

Comparative effect of constraint-induced movement therapy and proprioceptive neuromuscular facilitation on upper limb function of chronic stroke survivors

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Abstract

Introduction. Stroke is a leading cause of morbidity and mortality globally. The aim of this study was to compare the effect of constraint-induced movement therapy (CIMT) and proprioceptive neuromuscular facilitation (PNF) on upper limb function of chronic stroke survivors.

Methods. Overall, 30 stroke survivors were recruited via convenient sampling and consecutively assigned into 2 groups (15 participants each). Group A received CIMT while group B received PNF techniques. All treatments were administered on the affected upper limb, 3 times a week for 6 weeks. Fugl-Meyer assessment (FMA) scale was used to evaluate upper limb function. Descriptive statistics served to summarize the demographic characteristics of the participants and inferential statistics of t-test was used to determine the effect of the interventions within the groups and between the groups on the basis of FMA. All statistical analysis was performed with the Statistical Package for the Social Sciences (version 16.0) at the alpha level of 0.05.

Results. The participants' mean age was 59.53 ± 9.92 and 63.00 ± 7.27 years for group A and B, respectively. No significant baseline difference was observed between the groups in the upper limb FMA ($p > 0.05$). A statistically significant post-intervention effect was noted for both treatment approaches; however, when the groups were compared, CIMT resulted in a better improvement than PNF.

Conclusions. CIMT and PNF interventions are both beneficial in improving upper limb function, with CIMT being more advantageous. CIMT may be the preferred approach for the management of chronic upper limb post-stroke impairments.

Key words: proprioceptive neuromuscular facilitation, constraint-induced movement therapy, stroke, upper limb

Introduction

Stroke accounts for about 1.2% of hospital and 7.3% of medical wards admissions in Nigeria [1]. There is an increasing burden of stroke to the health care delivery system in Africa [2, 3]. Stroke is among the causes of high mortality, leading to death in about 1/3 of stroke admissions within 24 hours and more than 1/3 within 30 days in Nigeria [1, 4]. Among stroke survivors, a significant proportion ranging from 1/4 to 1/2 of the survivors present with some level of disability [5].

Recovery after stroke revolves around the severity of the initial impairments of motor, sensory, and cognitive functions [6]. Therefore, stroke rehabilitation is critical in shaping the functions and activities of the survivors [7]. It is focused on utilizing the principle of motor learning and neuroplasticity [8]. There have been several rehabilitation approaches for the management of post-stroke impairments [8]. These include, among others, aerobic exercises [9], Bobath approach, proprioceptive neuromuscular facilitation (PNF) [10], constraint-induced movement therapy (CIMT) [11], and mobilization and stimulation of neuromuscular tissue [12]. However, the choice of the appropriate method at a specified stage of recovery varies among practitioners [13]. CIMT is a neurological rehabilitation technique that can be applied at both acute and chronic stages of stroke [14–16] and different levels of impairments [17]. It can be administered in

hospital and home settings [17, 18]. Studies on upper limb post-stroke recovery showed a significant improvement of motor functions in favour of CIMT as compared with other rehabilitation approaches [19, 20]. In addition, CIMT is relatively inexpensive [21] and hence readily available for practice in low- and medium-income countries.

PNF is frequently used as a method to treat physical dysfunction resulting from damage or disease [22]. Studies conducted on stroke survivors have shown that PNF is effective through minimizing impairments and improving functions of limbs [23, 24] and trunk [25]. PNF techniques improve joint movement efficiency by inducing changes in the sequence of muscles that are activated [26]. This is mediated by changes in the excitation of the cortical motor area and the corresponding motoneurons [26]. Despite the benefits of PNF in stroke recovery, there are few certified International Proprioceptive Neuromuscular Facilitation Association (IPNFA) physiotherapists in Nigeria. This is due to lack of IPNFA training centres in Africa, placing a huge cost of travelling to other continents to acquire such knowledge.

Research to compare the effect of CIMT and PNF approaches have been conducted; however, most of these studies administered PNF in combination with other approaches. Furthermore, the duration of intervention in the studies was in favour of CIMT groups compared with PNF [27–31]. Therefore, this study is aimed to determine the comparative effect of CIMT and PNF on upper limb recovery.

