) groups. This improvement was observed in all domains of the FMA-UE: Upper extremity (Fig. 1A), wrist (Fig. 1B), hand (Fig. 1C) and coordination/speed (Fig. 1D). The total motor score of the two tested groups was similar (P>0.05) after 12 weeks of functional recovery (Fig. 1E). The aim of the present study was to determine if the intermittent recovery strategy differed from the continuous strategy. However, patients were recruited in both acute (<24 h post-stroke) and early sub-acute phases (within the first 72 h post-stroke), making the direct comparison difficult due to the different elapsed time from the stroke. Therefore, the present study, first investigated if there was any improvement within patients recruited in the continuous and intermittent groups. This was quantified as the percentage of improvement between the beginning and endpoint. There was no overall impact on the rehabilitation, as both acute and early sub-acute patients had similar improvements (P>0.05; Fig. S1).

Manual muscle testing (MMT) by EMG recordings detected no significant difference between the study groups. When MMT was measured for the biceps brachii (P=0.2718; Fig. 2A) and the triceps brachii muscle (P=0.3692; Fig. 2B), no significant difference was noted between the groups for the whole study period. The improvement in recovery between the beginning and end of the rehabilitation program in the continuous therapy group was significant, the biceps MMT score increased from 1.03±0.74 to 2.78±0.63 (P<0.0001) and the triceps MMT score increased from 0.79±0.63 to 2.39±0.69 (P<0.0001). A similar increase was observed in the intermittent therapy group for MMT [the biceps MMT score increased from 1.18±0.78 to 2.43±0.57 (P<0.0001) and the triceps MMT score increased from 0.78±0.60 to 2.08±0.57 (P<0.0001)]. The degree of spasticity evaluated by the Modified Ashworth Scale was did not differ significantly (P>0.05) during the study period (Fig. 2C).

Clinical monitoring of the patients based on the scoring scales developed for patients with stroke revealed no differences between the patients enrolled in the continues recovery program compared with those enrolled in the intermittent regimen (Fig. 3). The Barthel score was significantly improved between weeks 1 and 12 for both the continuous (n=48; 43.95±18.1 vs. 57.39±15.97; P<0.0001) and intermittent (n=20; 48.75±14.03 vs. 55±14.23; P=0.0003) groups (Fig. 3A). The same effects were observed for both iADL and ADL scores; after 12 weeks of stroke recovery procedures, both the continuous (n=48) and intermittent (n=20) groups improved in terms of iADL (P<0.0001) and ADL (P<0.0001) scores. Notably, no significant difference was recorded between the two groups at the final assessment on week 12 (iADL: 4.00±1.41 vs. 3.70±1.08, P=0.6075; ADL: 6.35±2 vs. 6.15±2.08, P=0.9171) (Fig. 3B and C).

As an objective measuring tool, the DFR was compared between the two groups, using the most basic clinical EMG

