BRAIN INJURY and MOBILISATION

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Cliniques universitaires
SAINT-LUC
UCL BRUXELLES

INTRODUCTION

NEURO-ICU

- Stroke / S.A.H. / T.B.I.

EARLY MOB

- Muscle wasting and disuse-related neural adaptations will create a significant problem when rehabilitation is eventually started at a later stage.
- Patients can be kept active without necessarily taking them out of bed
- Early activity makes use of a limited time window of heightened plasticity

- Early activity increases brain injury

EARLY MOBILIZATION and STROKE

- Initially reported during a Swedish consensus conference on stroke care in the mid 80's
- Early 90's: Indredavik : Marked reduction in mortality when stroke patients are treated in « Stroke Units » where EM is part of the protocol of care.

Indredavik et al. Stroke.1991; 22(8):1026-31

- Appear in national Stroke Guidelines in 1994
- 1st RCT in 2004 : AVERT II: safety and feasability – 71 patients

EARLY MOBILIZATION and STROKE

PRO:

- *Reducing Complications*

  Prevent and reduce immobility-related complications:

  DVT, infections, falls, …

  Prevent and reduce stroke-related inactivity changes:

  Loss of CV fitness, muscle atrophy, …
- *Promoting Brain recovery*

  Enhanced plasticity period after stroke

CON:

- Early upright activity might inhibit reperfusion of salvageable penumbral tissue ???
- Effect of mobilisation on blood pressure !!!

Very early versus delayed mobilisation after stroke (Review)

THE COCHRANE COLLABORATION®

3 Eligible RCT:

- **VERITAS study** – Scotland – ongoing
- **AVERT II study** – Australia – Safety and feasability study in 71 patients
- **AVERT III study** – Australia – ongoing

Bernhardt J et al. Cochrane Syst Rev Database.2009; CD006187

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Authors' conclusions

We found insufficient evidence to support or refute the efficacy of routine very early mobilisation after stroke, compared with conventional care. More research is required to determine the benefits and harms of very early mobilisation after stroke.

Bernhardt J et al. Cochrane Syst Rev Database.2009; CD006187

Bernhardt et al 2008[3] (AVERT)	71	• Recruited within 24 h of stroke, goal to start mobilization within 24 h of stroke • Emphasis on patient being upright and out of bed (sitting or standing) • At least twice a day for first 14 days or until discharge	Intervention (n=38): Median=18.1, IQR=12.8–21.5 Control (n=33): Median=30.8, IQR=23.0–39.9	Complications/safety Deaths: intervention=8/38, SC=3/33, absolute risk difference=12%, ns. Serious adverse events†: intervention =15, control=14, ns. Nonserious adverse events: intervention =61, control=76, *P*=0.04 Falls: intervention=27, SC=28, ns. Functional outcome mRS 0–2: intervention=39.5%, control =30.3%, adjusted‡ OR=4.10, *P*=0.05
Langhorne et al 2010[8] (VERITAS)	32	• Recruited within 24 h of admission, with goal to start mobilization within 24 h of stroke • Goal for patient to be sitting, standing or walking (adjusted to patient needs) • Continued at least four times a day, during the inpatient stay, or for one week after recruitment	Intervention (n=16): Mean=27.3 Range=26–29 Control (n=16): Mean=32.0 Range=22.5–47.3	Complications/safety Deaths: EM=0%, control=6% Complications§: EM=8, control=17 Complications (days 5–90): EM=8, control=8 Complications of immobility (days 0–5): intervention=0, control=3 Functional outcome mRS 0–2: intervention=75%, control =44%, adjusted‖ OR=2.3, (*P*=0.44)
Diserens et al 2011[10] (Lausanne trial)	50 (42 included in analysis)	• Recruited within 12 h of admission, with protocol started 24 h after stroke • Patient's head of the bed kept at 0° for first 24 h poststroke, followed by 45° for 24 h, then 90° for 4 h • At 52 h poststroke, patients were moved out of the bed to either sitting or standing	Intervention (n=25): Not reported Control (n=17): Not reported	Complications/safety Deaths: intervention=0%, control=6% Severe complications including death¶ (during hospitalization): intervention=8%, control=47% Minor complications (during hospitalization): intervention=20%, control=0%, ns. Functional outcome mRS 0–2: intervention=40%, control=30%, ns.
Sundseth et al 2012[9] (AKEMIS)	65 (56 included in analysis)	• Recruited if admitted to hospital within 24 h of stroke, with mobilization out of bed within 24 h of admission • No predefined mobilization protocol. Mobilization, defined as any out of bed activity, followed the stroke unit's standard routine for mobilization, adjusted to patients' needs • Mobilization occurred several times per day	Intervention (n=27): Median=13.1 IQR=8.5–25.6 Control (n=29): Median=33.3 IQR=26.0–39.0	Complications/safety Deaths: intervention=7/27, control =2/29, adjusted# OR=5.26, ns. Patients who experienced ≥1 complication: intervention=67%, control=66%, ns. Functional outcome mRS 0–2: intervention=40%. control=60.7%, adjusted** OR=2.7, ns.