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Subjects and methods

The participants in this quasi-experimental study were consecutively recruited and randomly assigned into 2 groups. The populations for the study were chronic hemiplegic stroke patients attending Aminu Kano Teaching Hospital and Muhammad Abdullahi Wase Specialist Hospital. Chronic stroke patients with mild spasticity (score of 2 or less on Modified Ashworth scale), good cognitive function (score of 20 more in Mini-Mental State Examination), as well as available range of motion of about 10° and 20° or more of fingers and wrist extension respectively (measured with a goniometer) were included. Participants who had had more than 1 episode of stroke or recent occurrence or cognitive impairment were excluded from the study.

Instruments

The upper extremity section of the Fugl-Meyer assessment (FMA) scale was used to measure the pre- and post-intervention recovery level. The FMA scale is a 226-point multi-item Likert-type scale developed as a measure to evaluate recovery from hemiplegic stroke. It is divided into 5 domains: motor function, sensory function, balance, joint range of motion, and joint [32]. FMA is a reliable and valid scale for recovery evaluation after stroke [33, 34].

Modified Ashworth scale was also applied. It is a 6-point scale, with scores ranging from 0 to 4, where lower scores represent normal muscle tone and higher scores stand for spasticity or increased resistance to passive movement [35]. Modified Ashworth scale is a reliable scale for the assessment of post-stroke elbow flexor spasticity [34, 36].

Procedure

All patients were informed about the purpose and procedure of the study, as well as the right to refuse to take part or quit from the study at any moment. A total of 43 patients consented to participate in the study but only 30 met the in-

clusion criteria and were recruited (Figure 1). The participants were recruited consecutively and randomly assigned into 2 groups: A and B (CIMT and PNF group, respectively), each of 15 subjects. The assessments were conducted at baseline by a rater and at 6th week of intervention by another rater. The raters were trained physiotherapists not involved in the administration of the study interventions and not aware of the group a participant belonged.

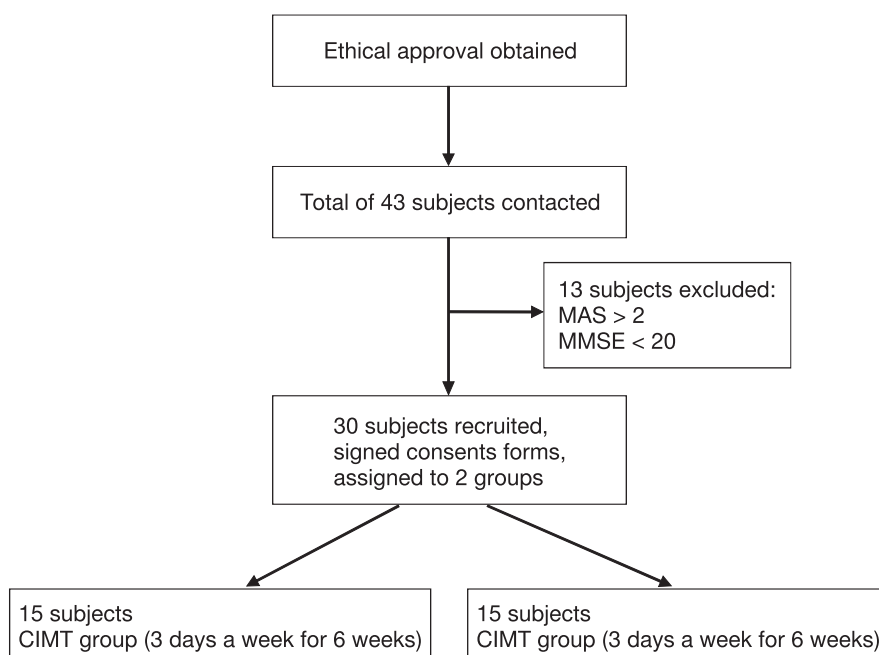
Interventions

Group A received CIMT for 45 minutes, with the unaffected upper limb restricted by using triangular bandage, by a trained and experienced physiotherapist. The intervention was conducted 3 times a week for a period of 6 weeks. CIMT was administered in a sitting position, with the hand on the table performing context-specific tasks, which included the use of spoons, cups, and combs repeatedly. The tasks were broken down into smaller components, starting with grasping the objects, and progressed until the task was completed. The exercises were performed at home while sitting, such as the ones practised in the hospital.

Group B received PNF intervention administered for 45 minutes to the upper limb 3 times a week for a period of 6 weeks. Context-specific tasks in this group were performed in the first diagonal (D1) of the upper limb (extension and flexion directions) through combined upper limb patterns (chopping and lifting). The techniques administered included rhythmic initiation, combination of isotonic techniques, normal timing, and timing for emphasis at wrist and elbow. The exercises were performed at home while sitting and lying, such as the ones practised in the hospital. The interventions were performed by a trained physiotherapist with a IPNFA certificate, who had practised for at least 5 years.

