INTRODUCTION
CHAPTER-I

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1.1 PREAMBLE

A stroke, also known as a brain stroke or brain attack or cerebro vascular accident (CVA), happens when there is an abrupt stoppage of blood flow to the cerebrum. 84% of strokes are due to the ischemic stroke, which causes blockage to the blood vessels of brain by thrombus or embolism. It reduces the oxygen supply and nutrients to the part of the brain and thus causes damage to the cerebrum. Remaining 16% of strokes are developed because of hemorrhagic stroke, which causes an artery burst, leads to a bruise in the brain. Individuals with cerebrovascular accident frequently complain of sudden weakness and numbness on one side of the body, trouble in seeing, talking, moving, understanding and difficulty in daily living activities. [1-3]

The World Health Organization (WHO) has defined stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin.” [4]

In 2013, American Stroke Association updated definition of stroke as “an acute episode of focal dysfunction of the brain, retina, or spinal cord lasting longer than 24 hour, or of any duration if imaging (CT or MRI) or autopsy show focal infarction or hemorrhage relevant to the symptoms”. [5]
Epidemiology:

Stroke is an universal health problem. It is the primary reason of death, serious long-standing disability and disease burden in both high economy as well as low and middle economy countries. [3, 6] The World Health Organization (WHO) pointed out that, globally brain attack causes 6.7 million deaths per year. [6] Just about 75% of the cerebrovascular accidents occur >65 years aged people, although brain-stroke may affect by any given age. [7]

Stroke in global scenario:

Worldwide, 16 million new cases of acute stroke occur every year, stroke causes death in about three million women and two and half million men every calendar year. [7, 8] Cerebrovascular accident is the 2nd most important reason of mortality over sixty years and 5th most important reason in people aged 15 to 59 years old. 12.6 million have moderate to severe disability after stroke. [9, 10, 11] The disability adjusted life year (DALY) is “a measure of overall disease burden, expressed as the number of years lost due to ill health, disability or premature death”. [12] The WHO predicts that, the disability adjusted life years (DALYs) missing due to stroke will increase from 38 million in 1990 to 61 million in 2020. [7]

Stroke in Indian scenario:

The latest population-based studies anticipated the accustomed occurrence rate of brain stroke range 334-424/100,000 in urban and 84-262/100,000 in rural regions. The incidence rate in India is 119-145/100,000 which is higher than the western nations. Stroke accounted for 7, 71067 deaths in 2002, in India. [13, 14]
The incidence of stroke:

World wide, incidence of stroke is around two per thousand, approximately two hundred new strokes occur in 100,000 populations per year. Incidence of stroke is about 19% higher in males than females. [6, 7]

The prevalence of stroke:

The prevalence of stroke varies from 44 to 842 per 1,00,000 population with a male preponderance. Cerebrovascular accident comprises 2% of all the hospital admissions, 1 to 5% of whole medical ward registrations and 9 to 30% of whole neurological registrations. [6, 7] The American Heart Association (AHA) estimated that worldwide; half billion cerebrovascular accident survivors are suffering with the physical, psychological, and higher mental deficits. [5]

Risk factors:

Several risk factors have been associated with stroke. They are classified into two groups such as risk factors that can be modified and fixed risk factors. Modifiable risk factors that can be altered with correcting life style include high blood pressure, type 2 diabetes mellitus, chronic smoking, associated cardiac disease (coronary artery disease, atrial fibrillation), hyperlipidemia (elevated lipids), excessive cholesterol markers, excessive consumption of alcohol, fatness, poor diet in aged population, lack of physical activity, increase in red blood cells, use of contraceptive pills, stress, blood clotting abnormalities, social isolation.[1, 15-20]
Risk factors that are fixed include advance age (>65 years), sex (male>female), race (Afro Americans), family or individual history of previous stroke or transient ischemic attack, malformations in the veins or arteries in the cerebrum, hereditary conditions, for instance sickle-cell anaemia, haemophilia, hereditary cardiac disease. [1, 16, 21]

Warning signs of stroke:

Stroke subjects experience sudden muscle weakness, sudden loss of sensation of one side of the body part, sudden trouble in speech, sudden trouble in vision, and sudden loss of movement. [22]
Consequences of bed rest/immobility/lack of physical activity in the hospital following stroke:

Bed rest after the stroke may delay in recovery and have a harmful effect on the heart, lung, gastrointestinal, musculoskeletal and nervous system. [23] Furthermore bed rest also causes development of serious medical conditions such as, DVT, lung infection-pneumonia, urinary tract infection, pressure ulcers, falls, fractures, abnormal mood and dependency in daily living activities. [23, 24]

Furthermore lack of physical activity during the hospital stay may cause atrophy of muscle, reduction in muscle power, reduced bone mineral density, maximal oxygen consumption, and postural hypotension. [23] Half of deaths happened in the first four weeks after cerebrovascular accident may be due to the bed rest. [24] There is strong evidence that bed rest is dangerous, delay recovery, and prolongs length of the hospital stay in most of the clinical conditions. [24]

Complications associated with stroke:

Most commonly seen life threatening adverse events associated with stroke are infections such as pneumonia and urinary tract infection; depression, fall and fracture. Immobility related complications are pressure ulcers, deep vein thrombosis, limb muscle contractures, shoulder pain, constipation and medical complications such as intracerebral bleed, another stroke and seizures. [25-32]
Pneumonia:

It is most frequently seen respiratory complication associated with stroke. Pneumonia causes difficulty in breathing, if untreated it may cause atelectasis and respiratory failure. Individuals with post stroke dysphasia frequently report aspirated pneumonia. Incidence of pneumonia in acute stroke is around 10%. [33]

Urinary Tract Infection (UTI):

It is a recognized serious adverse event of cerebrovascular accident. It can occur as a result of immobility, urinary catheter and advanced age. Incidence of UTI following stroke is around 10%. [33]

Falls:

Following stroke falls are regularly seen adverse event. It may cause fractures and further affects freedom in activities of daily living and fall is associated with poor trunk control and balance, severity and advanced age. Approximately half of the individuals with stroke experience fall. [34, 35]

Pressure ulcers:

The most commonly seen adverse effect of bed rest after stroke is pressure ulcers. Immobility or decreased movements may cause continuous pressure, friction, shear forces on underlying tissues results pressure sores. Frequency of pressure sore following stroke is around 17%. [35]
Deep venous thrombosis (DVT):

Deep vein thrombosis is the life threatening medical complication, routinely seen in acute cerebrovascular accident survivors. In general, prevalence of DVT after stroke is around 2-20%. [31] CLOTS trial reported that 11% of stroke subjects experienced DVT. [36] Blood clots form in veins of the legs because of immobilization following stroke. Pulmonary embolism results if DVT is formed and dislodged to land in pulmonary circulation.

