

## Early Mobilisation Following Stroke

Eitan Auriel<sup>1</sup> and Natan M Bornstein<sup>2</sup>

1. Physician; 2. Professor, Stroke Unit, Department of Neurology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Israel

### Abstract

Rehabilitation has been shown to influence brain recovery and to reduce the number of patients who are left handicapped following stroke; however, a question emerges in terms of the optimal time-point to initiate mobilisation. Very early mobilisation involves starting mobilisation including sitting up, getting out of bed, standing and walking, soon after stroke and continuing at frequent intervals. Several studies show evidence that very early rehabilitation has the potential to prevent complications and improve long-term outcomes compared with standard care. This article will discuss the benefits as well as safety concerns of this distinctive type of post-stroke care.

### Keywords

Early mobilisation, rehabilitation, stroke

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**Correspondence:** Natan M Bornstein, Tel Aviv Sourasky Medical Center, Tel Aviv 64239, Israel. E: strokeun@tasmc.health.gov.il

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Stroke is a sudden loss of cerebral blood flow caused either by occlusion (85 % of cases) or rupture of the cerebral artery manifesting with focal neurological deficits.<sup>1</sup> One-third of stroke patients are younger than and two-thirds are older than 65 years of age.<sup>2</sup> Stroke can have both immediate and ongoing physical consequences. Disability and mortality represent the most relevant clinical outcomes. The degree of disability varies from devastating outcome with total dependence on family/carer to minimal and manageable disability.<sup>3</sup> Within 12 months of stroke, one-third of stroke patients will die and another third are left with restriction in performing simple activities of daily living (ADL). Considering the high prevalence of the disease, the burden of post-stroke disability is of primary public health importance, translating to a substantial cost worldwide. In the US in 2008, for example, the direct and indirect costs of stroke are estimated to be more than \$65 billion.<sup>4</sup> Much of this cost probably relates to the physical disability. Any treatment that improves functional outcome can significantly reduce disability and costs, setting regaining of functional independence, defined as improvement in mobility and activities of ADL, as an important goal.<sup>4</sup> The potential for recovery varies substantially across stroke patients. Factors associated with poor functional recovery include stroke severity, age and, to a lesser extent, diabetes.<sup>5</sup>

Today, rehabilitation is recognised as a cornerstone of multidisciplinary stroke care and can reduce the number of patients who are left handicapped. Forty per cent of stroke patients require active rehabilitation services.<sup>3</sup> In recent years, rehabilitation has been shown to influence both brain recovery and reorganisation, especially in relation to motor impairment. Comprehensive rehabilitation programmes appear to improve functional recovery over standard care in terms of speed and extent of recovery.<sup>6</sup> It is noteworthy that neurological recovery is not linear and most of it occurs within the first 3–6 months, although some patients show recovery over prolonged timelines.

Rehabilitation intensity depends on the status of the patient and degree of disability. If the patient is unconscious, rehabilitation is passive to prevent contractions, pressure ulcers and to prevent distress when movement is regained.<sup>3</sup> However, there is still debate regarding the optimal intensity of physical therapy following stroke, with conflicting results across the different studies ranging from no benefit to significant functional improvement.<sup>6</sup> This discrepancy may reflect differences in methodology, patient selection and outcome scales.

### The Rationale Behind Very Early Mobilisation

Very early mobilisation (VEM) is a distinctive characteristic of care that involves starting mobilisation, including sitting up, getting out of bed, standing and walking, early after stroke and continuing at frequent intervals. However, the exact meaning of VEM is not well established and varies between 1 day to 3 months following symptoms onset.<sup>7</sup>

Previous studies have shown that induction of neurotrophic factors is associated with neural repair within the first 2 weeks after stroke and, thus, may modulate greater plasticity that may restore function in the peri-infarct tissue and supplementary motor areas.<sup>8</sup> This experience dependent cortical plasticity has been well documented in normal and injured brains.<sup>7</sup> It may also enable the brain to better respond to rehabilitation, suggesting that efficacy of therapy may vary considerably with the timeline of initiation. The interaction between plasticity and recovery is, however, complicated and individualistic; therefore, it is of importance to apply the appropriate rehabilitation strategy at the appropriate time. Efforts are being made to develop more efficient rehabilitate strategies that utilise current knowledge of cortical plasticity. In addition to enhancing plasticity, VEM may prevent complications with a high risk of causing harm such as deep vein thrombosis, pulmonary embolism, contractures, infections, sores, muscle atrophy and deterioration in cardiorespiratory

function. The complications associated with immobility were shown to be responsible for 51 % of deaths in patients with cerebral infarction.<sup>9</sup> In another analysis of stroke unit systems,<sup>9</sup> stroke unit care appeared to reduce complications of immobility, and infections, in particular. Early mobilisation may also have important psychological effects on a patient's motivation, well-being and quality of life.<sup>6</sup>