Data analysis

Descriptive statistics of mean, standard deviation, frequencies, and percentages were used to summarize the de-



MAS – Modified Ashworth scale, MMSE – Mini-Mental State Examination, CIMT – constraint-induced movement therapy, PNF – proprioceptive neuromuscular facilitation

Figure 1. Flow chart showing the recruitment procedure

mographic characteristics of the participants. Paired *t*-test was used to compare baseline data with post-intervention scores of upper limb function within the groups and unpaired *t*-test served to compare the post-intervention effects between the groups. The statistical analysis was conducted with the Statistical Package for the Social Sciences (SPSS), version 16.0; the *p* value of 0.05 was applied to determine statistical significance.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the ethical committees of Aminu Kano Teaching Hospital and Muhammad Abdullahi Wase Specialist Hospital.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

A total of 30 participants with chronic stroke (mean duration: 32.87 ± 5.54 weeks) completed the study. The mean age of participants was 59.53 ± 9.92 years in group A and 63.00 ± 7.27 years in group B. There was an equal distribution of males and females with right hemiparesis as the most frequently occurring (60%) in the study. The results showed that there was no significant difference in FMA scores between the 2 groups, which means that the groups were comparable, as presented in Table 1.

The study revealed a significant improvement in the upper limb function on the basis of pre- and post-intervention FMA scores within the CIMT group. On the same vein, a significant improvement was reported in the upper limb function on the basis of pre- and post-intervention FMA scores within the PNF group, as shown in Table 2.

Furthermore, a significant post-intervention difference was shown between the 2 groups, with a better improvement in the CIMT group, as shown in Table 3. When the upper limb function was compared across genders, there was no significant difference in the groups, as presented in Table 4.

Discussion

This study compared the effectiveness of PNF and CIMT in upper limb post-stroke recovery. The observation that no significant difference existed in the baseline scores of upper limb function implies that the participants in the 2 groups were comparable (Table 1). Therefore, any difference in upper limb post-intervention function can be attributed to the effect of the intervention in the groups.

The study revealed a significant post-intervention improvement in upper limb function in the PNF group (Table 2). The clinical implication of this finding is that upper limb treatment with PNF after stroke can lead to significant recovery of the ability to properly use the affected limb. This is line with the finding of De Moraes et al. [37], who observed a significant improvement of upper limb function in stroke survivors after 6 weeks of PNF intervention.

Similarly, the results of this study showed a significant post-intervention improvement in upper limb function in the CIMT group (Table 2). This implies that CIMT is an intervention that can significantly improve the function of the affected upper limb in stroke patients. The outcome corroborates

Table 1. Demographic and clinical characteristics of participants

Characteristics	CIMT group (n = 15) (mean ± SD)	PNF group (n = 15) (mean ± SD)	df	t	p value
Age (years)	59.53 ± 9.92	63.00 ± 7.27			
Males, n (%)	8 (50.7)	7 (49.3)			
Females, n (%)	7 (49.3)	8 (50.7)			
Right hemiparesis n (%)	8 (53.33)	10 (66.67)			
Left hemiparesis n (%)	7 (46.67)	5 (33.33)			
Disease duration (weeks)	31.60 ± 5.65	34.13 ± 5.32			
FMA score	36.80 ± 7.62	34.40 ± 9.760	28	0.750	0.459

CIMT – constraint-induced movement therapy
 PNF – proprioceptive neuromuscular facilitation
 SD – standard deviation, df – degree of freedom
 FMA – Fugl-Meyer assessment

Table 2. Comparison of upper limb FMA scores in the CIMT and PNF groups

Score	Mean ± SD	df	t	p value
CIMT				
Pre-test	36.8 ± 7.63	14	-10.8	0.000
Post-test	47.3 ± 7.46			
PNF				
Pre-test	34.4 ± 9.76	14	-10.2	0.000
Post-test	37.1 ± 9.53			

FMA – Fugl-Meyer assessment
 CIMT – constraint-induced movement therapy
 PNF – proprioceptive neuromuscular facilitation
 SD – standard deviation, df – degree of freedom