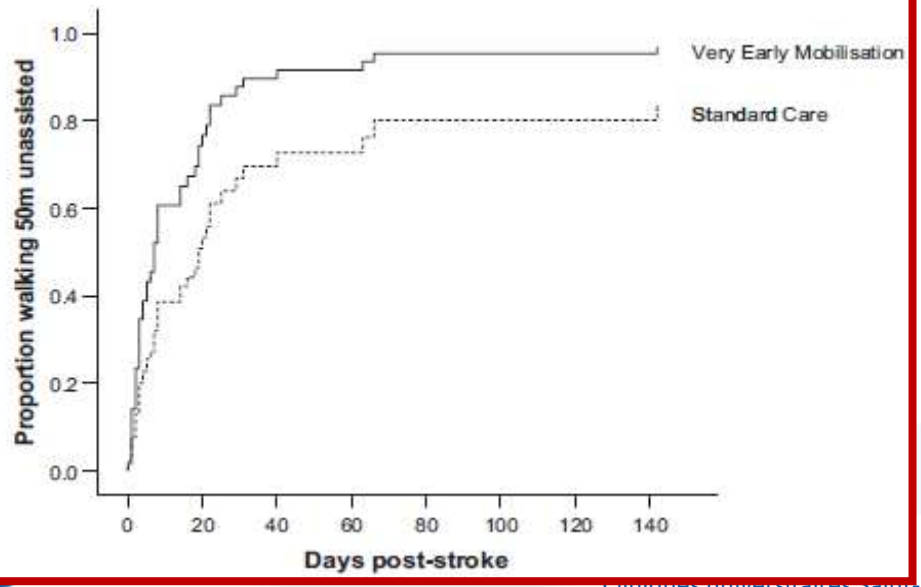
Bernhardt J et al. Stroke.2015; 46:1141-6.

Very Early Mobilization After Stroke Fast-Tracks Return to Walking

Further Results From the Phase II AVERT Randomized Controlled Trial

Table 2. Cox Regression for No. of Days to Walking 50 m Unassisted (N=71)

	Hazard Ratio	Lower CI	Upper CI	*P*
VEM	0.523	0.289	0.945	0.032
Age	0.967	0.944	0.990	0.005
Sex	0.679	0.374	1.233	0.204
NIHSS	0.864	0.815	0.916	<0.001
Premorbid mRS	0.867	0.645	1.165	0.344
Diabetes	2.147	1.020	4.520	0.044



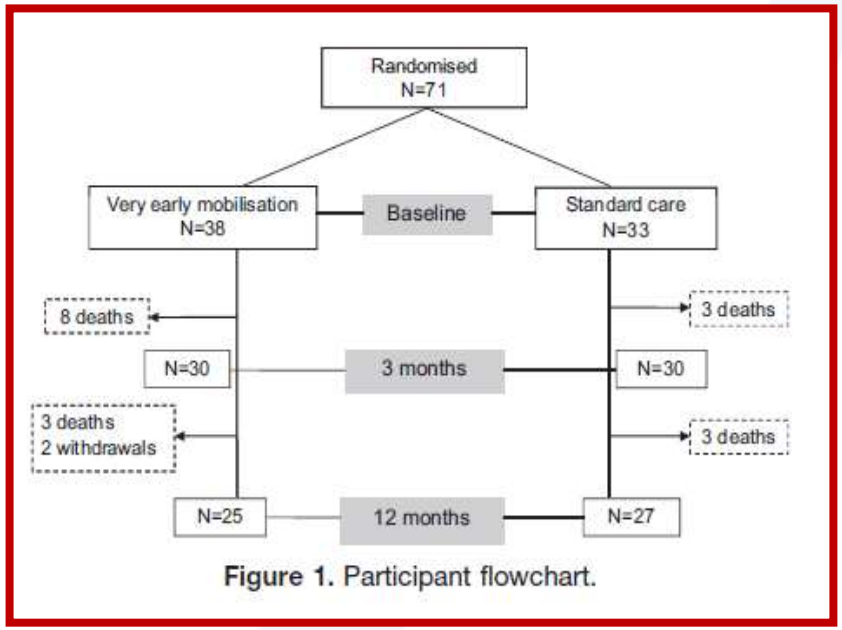


Figure 1. Participant flowchart.

Cumming TB et al. Stroke.2011; 42:153-8

Physical Activity Early after Stroke and Its Association to Functional Outcome 3 Months Later

		Time to first mobilization
	n	Mean (SD), h
All patients	106	30.0 (34.1)
Mild stroke (NIHSS score < 8)	63	21.3 (20.9)
Moderate stroke (NIHSS score 8-16)	27	30.1 (36.9)
Severe stroke (NIHSS score > 16)	16	64.3 (49.8)

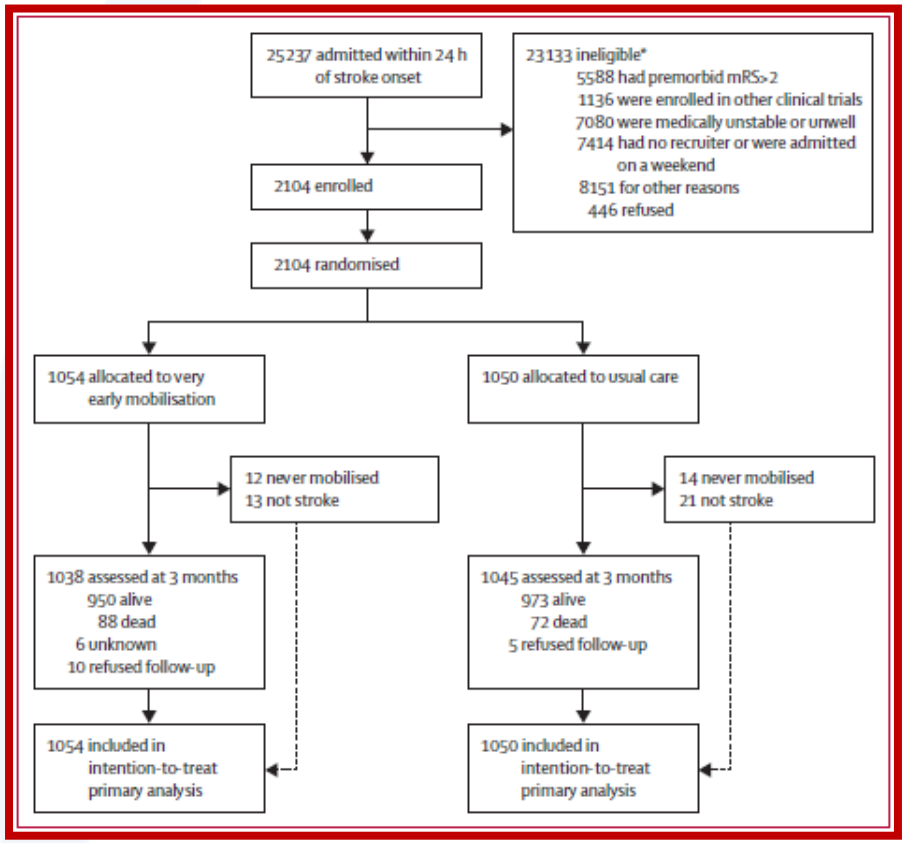
Table 4. *The partial proportional OR for poor outcome on mRS at 3 months follow-up*