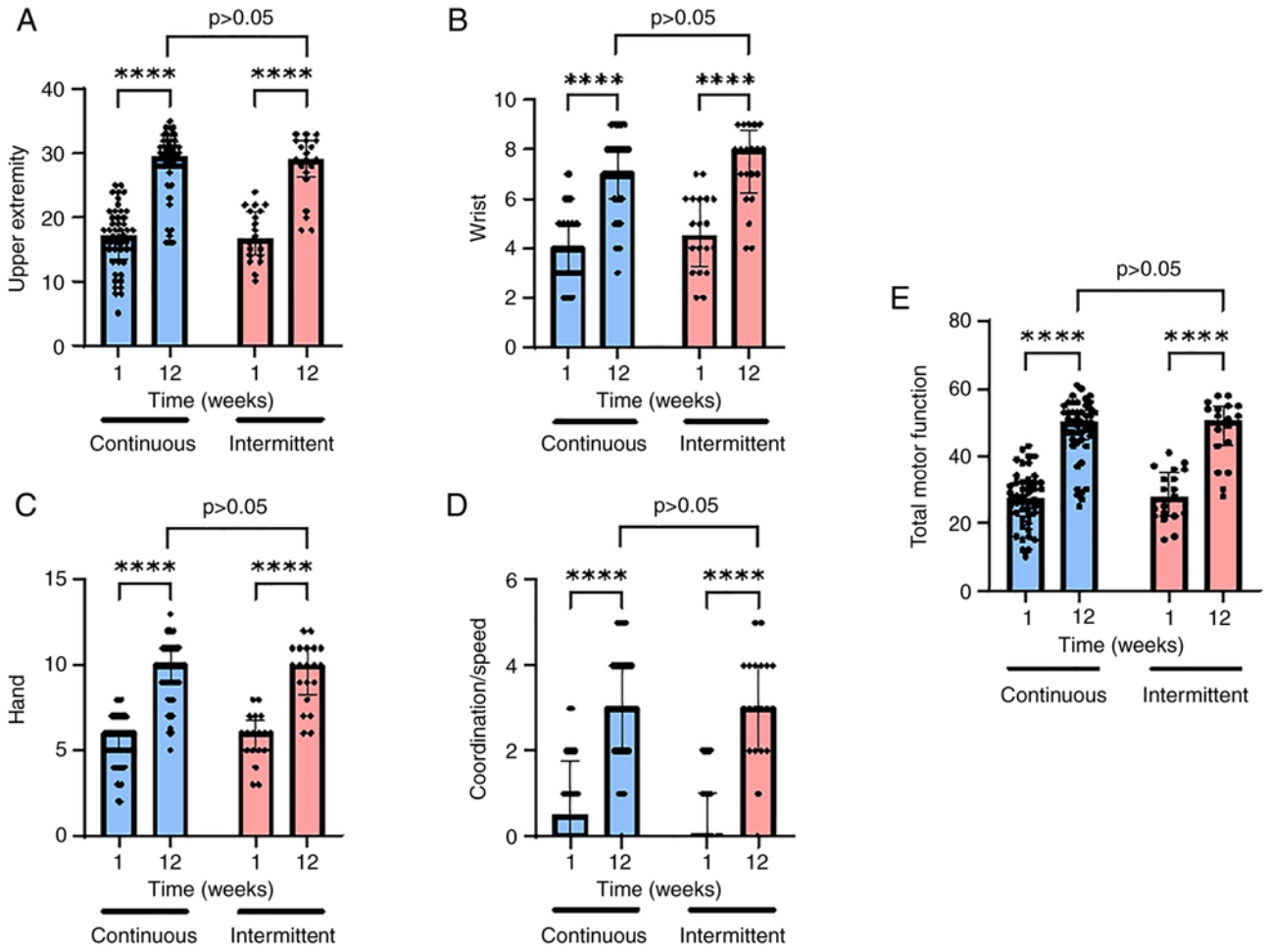


Figure 1. Comparison between FMA-UE scores during the study period. Improvement in all domains of the FMA-UE, (A) upper extremity, (B) wrist, (C) hand and (D) coordination/speed, was detected after 12 weeks. (E) Total motor score of the two tested groups was similar (P>0.05) after 12 weeks of functional recovery. The data are presented as the mean ± SD. ****P<0.001. FMA-UE, Fugl-Meyer Assessment Upper Extremity.

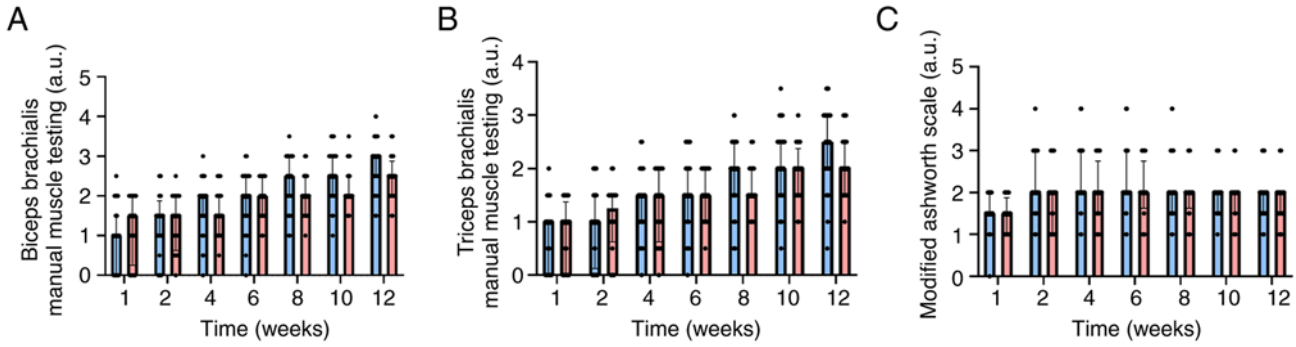


Figure 2. MMT and Modified Ashworth Scale of the subjects from the study groups. After 12 weeks of the physical rehabilitation program, the MMT estimations for (A) biceps brachialis (P=0.2718) and (B) triceps brachialis (P=0.3692) muscles between the two groups showed similar results. (C) Within the same interval, the two groups have shown a similar trend when measuring the degree of spasticity using the Modified Ashworth Scale, but this was not statistically significant (P>0.05). The data are presented as the mean ± SD. Blue bars represent the results for the 'Continuous' group, while the red bars indicate the results for the 'Intermittent' group. MMT, manual muscle testing; a.u., arbitrary units.

tests. No differences were observed among the two groups. The DFR was similar between the groups measured at week 12: Biceps brachii, 10.934±1.08 Hz in the continuous group vs. 10.62±1.89 Hz in the intermittent group; flexor carpi ulnaris, 9.81±1.54 Hz in the continuous group compared with 9.06±1.58 Hz (Fig. 4).