Table 3. Comparison of upper limb post-intervention recovery in the study groups

Group	Mean ± SD	df	t	p value
CIMT	47.6 ± 7.51	28	-2.7	0.002
PNF	37.1 ± 9.53			

SD – standard deviation, df – degree of freedom
 CIMT – constraint-induced movement therapy
 PNF – proprioceptive neuromuscular facilitation

Table 4. Comparison of upper limb post-intervention recovery between the groups across genders

Gender	n	Mean ± SD	df	t	p value
CIMT					
Males	8	38.0 ± 11.03	13	0.365	0.721
Females	7	36.14 ± 8.28			
PNF					
Males	7	46.5 ± 5.95	13	-0.628	0.541
Females	8	49.0 ± 9.30			

SD – standard deviation, df – degree of freedom
 CIMT – constraint-induced movement therapy
 PNF – proprioceptive neuromuscular facilitation

a study by Sethy et al. [38], in which better recovery was observed in upper limb function after CIMT in chronic stroke patients.

In this study, the participants in the CIMT group had significantly better scores of upper limb function than those in the PNF group (Table 3). The finding is supported by that of Rehman et al. [20], who observed a better post-intervention performance in the CIMT group when compared with Bobath approach. The difference in outcome between the CIMT and PNF groups after the intervention can be associated with the fact that PNF requires special handling by a physiotherapist, and a correct application of the technique by the participants at home may be minimal. Nevertheless, limb function recovery is not dependent only on rehabilitation intensity but also on other factors, such as socioeconomic status and type of stroke [39], which this study has not taken into consideration.

On the other hand, the results of this study have shown no significant difference in recovery in terms of gender (Table 4). This contradicts the findings by Yu et al. [40], who observed better recovery in males than in females. Alawieh et al. [39] also stated that females usually presented lower pre-stroke physical functioning than males. The contradiction with the previous studies may be a result of the difference in the characteristics of the participants. Our subjects were relatively younger than those in the study by Yu et al. [40] and as such would have functioned better, which could equate females' results with those of males.

The study provided information on the effectiveness of 2 interventions on upper limb post-stroke function. CIMT turned out to result in a more favourable outcome on stroke in the Nigerian subjects. The choice of intervention between PNF and CIMT will be at the discretion of the clinicians, especially when the opportunity to fund and access PNF training is not readily available.

Limitations

The study limitations include lack of a control group and the inability to assess long-term effects for retention. Another limitation is that the affected part of the brain was not evaluated with radiological investigations.

Conclusions

The study revealed that both PNF and CIMT were effective in the management of upper limb post-stroke function; however, CIMT might be the preferred technique for upper limb function recovery. Furthermore, no gender-related difference was observed in upper limb function post-intervention outcome among chronic stroke survivors. Further studies should be conducted to determine the long-term effect of the interventions.

Disclosure statement

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Conflict of interest

The authors state no conflict of interest.