	Simple multivariable model*			Complex multivariable model†		
Independent variables	OR	95% CI	*P* value	OR	95% CI	*P* value
Time in bed (%)	1.01‡	.98-1.05	.415	1.04	1.02-1.07	.001
Time in higher motor activities (%)	.96‡	.92-1.01	.100	.97‡	.93-1.02	.283
Time to first mobilization (h)	1.00	.99-1.02	.405	.99	.98-1.01	.397

Askim T et al. J Stroke Cerebrovasc Dis.2014; 23(5):e305-e312

Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial

The AVERT Trial Collaboration group*



- Parallel-group, single blind, RCT
- 56 Acute Stroke Unit - 5 countries
- Ischaemic or Haemorrhagic stroke

Usual Stroke Unit Care or
Usual care + very early mobilisation

- Outcome at 3 months
- Modified Rankin Scale (0 – 2)
- ITT

Lancet.2015; 386:46-55

Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial

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	Very early mobilisation (n=1054)	Usual care (n=1050)	p value
Time to first mobilisation (h)	18·5 (12·8–22·3; n=1042*)	22·4 (16·5–29·3; n=1036*)	<0·0001
Frequency per person†	6·5 (4·0–9·5)	3 (2·0–4·5)	<0·0001
Daily amount per person (min)‡	31 (16·5–50·5)	10 (0–18)	<0·0001
Total amount per person (min)§	201·5 (108–340)	70 (32–130)	<0·0001

	Very early mobilisation (n=1038*)	Usual care (n=1045*)	Adjusted analysis		Unadjusted analysis	
			OR, generalised OR, or HR† (95% CI)	p value	OR generalised OR, or HR† (95% CI)	p value
Primary						
Favourable outcome‡	480 (46%)	525 (50%)	0·73 (0·59–0·90)	0·004	0·85 (0·72–1·0)	0·068
Secondary						
mRS category	..	..	0·94 (0·85–1·03)	0·193	0·94 (0·85–1·03)	0·202
0	90 (9%)	96 (9%)	..	..	..	..
1	200 (19%)	204 (19%)	..	..	..	..
2	190 (18%)	225 (22%)	..	..	..	..
3	238 (23%)	218 (21%)	..	..	..	..
4	140 (14%)	127 (12%)	..	..	..	..
5	92 (9%)	103 (10%)	..	..	..	..
6	88 (8%)	72 (7%)	..	..	..	..
Walking 50 m unassisted§	6 (5–7; n=1051)	7 (6–8; n=1049)	1·04 (0·94–1·15)	0·459	1·05 (0·95–1·16)	0·331

46-55

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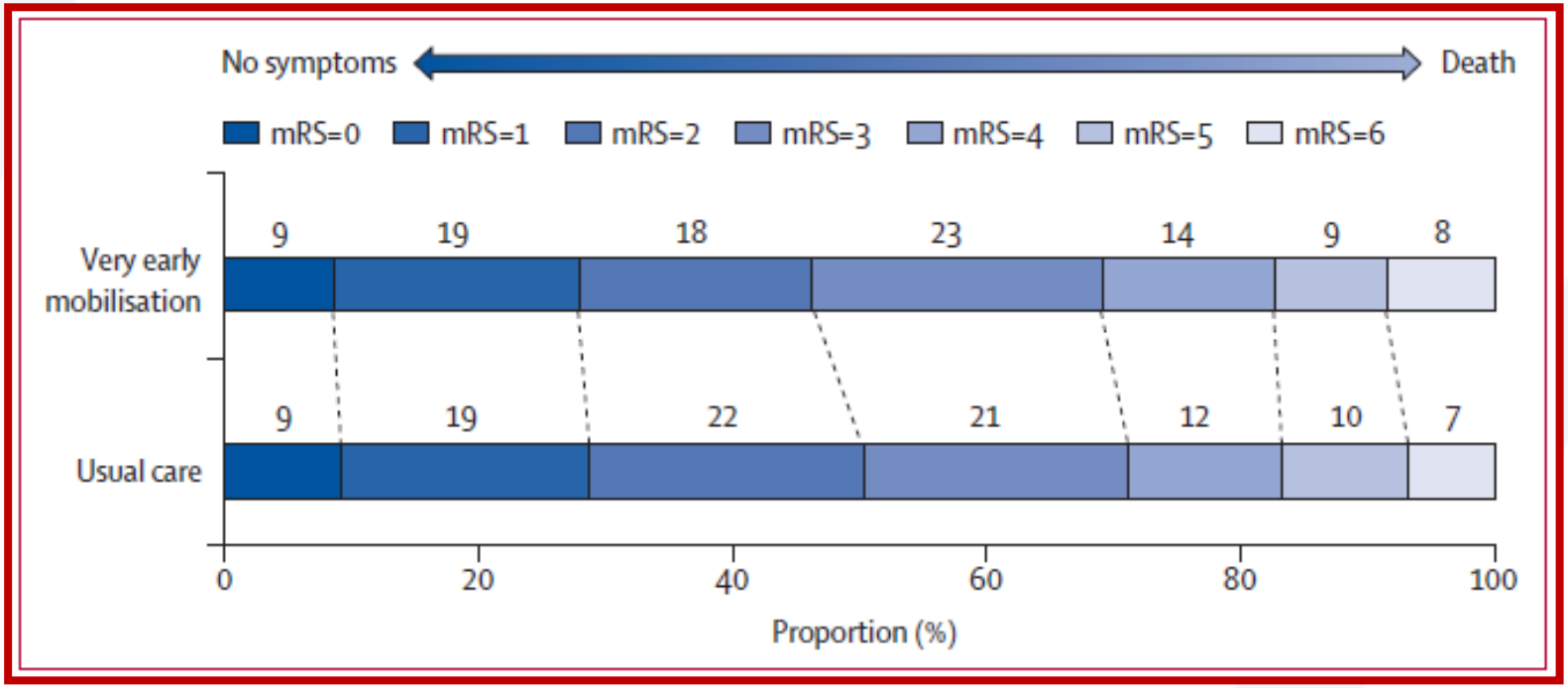