Analysing the relationship between FMA-UE scores on all four domains and socio-demographic data, it was revealed that for both study samples the evolution of recovery in terms of improvement during the 12 weeks of therapeutic process was statistically significant independent of sex and residence (P<0.01; Table IV).

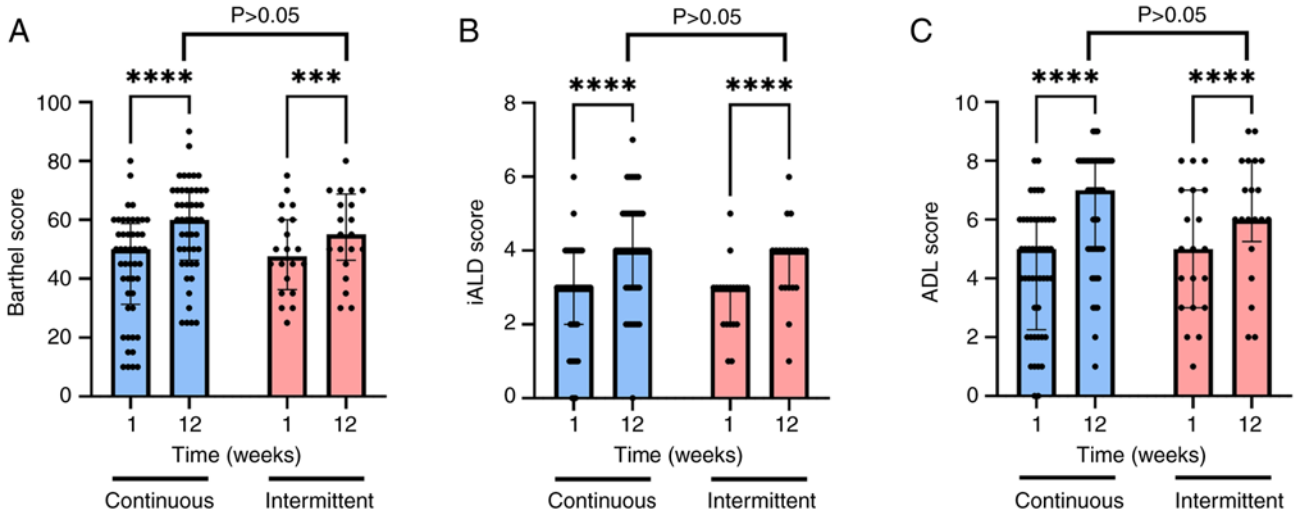


Figure 3. Comparison between the functional ability of subjects. No differences were observed between the two recovery groups regarding (A) Barthel Index, (B) iADL scale and (C) ADL scale. The data are presented as the mean ± SD. ***P<0.001 and ****P<0.001. ADL, activities of daily living; iADL Instrumental ADL.

