

# Very Early Mobilization of Individuals with Acute Stroke after Receiving Thrombolytic Therapy

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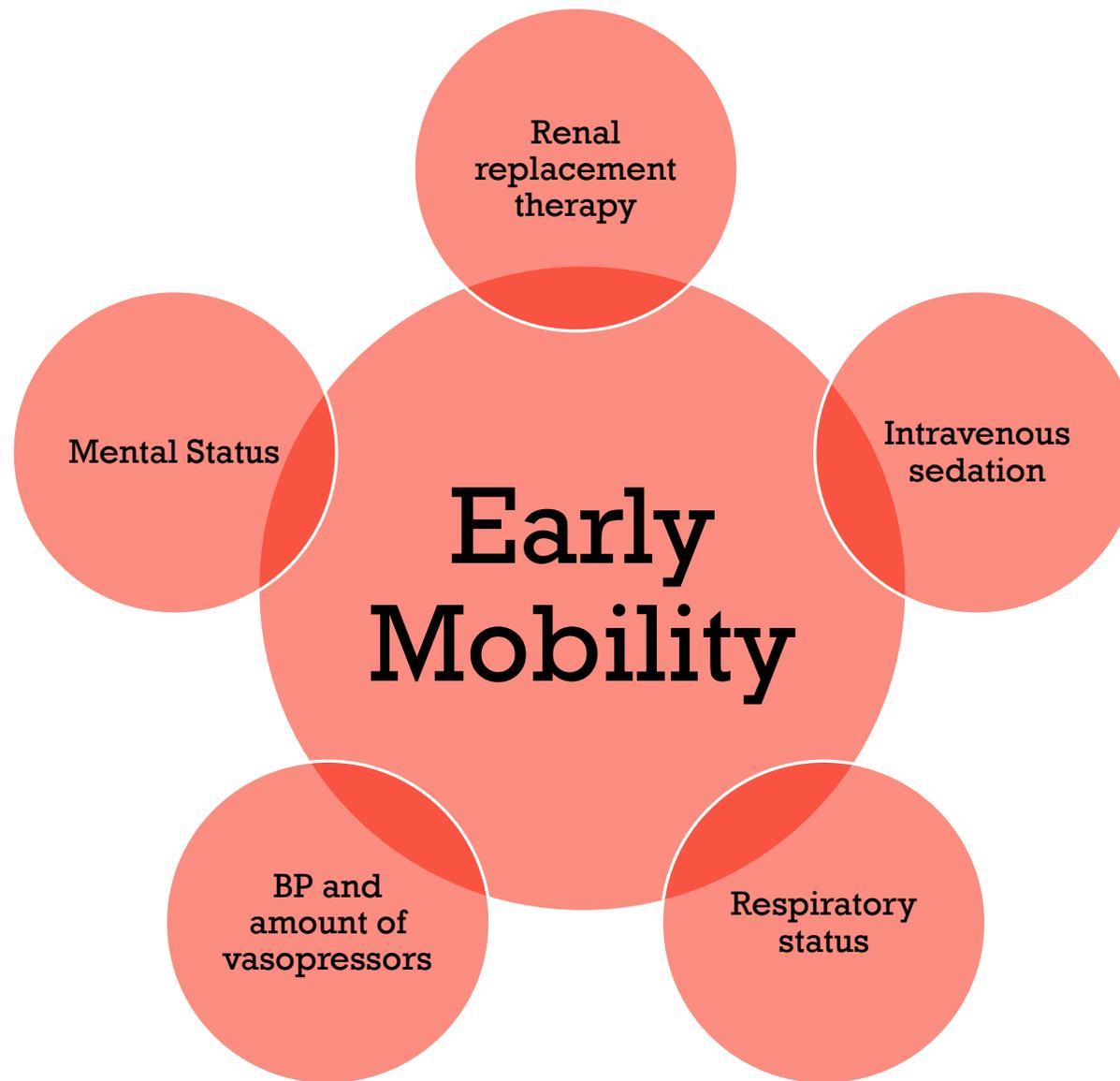
# Disclosures

- I have no financial interests or relationships to disclose.