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References

1. Abubakar SA, Sabir AA. Profile of stroke patients seen in a tertiary health care center in Nigeria. *Ann Nigerian Med.* 2013;7(2):55–59; doi: 10.4103/0331-3131.133097.
2. Adeloye D. An estimate of the incidence and prevalence of stroke in Africa: a systematic review and meta-analysis. *PLoS One.* 2014;9(6):e100724; doi: 10.1371/journal.pone.0100724.
3. Badaru UM, Ogwumike OO, Adeniyi AF. Quality of life of Nigerian stroke survivors and its determinants. *Afr J Biomed Res.* 2015;18(1):1–5.
4. Ekeh B, Ogunniyi A, Isamade E, Ekrikpo U. Stroke mortality and its predictors in a Nigerian teaching hospital. *Afr Health Sci.* 2015;15(1):74–81; doi: 10.4314/ahs.v15i1.10.
5. DoCarmo JF, Morelato RL, Pinto HP, de Oliveira ERA. Disability after stroke: a systematic review. *Fisioter Mov.* 2015;28(2):407–418; doi: 10.1590/0103-5150.028.002.AR02.
6. Mercier L, Audet T, Hébert R, Rochette A, Dubois M. Impact of motor, cognitive, and perceptual disorders on ability to perform activities of daily living after stroke. *Stroke.* 2001;32(11):2602–2608; doi: 10.1161/hs1101.098154.
7. Lum PS, Mulroy S, Amdur RL, Requejo P, Prilutsky BI, Dromerick AW. Gains in upper extremity function after stroke via recovery or compensation: potential differential effects on amount of real-world limb use. *Top Stroke Rehabil.* 2009;16(4):237–253; doi: 10.1310/tsr1604-237.
8. Takeuchi N, Izumi S-I. Rehabilitation with poststroke motor recovery: a review with a focus on neural plasticity. *Stroke Res Treat.* 2013;2013:128641; doi: 10.1155/2013/128641.
9. Kolapo HT, Nelson EE. Aerobic training in stroke rehabilitation: what is known and what needs to be addressed – a systematic review. *Nigerian J Med Rehabil.* 2015;18(1).
10. Kawahira K, Shimodozono M, Ogata A, Tanaka N. Addition of intensive repetition of facilitation exercise to multidisciplinary rehabilitation promotes motor functional recovery of the hemiplegic lower limb. *J Rehabil Med.* 2004; 36(4):159–164; doi: 10.1080/16501970410029753.
11. Abdullahi A. Is time spent using constraint induced movement therapy an appropriate measure of dose? A critical literature review. *Int J Ther Rehabil.* 2014;21(3):140–146; doi: 10.12968/ijtr.2014.21.3.140.
12. Athanasiadis D, Protosaltis S, Stefanis E. The effects of Mobilization and Stimulation of Neuromuscular Tissue on the hemiplegic upper limb: a case report. *Physiother Quart.* 2019;27(1):6–11; doi: 10.5114/pq.2019.83055.
13. Abdullahi A, Abdu YY, Abba MA. What do physiotherapists do in stroke rehabilitation? A focus group discussion. *Nigerian J Med Rehabil.* 2015;18(2); doi: 10.34058/njmr.v18i2.125.
14. Miltner WHR, Bauder H, Sommer M, Dettmers C, Taub E. Effects of constraint-induced movement therapy on patients with chronic motor deficits after stroke: a replication. *Stroke.* 1999;30(3):586–592; doi: 10.1161/01.STR.30.3.586.
15. Grotta JC, Noser EA, Ro T, Boake C, Levin H, Aronowski J, et al. Constraint-induced movement therapy. *Stroke.* 2004;35(11 Suppl. 1):2699–2701; doi: 10.1161/01.STR.0000143320.64953.c4.
16. Wolf SL, Winstein CJ, Miller JP, Taub E, Uswatte G, Morris D, et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *J Am Med Assoc.* 2006;296(17):2095–2104; doi: 10.1001/jama.296.17.2095.