+ Time to walking unassisted: similar
  Mortality: similar
  Non-fatal SAE and Immobility related AE: similar

Lancet.2015; 386:46-55

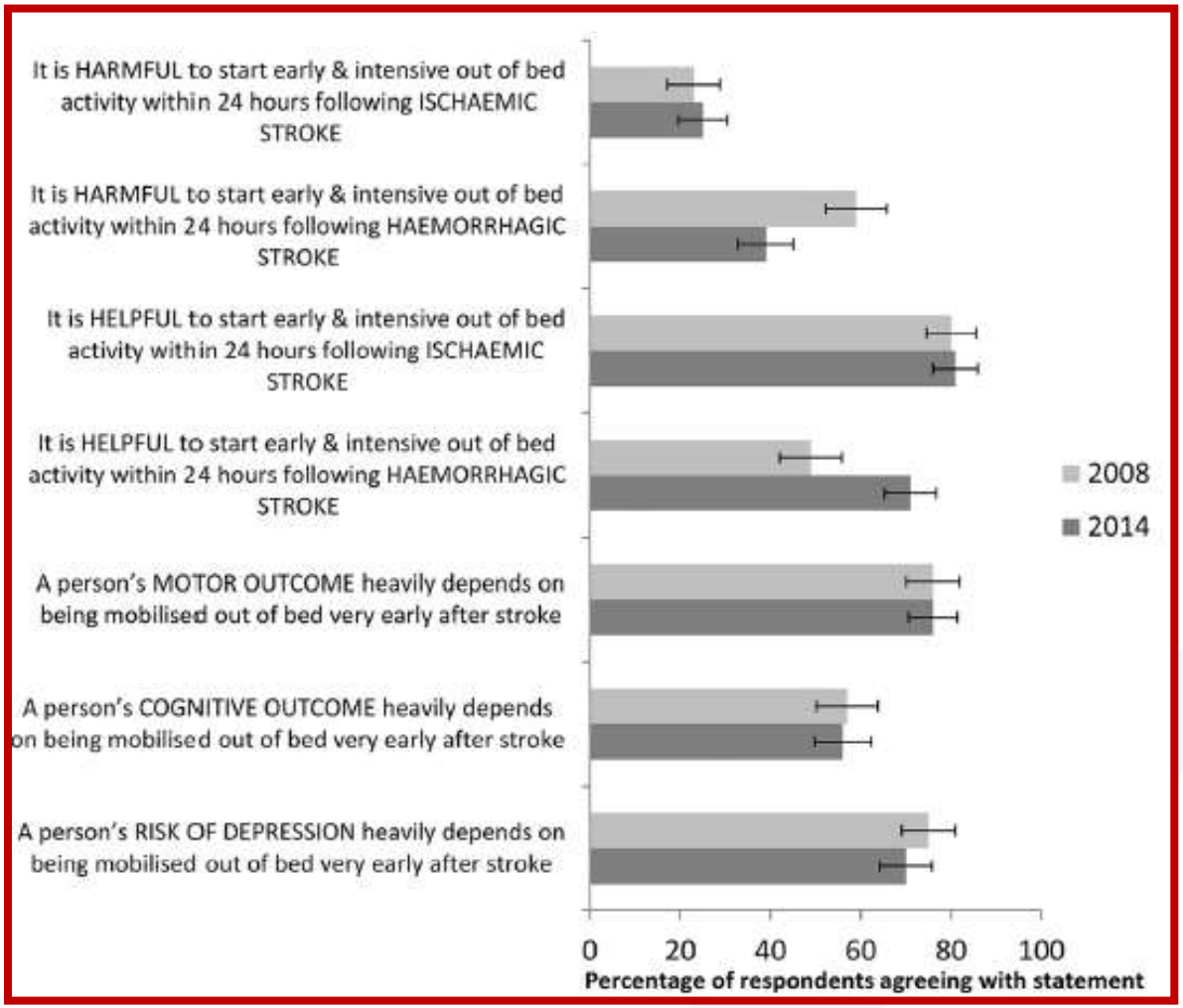
Critique of A Very Early Rehabilitation Trial (AVERT)

- m Rankin Scale (≤ 2 or > 2):
  Rather broad assessment of stroke outcome
- Other outcome scale ? Extended Barthel Index ?
- Time difference to first mobilization between groups: 4 hours !!!
- 92% of patients (and 59% in the late group) were treated within 24 hours

Luft AR et al. Stroke.2016;47:291-2.