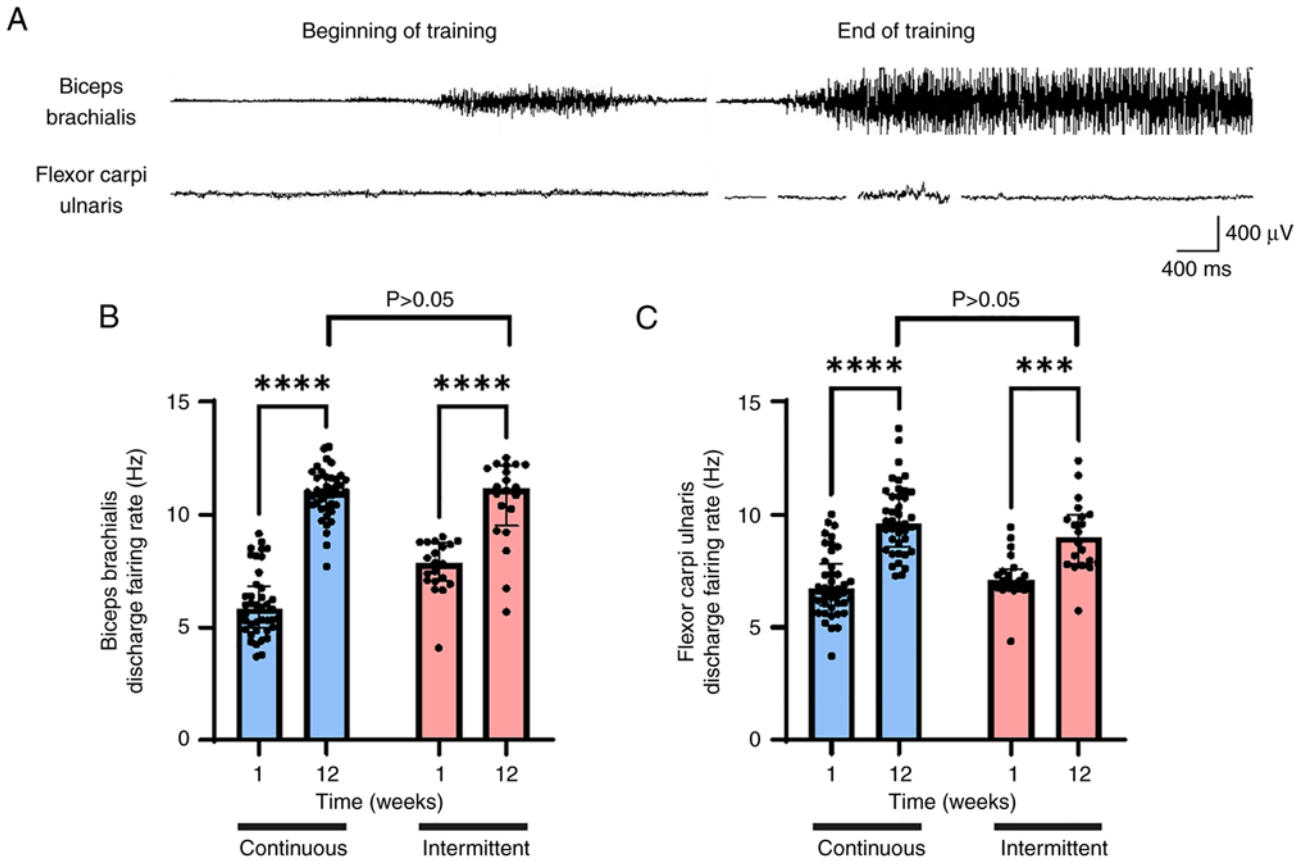


Figure 4. DFR extracted from electromyography recordings. (A) Example of improvement of DFR in the biceps brachialis and flexor carpi ulnaris after 12 weeks. (B) Biceps brachialis and (C) flexor carpi ulnaris DFR was improved in both groups after 12 weeks of rehabilitation therapies. The data are presented as the mean ± SD. ***P<0.01 and ****P<0.001. DFR, discharge-firing rate.

The present study examined the influence of demographics (sex and environment) on the evolution of recovery from week 1 to 12 in both groups. The improvement in the level of functional ability for ADL, iADL and Barthel, as expressed by the average scores of the working tools, was significant (P<0.05) in the intermittent and highly significant (P<0.001) in the continuous group, associated with both sex and residency (Table V).

The association between risk behaviours (smoking) and medical conditions (diabetes, hypertension and dyslipidaemia) with recovery outcomes, as measured by mean FMA-EU scores, were also statistically analysed. Notably,

Table IV. Association between FMA-UE scores and demographic data during the recovery process.