Conventionally stroke survivors who developed DVT were medically managed using low molecular weight heparin, compression therapy and strict bed rest. [36-38] However recent research suggests that early mobilisation including ambulation may prevent deep vein thrombosis and pulmonary embolism. [37, 38]

Muscle contractures:

Muscle contractures are frequently seen immobility related complication of post acute stroke. Contracture is an adaptive shortening of the muscle due to abnormal position of limbs in bed, wheel chair and lack of movement. 43% of individuals with stroke develop contractures in limb muscles due to bed rest. Contractures were estimated as one third of the restriction in range of motion of the joint. [35]

Shoulder pain:

Impingement of shoulder joint occurs, when an individual with stroke positioned on affected side. Weakness, spasticity may pull the shoulder joint inferiorly may also cause shoulder pain. Support should be provided while
transfer, positioning and mobilisation of the stroke survivor. Approximately 39% of stroke survivors complain shoulder pain. [35, 39]

**Constipation:**

Constipation is most commonly reported an immobility related complication in acute stroke survivors. Constipation disturbs mood, discomfort and uneasiness complained during physiotherapy and addressed with medical intervention and high fiber diet. Physiotherapist uses early mobilisation including standing therapy to address this issue. [40]

**Quick evaluation of suspected cerebrovascular accident survivor:** [41]

- **F**- Face drooping while attempting smile.
- **A**- Arm drifts while attempting to lift both upper extremities.
- **S**- Speaking ability.
- **T**- Time left from onset of stroke to emergency medical room, call emergency department/108 in India.

**Emergency medical management of stroke:**

An ischemic stroke survivor, if admitted within three hours of stroke onset, thrombolytic drug, intravenous tissue plasminogen activator (Rt-PA) is administered to reduce catastrophic events like death and permanent disability following stroke. [42, 43] Anticoagulants, [44] Anti platelet drug such as aspirin [45-47] given to save person life.

**Definition of Mobilisation:**

Traditionally ‘mobilisation’ is considered as any physical activity within the bed, activities such as passive and active limb range of motion exercises,
stretching, trunk stability exercises, balance activities in sitting position within bed. [48, 49]

**Definition of Very Early Mobilisation (VEM):**

The terminology ‘Very Early Mobilisation’ or ‘Early Rehabilitation’ following cerebrovascular accident is ambiguous. Early and repetitive rehabilitation consist of out of bed activities, which start inside 24 hours up to 12 weeks after cerebrovascular accident onset. Many of the researchers in their studies used the term ‘early mobilisation’ and ‘very early mobilisation’ was similar. [48, 50, 51]

In this study the term “very early” is defined as inside the earliest 48 hours following stroke symptom onset. The term “mobilisation” is stated as upright activities such as sit upright, stand upright, sit to stand transfer and walking activities perform through out the day. The term ‘Very Early Mobilisation’ (VEM) is defined as out of bed upright activities including sit upright, sit to stand, stand upright, and walking within 48 hours post-stroke.

Encourage and involve in active training of upright and out of bed activities within 48 hours, when individuals with cerebrovascular accident can tolerate to upright activity without disturbing his/her neurological and cardio respiratory status.

Very early mobilisation is recommended in most of the countries guidelines for acute stroke subjects. [50, 52] Very early mobilisation (VEM) is a safe and practical, simple and effortless to deliver treatment, hardly needed any
apparatus. It can be tolerated by most of the subjects with the cerebrovascular accident. [53]

Early mobilisation started inside one calendar day of acute ischemic cerebrovascular accident individuals who has received IV rtPA/Thrombolytic therapy turn up to be fairly safer and practical and require intensive care and monitoring of neurologic and vital signs. [54, 55]

Advantages of very early mobilisation:

Few recent trials demonstrated that the very early mobilisation coupled with the standard care enhances the independence in activities of daily living, reduces cost, early discharge to home and improves the quality of life, patient satisfaction and psychological well being, furthermore reduces the cognitive impairment and serious medical complications such as pneumonia, pressure sores, deep vein thrombosis therefore reduces the disability and death rate following acute stroke. [56-65]

Disadvantages of very early mobilisation:

Very few studies reported the harms related to the very early mobilisation following acute stroke. Many health care professionals believe that early, high intensity and frequent upright activities initiated inside one calendar day onset of cerebrovascular accident may reduce perfusion along with expand brain ischemia area and it may abnormally affect the blood pressure regulation, however after few minutes completion of mobilisation, blood pressure remains normal. An abnormal change in intra cranial pressure, furthermore hemorrhagic stroke victims may further bleed. [66, 67] However the contemporary HeadPoST
multicentre trial with an objective of lying strictly in flat position compared with sit up and elevated head position within 24 hours of cerebrovascular accident shown head end elevation > 30 degree is safe and feasible and results did not show any statistical significance difference on disability. [68]

Factors affecting delivering early mobilisation in acute stroke survivors:

Factors such as advanced age, abnormal vitals, ICU admission, co-morbidity, stroke type and severity can affect the delivery of early mobilisation. [53]

Stroke unit care versus usual care:

Level-1 evidence is available for the stroke unit care for better functional recovery in acute stroke survivors. Stroke unit care includes interdisciplinary team work mainly includes early mobilisation and physical therapy. [69]

RepetetiveTask training:

There exist systematic review evidence for high intensity, repetitive functional or task oriented training in acute stroke which includes repetitive functional activities or task specific activities such as rolling, supine to sit, sit to stand, stand to sit, standing, walking and stair climbing activities. [70]

The standard physiotherapy care given in acute phase of stroke:

The standard physiotherapy in acute stroke includes, correct positioning in the bed, passive and active range of motion exercises of the affected extremity, mobilisation in the bed, sitting balance activities, and education of subjects and caregivers. [71, 72]
Activities of Daily Living (ADL):

ADL are classified as basic ADL for instance, eating food, bathing, wearing cloths, sphincter care, transfers, walking and flight of stairs and work related activities like keyboard typing, writing, manual labor job and so on.

Mortality:

Death rate associated with the stroke is significantly reduced in western countries than eastern countries. Numerous factors contribute for the death after stroke including but not limited to another stroke, intracerebral bleed, fall and fractures, pneumonia, urinary tract infections and pressure sores. \[^{1, 5, 6}\]

Disability:

Disability is limitation to perform activities. “It is an intricate process, involving the interaction between an individual with a health condition and the environment.” according to the International Classification of Functioning, Disability and Health (ICF). For example, an individual with stroke may experience weakness on one side of the body part (impairment) that may perhaps decrease an individual ability to perform daily routines such as eating, walking (disability) and that further can lead to an inability to participate in social activities such as going to work place and social activities and meeting friends (Handicap). \[^{73}\]

Disability associated with stroke:

Most of the individuals with stroke survive but experience serious disability. Many factors contribute to the disability post stroke such as immobility related or bed ridden. \[^{59}\]
Quality of Life (QoL):

‘An individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. “It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships, and their relationship to salient features of their environment.” [74, 75] Stroke often reduces the quality life of the survivors.