- 8 years
- 7% of patients in the usual care group were still in bed at H48

Early Mobilization after Stroke: Changes in Clinical Opinion Despite an Unchanging Evidence Base



Lynch EA et al. J Stroke Cerebrovasc Dis.2017; 26(1): 1-6

Very Early Mobilization in Stroke Patients Treated with Intravenous Recombinant Tissue Plasminogen Activator

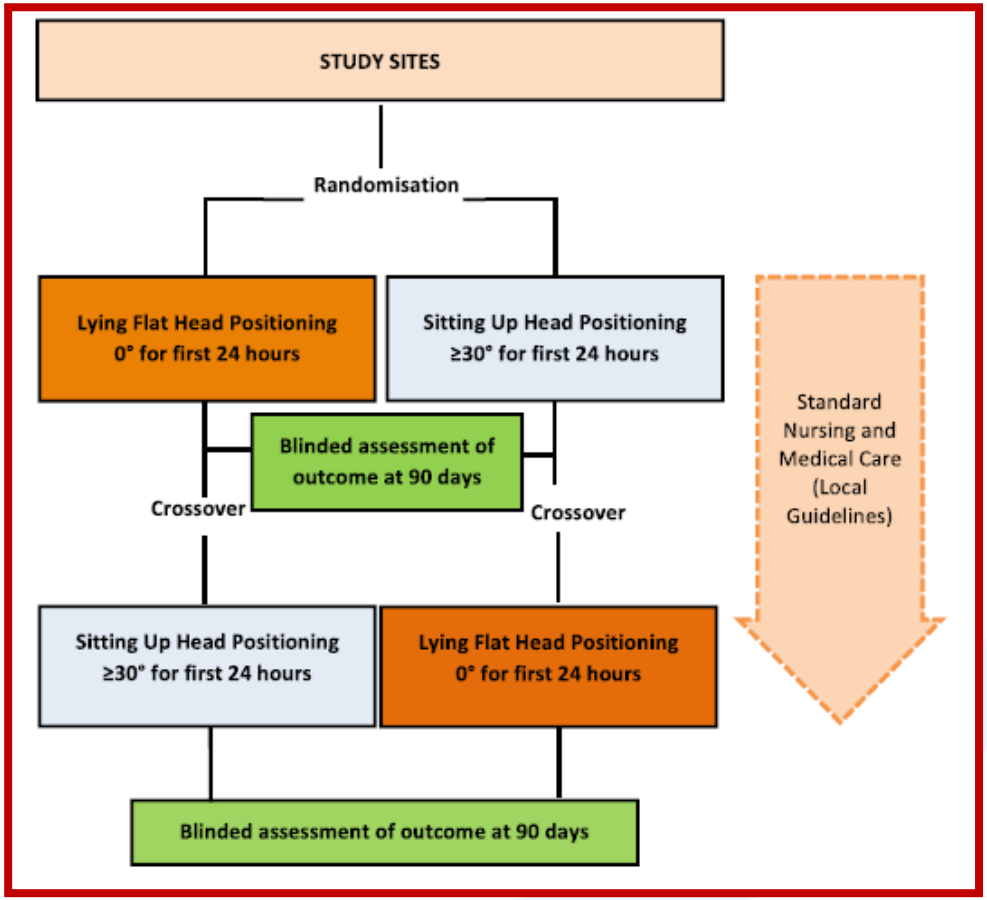
Variables	Summary (n = 18)
Patient characteristics	
Age (y)	69 (35-89)
Gender (male)	12 (66.7)
Race (white)	18 (100.0)
NIHSS score	
Minor stroke (NIHSS <7)	7 (38.9)
Moderate stroke (NIHSS 7-15)	6 (33.3)
Moderate/severe stroke (NIHSS >15)	5 (27.8)

Adverse response	Number (%) of patients (n = 18)	95% CI
Any adverse response (including orthostasis)	5 (27.8)	9.7-53.5
Any adverse response (excluding orthostasis)	3 (16.7)	3.6-41.4
Individual adverse responses		
Orthostasis*	3 (16.7)	3.6-41.4
DBP >105	1 (5.6)	.1-27.3
Dizziness	1 (5.6)	.1-27.3
Heart rate >100	0 (.0)	.0-18.5
Neurologic signs†	1 (5.6)	.1-27.3
Active bleeding	0 (.0)	.0-18.5
Pallor	0 (.0)	.0-18.5
Diaphoresis	0 (.0)	.0-18.5
Intense anxiety	0 (.0)	.0-18.5
Pain	0 (.0)	.0-18.5
Syncope	0 (.0)	.0-18.5

of neurologic deficits. *Conclusions:* Very early mobilization within 24 hours of ischemic stroke for patients who receive IV rtPA appears to be relatively safe and feasible in most patients. Patients who are mobilized within 24 hours of IV rtPA require detailed neurologic and vital sign monitoring. **Key Words:** Early