## Stroke Unit Care Effectiveness

The concept of comprehensive dedicated stroke units is that stroke patients are accepted acutely, and during admission undergo work-up, secondary prevention and rehabilitation.<sup>10</sup> Organised stroke unit care is provided by experienced multidisciplinary teams that exclusively manage stroke patients in a dedicated ward. It has been recognised over the last few years that patients who are managed in an organised inpatient stroke unit setting are more likely to survive and rapidly regain a greater degree of independence compared with those managed in conventional care settings. Indeed, several trials showed better outcomes for stroke patients treated in stroke units compared with general wards.<sup>11–19</sup> These positive effects can persist for years. In addition, stroke unit care can be given to a broad number of patients, regardless of stroke severity.<sup>20</sup>

A meta-analysis of 31 trials,<sup>21</sup> involving 6,936 participants, compared stroke unit care with an alternative service: more organised care was consistently associated with improved outcomes. Twenty-six trials (5,592 participants) compared stroke unit care with general wards. Stroke unit care showed reductions in the odds of death (odds ratio [OR] 0.86, 95 % confidence interval [CI] 0.76 to 0.98;  $p=0.02$ ), the odds of death or institutionalised care (OR 0.82, 95 % CI 0.73 to 0.92;  $p=0.0006$ ) and death or dependency (OR 0.82, 95 % CI 0.73 to 0.92;  $p=0.001$ ). Another analysis showed that in a population of one million people with 2,400 stroke cases per year, stroke unit care prevents 107 deaths with the number needed to treat of 18 (more than aspirin and thrombolysis therapy combined).<sup>22</sup> However, few factors in the medical, nursing and therapy aspects of care may account for this striking difference and it is not clear how exactly gain is achieved. Indredavik et al. found that the most important factor associated with discharge home is a shorter time to start mobilisation,<sup>12</sup> which outweighs other major factors, such as blood pressure, temperature and glucose levels. In that study, the better outcome in stroke units seems to be due not to more occupational therapy, but to early initiation. In stroke units, all patients were assessed by a physiotherapist within 24 hours and most of them within 8 hours. In the general ward, physiotherapy had to be ordered by a physician, and there was often a delay of 2 to 3 days before the patients received physiotherapy and mobilisation. It should be noted, however, that other confounding factors associated with stroke units reasonably promote better outcomes, such as specially trained staff and integration between nursing and rehabilitation, could not be measured reliably. Other parameters such as the motivation of individual patients and attention paid by the therapist may have confounded results as well.

## Optimal Timing for Initiating Mobilisation

A debate exists as to the optimal exact time to begin mobilisation.<sup>23</sup> In terms of bed rest, in general, following medical conditions it seems that one should not assume any benefit. In 24 trials investigating bed rest following a medical procedure no outcomes improved significantly and eight worsened significantly in some procedures (lumbar puncture, spinal anaesthesia, radiculography and cardiac catheterisation). In 15 trials investigating bed rest as a primary treatment, no outcomes improved significantly and nine worsened significantly for some

conditions (acute low back pain, labour, proteinuric hypertension during pregnancy, myocardial infarction and acute infectious hepatitis).<sup>24</sup>

When looking particularly at stroke patients, several studies have demonstrated efficacy of early rehabilitation. In a cohort study among 20 rehabilitation hospitals and wards (total of 1,716 stroke patients),<sup>25</sup> patients who initiated rehabilitation early (within 7 days after stroke) had better long-term outcomes than those who initiated the rehabilitation after more than 1 month (OR 2.12, 95 % CI 1.35–3.34) or from 15 to 30 days after the symptoms presented (OR 2.11, 95 % CI 1.37–3.26).

Other studies reinforce these findings. In an observational cohort study of 200 consecutive post-stroke rehabilitation patients,<sup>23</sup> fewer days from stroke symptom onset to rehabilitation admission was associated significantly with better functional outcomes and shorter length of stay. In another case-control study<sup>26</sup> among 145 consecutive stroke inpatients the functional outcome, as measured by the Barthel index, and probability of excellent therapeutic response were significantly higher in favour of a shorter interval of rehabilitation from the time of admission (<20 days). A recent study showed, using onsite 3D-kinematic measurements, that the smoothness of paretic upper limb movements improves within the first few weeks following stroke, which also supports the concept of early time window for functional improvement.<sup>27</sup> Early mobilisation was also found to be beneficial in stroke animal models.<sup>28</sup>

As consensus seems to emerge that early implementation of stroke mobilisation is associated with enhanced and faster improvement, VEM is a more complicated, especially concerning safety concerns and therefore poses a challenge. In a pooled analysis of two trials (A Very Early Rehabilitation Trial [AVERT] in Australia and the Very Early Rehabilitation or Intensive Telemetry after Stroke trial [VERITAS] in the UK)<sup>29</sup> patients were between 27 and 97 years old, had first or recurring stroke and were treated within 36 hours after stroke onset. Time-to-first mobilisation from symptom onset was significantly shorter among VEM patients (median 21 hours; interquartile range 15.8–27.8 hours) compared with standard care patients (median 31 hours; interquartile range 23.0–41.2 hours). There were no other significant differences in baseline characteristics between the treatment groups. VEM patients had significantly greater odds of independence at 3 months compared with standard care patients (adjusted OR 3.11, 95 % CI 1.03–9.33). Patients in both trials who underwent VEM also appeared to have a lower rate of complications associated with immobility in the acute stage.

