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[REVIEW ARTICLE]

Characteristics of Longitudinal Studies Analysing Functional Recovery in Patients with Stroke: - A Systematic Review

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ABSTRACT :

Background- Stroke is a common neurological disorder that represents a major cause of disability.Stroke is a major cause of short-term functional impairment in developed countries, in the absence of adequate treatment and rehabilitation, which can lead to significant long-term functional impairment.

Objectives- This present systematic review is aimed to explore the literature-related longitudinal studies conducted on patients with Stroke concerning the number of subjects included, follow-up time, number of centers involved, percentage of dropouts, and type of outcome measures used to assess the effect of treatment.

Methods- PubMed databases were searched to identify eligible studies using the keywordsStroke, Functional recovery, and longitudinal studies. Only longitudinal studies published in the last 12 years (2010-2022) were included in this review.

Results- Nine studies were included in the review conducted on functional recovery in Stroke patients. All studies investigated Functional recovery over a longer period using different outcome measures with different follow-up times. It was found that functional recovery occurs over a longer period.

Conclusion- This review concludes that multicentric longitudinal studies with specifically related outcome measures focus on activity & participation as stated in ICF guidelines with an option of telerehabilitation in the chronic stage to reduce attrition rate may be undertaken by the researcher in the field of Stroke rehabilitation.

Keywords: *Functional recovery, Longitudinal study, Stroke.*

Introduction:

Stroke is a common neurological disorder that represents a major cause of disability. It is a significant health problem that needs continuous rehabilitation. It had been positioned as 6th driving cause of disability within the year 1990 and is projected to rank fourth by the year 2020.[1]Worldwide stroke prevalence in 2016 was 80.1 million (95% CI 74.1–86.3): 41.1 million (38.0–44.3) in women and 39.0 million (36.1–42.1) in men.[2] In the United States, the prevalence of stroke is about 3% in adults 20 years or older, which accounts for approximately 7 million strokes in the population.[3]In 2016, the Global Burden of Disease project[2] estimated the number of stroke incidents in India to be 1,175,778. In a recent systematic review, consisting mainly of cross-sectional studies, a review showed that the crude stroke prevalence in different parts of India ranged from 44.29 to 559/per 100,000 persons during the past two decades. The cumulative incidence of stroke in India ranged from 105 to 152/per 100,000 persons per year during the past two decades in different parts of the country.[4] Stroke is a major cause of short-term functional impairment in developed countries, in the absence of adequate treatment and rehabilitation, which can lead to significant long-term functional impairment.[5] Up to 70% of stroke patients show hemiparesis in the acute phase, and 40% of those do not regain independence in the execution of activities of daily living (ADL) within the first 6 months after stroke.[5] Stroke is a