# Objectives

By the end of the presentation the audience will be able to:

1. Differentiate between very early mobility and early mobility
2. Discuss literature regarding very early mobility after the use of thrombolytic therapy
3. Verbalize guidelines for very early mobility after the use of thrombolytic therapy
4. Describe patient interventions and modifications used to increased independence of the post-acute stroke patient as it relates to mobility, ADLs, and communication.



Linke, C. et al. (2020). Early mobilization in the ICU: A collaborative, integrated approach. *Critical Care Explorations*, 2(4). doi:10.1097/CCE. 0000000000000090.

Lipshutz, A., & Groper, M. (2013). Acquired neuromuscular weakness and early mobilization in the intensive care unit. *Anesthesiology*, 1(118), 202-215.

Naito, Y, Kamiya, M., Morishima, N., & Ishikawa, T. (2020). Association between out-of-bed mobilization and complications in acute phase of severe stroke: A retrospective observation study. *Journal of Stroke and Cerebrovascular Diseases*, 29(10), 1-4. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105112>.



Why very early  
mobility/early  
mobility?

- Physiological consequences of immobility
- Survival rate of critical illness is increasing

Linke, C. et al. (2020). Early mobilization in the ICU: A collaborative, integrated approach. *Critical Care Explorations*, 2(4). doi:10.1097/CCE.000000000000090.

Lipshutz, A., & Groper, M. (2013). Acquired neuromuscular weakness and early mobilization in the intensive care unit. *Anesthesiology*, 1(118), 202-215.

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# Early Mobility and Patients Receiving Thrombolytic Therapy after Acute Ischemic Stroke

1994 Early mobilization adopted for care of patients with stroke

2004 First RCT for individuals with stroke receiving early mobility

2024 Varying guidelines regarding timeline of early mobility/dose of mobility after receiving thrombolytic therapy

Arnold, S., et al. (2015). Very early mobilization in stroke patients treated with with intravenous recombinant tissue plasminogen activator. *Journal of Stroke and Cerebrovascular Diseases*, 6(24), 1168-1173. <http://dx.doi.org/10.1016/j.strokecerebrovasdis.2015.01.007>.

Bernhardt, J., et al. (2015). Efficacy and safety of very early mobilization with 24 h of stroke onset (AVERT): A randomized controlled trial. *Lancet*, 386, 46-55. [http://dx.doi.org/10.1016/S0140-6736\(15\)60690-0](http://dx.doi.org/10.1016/S0140-6736(15)60690-0).

Olkowski, B. & Shah, S. (2017). Early mobilization in the neuro-ICU: How far can we go? *Neurocrit care*, 27, 141-150. doi: 10.1007/s112028-016-0338-7.

# What's stopping us?

- Concerns of intracranial or systemic bleeding
- Adverse outcomes
- Reduction of cerebral blood flow
- Team Readiness
- Research

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Olkowski, B. & Shah, S. (2017). Early mobilization in the neuro-ICU: How far can we go? *Neurocrit care*, 27, 141-150. doi: 10.1007/sl12028-016-0338-7.

Silver, B. et al. (2020) 12 versus 24 hour bed rest after acute ischemic stroke thrombolysis. *Journal of Neurological Science.*, 409. doi:10.1016/j.jns.209.116618.

# The Research: A Very Early Rehabilitation Trial (AVERT)

- **Objectives:**

1. Does VEM reduce death and disability at 3 months post stroke?
2. Does VEM reduce the number and severity of complications at 3 months post stroke?
3. Does VEM improve quality of life at 12 months post stroke?
4. Is VEM cost-effective?