17. Bonifer N, Anderson KM. Application of constraint-induced movement therapy for an individual with severe chronic upper-extremity hemiplegia. *Phys Ther.* 2003; 83(4):384–398; doi: 10.1093/ptj/83.4.384.
18. Barzel A, Ketels G, Tetzlaff B, Krüger H, Haevernick K, Daubmann A, et al. Enhancing activities of daily living of chronic stroke patients in primary health care by modified constraint-induced movement therapy (HOME CIMT): study protocol for a cluster randomized controlled trial. *Trials.* 2013;14:334; doi: 10.1186/1745-6215-14-334.
19. Hakkennes S, Keating JL. Constraint-induced movement therapy following stroke: a systematic review of randomised controlled trials. *Aust J Physiother.* 2005;51(4): 221–231; doi: 10.1016/s0004-9514(05)70003-9.
20. Rehman B, Rawat P, Agarwal V, Verma SK. A study on the effectiveness of Bobath approach versus constraint induced movement therapy (CIMT) to improve the arm motor function and the hand dexterity function in post stroke patients. *Int J Physiother Res.* 2015;3(2):912–918; doi: 10.16965/ijpr.2015.102.
21. Boyd LA, Walker MF. Critique of home constraint-induced movement therapy trial: constraint-induced movement therapy study prompts the need for further research. *Stroke.* 2016;47(7):1960–1961; doi: 10.1161/STROKEAHA.116.012423.
22. Lee J-H, Park S-J, Na S-S. The effect of proprioceptive neuromuscular facilitation therapy on pain and function. *J Phys Ther Sci.* 2013;25(6):713–716; doi: 10.1589/jpts.25.713.
23. Akosile CO, Adegoke BOA, Johnson OE, Maruf FA. Effects of proprioceptive neuromuscular facilitation technique on the functional ambulation of stroke survivors. *J Nig Soc Physio.* 2011;18–19:22–27.
24. Yeole UL, Arora SP, Gharote GM, Panse RB, Pawar PA, Kulkarni SA. Effectiveness of proprioceptive neuromuscular facilitation on spasticity in hemiplegia: randomised controlled trial. *J Med Sci Clin Res.* 2017;5(1):15567–15572; doi: 10.18535/jmscr/v5i1.61.
25. Hariharasudhan R, Balamurugan J. Enhancing trunk stability in acute poststroke subjects using physio ball exercise and proprioceptive neuromuscular facilitation technique: a pilot randomized controlled trial. *Int J Adv Med Health Res.* 2016;3(1):5–10; doi: 10.4103/2350-0298.184681.
26. Shimura K, Kasai T. Effects of proprioceptive neuromuscular facilitation on the initiation of voluntary movement and motor evoked potentials in upper limb muscles. *Hum Mov Sci.* 2002;21(1):101–113; doi: 10.1016/s0167-9457(01)00057-4.
27. Page SJ, Levine P, Leonard A, Szaflarski JP, Kissela BM. Modified constraint-induced therapy in chronic stroke: results of a single-blinded randomized controlled trial. *Phys Ther.* 2008;88(3):333–340; doi: 10.2522/ptj.20060029.
28. Atteya AA. Effects of modified constraint induced therapy on upper limb function in subacute stroke patients. *Neurosciences.* 2004;9(1):24–29.
29. Page SJ, Sisto S, Levine P, McGrath RE. Efficacy of modified constraint-induced movement therapy in chronic stroke: a single blinded randomized controlled trial. *Arch Phys Med Rehabil.* 2004;85(1):14–18; doi: 10.1016/s0003-9993(03)00481-7.
30. Page SJ, Sisto S, Johnston MV, Levine P. Modified constraint-induced therapy after subacute stroke: a preliminary study. *Neurorehabil Neural Repair.* 2002;16(3): 290–295; doi: 10.1177/154596830201600307.
31. Page SJ, Sisto SA, Levine P, Johnston MV, Hughes M. Modified constraint induced therapy: a randomized feasibility and efficacy study. *J Rehabil Res Dev.* 2001;38(5): 583–590.
32. Gladstone DJ, Danelles CJ, Black SE. The Fugl-Meyer assessment of motor recovery after stroke: a critical review of its measurement properties. *Neurorehabil Neural Repair.* 2002;16(3):232–240; doi: 10.1177/154596802401105171.
33. Kim H, Her J, Ko J, Park D-S, Woo J-H, You Y, et al. Reliability, concurrent validity, and responsiveness of the Fugl-Meyer Assessment (FMA) for hemiplegic patients. *J Phys Ther Sci.* 2012;24(9):893–899; doi: 10.1589/jpts.24.893.
34. Zwolińska J, Drużbicki M, Perenc L, Kwolek A. A method of hand motor control assessment in patients with post-stroke spasticity. *Adv Rehabil.* 2017;(3):55–70; doi: 10.1515/rehab-2015-0073.
35. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther.* 1987;67(2):206–207; doi: 10.1093/ptj/67.2.206.
36. Kaya T, Karatepe AG, Gunaydin R, Koc A, Altundal Ercan U. Inter-rater reliability of the Modified Ashworth Scale and modified Modified Ashworth Scale in assessing poststroke elbow flexor spasticity. *Int J Rehabil Res.* 2011;34(1):59–64; doi: 10.1097/MRR.0b013e32833d6cdf.
37. De Moraes KR, De Freitas EL, Gomes D, Possa SS, Barcala L. Effects of PNF method for hemiplegic patients with brachial predominance after stroke: controlled and blinded clinical trial. *Neurol Res Ther.* 2014;2(1):101; doi: 10.14437/NRTOA-1-101.
38. Sethy D, Bajpai P, Kujur ES, Mohakud K, Sahoo S. Effectiveness of modified constraint induced movement therapy and bilateral arm training on upper extremity function after chronic stroke: a comparative study. *Open J Ther Rehabil.* 2016;4(1):1–9; doi: 10.4236/ojtr.2016.41001.
39. Alawieh A, Zhao J, Feng W. Factors affecting post-stroke motor recovery: implications on neurotherapy after brain injury. *Behav Brain Res.* 2018;340:94–101; doi: 10.1016/j.bbr.2016.08.029.
40. Yu C, An Z, Zhao W, Wang W, Gao C, Liu S, et al. Sex differences in stroke subtypes, severity, risk factors, and outcomes among elderly patients with acute ischemic stroke. *Front Aging Neurosci.* 2015;7:174; doi: 10.3389/fnagi.2015.00174.