Determinants of post stroke quality of life:

Many factors contribute to cause decrease in QoL after cerebrovascular accident. Following factors contribute to reduction in QoL after stroke, such as, old age, severity of stroke, social isolation, couldn’t go to work place, decreased higher mental function, and the complications associated with disease. Numerous researchers confirmed that there is a strong relationship between dependency in ADL and QoL after cerebrovascular accident. [76, 77]

Psychological wellbeing:

The majority of stroke individuals are associated with sharp decline in psychological well-being at the time of the episode. Anxiety and depression is the most general adverse events seen after stroke. [78, 79]

Definition of depression:

It is defined as “a feeling of helplessness and hopelessness, feeling of empathy, suicidal thoughts”. An electronic database review by Hackett M et al. asserted that 33% of all cerebrovascular accident subjects encounter depression.
Depression is associated with poor functional recovery, increased mortality and decreased quality of life following acute phase of stroke. [81-83]

**Definition of Anxiety:**

It is defined as a feeling of fear and anxiousness. Majority of stroke individuals experience anxiety after stroke. Stroke patients with depression and anxiety have declined functional status, diminished psychosocial outcome, reduced quality of life and higher death rates than stroke patients without depression. [83, 84]

**Cost effectiveness of very early mobilisation:**

Stroke unit care is expensive and requires multidisciplinary care. So developing countries find it difficulty to establish stroke units in their hospitals. Early mobilisation is simple and easy to administer intervention which prevents serious adverse events following acute stroke. Further it requires little or no usage of equipment’s so it minimizes the cost of hospitalization. [64]

**Length of hospital stay:**

Advanced age and severity of stroke is the most common cause of greater length of stay in hospital following acute stroke. Further bed rest or immobility related adverse events may delay early discharge from the hospital. Research evidence says that very early, frequent and intensive mobilisation activities including out of bed activities help in reducing the length of the hospital stay. [85, 59]
NEED FOR THE STUDY

There is no standardized practice of stroke unit care in India. Any interventions which has ability to improve functional status, quality of life and reducing immobility related adverse events has to be adopted in routine stroke care for better recovery. However stroke unit care is very expensive and causes economical burden on stroke survivor or caregiver. Hence simple and economical therapeutic interventions are required to overcome the post stroke burden. Therefore early mobilisation is tested in this study.

Very early mobilisation protocol is simple, economical and practical to apply to the most of acute stroke survivors. Previous randomized controlled studies demonstrated that very early mobilisation is safe and feasible,\textsuperscript{[53]} reduces serious clinical adverse events for instance bed sores, lung infections, further deep vein thrombosis following acute stroke.\textsuperscript{[57, 59]}

Early mobilisation after stroke is approved and recommended by almost 22 countries in their clinical guidelines of stroke.\textsuperscript{[52]} There is an early adaptation of early mobilisation practice in stroke units in many countries guidelines, however there is limited or no high quality randomized trials performed on the effect of very early and frequent upright activities (initiated inside 48 hours of cerebrovascular accident onset) on the complications, activities of daily living, disability, quality of life, and psychological well-being immediately after the stroke, to make any approvals on the clinical practice.\textsuperscript{[50]} Thus less is known about the knowledge of mobilising very early after stroke and their dosage, benefits after acute cerebrovascular accident.
Therefore current RCT was an endeavour to find out the effect of very early mobilisation which is initiated within 48 hours of cerebrovascular accident onset on the prevention of adverse effects, activities of daily living, disability, quality of life, and psychological well-being post acute stroke.

1.2 LITERATURE SURVEY

Search strategy:

Search methods used for finding of research studies:

We explored the popular medical and physiotherapy databases for articles published from 1965 to July 2017. Search comprised from the apex to the bottom of the evidence based pyramid in English language only. We used the following search terms: (Stroke or Cerebro vascular accident in combination with very early mobilisation or early mobilisation or early rehabilitation/early physiotherapy) and (Functional status, disability, complications, psychological wellbeing, and quality of life). We also searched the primary registry for clinical trials in India (www.ctri.nic.in) for ongoing and recently completed trials.

Very Early Mobilisation (VEM) and Acute Cerebrovascular accident:

In 2006, Department of neurology and Neuro rehabilitation, centre Hospitalier Universitaire Vaudois, Rue de Bugnon, Switzerland did the literature synthesis on early mobilisation after cerebrovascular accident. A popular medical database search was performed from 1950 to August 2005. The findings of their review recommend that early out of bed activities may be useful for acute stroke individuals. Nevertheless, no RCT’s were available to contrast the early and frequent mobilisation (e.g. within three days) versus delayed (e.g. 7 days to 14
days) mobilisation. They concluded, not a single RCT was accessible to provide evidence of the usefulness of early out of bed activities after acute cerebrovascular accident. Thus, according to Diserens K et al (2006) early mobilisation benefits acute stroke survivors; however results obtained from the observational studies pointed out that, there were no randomized controlled trials which existed on this topic. Future research should focus on randomized controlled trials on this topic. [48]

Bernhardt J et al. [50] in 2009 performed a systematic review on the effect of dose comparison of mobilisation following cerebrovascular accident; one completed randomized controlled trial with 71 stroke survivors included for analysis after screening of 39 relevant trials. And authors concluded that inadequate proof to endorse or refute benefits of early and intensive out of bed activities following cerebrovascular accident compared with usual care. Thus according to Bernhardt J et al (2009) very few RCT’s were available on benefits and harms of early and frequent out of bed activities following acute cerebrovascular accident. Therefore larger, high-quality randomized controlled trials of very early mobilisation after stroke were needed.

Arias M and smith LN (2007). [86] did a postal survey in Scotland to examine the health professional’s opinions on early mobilization of acute stroke individuals. 99 healthy professionals of whom 39 were nurses, 39 doctors and 21 physiotherapists took part in the study. Results showed there was an ambiguity across three professions in terms of meaning of ‘early mobilization’ and dosage of it. Thus according to the Arias M and smith LN evidence based support to
practice early mobilisation in acute stroke survivors is missing. Therefore a strong research gap was identified on this topic.

Sjoholm A et al (2011). [87] Conducted a survey to explore stroke care professional’s opinion on very mobilisation and its effectiveness and dosage following acute stroke, survey results state that the lack of understanding, agreement and broaden in opinion on timing and benefits of very early mobilisation after stroke, which suggests further research is required.