| | Continuous therapy group, n=48 | | | Intermittent therapy group, n=20 | | |
|---|---|---|---|---|---|---|
| | FMA-UE scores | | | FMA-UE scores | | |
| Patients | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Male patients | | | | | | |
| A-upper extremity | 17.00 (13.00-20.00) | 30.00 (28.00-31.00) | <0.001 | 16.00 (13.50-18.75) | 29.00 (22,00-30.75) | <0.010 |
| B-wrist | 4.00 (3.00-5.00) | 7.00 (7.00-8.00) | <0.001 | 4.00 (3.25-5.00) | 8.00 (6.25-8.00) | <0.010 |
| C-hand | 6.00 (4.75-6.00) | 10.00 (9.00-11.00) | <0.001 | 6.00 (5.00-6.00) | 10.00 (7.25-10.75) | <0.010 |
| D-coordination/speed | 0.50 (0.00-1.25) | 3.00 (2.00-4.00) | <0.001 | 0.00 (0.00-0.75) | 3.00 (2.25-4.00) | <0.010 |
| Female patients | | | | | | |
| A-upper extremity | 17.50 (15.00-20.25) | 28.50 (27.75-32.25) | <0.001 | 18.50 (14.50-22.00) | 30.50 (27.25-32.75) | <0.010 |
| B-wrist | 4.00 (3.00-5.00) | 6.50 (5.75-8.00) | <0.001 | 5.50 (4.00-6.00) | 7.50 (7.00-9.00) | <0.010 |
| C-hand | 6.00 (5.00-6.25) | 9.50 (8.00-11.00) | <0.001 | 5.50 (5.00-7.00) | 10.00 (9.00-11.00) | <0.010 |
| D-coordination/speed | 0.50 (0.00-1.25) | 3.00 (2.00-3.25) | <0.001 | 0.50 (0.00-1.75) | 3.00 (2.25-4.00) | <0.010 |
| Living in urban areas | | | | | | |
| A-upper extremity | 15.50 (13.00-18.25) | 28.00 (24.50-31.00) | <0.001 | 16.50 (14.75-20.25) | 29.00 (27.75-31.25) | <0.010 |
| B-wrist | 3.50 (3.00-4.00) | 7.00 (6.00-8.00) | <0.001 | 4.50 (4.00-6.00) | 8.00 (7.00-8.00) | <0.010 |
| C-hand | 5,00 (4.00-6.00) | 9.50 (8.00-10.00) | <0.001 | 6.00 (5.00-6.00) | 10.00 (8.75-11.00) | <0.010 |
| D-coordination/speed | 0.00 (0.00-1.00) | 3.00 (2.00-3.00) | <0.001 | 0.00 (0.00-1.00) | 3.00 (2.75-4.00) | <0.010 |
| Living in rural areas | | | | | | |
| A-upper extremity | 18.50 (16.75-21.25) | 30.00 (28.75-32.25) | <0.001 | 17.50 (12.50-22.00) | 30.00 (24.00-33.00) | <0.010 |
| B-wrist | 5.00 (4.00-5.00) | 7.50 (7.00-8.00) | <0.001 | 4.50 (2.75-6.25) | 7.50 (5.50-9.00) | <0.010 |
| C-hand | 6.00 (5.00-7.00) | 10.00 (9.75-11.00) | <0.001 | 5.50 (4.50-7.00) | 9.50 (8.25-11.00) | <0.010 |
| D-coordination/speed | 1.00 (0.00-2.00) | 4.00 (3.00-4.00) | <0.001 | 0.00 (0.00-2.00) | 3.50 (2.00-4.00) | <0.010 |

Wilcoxon signed-rank test, week 1 vs. week 12. FMA-UE, Fugl-Meyer Assessment Upper Extremity.

no differences were identified in the recovery period for both groups. Thus, during the 12 weeks of the study period, all subjects showed a significant improvement (P<0.005) in their health status where comorbidities were recorded, even if the recovery procedures were applied continuously or intermittently, according to the study methodology (Table VI). The low number of patients with diabetes mellitus and diabetes mellitus in association with hypertension did not allow for statistical analysis (n.a. in Table VI).

The association between risk behaviours (smoking) and comorbidities (as identified through clinical assessment) with positive outcomes of the rehabilitation program was also statistically significant (P<0.05). Thus, the efficiency of the recovery process was not impacted by these clinical aspects for the subjects who followed the continuous rehabilitation program, as well as for those who received intermittent procedures (Table VII). The low number of patients with diabetes mellitus and diabetes mellitus in association with hypertension did not allow for statistical analysis (n.a. in Table VII).

## Discussion

The present study investigated the benefits of the rehabilitation programs for stroke survivors in its continuous and intermittent variants. The clinical characteristics of the study subjects from both groups were similar to those mentioned by the specialized literature in terms of the presence of behavioural and clinical risk factors, including modifiable (hypertension, diabetes mellitus, high blood cholesterol, dyslipidaemia, smoking) (4) and nonmodifiable risk factors (age and sex) (5,24).

For the patients in the acute and sub-acute phases of stroke involved in the present study, the degree of functional improvement after the initial recovery program was significant, and could be considered a short-term recovery in functional status, as mentioned in previous studies (25,26). Thus, the initial approach of the rehabilitation process was the correctly selected, according to the clinical status of the subjects involved in the study. Based on the outcomes of the therapeutic process, it became clear that for the best possible recovery, the procedures should be initiated as soon as possible (18). Moreover, after the first series of rehabilitation procedures applied for 12 weeks, clinical evaluation is necessary to provide a clear and complete picture of the stroke survivor. The results of this evaluation will provide the background for the subsequent monitoring and recovery processes, in order to avoid a possible worsened evolution of the functional abilities as described in long-term studies (26,27).

Even if the medical conditions identified (hypertension, diabetes and dyslipidaemia) in the present subjects were not significantly involved in the deterioration of the evolution

Table V. Association between demographic data and evolution of the recovery process.