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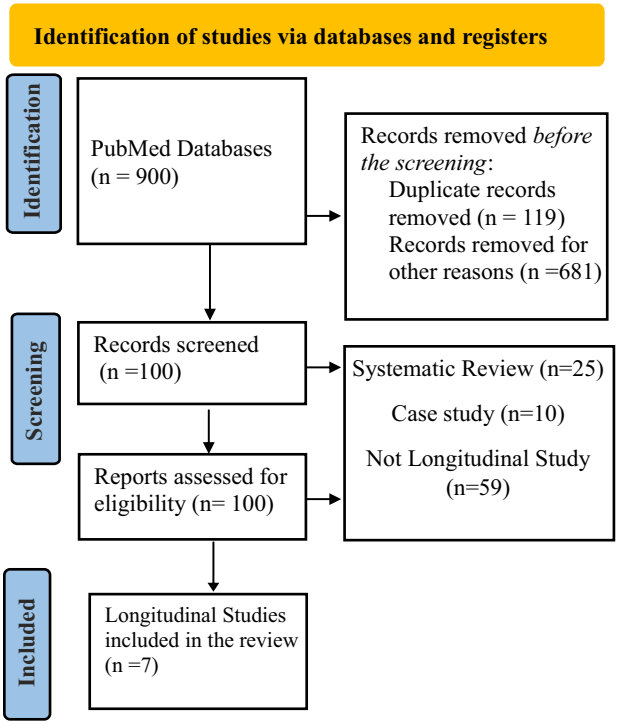
main cause of physical disability in adults, with up to 85% of survivors experiencing upper limb paresis. About 50% of stroke patients show impaired hand function in the chronic phase. Importantly, in addition to reduced gross arm and hand movement control, the persistence of impaired manual dexterity has a specific impact on activities of daily living and may decrease quality of life.[6] Conversely, recovery of the global upper limb and hand motor impairment (i.e., strength, gross arm, and hand function, simple grasp movements) has been more extensively studied and shown to take place during the first two to three months after stroke onset.[7] Upper limb rehabilitation trials designed to improve recovery rates have been largely unsuccessful. As a result, the burden of upper limb impairment after a stroke remains high.[8] Therefore, understanding how to improve the potential for recovery of upper limb function remains a major scientific, clinical, and patient priority.[9] The initial deficit and the degree of motor recovery after an ischemic stroke vary greatly and are related to such factors as lesion type, topography, and size. Brain imaging (positron-emission tomography [PET] or functional MRI [fMRI]) has revealed a cortical "reorganization" in patients with complete or partial upper limb recovery. These studies showed activation of the contralateral as well as the ipsilateral sensorimotor cortex (SMC) and other cortical regions such as the premotor areas, supplementary motor area (SMA), and parietal cortex, suggesting the involvement of a widespread network in recovery.[10] From the several days immediately after stroke onset up to years, innate physiological and structural plasticity, which usually started & were reported to be the fundamental process underlying motor function recovery after stroke.[11] During the past decade, several models for the prediction of UL recovery have been proposed.[12] Five prospective longitudinal studies showed that most patients recover roughly 70% of their lost UL motor capacity within 3 & 6 months after stroke.[13] Longitudinal studies are important in public health research for identifying risk factors related to negative health outcomes. However, a major concern in such studies is that the longer the follow-up period, the higher the chances are for drop-out.[14] Attrition rates from 30 to 70% are often reported. Thus, it is important to study the effect of attrition on the generalizability of findings from long-term longitudinal studies.[14]

This present systematic review is aimed to explore the literature-related longitudinal studies conducted on patients with Stroke concerning the number of subjects included, follow-up time, number of centers involved, percentage of dropouts, and type of outcome measures used to assess the effect of treatment.

Methodology

A systematic search was undertaken in a commonly used search engine (PubMed) for the period from January 2010 to December 2022. The search strategy comprised of the following terms: Functional Recovery, Stroke, and Longitudinal Study.



Selection Criteria For Observation Studies:

Only Longitudinal studiespublished in the English language evaluating Functional Recovery in patients with stroke were included. The Exclusion criteria were Randomized Control Trials (RCT) and experimental studies as the study design.

Data Extraction:

The data analysis was done through Pub Med Electronic Database and was searched by SM. The Title and Abstract of all the retrieved results were then screened for eligibility by SM & SG. The Screening process was aimed at narrowing down the volume of articles by rejecting the studies that are not relevant or appropriate according to previously stated criteria, Full text versions of all relevant articles were

evaluated by SM and SG.

Data Analysis:

The selected studies were analyzed in terms of specific study design, no. of subjects included, drop-outs, whether it is single-centric or multicentric, time points for follow-up, the procedure performed, outcome measures used in the study & conclusion.

Analysis of the study design helped to confirm the Longitudinal study. Details of participants suggested the stage of stroke, whether subacute or chronic. The procedure of each study revealed how the functional recovery was assessed.

Result:

Table no. 1: Summary of Observational Studies:

Sr. No.	Author name	No. of Patients Included in the study	Dropouts	Multicentric or single centric	Time points for follow up	Objectives	Outcome measures	Result
1.	Jeanette Plantin, PT, MSc et 2021[15]	89 patients with first-ever stroke	5 Dropouts (84 Patients up to the last follow-up)	Single centric study	3 weeks and 3 and 6 months after stroke onset.	Measures bimanual activity performance & Unimanual arm and hand motor impairment	Adult Assisting Hand Assessment Stroke & Fugl-Meyer Assessment	Ad-AHA performance was improved over time in all (mild-severe) impairment subgroups. Ad-AHA correlated with FMA at each time point ($r > 0.88$, $p < 0.001$), and recovery was similar
2.	Zhiyuan Wu,1 etal 2017[16]	12 Stroke Patients		Single centric study	Less than 10 days, two weeks, one month, and three months	To investigate functional activation-informed structural changes during stroke recovery	MRI scan & Fugl-Meyer Index	The GMV of contralesional activated brain regions & LIGMV increased during stroke recovery LIGMV was positively correlated with FMI aGMV negatively correlates with FMI
3.	Fidel López-Espuela 2016[17]	175 participated in the study.	23 Dropouts	Multicentric study	within 48 hours of admission, at hospital discharge, & 6 months after stroke.	To evaluate basic activities of daily living in stroke survivors & detect any predictors of functional outcome at 6 months after stroke.	BI, Charlson Comorbidity Index, Hamilton rating scale for depression, NIHSS	Scores on BI 6 months after stroke correlated with baseline scores on NIHSS. Age, female sex, stroke severity (NIHSS score), social risk, and depression as the baseline variables independently associated with functional disability at 6 months
4.	Jitka Veldema etal 2017[18]	18 Stroke patients	9 Dropouts	Single centric study	At baseline & weekly over 7 weeks	Relationship between changes of cortico-spinal excitability and motor recovery of the affected hand after stroke.	Corticospinal excitability measures - resting motor thresholds & motor evoked potentials, Wolf Motor Function and Action Research Arm test	Severe hand dysfunction strong suppression of ipsilesional cortico-spinal excitability and a shift of excitability towards the contralesional hemisphere Mild hand impairment was associated with a shift of corticospinal excitability towards the ipsilesional hemisphere.

5.	Dongni Buvarp etal 2020[19]	135 patients included in the study	44 dropouts	Single centric	5 days after onset, within 24 hours after discharge, 1 month after discharge, 3 months, & 1 year poststroke.	To determine longitudinal changes in functional mobility after stroke	Timed Up-and-Go, Fugl-Meyer Assessment , NIHSS	Patients with moderate stroke had a maximum rate of improvement in functional mobility during the first 3 months poststroke & then declined significantly at 1 year
6.	Leighton Chan et al 2013[20]	287 stroke patients	65 drop-outs	Multicentric centric study	Baseline and 6-month assessments were performed	To determine the impact of post-acute care sites on stroke outcomes	Activity Measure for Post-Acute Care (AM-PAC)	Patients with stroke may make more functional gains if their post-acute care includes an IRF than home health care (HH), outpatient (OP), or institutional settings (skilled nursing facility [SNF]
7.	Julia Birchenall 2018[21]	6 Stroke Patients		Single centric	Two weeks, three & six months post-stroke	Investigated how manual dexterity recovery was related to corticospinal tract (CST) injury & excitability in patients undergoing conventional rehabilitation.	MRI was obtained to calculate CST lesion load & FM-UE hand & transcranial magnetic stimulation (TMS)	At 6 months post-stroke, complete recovery of hand gross motor impairment had occurred in 3 patients & 4 patients had recovered the ability to accurately control finger force.

Discussion:

This systematic review mainly focuses on Functional Recovery in patients with Stroke over a longer period. Some studies show most of the neurologic and functional improvements occur within the first three months after a stroke.[22]and time-dependent recovery of body function and activities has been shown to decline significantly 10 weeks after stroke.[23]Inthe reviewed articles, the Fugl-Meyer Assessment was a commonly used outcome measure to assess functional recovery.

In the current systematic review, the number of patients included in the study varied from a minimum of 6 patients to a maximum of 287 patients. Five studies were Single centric & only two were multicentric.

Single-center trials are usually set up in a particular hospital, clinic, or general practice. Single-centric studies are usually small-scale and cheaper to conduct than multicentre trials. The multicentre trial is an accepted way of evaluating a new technology more efficiently; under some circumstances, they may have several centers with a large number of subjects per center. The advantages of multicenter trials are numerous: quicker recruitment of the necessary number of patients, clearer results that are more convincing and whose acceptance is higher, as the patient sample of multicenter trials is supposed to be representative.[24]