The most recent single-center, randomized control trial performed by Herisson F et al. (2016) aimed to compare the effect of early out of bed sitting activity initiated within a day with progressively sitting activity started third day of ischemic stroke onset. Their study results suggest that early upright activity is useful in ischemic stroke survivors. However no distinction found among interventions in support of a favorable outcome on modified rankin scale (0-2) score, barthel index and adverse events reported at three months post ischemic stroke. Further they also stated that early sitting procedure was safe and feasible. [65]

**Effect of early supported standing in acute stroke individuals:**

Allison R et al. [88] performed a pilot randomized controlled trial to investigate whether early supported standing enhances functional ability in people with acute stroke. Their research trial results confirmed that the gross functional tool section of the River mead Motor assessment achieved higher median scores. In addition, the Berg Balance Scale reflected higher scores at the completion of study. Authors concluded that supported standing improved functional ability and balance in people with acute stroke. Thus according to Allison R et al. Early supported standing of acute stroke survivors improves
independence in activity of daily living and postural control. However small sample size of pilot study results can’t be generalized to whole stroke population. Therefore larger sample size with high quality randomized controlled trials were recommended.

However Bagley et al. \cite{89} and Ferrarello et al. \cite{90} study results demonstrate that, supported standing therapy in conjunction with traditional physical therapy post stroke, does not improve functional ability including mobility and balance compared to traditional physical therapy alone.

**Frequency of adverse events/complications reported in hospital and first three months after stroke:**

Langhorne P and colleagues \cite{91} conducted a prospective cohort study on 311 stroke survivors to determine the frequency of medical, immobility, and stroke related adverse events up to thirty months following cerebrovascular accident. The results of this study confirmed that, illness due to infections and fall are regular, furthermore, pressure sores, shoulder impingements, and depression were reported in their study.

**Effect of Very early mobilisation to prevent adverse events associated with stroke:**

Sorbello D et al. \cite{92} did a randomized controlled trial to explore whether very early mobilisation affected immobility related complication type, amount and severity in the first twelve weeks after the cerebrovascular accident. And the results showed that falls were routinely seen adverse event, and the number of bedridden complications was associated with length of hospital stay.
Diserens K et al. [60] carried out a pilot RCT among 50 ischemic cerebrovascular accident subjects (with a NIHSS score >6) to compare early initiation of out of bed activities with postpone out of bed activities to reduce adverse events. Authors found that early mobilisation subjects had noticeable decrease in high risk adverse events, and no change in overall adverse events.

Langhorne P et al. [57] did an assessor blinded, pilot randomized trial to compare the standard stroke care with an additional very early and high frequency mobilisation and automated monitoring protocol following acute cerebrovascular accident. It was concluded that early and frequent mobilisation was connected to less immobility related complications and more subjects were independent at three months post stroke. Further they also confirmed that early and frequent out of bed activities are safe and feasible to deliver for acute stroke individuals.

Wijk RV and associates [93] conducted a single blind, multicenter, RCT on effect of an early rehabilitation programme initiated within a calendar day after cerebro vascular disease onset on adverse events reported at 12 weeks follow-up, concluded that adverse events associated with bed rest were not connected with the therapy duration, frequency and intensity of upright activities.

VEM and Activities of daily living following acute stroke:

Cumming TB et al. [56] in a RCT established that, almost half the individuals of early out of bed activities group, had a better effect on the independence in activity of daily living (Barthel ADL Index) by three months, contrast with 28% of the standard care individuals with acute stroke (p=0.136).
Chippala and Sharma (2016) conducted a prospective randomized control trial in India on 83 subjects with acute cerebrovascular accident, compared early and repetitive mobilisation which was initiated within 24 hours of stroke onset with the routine care, concluded that 85% of very early mobilisation group subjects were improved independence in activities of daily living. Further statistical significant difference ($p<0.05$) shown between groups on freedom in activities of daily living at 3 months follow-up after acute cerebrovascular accident. Thus very early mobilisation is effective in augmenting freedom in daily living activities. \cite{58}

On the contrary Bernhardt J et al.\cite{53} and Langhorne P et al.\cite{57} found that early rehabilitation group shown a non Significant Summary Effect Size (SES) on freedom in activities of daily living at 3 months follow-up after acute cerebrovascular accident.

Craig LE et al.\cite{94} conducted meta-analysis to find out the influence of early mobilisation after stroke on freedom in ADL through putting together information gathered from two promising trials, one from the Australia, AVERT and other trial from the UK, VERITAS study and concluded that very early mobilisation was related with enhanced freedom in ADL at 12 weeks equated with routine treatment. Nevertheless both studies were restricted by small size.

In 2011, Kuwabara et al.\cite{95} did an observational study using a Japanese administrative database on 45,014 stroke individuals to investigate whether early initiation of rehabilitation produces functional recovery in acute stroke individuals. They reported that early rehabilitation did not improve functional recovery. Further they stated that longer the length of stay would affect functional recovery.
Matsui and his colleagues. \cite{96} did a nationwide retrograde group survey in Japan, to explore the relationship between early initiation of rehabilitation (started three days of stroke onset) and functional outcome for the individuals with acute ischemic cerebrovascular accident. Their results indicated that very early initiation of rehabilitation was safe and it improves functional outcome following acute cerebrovascular accident.

**Effect of Very early mobilisation on reduction of death rate following acute stroke:**

Bernhard et al. \cite{97} conducted a very large scale multicentre randomized control trial on effect of early and frequent mobilisation on reduction of death rate and disability following acute cerebrovascular accident. Their study revealed surprise results that outcomes at three months, very early high intensity repetitive mobilisation along with the usual care started within twenty four hours after stroke, reported more fatalities than the usual care.

Sundseth et al. \cite{98} performed single centred RCT, to find the effect of VEM initiated within twenty four hours on death and dependency following acute stroke. Their study results showed that more individuals in the very early mobilisation group reported fatalities and didn’t improve the functional status than control group.

**Effect of very early mobilisation on quality of life following acute stroke:**

Tyedin K et al. \cite{62} performed a stage II randomized control trial on 71 subjects with cerebrovascular accident, with an objective to explore the consequence of VEM on the HRQoL. Health-Related Quality of Life measured with Assessment of Quality of Life (AQoL) questionnaire at one year post stroke.
and concluded that VEM group reported improved long term quality of life especially independent physical functioning after stroke.

In 2016 Hokstad A et al. [99] did a prospective cohort multi-centre study on 390 subjects with cerebrovascular accident in Norway to find out the association between the higher the amount of early and frequent out of bed activities and good outcome (mRS), Participation limitation (HRQoL) at 3 months following stroke? Their trial results authenticated that there was strong association of early and higher the amount of upright activity and good outcome (mRS), QoL after stroke.

Indredavik and his associates in 1998 performed a RCT with an aim to find out effectiveness of initial organized stroke therapy given in stroke unit versus routine therapy given in general ward on lasting QoL assessed five years following cerebrovascular accident. Their study results demonstrated that organized stroke unit care improved QoL 5 years following cerebrovascular accident. [100]

A review was conducted by Artal FJ and Egido JA [101] on QOL following cerebrovascular accident. Authors pointed that decreased incidence of mortality and the presence of medical complications and dependency in activity of daily living in stroke survivors reduces their HRQoL. Dependency in ADL, reduced disability and depression are common causes of quality of life after stroke. Other causes include advanced age, female sex, and psychological adaptation, coping style, and decreased social support.
Frequency of depression after stroke:

Rastenytė D and Krančiukaitė D[^81] did a review on post stroke depression and its impact on quality of life. Summary of their review states that depression is one of the most recognized complications after stroke and is associated with poor quality of life and poor psychosocial outcome. Depression after stroke can affect anyone regardless of his/her age, gender, ethnicity and the severity of stroke. Cerebrovascular accident subjects with depression have lesser independence in activities of daily living, higher mental issues, and high death rate than individuals with no post stroke depression.