A, Continuous therapy group, n=48

| | Barthel | | | iADL | | | ADL | | |
|---|---|---|---|---|---|---|---|---|---|
| Patients | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Male | 50.00 (27.50-60.00) | 60.00 (48.75-70.00) | <0.0010 | 3.00 (2.00-3.25) | 4.00 (3.00-5.00) | <0.0010 | 5.00 (2.75-6.00) | 7.00 (5.00-8.00) | <0.0010 |
| Female | 45.00 (35.00-55.00) | 57.50 (48.75-70.00) | <0.0010 | 3.00 (2.00-4.00) | 4.00 (3.75-5.00) | <0.0010 | 4.50 (2.75-6.00) | 6.50 (5.00-8.00) | <0.0010 |
| Urban | 42.50 (20.00-51.25) | 55.00 (43.75-70.00) | <0.0010 | 3.00 (1.75-3.25) | 4.00 (2.75-4.25) | <0.0010 | 4.00 (2.00-6.00) | 6.00 (4.75-8.00) | <0.0010 |
| Rural | 55.00 (48.75-60.00) | 65.00 (57.50-70.00) | <0.0010 | 3.00 (3.00-4.00) | 4.50 (4.00-5.00) | <0.0010 | 5.00 (3.75-6.25) | 8.00 (6.50-8.00) | <0.0010 |

B, Intermittent therapy group, n=20

| | Barthel | | | iADL | | | ADL | | |
|---|---|---|---|---|---|---|---|---|---|
| Patients | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Male | 47.50 (32.50-50.00) | 55.00 (37.50-60.00) | <0.0500 | 3.00 (2.25-3.00) | 4.00 (3.00-4.00) | 0.0110 | 4.50 (2.50-5.75) | 6.00 (3.75-7.00) | <0.0100 |
| Female | 52.50 (45.00-65.00) | 57.50 (50.00-70.00) | <0.0100 | 3.00 (2.00-3.00) | 4.00 (3.25-4.75) | 0.0015 | 5.50 (3.25-7.75) | 6.50 (6.00-8.00) | <0.0500 |
| Urban | 47.50 (43.75-51.25) | 55.00 (48.75-61.25) | <0.0100 | 3.00 (2.75-3.00) | 4.00 (3.00-4.00) | 0.0015 | 5.00 (3.75-6.00) | 6.00 (6.00-7.00) | <0.0100 |
| Rural | 52.50 (33.75-66.25) | 60.00 (45.00-70.00) | <0.0500 | 2.50 (1.75-3.25) | 4.00 (2.75-5.00) | 0.0133 | 5.50 (2.75-7.25) | 6.50 (3.50-8.25) | <0.0500 |

Wilcoxon signed-rank test, week 1 vs. week 12. ADL, activities of daily living; iADL, Instrumental ADL.

Table VI. Association between clinical data and the FMA-UE scores during the recovery process.