Drop-out is a prevalent complication in the analysis of data from longitudinal studies.[25]In the current review, the percentage of drop-out patients varied according to the sample size present in different studies, whether it was small or large.Attrition rates from 30 to 70% are often reported.A study by Veldema et al. had 50% drop-outs where the sample size was 18 [18], And another study by Dongni Buvarp et al. had 32% drop-outs where the sample size was 135.[19]Three reviewed articles in this systematic review didn't mention the drop-outs, but as it is a type of longitudinal study drop-outs need to be mentioned. Dropout in longitudinal surveys has three separate sources: failure to locate research participants, failure to contact research participants, and failure to achieve cooperation.[26]

The articles studied in this systematic review had different follow-up time points; the maximum follow-up time was 1 year, and the minimum follow-up time was 48 hours after the Stroke. Dongni Buvarp et al 2020 mentioned that they follow up with the

patients 5 days after onset, within 24 hours after discharge, 1 month after discharge, 3 months, & 1 year poststroke.A major advantage of frequently repeated measurements over time is that it represents reality far better than one or two measurements.[27] In 1-2, studies 1 month to 6 months was the common follow-up time for the patients. Where they assessed the patients for 1 month, 3 months, and 6 months after the Stroke. The variability in the timing of the assessment of the outcome has made comparisons between prognostic studies difficult.[27]

Fugl Meyer was a commonly used outcome measure.The Fugl-Meyer scale assesses the body functions according to ICF and has an excellent psychometric property. The Fug was developed as the first quantitative evaluative instrument for measuring sensorimotor stroke recovery, based on Twitchell and Brunnstrom's concept of sequential stages of motor return in the hemiplegic stroke patient. The Fugl-Meyer is a well-designed, feasible, and efficient clinical examination method that has been tested widely in the stroke population.[28]

The author Jeanette Plantin et al Measured bimanual activity performance & Unimanual arm and hand motor impairment by using Adult Assisting Hand Assessment Stroke & Fugl-Meyer Assessment as outcome measures and they found that Ad-AHA performance was improved over time in all (mild-severe) impairment subgroups and Ad-AHA correlated with FMA at each time point.

Zhiyuan Wu et al. in 2017investigated functional activation-informed structural changes during stroke recovery by using MRI scans & Fugl-Meyer Index. He found that a GMV of contralesional activated brain regions & LIGMV increased during stroke recovery. LIGMV was positively correlated with FMI, and a GMV negatively correlated with FMI.

Fidel López-Espuela et al in 2016, performed a study to evaluate basic activities of daily living in stroke survivors & detect any predictors of functional outcome 6 months after a stroke & they found that scores on BI 6 months after stroke correlated with baseline scores on NIHSS. Age, female sex, stroke severity (NIHSS score), social risk, and depression as the baseline variables independently associated with functional disability at 6 months. BI is a widely used measure of functional disability. The index was developed for use in rehabilitation patients with Stroke and other neuromuscular or musculoskeletal disorders. The BI is not designed for clinical trials and not specifically a stroke scale, BI has been used as a trial endpoint, either singly or as part of a "global" measure, in landmark studies of thrombolysis and acute stroke units.[29]

Dongni Buvarp et al 2020 performed a study to determine longitudinal changes in functional mobility after stroke by Time up and go & FMA scale for functional recovery, and NIHSS for Stroke severity& they found that the maximum rate of improvement in functional mobility during the first 3 months poststroke & then declined significantly at 1 year in patients with moderate stroke.

In the last decade, 2010-2020, only 7 longitudinal studies on patients with Stroke have been reported in the literature, considering the long duration of treatment required for patients with neurological dysfunction.[30]Longitudinal studies investigating the broader impact on patients as an individual are expected to be conducted by the researcher functional profile with individual variations among patients with Stroke due to age, gender, psychological status, and pre-stroke functional status[31] may warrant more multicentric studies to better generalize the results in the present review only, the study is multicentric.

Despite the WHO providing the uniform language of functioning in the form of ICF. The studies included in the review did not use outcome measures mentioned in the ICF booklet.

Articles included mentioning a 32-50% attrition rate however does not mention any other strategy to reduce the attrition rate.

Conclusion:

This review concludes that multicentric longitudinal studies with specifically related outcome measures focus on activity & participation as stated in ICF guidelines with an option of telerehabilitation in the chronic stage to reduce attrition rate may be undertaken by the researcher in the field of Stroke rehabilitation.

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