In 2015, Sugawara et al.[^102] did a retrospective study to identify the consequence of post cerebrovascular accident depression symptoms on the duration of stay at the hospital in acute stroke individuals of Japan, concluded that the depression was associated with long duration of stay at the hospital; furthermore it causes dependency in ADL and poor progress in stroke outcomes.

Caeiro L et al.[^103] did a prospective study in Portugal to analyse the frequency of depression in acute stroke survivors. They observed 178 acute stroke (≤ 4 days) individuals with depression from 218 stroke survivors and they concluded that the frequency of depression (lack of interest and apathy) was noted in 46% of the acute stroke survivors.

In an electronic database review by Hackett et al.[^80] reported that 33% of stroke survivors reported risk of depression in first six months of cerebrovascular accident.
Very Early Mobilisation and Exercises on psychological wellbeing following acute stroke:

Cumming TB et al. [63] in 2008 did a randomized controlled trial on 71 individuals diagnosed with stroke to investigate the effect of very early initiation of mobilization (started within the first day of the cerebrovascular accident onset) on levels of depression, anxiety and irritability. Their results demonstrated that at discharge (at seven days) intervention group subjects were less depressed and slightly less anxious than usual care patients.

Aider FJ et al. [104] investigated the benefits and hazards of water based physical activity on mood in thirty individuals with ischemic cerebrovascular accident. Their results demonstrated that the aquatic exercises significantly improved the psychological wellbeing including anxiety and depression (p<0.05) of ischemic stroke survivors.

VEM and the level of disability following acute cerebrovascular accident:

The most recent multi-center, large RCT conducted by AVERT collaboration group aimed to compare the effect of frequent, high dose, early out of bed activities with standard care after stroke. 2104 stroke subjects were haphazardly allocated to any intervention group (n=1054) or usual care (n=1050); results of this trial showed that higher intensity, very early initiation of mobilisation was linked with a decrease in the likelihood ratio of a favorable result (0-2) on modified rankin scale (mRS) at 3 months. [97]

Sundseth et al. [98] conducted a randomized, controlled trial at Akershus University Hospital, Norway, to investigate the effect of early out of bed
mobilization activities initiated within twenty hours of acute stroke on disability outcomes. Results identified that an unfavourable outcome on mRS, increased mortality, and dependency in activities of daily living with very early mobilisation group (<24 hours of stroke onset) than people with stroke mobilized between 24 and 48 hours.

In 2016, Herisson F and colleagues \cite{65} did a RCT to investigate the effect of early mobilisation including sitting out of couch movements, which are initiated inside 24 hour of cerebrovascular accident onset comparing it with progressively sitting where angle of bed changed progressively to sitting upright at third day stroke onset. Their results suggest that no distinction between interventions for both a favourable result on modified rankin score (0-2) and Barthel index and adverse events collected at three months post stroke. However early sitting procedure was safe and feasible.

**Economic evaluation of very early mobilisation (VEM) following acute cerebrovascular accident:**

Tay-Teo K et al. \cite{64} did a randomized controlled trial to find out the economic evaluation of early initiation of out of bed activities and the routine therapy contrasted with the routine therapy alone in people with acute stroke. Study results demonstrated that intervention group was proven to be economical.
Safety, feasibility of very early mobilisation following acute cerebrovascular accident:

Bernhardt J et al. [53] and Langhorne P et al. [57] found that very early and frequent mobilisation started within twenty-four hours of cerebrovascular accident symptom onset is practical and not harmful.

Poletto SR et al. [61] did a pilot RCT on harmless and practicality of early mobilization following acute ischemic stroke. Their study results showed that frequency of immobility related complications and death were alike in the early mobilisation group and routine care group. Dependency in daily living activities and levels of disability were found to be no meaningful difference between the groups at the 12weeks follow-up. Furthermore early initiation of out of bed activities was harmless and practical following acute ischemic cerebrovascular accident.

Olkowski and his associates performed a backward looking trial to determine safety and feasibility of an early initiation mobilisation program for individuals with aneurysmal subarachnoid hemorrhagic stroke. Researchers concluded that early mobilisation activities including positioning, education, functional training and therapeutic exercises were safer and practical for aneurysmal subarachnoid hemorrhagic stroke survivors. [105]
Effect of dose response (timing of initiation, intensity, frequency) of very early mobilisation following acute stroke:

In 2016, Bernhardt et al. performed pre specified dosage reaction testing of AVERT following acute phase of cerebrovascular accident. Their study analysis suggests that early, shorter and more repeated out of bed activities but not the high intensity may help in functional recovery.\textsuperscript{[106]}

Effect of early, intensive rehabilitation (Physiotherapy) on acute stroke survivors:

A systematic review and meta-analysis conducted in the International Centre for Allied Health Evidence, School of Health Sciences, Sansom Institute for Health Research, University of South Australia, Adelaide, Australia with an objective to find out the effect of early (within 7 days of stroke) physical therapy on death, functional status and adverse events following acute phase of cerebrovascular accident. Their review and meta-analysis of three randomized controlled trial (total 159 stroke subjects) suggests that early physical therapy within three days of stroke is beneficial. Conversely clinical benefits of very early mobilisation started within twenty four hours over standard care are not clearly demonstrated and increased possibility of death within three months of cerebrovascular accident.\textsuperscript{[107]}

The Institute of Biomedical Technologies, National Research Council, Milan, Italy attempted multicentre cohort study to find out the influence of timing of beginning and time of rehabilitation on death and long term functional disability and quality of life after stroke. Review recommended that early initiation of physiotherapy may decide improvement in functional disability and quality of life after acute stroke.\textsuperscript{[108]}
Peurala S H et al. \cite{109} performed an experimental study on 22 subjects with stroke in the Department of Neurology and Physical Medicine and Rehabilitation, Kuopio University Hospital, Kuopio, Finland to evaluate the effects of three weeks intensive and task specific walking training in early acute stroke subjects, concluded that the early three weeks of intensive task specific gait training is safe and improved activities of daily living furthermore improved walking ability at three months and six months follow-up.

The department of physiotherapy, University hospital Vrije Universiteit, Amsterdam \cite{110} conducted a meta-analysis and data based study on the effects of additional physiotherapy following cerebrovascular accident using popular medical and physiotherapy electronic databases that reviewed papers published from 1966 to November 2003, they selected twenty randomized controlled trials for meta-analysis based on relevant key areas in intensive physiotherapy, conventional therapy and stroke, they concluded that intensive physiotherapy approximately 16 hours extra than routine care results in a little progress in activities of daily living within six months following cerebrovascular accident. However more than two hours of physical therapy in a day is not practical for most of the individuals with acute stroke, because lack of ability to tolerate the extra therapy time.