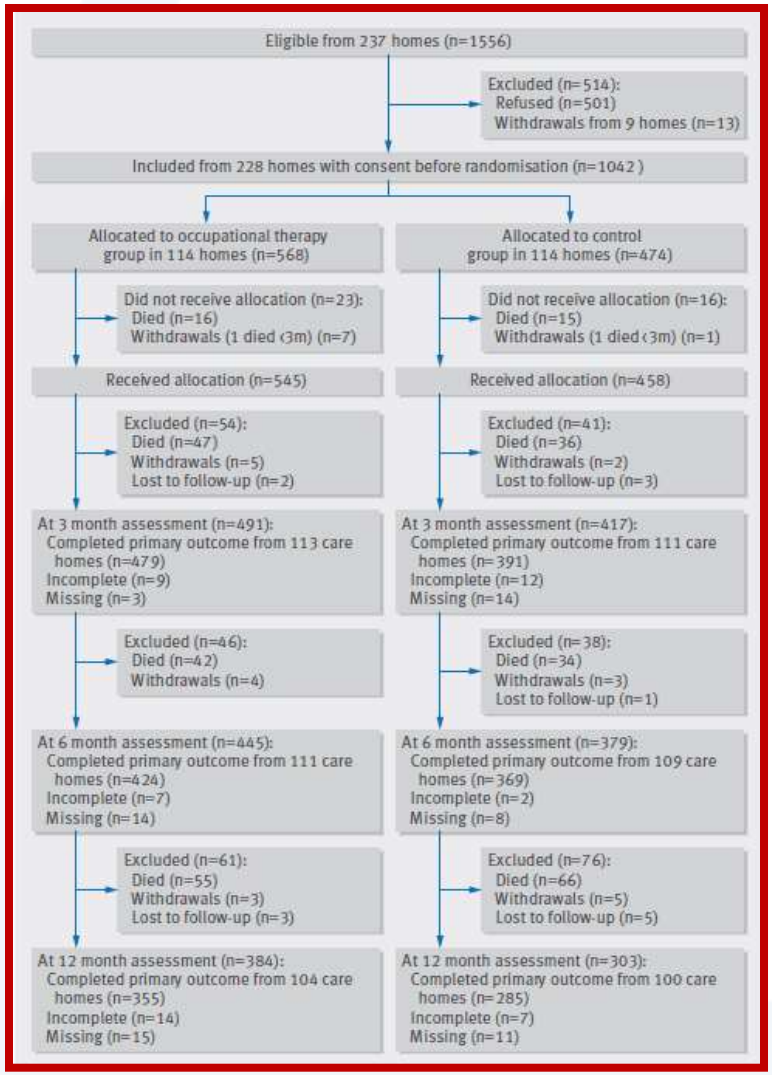
Arnold SM et al. J Stroke Cerebrovasc Dis.2015; 24(6): 1168-73

Head Position in Stroke Trial (HeadPoST) – sitting-up vs lying-flat positioning of patients with acute stroke: study protocol for a cluster randomised controlled trial



Munoz-Venturelli et al. Trials.2015; 16: 256

An occupational therapy intervention for residents with stroke related disabilities in UK care homes (OTCH): cluster randomised controlled trial



CONCLUSIONS

This large phase III study provided no evidence of benefit for the provision of a routine occupational therapy service, including staff training, for care home residents living with stroke related disabilities. The established three month individualised course of occupational therapy targeting stroke related disabilities did not have an impact on measures of functional activity, mobility, mood, or health related quality of life, at all observational time points. Providing and targeting ameliorative care in this clinically complex population requires alternative strategies.

Sackley CM et al. BMJ.2015; 350: h468

EARLY MOBILIZATION and S.A.H.

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Connolly ES Jr et al. Stroke.2012; 43(6):1711-37

European Stroke Organization Guidelines for the Management of Intracranial Aneurysms and Subarachnoid Haemorrhage

Stzeiner T et al. Cerebrovasc Dis.2013; 35:93-112

Clinical management guidelines for subarachnoid haemorrhage. Diagnosis and treatment☆

Vivancos J et al. Neurologia.2014; 29(6):353-70

Early Ambulation Produces Favorable Outcome and Nondemential State in Aneurysmal Subarachnoid Hemorrhage Patients Older than 70 Years of Age

Number of cases	71
Median age (IQR, range)	76 (73–80, 71–87)
Male/female	8/63
Hunt-Hess grade (1/2/3)	11/31/27
Premorbid conditions, n (%)	11 (15)
Treatment methods (Clipping:coiling)	56:15
Mean days to ambulation after the ictus	10.7 ± 9.3
Distribution of ambulation (days) (0–5/ 6–10/11–15/16-)	26/15/11/19
Symptomatic vasospasm, n (%)*	30 (45)
Angioplasty for vasospasm, n (%)	25 (83)
Postoperative complication, n (%)	13 (18)
Hydrocephalus†	13 (20)

Table 5. Relation Between Ambulation Date and Clinical Factors or Outcome

	Ambulation Date			
	0–5	6–10	11–15	16-
Premorbid conditions (no/yes)	21/5	13/2	11/0	15/4
Symptomatic vasospasm* (no/yes)	17/8	8/7	6/5	6/11
Postoperative complications (no/yes)	22/4	13/2	9/2	13/6
Hydrocephalus† (no/yes)	20/5	10/2	10/1	13/5
Glasgow Outcome Scale‡ (GR and MD: SD, VS, and D)	23/3	8/7	8/3	8/11
Revised-Hasegawa Dementia Scale† (30-21/20-11/10-0)	16/3/7	4/2/9	5/1/5	2/2/15

Shimamura N et al. World Neurosurg. 2010; 81(2):330-4.

Early versus delayed mobilisation for aneurysmal subarachnoid haemorrhage (Review)

Main results

In the absence of any suitable RCTs addressing this topic, we were unable to perform a meta-analysis. Data from recent observational studies suggested the period of greatest risk for rebleeding occurs more frequently in the early period, especially within 24 hours of the initial SAH. The impact of bedrest on aneurysm care should be clarified.

Authors' conclusions

There are no RCTs or controlled trials that provide evidence for, or against, staying in bed for at least four weeks after symptom onset in patients with aneurysmal SAH, who have not had, or could not have, surgical treatment for the aneurysm. Treatment strategies to reduce the risk of rebleeding in SAH patients before aneurysm ablation, or in those not suitable for surgical treatment, or who prefer conservative treatments, deserve attention.