- **Setting:** 56 hospitals in 5 countries

- **Participants:** Acute stroke admitted within 24 hours onset of symptoms (MD took special consideration when enrolling tPA pt to investigation)

- **Sample Size:** 2104 patients recruited from July 2006 through October 2014

- **Intervention:** RCT, VEM was delivered in 3 out of bed session per day versus the usual care group

# The Research: A Very Early Rehabilitation Trial (AVERT)

## Phase I

- Observational study
- Demonstrated most individuals with stroke were inactive most of the time
- Varied opinions of health care professionals regarding VEM

## Phase II

- **Hypothesis:** VEM will be safe and feasible.
- **Conclusion:** Safe and feasible indicating signals for improvement with recovery and likeliness of cost effectiveness

# The Research: A Very Early Rehabilitation Trial (AVERT)

- **Phase III**
  - **Hypothesis:** VEM would improve functional outcome at 3 months, reduce immobility-related complications, accelerate walking recovery, improve quality of life at 12 months and be cost effective
  - **Participants:** 2104 with 24% receiving tPA
  - **Method:** Vitals assessed at each stage of movement (head of bed greater than 70 degrees, sit edge of bed, sitting for 5 minutes, transfer to chair)
  - **Treatment Compliance:** VEM mobilized at a median of 18.5 hours UC at 23.5 hours
  - **Discussion:** VEM reduced favorable outcome at 3 months, safety concerns for elderly patients and patients with hemorrhagic stroke
  - **Conclusion:** No difference in complications between VEM group and UC group, mobility at early phase of recovery may influence long-term outcomes, more practice may not always be better, frequency may be more important than other aspects of treatment

# Research on Early Mobility of Patients who Received Thrombolytics

- **Fatal and Nonfatal Events Within 14 Days after Early, Intensive Mobilization Poststroke**
  - **Objective:** Tertiary analysis from AVERT examined fatal and nonfatal serious adverse events at 14 days.
  - **Method:** Review of the AVERT trial. The primary early safety outcome was fatal serious adverse events at 14 days. The secondary outcomes were nonfatal serious adverse events classified as neurological, immobility-related and other.
  - **Results:** By 14 days, 48 had died in the VEM, 32 in the UC group. Stroke progression more common in VEM. Higher odds of death and intracerebral hemorrhage in 80+ group. No difference in nonfatal SAE's found.
  - **Conclusion:** Stroke progression more common in VEM.

# Research on Early Mobility of Patients who Received Thrombolytics

- **A phase III, multi-arm multi-stage covariate-adjusted response-adaptive randomized trial to determine optimal early mobility training after stroke (AVERT DOSE)**
  - **Objective:** Define early mobility intervention for people with mild to moderate stroke
  - **Method:** 3 dose intervention groups with one reference group, randomize, treatment provided for 14 days or until discharge
  - **Participants:** acute ischemic stroke, may have received thrombolytics, NIHSS <17
  - **Intervention:** 10-40 minutes of task training/day spread over 1-4 sessions

- Bernhardt, J. Et al., (2023). A phase III, multi-arm multi-stage covariate-adjusted response-adaptive randomize trial to determine optimal early mobility training after stroke (AVERT DOSE). *International Journal of Stroke*, 18(6), 745-750.

# Research on Early Mobility of Patients who Received Thrombolytics

- **Enhancing Patient Outcomes After Stroke: Acute Care and Beyond**
  - Presentation provided by Physical Therapists at JFK Medical Center in 2017
    - Report
      - **Participants:** over 20 cases of patients who received tPA mobilized under 12 hours
      - No adverse events reports

Lieberman, A. & Dubuisson, G. (2017). Enhancing patient outcomes after stroke: Acute care and beyond. Combined Sections Meeting, San Antonio, TX. JFK Medical Center, Johnson Rehabilitation Institute, Edison NJ.