A RCT conducted on sixty individuals with stroke (11 men, 14 women) in the Department of neurology, U.O. Neurologia, Caserta, Italy, with an objective of comparing intensive physiotherapy with routine physiotherapy in acute ischemic cerebrovascular subjects. They concluded that fourteen days of an intensive physiotherapy didn’t reduce disability and improved the activities of daily living at
14 days and 6 month follow-up of the acute thrombotic cerebrovascular accident subjects.\[111\]

Department of Physical Medicine and Rehabilitation, and Stroke Center, Chiayi Taiwan conducted the retrospective review on 76 stroke survivors (39 men, 37 women) to determine the effect of early initiation and amount of physiotherapy program on improvement of ADL of cerebrovascular accident survivors. Barthel index tool was used to measure the functional status at admission, 1 month, 3 months, 6 months and 1 year post cerebrovascular accident. Study results demonstrated that early initiation of physiotherapy (approximately seven days) has had an effect on the recovery of function of cerebrovascular accident individuals up to 12 months.\[112\]

Department of physical medicine and rehabilitation, Department of neurology of National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan, conducted a prospective cohort study using regression analysis on 154 (99 men, 55 women) acute cerebrovascular accident subjects, to find put effect of early intensive rehabilitation on activities of daily living and walking ability, concluded that individuals with acute cerebrovascular accident improved in their functional ability and walking function at discharge. Thus early initiation and intensive rehabilitation improved functional status and walking ability following acute stroke. However cohort studies results can’t be generalized to the entire stroke population.\[113\]

Department of Neurology, Sun Yat-Sen University Hospital, Guangzhou, Southern China, performed on prospective RCT on 156 stroke subjects to
examine the effect of early initiation (less than a week) of physical therapy on activities of daily living and disability after acute cerebrovascular accident, concluded that early commencement of physical therapy improves activities of daily living and reduces disability after acute cerebrovascular accident.\[114\]

Department of Physiotherapy and Rehabilitation and Department of Neurology, St. Anne’s Faculty Hospital, Masaryk University, Brno, Czech Republic, did a study on 96 subjects (60 men, 36 women) to find out the efficacy of physical therapy on disability and health related quality of life (HQOL) in acute cerebrovascular accident, concluded that rigorous physical therapy reduced disability and improved quality of life at discharge. However they didn’t find the correlation between disability measure FIM and quality of life measure SF-36. Limitations of this study were, control group was not included.\[115\]

Maulden et al.\[116\] did an observational cohort study 969 stroke subjects to investigate relationship between the early rehabilitation and functional outcomes, concluded that early rehabilitation after stroke onset has positive effect on the independence in daily living activities and an early discharge from the hospital.

Langhorne P et al.\[117\] did a systematic review on the effective stroke unit care parts. This review provides a description about median of 45 minutes (30-60) early mobilisation per day was given by physiotherapy in stroke unit care.

Effect of bed rest and body position in acute stroke patients:

Bernhardt J et al.\[23\] published a review article in Annals of Indian Academy of Neurology in 2008, on the effects of bed rest and early, intensive
mobilisation after acute cerebrovascular accident and concluded that very early mobilisation is simple and effortless to deliver treatment, hardly needed any apparatus. It can be tolerated by most of the subjects with the cerebrovascular accident.

Centre for General Practice, Graduate School of Medicine, University of Queensland, Herston Queensland, Australia, performed a database review on immobility due to recumbent position and its hazards, using popular medical electronic databases that reviewed papers published from 1966 to June 1998. They selected thirty-nine trials for review based on relevant key areas in bed rest, immobilisation, early activity, and early rehabilitation following medical conditions. It concluded that the strict bed rest or immobility following medical and post-surgical conditions prescribed as primary therapy don’t provide any benefit and may cause serious adverse events such as DVT, infections in the lung, and pressure ulcers following medical conditions and post-surgery. [24]

Tyson and Nightingale [118] did a systematic review to assess the outcome of body position on saturation of oxygen in acute cerebrovascular accident subjects and authors concluded that, convincing support about position of the human body didn’t influence saturation of oxygen in subjects with no hypoxia or significant risk factors. There was an inadequate proof that individuals with/or risk of hypoxia should be positioned as upright as possible and avoid lying positions.

Askim T et al. [119] stated that individuals with cerebrovascular accident shouldn’t be idle in the bed in the initial 12 days of cerebrovascular accident onset and an early physiotherapy may benefit such individuals, concluded that
early and intensive rehabilitation is practical, safe, can be tolerated by severe stroke subjects.

**Head end position and stroke:**

The prospective multi centre HeadPoST trial published in 2017, compared Effect of lying in flat position and Sitting up with head end elevation (>30°) initial 24 hours of stroke onset on level of disability. Study results shown that sitting up position with head end elevation initial 24 hour stroke onset is safe and feasible. However no statistical significance difference observed between groups. [68]

In 2006, Department of neurology and Neuro rehabilitation, centre Hospitalier Universitaire Vaudois, Rue de Bugnon, Switzerland, developed an early mobilisation protocol for acute cerebrovascular accident subjects. An early mobilisation protocol, begins with lying in flat position initial 24 hours of brain stroke, then second day progress to head end of the bed is elevated to 45 degree, if subject can tolerate and medically stable, then third day progress to head end elevated to 90 degree for minimum four hours, if subject is medically stable, then progress to start out of bed activities like sitting, standing, and walking. [48]

**Effect of very early mobilisation on Brain plasticity in acute stroke subjects:**

The potential explanation for faster and better improvement with very early mobilisation could be; activity is the powerful modulator of brain reorganization. [120]

An earlier trial has pointed out that generation of proteins is linked by greater neuro-plasticity in the initial 14 days following the onset of ischemic cerebrovascular accident. [121-123] This evidence suggests that the early initiation
and frequent mobilisation after acute stroke provided significant functional gains and enhanced brain plasticity.

Outcome measures:

For comprehensive assessment of stroke recovery, reliable and valid outcome measures are necessary. To date, Barthel Index, Modified Rankin Scale (mRS), Medical Outcomes short form questionnaire (SF-36 v2), Depression and Anxiety measurement Scale (HADS) to measure mood during hospital stay are frequently been used in randomized controlled trials with stroke.