Ma Z et al. Cochrane Database Syst Rev.2013; 5:CD008346

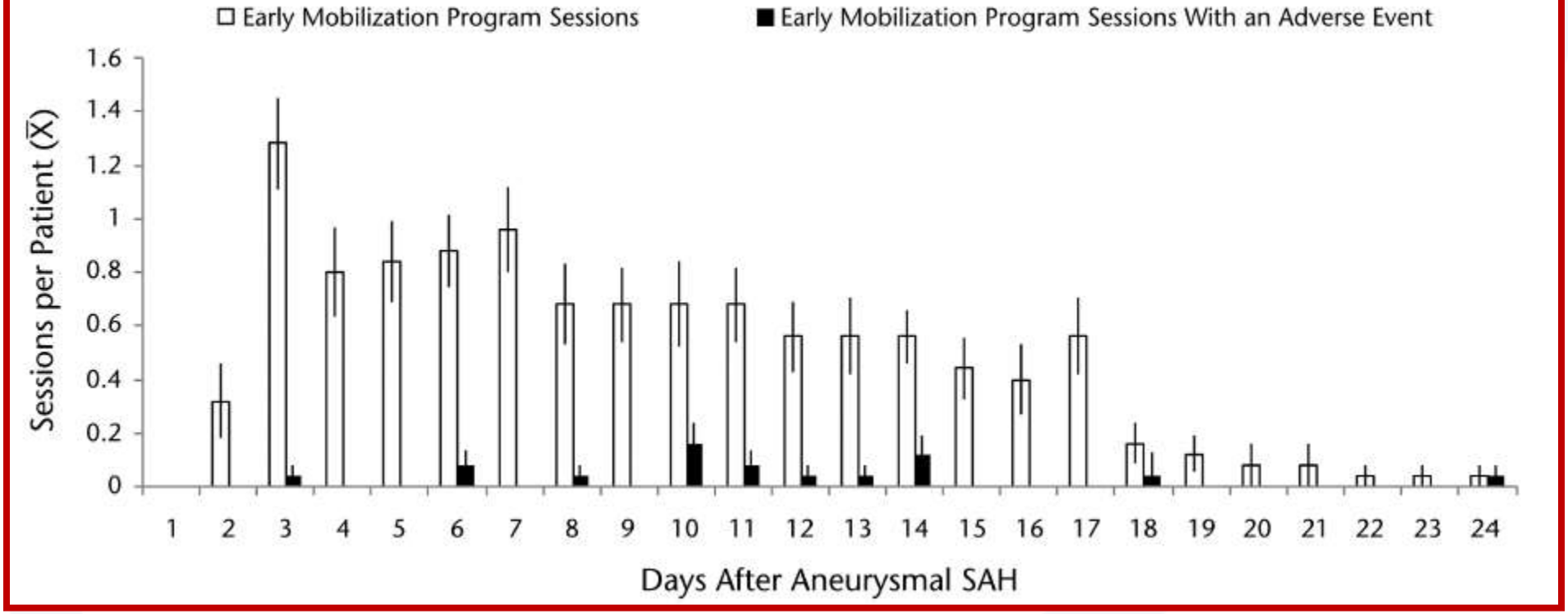
Safety and Feasibility of an Early Mobilization Program for Patients With Aneurysmal Subarachnoid Hemorrhage

- Retrospective analysis
- 25 patients
- Early mobilisation in stable patients
- Primary Outcome: Safety and feasability
- 286 sessions on 332 attempts

- Secured aneurysm or no underlying aneurysm identified
- Lindegaard ratio ≤3.0 or MCA MFV ≤120 cm/s
- Mean arterial pressure ≥80 and ≤110 mm Hg
- Heart rate ≥40 and ≤130 bpm
- Respiratory rate ≤40 breaths/min
- Pulse oximetry ≥88%
- Intracranial pressure ≤15 mm Hg
- No evidence of seizure activity
- Stable neurologic examination
- Able to open eyes in response to voice
- Ability to move one extremity on command

Olkowski BF et al. Phys Ther.2013; 93(2):208-15

Safety and Feasibility of an Early Mobilization Program for Patients With Aneurysmal Subarachnoid Hemorrhage



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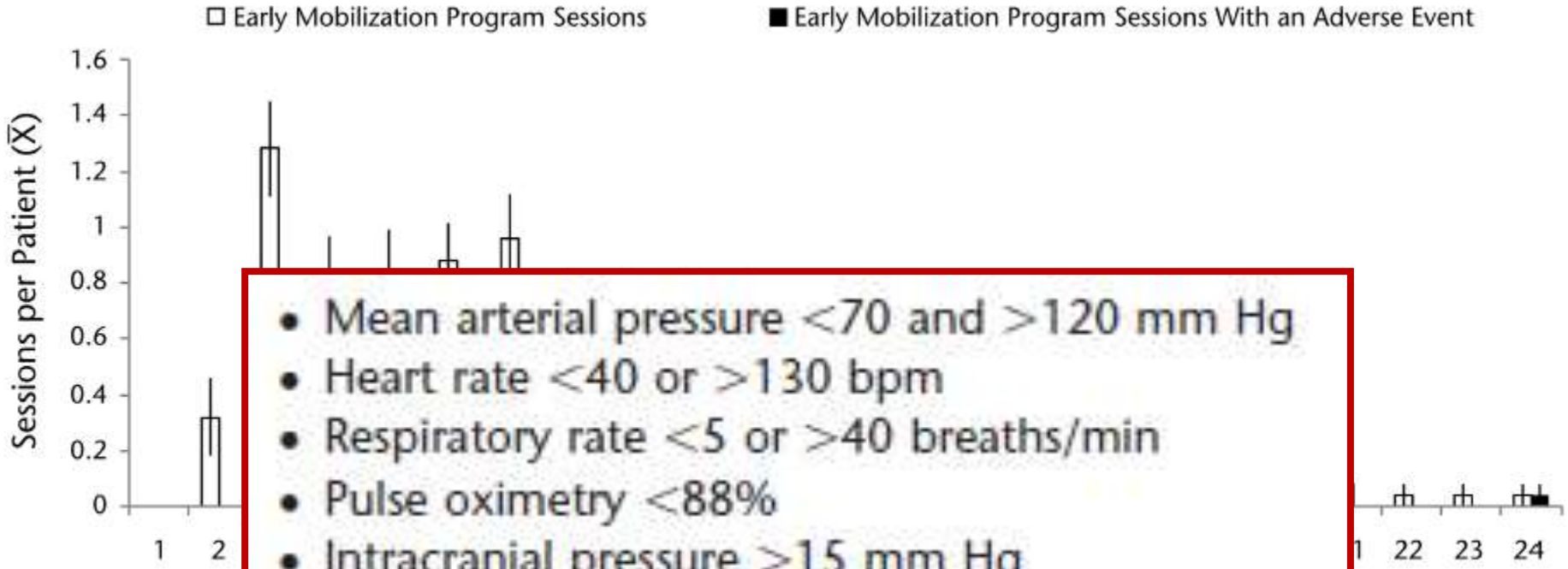