Further results from the phase II AVERT study<sup>30</sup> also endorse the previous findings. This randomised controlled trial included 71 patients with both haemorrhagic and ischaemic strokes admitted within the first 24 hours after symptom presentation. Patients were randomised to VEM while control patients received standard stroke unit care. Both VEM and control groups received standard care from ward therapists and nursing staff in the stroke units. Patients randomised to the VEM group began mobilising as soon as practical after randomisation, with the goal of first mobilisation within 24 hours of symptoms onset. The VEM group also received additional interventions, with the aim of assisting patients to be upright and out of bed at least twice per day. Although having more patients with moderate to severe strokes, the study group returned to walking (50 metres unassisted) significantly faster than controls ( $p=0.032$ ). VEM was also independently associated with good functional outcome in ADL (Barthel Index) at 3 months ( $p=0.008$ ) and in motor function (Rivermead Motor Assessment) at 3 months ( $p=0.050$ ) and 12 months ( $p=0.024$ ).

## Safety Concerns

The AVERT data support the hypothesis that introducing earlier and more frequent mobilisation seems to be safe and feasible. In light of these encouraging results, the question emerges whether, in some circumstances, VEM may be harmful. In the setup of disturbed autoregulation, upright position may decrease perfusion pressure.<sup>7</sup> An upright position may promote ischaemic core extension within the penumbra<sup>31</sup> resulting in worse outcome, especially in patients prone to orthostatic hypotension, similar to patients with neurodegenerative diseases such as Parkinson's disease, peripheral neuropathy and antihypertensive treatments.<sup>7</sup> Small transcranial Doppler (TCD)-based studies<sup>32,33</sup> showed that acute stroke patients may benefit from flat head positioning as it may promote residual flow to the ischaemic, potentially salvageable, tissue at risk, resulting in reduced final infarct volume. Given these concerns, Diserens et al.<sup>7</sup> have developed a partially individualised procedure with precise entry and exit points for early mobilisation according to clinical status. Based on their recommendations, acute stroke patients within the first 24 hours with any degree of stroke (not transient ischaemic attack) should remain at 0°. In this position, mobilisation in bed with the assistance of a nurse and physiotherapist, and if possible by the patients themselves, starts immediately. As this approach does not delay mobilisation, yet maintaining adequate residual flow, we believe it is reasonable as well as feasible.

## Future Prospects

Combination of early mobilisation and pharmacological therapies may have an additive effect in accelerating neural plasticity and brain recovery following stroke. Agents that may promote early mobilisation, for example, may have the potential to enhance recovery. Some of these agents, identified in experimental animal research and are already in clinical use, include levodopa, D-amphetamine, fluoxetine niacin and

inosine.<sup>34</sup> Cerebrolysin is a neurotrophic drug that was found to promote recovery and prevent neuronal damage in ischaemic models.<sup>35</sup> In a recent trial,<sup>36</sup> 119 acute stroke patients were randomised to receive a combined treatment with alteplase plus cerebrolysin or placebo. Although no benefit in the modified Rankin Scale (mRS) for cerebrolysin on day 90 compared with placebo was found in a secondary analysis there were significantly more patients with an improvement of 6 or more points in the National Institutes of Health Stroke Scale (NIHSS, range from 0 to 42) in the treatment group after 2, 5, 10 and 30 days. A similar positive trend towards improvement in the mRS in the cerebrolysin group at early time-points was demonstrated too, in particular at day 5 and 10. This accelerated, even temporary, recovery in the treatment group at early time-points may promote earlier mobilisation, suggesting a potential combined synergistic effect for long-term outcomes, a well-deserved aim to study in future studies. Another potential agent for early improvement is the administration of normobaric oxygen. A pilot study<sup>37</sup> found that high-flow, normobaric oxygen, started within 12 hours of stroke onset, may be associated with a transient improvement in neurological impairment suggesting a window of opportunities for early mobilisation.

## Summary

To date, some evidence indicates that providing earlier and more intensive mobilisation after stroke can maximise gain from therapy, accelerate recovery and improve functional outcomes. Stroke patients undergoing VEM were shown to perform better compared with their standard care counterparts, thereby having improved quality of life. We also believe that VEM is one of the main factors in contributing to the reported better functional outcomes in patients admitted to a dedicated stroke units. Although some concerns exist when initiating mobilisation within the first 24 hours, careful and tailor-made approach based on a patient's disability and neurological status may overcome them. ■

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