Barthel Index (BI):

Barthel Index is routinely used standard tool for assessing activity of daily living; The Barthel Index is an ordinal scale. It contains 10 self-care, bladder and bowel, and mobility items. Transfers and mobility items (both wheel chair transfers and ambulation encompass 30%, and toileting and bathing a further 10% of the total score). The BI has established psychometric properties and has high association with established tools used for measuring impedence in daily living activities. [124]

A recent systematic review and meta-analysis performed by Duffy et al.[125] pointed out that the BI has high agreement between rater (kw=0.93) for assessment of performance of activity of daily living in stroke survivors and further stated that Barthel Index appears a suitable outcome measurement tool for stroke trials and practice.
Hsueh et al.\textsuperscript{[126]} demonstrated that the Barthel index is reliable (k= 0.53-0.94, ICC=0.94), valid (Pearson r≥0.78) and responsive measure (effect size, d=0.85 at 14-30 days after stroke) in stroke individuals of Taiwan.

A systematic review was done by Sulter G et al.\textsuperscript{[127]} with an objective to find out usage and interpretation of modified rankin scale and barthel index in acute cerebrovascular research studies. Results shows that, for the barthel index, favourable outcome was >60. And for modified rankin scale favourable outcome was <3.

**Modified Rankin Scale (mRS):**

It is a most prevalent outcome measure for measuring global disability of acute stroke survivors in contemporary published stroke trials. mRS is a 7 points Likert scale, score ranges from 0-6, where zero indicates no disability, five indicates severe disability and six indicates death. It is simple and easy to administer and, time efficient i.e., not more than 5 minutes. Further it requires limited training. mRS has good inter-rater reliability, good validity and responsive, sensible, feasible tool, it has limited floor and ceiling effect. Interpretation of modified rankin scale: Poor outcome can be defined as >3 mRS, favourable outcome can be defined as <3 mRS.\textsuperscript{[128]}

Quinn et al.\textsuperscript{[129]} performed a systematic review on reliability of modified rankin scale. Concluded that the modified rankin scale (mRS) has excellent intra observer reliability but also demonstrated variability in inter-rater reliability (weighted k=0.95 to k=0.25) for the analysis of global disability in stroke survivors.
and further stated that modified rankin scale appears a suitable outcome measurement tool for stroke trials and practice.

In a recent systematic review, Nunn A et al. [130] analysed the mRS use in acute ischemic cerebrovascular accident studies from 2007- to- 2014. Authors stated that recent trials favoured the use of dichotomous statistical analyses over ordinal.

Zhao H et al stated that the Modified Rankin Scale has got good inter rater reliability but doubtful validity in acute stroke survivors. [131]

**Medical Outcome Short Form Questionnaire (SF-36 v2):**

It is most widely used self-rated measuring tool for QoL of generic and medical conditions. It has 8 items, the medical outcome short form questionnaire (SF-36) has been commonly recommended for use in clinical research of individuals with stroke. [132-134] It has excellent within rater and between rater reliability and adequate validity.

**Strength:** Self-administered questionnaire takes not more than 15 minutes to complete the form. It measures disease burden and set up efficient and less expensive selection of intervention.

**Weakness:** Subjects who are very sick and complete dependency in daily living activities may have ‘floor effect’.
Hospital Anxiety and Depression Scale (HADS):

The most widely recommended self-administered outcome tool to measure the psychological well-being is Hospital Anxiety and Depression Scale. It is a reliable, valid screening tool measures anxiety and depression in stroke individuals as well as in general hospital subjects. Administration time ranges from 2-5 minutes. [135-138]

It has 14 items in total that examine the client to reflect on their mood in the past week. Seven items assess depression, 5 of which are markers for anhedonia (lack of interest), and 2 concern appearance and feelings of lingering down. Seven items assess anxiety, of which 2 assess autonomic anxiety (fear and butterflies in the stomach), and the remaining 5 assess nervousness and agitation. [135, 136]

Bjell I and associates performed a review on the legitimacy of the Hospital Anxiety and Depression Scale (HADS). 747 papers were reviewed that used HADS and found that HADS can evaluate clearly the severity and diagnosis of depression and anxiety in physical, cognitively impaired subjects. [137]
Table 1: Primary outcome measures: Description and Psychometric Properties of Barthel Index (BI), Modified Rankin Scale (mRS).

+++ =Excellent, ++=Adequate, +=Poor

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Components &amp; Description</th>
<th>Scoring</th>
<th>Psychometric Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reliability</td>
</tr>
<tr>
<td>Barthel Index (BI)</td>
<td>10 ADL items</td>
<td>Total score range is 0-100</td>
<td>+++ (TR)</td>
</tr>
<tr>
<td></td>
<td>Very simple, easy to administer, cost effective, quick time (5-10 min)</td>
<td></td>
<td>+++ (IO)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+++ (IC)</td>
</tr>
<tr>
<td>Modified rankin scale (mRS)</td>
<td>Simple, easy and time efficient, feasible</td>
<td>0-6 Based on level of disability</td>
<td>+++ (TR)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>++ (IO)</td>
</tr>
</tbody>
</table>

TR=Test retest reliability, IO=Inter-rater reliability, IC=Intra rater reliability.
Table 2: Secondary outcome measures: Description and Psychometric Properties of SF-36V2, Hospital anxiety depression scale (HADS).

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Components &amp; Description</th>
<th>Scoring</th>
<th>Psychometric Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reliability</td>
</tr>
<tr>
<td>SF-36V2</td>
<td>8 domains, 36 Items simple, self completed, &lt;10 minutes</td>
<td>0-100</td>
<td>++ (TR)</td>
</tr>
<tr>
<td>Quality of Life</td>
<td></td>
<td></td>
<td>++ (IC)</td>
</tr>
<tr>
<td></td>
<td>HADS-Anxiety (7 Items)</td>
<td></td>
<td>++ (IO)</td>
</tr>
<tr>
<td></td>
<td>HADS-Depression (7 Items)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital Anxiety Depression Scale (HADS)</td>
<td>HADS-A 0-21</td>
<td>+++ (TR)</td>
<td>+++</td>
</tr>
<tr>
<td></td>
<td>HADS-D 0-21</td>
<td></td>
<td>++ (IO)</td>
</tr>
</tbody>
</table>

+++ =Excellent, ++=Adequate, +=Poor

TR=Test retest reliability, IO=Inter-rater reliability, IC=Intra rater reliability.
Table 3: Summary of important trials related to the Effect of very early mobilisation on acute stroke.