| Risk behaviour/ comorbidities | Continuous therapy group, n=48 | | | Intermittent therapy group, n=20 | | |
|---|---|---|---|---|---|---|
| | FMA-UE scores | | | FMA-UE scores | | |
| | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Smokers | | | | | | |
| A-upper extremity | 18.00 (15.00-20.00) | 30.00 (28.00-31.00) | <0.001 | 16.00 (14.00-20.50) | 28.50 (26.25-31.00) | <0.001 |
| B-wrist | 4.00 (3.00-5.00) | 7.00 (6.50-8.00) | <0.001 | 4.50 (3.25-5.75) | 7.50 (6.25-8.00) | <0.001 |
| C-hand | 6.00 (5.00-6.00) | 10.00 (9.00-10.50) | <0.001 | 5.50 (5.00-6.00) | 10.00 (9.00-11.00) | <0.001 |
| D-coordination/speed | 1.00 (0.00-1.00) | 3.00 (3.00-4.00) | <0.001 | 0.00 (0.00-0.75) | 3.00 (2.00-3.75) | <0.001 |
| Diabetes | | | | | | |
| A-upper extremity | 14.00 (11.00-18.00) | 28.00 (25.75-29.00) | <0.001 | 15.00 (13.25-18.00) | 25.00 (20.25-30.00) | n.a. |
| B-wrist | 3.00 (3.00-4.00) | 7.00 (6.00-8.00) | <0.001 | 3.00 (2.75-4.00) | 6.00 (4.75-7.50) | n.a. |
| C-hand | 5.00 (4.00-6.00) | 9.00 (8.25-10.00) | <0.001 | 4.50 (3.75-5.75) | 8.50 (6.75-10.50) | n.a. |
| D-coordination/speed | 0.00 (0.00-1.00) | 3.00 (2.00-3.00) | <0.001 | 0.00 (0.00-0.5) | 2.50 (1.50-3.25) | n.a. |
| Hypertension | | | | | | |
| A-upper extremity | 17.00 (14.00-20.00) | 29.00 (28.00-31.50) | <0.001 | 17.50 (15.00-21.00) | 30.00 (27.25-32.00) | <0.001 |
| B-wrist | 4.00 (3.00-5.00) | 7.00 (6.50-8.00) | <0.001 | 5.00 (3.25-6.00) | 8.00 (7.00-9.00) | <0.001 |
| C-hand | 6.00 (5.00-6.50) | 10.00 (9.00-11.00) | <0.001 | 6.00 (5.00-6.75) | 10.00 (8.25-11.00) | <0.001 |
| D-coordination/speed | 0.00 (0.00-1.00) | 3.00 (2.00-4.00) | <0.001 | 0.00 (0.00-1.00) | 4.00 (2.25-4.00) | <0.001 |
| Diabetes + hypertension | | | | | | |
| A-upper extremity | 14.00 (10.25-17.25) | 28.00 (25.75-29.75) | <0.010 | 16.00 (13.50-20.00) | 29.00 (23.50-31.00) | n.a. |
| B-wrist | 3.00 (3.00-4.00) | 7.00 (6.25-8.00) | <0.010 | 3.00 (2.50-5.00) | 7.00 (5.50-8.00) | n.a. |
| C-hand | 5.00 (4.00-5.75) | 9.00 (8.25-10.00) | <0.010 | 5.00 (4.00-6.50) | 10.00 (8.00-11.00) | n.a. |
| D-coordination/speed | 0.00 (0.00-0.75) | 2.50 (2.00-3.00) | <0.010 | 0.00 (0.00-1.00) | 3.00 (1.50-3.50) | n.a. |
| Dyslipidaemia | | | | | | |
| A-upper extremity | 17.00 (12.00-19.00) | 29.00 (27.5-31) | <0.001 | 16.00 (14.00-21.00) | 29.00 (26.50-32.00) | <0.001 |
| B-wrist | 4.00 (3.00-5.00) | 7.00 (7.00-8.00) | <0.001 | 5.00 (3.50-6.00) | 8.00 (6.50-8.50) | <0.001 |
| C-hand | 6.00 (5.00-6.00) | 10.00 (9.00-10.5) | <0.001 | 6.00 (5.00-6.50) | 10.00 (8.50-11.00) | <0.001 |
| D-coordination/speed | 0.00 (0.00-1.00) | 3.00 (2.00-4.00) | <0.001 | 0.00 (0.00-1.00) | 3.00 (2.00-4.00) | <0.001 |

Wilcoxon signed-rank test, week 1 vs. week 12. FMA-UE, Fugl-Meyer Assessment Upper Extremity; n.a., not applicable.

and prognosis during the post-stroke period, the presence of cardiac and metabolic comorbidities are associated with reduced survival after stroke, and this is another aspect that necessitating a mandatory long-term monitoring and recovery program (28).

Assessment in the acute phase using EMG has been recognized as the most accurate, accessible and useful tool for diagnosis, and has also shown its value as a long-term monitoring tool. The EMG assessment provides data on both the temporal course and rate of recovery of the lesion (11,29). The evaluation method used in the present study was similar to that of other studies, measuring the movement control of the upper extremities in patients in the sub-acute and acute phases following a stroke (30). Based on the results obtained by the present study and another study (31), it is recommended that this type of evaluation is used for the long-term monitoring process of chronic stroke survivors.

Previous studies have highlighted the importance of complex rehabilitation programs for patients following stroke in both the acute and chronic phases, based on the individualized evaluation of each patient, rather than that provided by guidelines (32,33). The program proposed in the present study (kinesiotherapy, cryotherapy, thermotherapy, electrotherapy and massage) covered the entire spectrum of the patients' needs, as reflected in the positive outcomes measured by the working tools. Moreover, the way in which the therapeutic program was administered, either continuous or intermittent, did not influence the benefits of the rehabilitation. Although the number of subjects undergoing the intermittent program (n=20) was not substantial enough to impose this approach as a reliable and standardized one, which could be considered one of the limitations of the present study, the results after 12 weeks were promising. Another limitation of the current study could be the lack of long-term monitoring of the evolution of patients following the study period.

In conclusion, the rehabilitation process of stroke survivors represents one of the most important elements for their future quality of life. Intermittent physical recovery could be considered a valid approach for sub-acute and acute stroke survivors following an individualized clinical evaluation. Future studies

Table VII. Association between clinical data and evolution of the recovery process.