# Research on Early Mobility of Patients who Received Thrombolytics

- **Abstract NS6:** Early Mobility Initiated at 12 Hours Post Thrombolytic Therapy for Stroke Increases Likelihood for Discharge to Home
  - **Purpose:** To assess patient safety and discharge outcomes of initiating early mobility after 12 hours of receiving tPA for stroke at primary stroke center.
  - **Methods:** Early Mobility Protocol was implemented within 24 hours of receiving tPA. 44 patients received tPA.
  - **Discussion:** Among the early mobility group there were no falls or adverse physiological events. Patients in early mobility were more likely to discharge home. No significant difference in length of stay.
  - **Conclusion:** Providing early mobility to patients post thrombolytic therapy between 12-24 hours does not cause an increase in adverse physiological events. It has a positive impact on patient discharges to home.

Gwilliam, J. & McNicholas, M. (2020). Abstract NS6: Early mobility initiated at 12 hours post thrombolytic therapy for stroke increases likelihood for discharge to home. *Stroke*, 51. [https://doi.org/10.1161/str.51.suppl\\_NS6](https://doi.org/10.1161/str.51.suppl_NS6).

# Research on Early Mobility of Patients who Received Thrombolytics

- **Efficacy and safety of very early mobilization after thrombolysis in acute ischemic stroke: A randomized clinical trial**
  - **Objective:** To assess efficacy and safety of VEM after receiving thrombolytics
  - **Methods:** Prospective randomized trial with participants receiving thrombolytic after mild to moderate stroke. Reassessed at discharge or 7 days and 90 days
    - **Intervention:** VEM (51 participants) received 2, 15-minute therapy sessions within 12 hours of thrombolytic and the UCG (53 participants) mobilizing post 24 hours
  - **Conclusion:** No significant difference between length of stay and complications, no evidence of benefits compared to UCG

# Research on Early Mobility of Patients who Received Thrombolytics

- **12 Versus 24 Hour Bed Rest after Acute Ischemic Stroke Thrombolysis**
  - **Objective:** To compare outcomes of patients who received 12 hours of bedrest versus patients who received 24 hours of bedrest following acute ischemic stroke after receiving thrombolysis.
  - **Methods:** Retrospective investigation of patients who received thrombolysis after stroke 12 and 24 hours. NIHSS collected at 8 hours, 24 hours and discharge, adverse outcomes and discharge disposition.
  - **Results:** 203 patients in the 24-hour group and 189 in the 12-hour group. No significant difference in discharge disposition between the 2 groups. The 12-hour group showed lower NIHSS at discharge, decreased rate of pneumonia and lower lengths of stay. (Of note: the 12-hour group mean time to begin therapy was 38 hours with 25% of the patients initiating therapy less than 24 hours.)
  - **Limitations:** Dose of therapy, 3-month follow-up, groups from different time periods, no random assignment and definition of discharge outcome not clearly defined

# Understanding the Research

- Most trials suggest feasibility with mobilization 12 hours after receiving thrombolytics with no increase in adverse reactions for those with mild to moderate stroke
- Varying information exists regarding the benefits of very early mobility
- The largest known RCT AVERT reports frequency of mobilization over duration and doses are being investigated

Arnold, S., et al. (2015). Very early mobilization in stroke patients treated with intravenous recombinant tissue plasminogen activator. *Journal of Stroke and Cerebrovascular Diseases*, 6(24), 1168-1173. <http://dx.doi.org/10.1016/j.strokecerebrovasdis.2015.01.007>.

Bernhardt, J., Borschmann, K., Collier, J., Thrift, A., Langhorn, P., Middleton, S., et al. (2021). Fatal and nonfatal events within 14 days after early, intensive mobilization poststroke. *American Academy of Neurology*, 96, e1156-e1166. <https://doi.org/10.1212/WNL.00000000000011106>.

Gwilliam, J. & McNicholas, M. (2020). Abstract NS6: Early mobility initiated at 12 hours post thrombolytic therapy for stroke increases likelihood for discharge to home. *Stroke*, 51. [https://doi.org/10.1161/str.51.suppl\\_NS6](https://doi.org/10.1161/str.51.suppl_NS6).