<table>
<thead>
<tr>
<th>Authors, year, country, Trial name</th>
<th>Methods</th>
<th>Sample Size (n=)</th>
<th>Intervention</th>
<th>Outcome measures</th>
<th>Results /Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernhardt et al. 2015, Australia AVERT</td>
<td>Multi centered parallel group Single blinded RCT Concealed allocation, Assessor blinded</td>
<td>2104</td>
<td>VEM (n=1054) Usual care (n=1050)</td>
<td>Poor outcome (mRs), total number of serious adverse events at 3 months</td>
<td>VEM was associated with no reduction in disability, death and complications.</td>
</tr>
<tr>
<td>Poletto et al. 2015 Brazil</td>
<td>Pilot RCT parallel group</td>
<td>39</td>
<td>Early mobilisation (n=19) Usual care (n=20)</td>
<td>Favorable outcome-mRS score Complications</td>
<td>No difference between groups Safe and practical</td>
</tr>
<tr>
<td>Chippala and Sharma. 2016 India</td>
<td>RCT, Single blinded Concealed allocation Assessor blinded</td>
<td>86</td>
<td>VEM (n=43) Usual care (n=43)</td>
<td>Barthel Index at discharge, at three months</td>
<td>Functional independence at discharge, at three months post stroke, Statistically significant group difference</td>
</tr>
<tr>
<td>Morreale et al. 2016 Italy</td>
<td>Prospective multi center RCT, Single blinded, Concealed allocation, Block randomization</td>
<td>340</td>
<td>Early rehabilitation (n=220) Usual care (n=120)</td>
<td>Favorable outcome-mRS score, BI score at twelve weeks, Complications at three month follow-up</td>
<td>No statistical difference between groups</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Patients</td>
<td>Intervention 1</td>
<td>Intervention 2</td>
<td>Outcome Measures</td>
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<tr>
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<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Herisson et al [65]</td>
<td>Prospective multicenter RCT, Single blinded, Concealed allocation, Block randomization</td>
<td>167</td>
<td>Early sitting within 24 hours (n=82)</td>
<td>Progressive sitting (n=85)</td>
<td>Favorable outcome- mRS score, BI score at three months</td>
</tr>
<tr>
<td>Cumming TB et al. [56]</td>
<td>RCT, Single blinded Concealed allocation, Assessor blinded, Intention to treat analysis</td>
<td>71</td>
<td>VEM (n=38)</td>
<td>Usual care (n=33)</td>
<td>Barthel Index River mead Motor assessment</td>
</tr>
<tr>
<td>Bernhardt et al. [53]</td>
<td>RCT Single blinded Concealed allocation Assessor blinded</td>
<td>71</td>
<td>VEM (n=38)</td>
<td>Routine care (n=33)</td>
<td>Safety (mRS), Total number of serious adverse events at 3 months</td>
</tr>
<tr>
<td>Langhorne et al. [57]</td>
<td>Observer blinded 2*2 Pilot RCT</td>
<td>32</td>
<td>Early Mobilisation (EM) (n=16)</td>
<td>Control EM (n=16) Augmented monitoring (AM) (n=16) Control AM (n=16)</td>
<td>Complications, Barthel Index, River mead mobility, Borg exertion scale</td>
</tr>
<tr>
<td>Study Authors and Year</td>
<td>Country</td>
<td>Design</td>
<td>Intervention</td>
<td>Sample Size</td>
<td>Outcome Measures</td>
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<tr>
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<tr>
<td>Tyedin K et al. [62] 2010</td>
<td>Australia</td>
<td>RCT, Single blinded</td>
<td>Concealed allocation, Assessor blinded, Intension to treat analysis</td>
<td>71</td>
<td>VEM (n=38) Standard care (n=33)</td>
</tr>
<tr>
<td>Sundseth A et al. [98] 2012</td>
<td>Norway</td>
<td>RCT</td>
<td>Blinded assessor at follow up</td>
<td>56</td>
<td>VEM (n=27) Control (n=29)</td>
</tr>
<tr>
<td>Diserens et al. [60] 2011</td>
<td>Switzerland</td>
<td>Pilot RCT, Computer generated number numbers, Concealed allocation</td>
<td>50</td>
<td>Early mobilisation (n=25) Delayed mobilization (n=25)</td>
<td>Complications mRs score, NIHSS Length of stay</td>
</tr>
<tr>
<td>D Sorbello et al. [92] 2008</td>
<td>Australia</td>
<td>RCT, Single blinded, Concealed allocation, Assessor blinded, Intension to treat analysis</td>
<td>71</td>
<td>VEM (n=38) Usual care (n=33)</td>
<td>Complications reported in the first three after stroke</td>
</tr>
<tr>
<td>Cumming TB et al. [63] 2008</td>
<td>Australia</td>
<td>RCT, Single blinded, Concealed allocation, Assessor blinded</td>
<td>71</td>
<td>VEM (n=38) Standard care (n=33)</td>
<td>Irritability, depression and anxiety (IDA) scale</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Setting</td>
<td>Participants</td>
<td>Outcomes</td>
<td>Findings</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Tay-Teo K et al. [64] 2008 Australia AVERT</td>
<td>RCT Single blinded Concealed allocation Assessor blinded</td>
<td>VEM (n=38) Standard care (n=33)</td>
<td>Cost effective analysis of VEM after stroke</td>
<td>VEM was found to be cost effective.</td>
<td></td>
</tr>
<tr>
<td>Oklowski, BF et al. [105] USA 2013</td>
<td>Retrospective analysis</td>
<td>Stroke rehabilitation</td>
<td>Frequency of medical, immobility, and stroke related complications up to 30 months after stroke.</td>
<td>Infections and fall, pressure sores, shoulder pain, and depression were reported.</td>
<td></td>
</tr>
<tr>
<td>Hokstad A et al. [99] 2016 Norway</td>
<td>A prospective Observational multi-centre study</td>
<td>VEM (n=25) It includes positioning, education, functional training and therapeutic exercise.</td>
<td>mRs Barthel Index</td>
<td>Early mobilisation program for individuals with aneurismal subarachnoid hemorrhage (SAH) was safe and feasible</td>
<td></td>
</tr>
</tbody>
</table>
AIM

The aim of the present randomized controlled trial is to explore the possible beneficial effects very early mobilisation (initiated within 2 days of cerebrovascular accident onset) coupled with regular physiotherapy compared with regular physiotherapy alone following acute stroke.

OBJECTIVES

Primary Objectives
(1) To find out the effect of Very Early Mobilisation (VEM) on Prevention of adverse effects following acute stroke.
2) To find out the effect of Very Early Mobilisation (VEM) on Activity of daily living following acute stroke.
3) To find out the effect of Very Early Mobilisation (VEM) on the Level of disability following acute stroke.

Secondary Objectives
(1) To find out the effect of Very Early Mobilisation (VEM) on Quality of Life (OoL) following acute stroke.
(2) To find out the effect of Very Early Mobilisation (VEM) on Depression and anxiety following acute stroke.
HYPOTHESIS

Experimental Hypothesis:

Very early mobilisation (Additionally to the routine care) contrast with routine care only will:

1. Prevent the adverse events suffered by cerebrovascular accident subjects.
2. Improve freedom in functional activities.
3. Reduce the level of disability post cerebrovascular accident.
4. Improve quality of life.
5. Improve the psychological well-being.

Null Hypothesis:

Very early mobilisation (Additionally to the routine care) contrast with routine care only will not:

1. Prevent the adverse events suffered by cerebrovascular accident subjects.
2. Improve freedom in functional activities.
3. Reduce the level of disability post cerebrovascular accident.
4. Improve quality of life.
5. Improve the psychological well-being.