A, Continuous therapy group, n=48

| Risk behaviour/ Comorbidities | Barthel | | | iADL | | | ADL | | |
|---|---|---|---|---|---|---|---|---|---|
| | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Smokers | 50.00 (40.00-57.50) | 60.00 (50.00-70.00) | <0.001 | 3.00 (2.50-4.00) | 4.00 (3.00-5.00) | <0.001 | 5.00 (3.50-6.00) | 7.00 (5.00-8.00) | <0.001 |
| Diabetes | 40.00 (22.50-45.00) | 47.50 (45.00-55.00) | n.a. | 2.50 (1.25-3.00) | 3.00 (3.00-4.00) | n.a. | 3.50 (2.00-4.75) | 5.00 (5.00-6.75) | n.a. |
| Hypertension | 50.00 (32.50-57.50) | 60.00 (45.00-70.00) | <0.001 | 3.00 (2.00-3.50) | 4.00 (3.00-4.50) | <0.001 | 5.00 (2.50-6.00) | 7.00 (5.00-8.00) | <0.001 |
| Diabetes + hypertension | 35.00 (22.50-48.75) | 45.00 (37.50-65.00) | <0.010 | 2.50 (1.00-3.00) | 3.00 (2.25-4.00) | <0.050 | 3.50 (2.00-5.50) | 5.00 (4.25-6.75) | <0.010 |
| Dyslipidaemia | 50.00 (30.00-55.00) | 60.00 (45.00-67.50) | <0.001 | 3.00 (2.00-3.50) | 4.00 (3.00-5.00) | <0.001 | 4.00 (2.00-6.00) | 7.00 (5.00-8.00) | <0.001 |

B, Intermittent therapy group, n=20

| Patients | Barthel | | | iADL | | | ADL | | |
|---|---|---|---|---|---|---|---|---|---|
| | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value | Week 1 | Week 12 | P-value |
| Smokers | 45.00 (37.50-57.50) | 52.50 (50.00-63.75) | <0.010 | 3.00 (2.00-3.00) | 4.00 (3.00-4.00) | <0.010 | 4.50 (3.00-5.75) | 6.00 (5.25-7.00) | <0.001 |
| Diabetes | 40.00 (33.75-52.50) | 50.00 (45.00-57.50) | n.a. | 2.00 (1.75-2.50) | 3.50 (2.50-4.25) | n.a. | 3.00 (2.75-4.25) | 5.50 (4.25-6.75) | n.a. |
| Hypertension | 50.00 (37.50-60.00) | 57.50 (50.00-68.75) | <0.001 | 3.00 (2.25-3.00) | 4.00 (4.00-4.00) | <0.001 | 5.00 (3.25-7.00) | 6.00 (5.25-8.00) | <0.001 |
| Diabetes + hypertension | 35.00 (32.50-55.00) | 50.00 (40.00-65.00) | n.a. | 2.00 (1.50-3.00) | 4.00 (2.50-4.50) | n.a. | 3.00 (2.50-5.50) | 5.00 (3.50-7.00) | n.a. |
| Dyslipidaemia | 45.00 (40.00-57.50) | 55.00 (50.00-65.00) | <0.001 | 3.00 (2.00-3.00) | 4.00 (3.00-4.00) | <0.001 | 5.00 (3.00-6.50) | 6.00 (5.50-7.50) | <0.010 |

Wilcoxon signed-rank test, week 1 vs. week 12. ADL, activities of daily living; iADL, Instrumental ADL; n.a., not applicable.

are required to confirm the findings for the chronic stages of this disease.

**Acknowledgements**

The authors gratefully acknowledge Dr Mihail Cristian Pirlog (Department of Medical Sociology, University of Medicine and Pharmacy Craiova, Craiova, Romania) for critical discussion and valuable support during the realization of the study, and Dr Bogdan Catalin (Department of Physiology, University of Medicine and Pharmacy Craiova, Craiova, Romania) for technical assistance with electromyography recording.

**Funding**

No funding was received.

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request and after the approval of the Ethics Committee of the University of Medicine and Pharmacy of Craiova, Craiova, Romania.

**Authors' contributions**

AMP, ATB, SCB and OCR conceptualized the present study. AMP, GC, ATB, SCB and OCR were major contributors to writing the manuscript and collected the clinical data and analyzed the data. The methodology used was established by AMP, ATB, GC and OCR. Software input was performed by AMP and GC. Data curation was performed by GC. The original draft was prepared by AMP and GC. The editing and rewriting of the manuscript was performed by ATB and OCR. ATB and OCR supervised the project. AMP and GC confirm the authenticity of all the raw data. All have authors read and approved the final manuscript.

**Ethics approval and consent to participate**

The present study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova (approval no. 167/12.06.2017; Craiova, Romania) and was in line with The Declaration of Helsinki. Written informed consent was obtained from all subjects involved in the study.

**Patient consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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