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Muhl, L., et al. (2014). Mobilization after thrombolysis (rtPA) within 24 hours of acute stroke: What factors influence inclusion of patient in A Very Early Rehabilitation Trial (AVERT). *BMC Neurology*, 14(163). doi:10.1186/s12883-014-0163-6.

Olkowski, B. & Shah, S. (2017). Early mobilization in the neuro-ICU: How far can we go? *Neurocrit care*, 27, 141-150. doi: 10.1007/s112028-016-0338-7.

# Next Steps

Very early mobility may be safe and feasible

Mobility should be progressive and closely monitored

Duration of task specific training and mobility should be low with a higher frequency

MD should guide who is able to be mobilized after receiving thrombolytics

More research

Arnold, S., et al. (2015). Very early mobilization in stroke patients treated with intravenous recombinant tissue plasminogen activator. *Journal of Stroke and Cerebrovascular Diseases*, 6(24), 1168-1173. <http://dx.doi.org/10.1016/j.strokecerebrovasdis.2015.01.007>.

Bernhardt, J., Borschmann, K., Collier, J., Thrift, A., Langhorn, P., Middleton, S., et al. (2021). Fatal and nonfatal events within 14 days after early, intensive mobilization poststroke. *American Academy of Neurology*, 96, e1156-e1166. <https://doi.org/10.1212/WNL.00000000000011106>.

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# Potential Inclusion Criteria for Very Early Mobility

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**Systolic blood pressure (SBP) 110-220**

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**Oxygen saturation of greater or equal to 92%**

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**Resting heart rate of 40-110 beat per minutes (b.p.m.)**

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**Temperature 101.3 degrees F. or less**

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**At a minimum, patient must at least react to verbal commands**

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Langhorn, P., Wu, O., Rodgers, H., Ashburn, A., & Bernhardt, J. (2017). A very early rehabilitation trial after stroke (AVERT): A phase III, multicenter, randomized controlled trial. *Health Technology Assessment, 21*(54), 1-119. doi:10.3310/hta21540.

## Stages of Very Early Mobility

- **Monitor Vitals**
- **Raise bed to 70 degrees hip flexion, monitor vitals**
- **Sit edge of bed, monitor vitals**
- **Sit for 5 minutes, monitor vitals**
- **Transfer to chair/functional activity, monitor vitals**

## Return patient to bed if . . .

- **Clinical judgement suggests patient is not tolerating**
- **SBP is outside the order set by MD**
- **SBP decreased by 30**
- **HR greater than 120**
- **O2 sat less than 90**

Langhorn, P., Wu, O., Rodgers, H., Ashburn, A., & Bernhardt, J. (2017). A very early rehabilitation trial after stroke (AVERT): A phase III, multicenter, randomized controlled trial. *Health Technology Assessment, 21*(54), 1-119. doi:10.3310/hta21540.

## Dose of Activity

### ■ **Potential Doses Based on Research Methods**

- Estimated amount of actual movement/activity 15 minutes
- 15 minutes of activity provided twice a day
- 10-40 minutes of training spread over 1-4 sessions

### ■ **Research is Ongoing**

Bernhardt, J. Et al., (2023). A phase III, multi-arm multi-stage covariate-adjusted response-adaptive randomize trial to determine optimal early mobility training after stroke (AVERT DOSE). *International Journal of Stroke*, 18(6), 745-750.

Motta Anjos, J. et al. (2023). Efficacy and safety of very early mobilization after thrombolysis in acute ischemic stroke: A randomized control trial. *Journal of Neurology*, 270, 843-850. <https://doi.org/10.1007/s00415-022-11411-5>

Silver, B., et al. (2020) 12 versus 24 hour bed rest after acute ischemic stroke thrombolysis. *Journal of Neurological Science*, 409. doi:10.1016/j.jns.2019.116618.

## Conclusion

- **Very early mobility for patients receiving thrombolytics is possible under the direction of an MD. Frequency may be more beneficial than duration in the early stages of stroke recovery.**



Questions

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