- Mean arterial pressure <70 and >120 mm Hg
- Heart rate <40 or >130 bpm
- Respiratory rate <5 or >40 breaths/min
- Pulse oximetry <88%
- Intracranial pressure >15 mm Hg
- Fall
- Acute change in neurologic presentation

Olkowski BF et al. Phys Ther.2013; 93(2):208-15

Safety and Feasibility of an Early Mobilization Program for Patients With Aneurysmal Subarachnoid Hemorrhage

Outcome	Value
Early mobilization program sessions	286 (100.0)
Sessions including out-of-bed activity	167 (58.4)
Sessions including walking ≥15.24 m (50 ft)	51 (17.8)
Sessions per patient, $\bar{X}$ (SD)	11.4 (4.3)
Days from subarachnoid hemorrhage to initial early mobilization program session, $\bar{X}$ (SD)	3.2 (1.3)
Days from admission to out of bed, $\bar{X}$ (SD)	5.4 (4.2)
Days from admission to walking ≥15.24 m, $\bar{X}$ (SD)	10.7 (6.2)
Modified Rankin Scale score at discharge, median (range)	2 (1.5)
Barthel Index at discharge, $\bar{X}$ (SD)	59.8 (35.5)
Patients discharged home	15 (60.0)
Patients discharged to an inpatient rehabilitation facility	10 (40.0)

Olkowski BF et al. Phys Ther.2013; 93(2):208-15

IMPACT OF EARLY MOBILIZATION AND REHABILITATION ON GLOBAL FUNCTIONAL OUTCOME ONE YEAR AFTER ANEURYSMAL SUBARACHNOID HAEMORRHAGE

Variables	Control group ($n=76$)	Early rehabilitation group ($n=92$)
Demographic characteristics		
Age, years, mean (range)	54 (25–79)	56 (25–81)
Sex, male/female, %	37/ 63	30/ 70
Years of education, %		
≤12 years	80	68
>12 years	20	32
Clinical characteristics		
Aneurysmal source of bleeding, %		
Anterior cerebral arteries	50	46
Middle cerebral – and internal carotid arteries	37	40
Vertebro-basilar arteries	13	14
Surgical aneurysm repair, %	50	47
Hunt and Hess score just prior to aneurysm repair, % of patients		
1	28	22
2	36	37
3	14	23
4	17	11
5	5	7
WFNS at transfer to NIW, % of patients		
1	33	33
2	29	34
3	22	16
4	13	14
5	3	3

- Prospective, Controlled, Interventional study
- Patients in neuro intermediate ward
- Standard treatment vs ST + early mobilisation program
- Outcome: mRS and GOSE at 1 year

Karic T et al. J Rehabil Med.2016; 48:676-82

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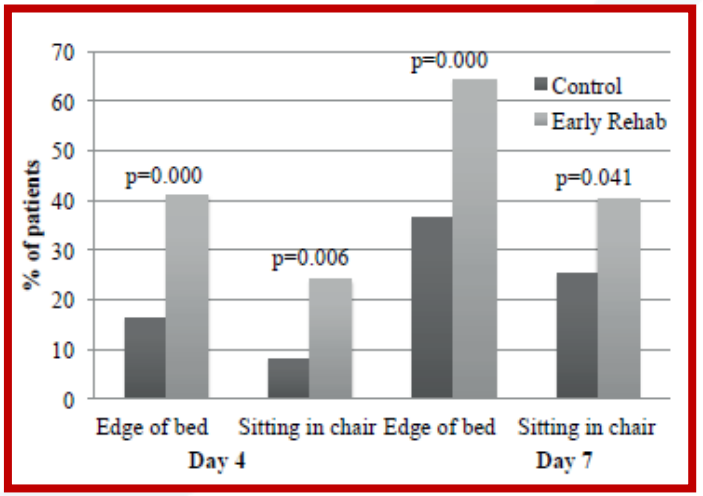


Karic T et al. J Rehabil Med.2016; 48:676-82

IMPACT OF EARLY MOBILIZATION AND REHABILITATION ON GLOBAL FUNCTIONAL OUTCOME ONE YEAR AFTER ANEURYSMAL SUBARACHNOID HAEMORRHAGE

Good recovery 79 Moderate disability 64 Severe disability 14 Dead 11	Adjacent-category logistic regression for all patients			
	Univariate		Multivariate	
	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Early rehabilitation	0.982 (0.69–1.39)	0.922	1.30 (0.836–2.037)	0.242
Age (years)	0.95 (0.93–0.97)	**0.000**	0.95 (0.929–0.972)	**0.000**
Hunt and Hess grade (23)	1.38 (1.18–1.63)	**0.000**	1.39 (1.16–1.67)	**0.000**
Time to 12 months follow-up (days)	1.00 (0.99–1.01)	0.102	1.00 (0.999–1.01)	**0.052**
Surgical aneurysm repair	1.01 (0.711–1.43)	0.962	1.25 (0.823–1.904)	0.292
Male sex	0.98 (0.67–1.42)	0.900	1.189 (0.756–1.872)	0.453

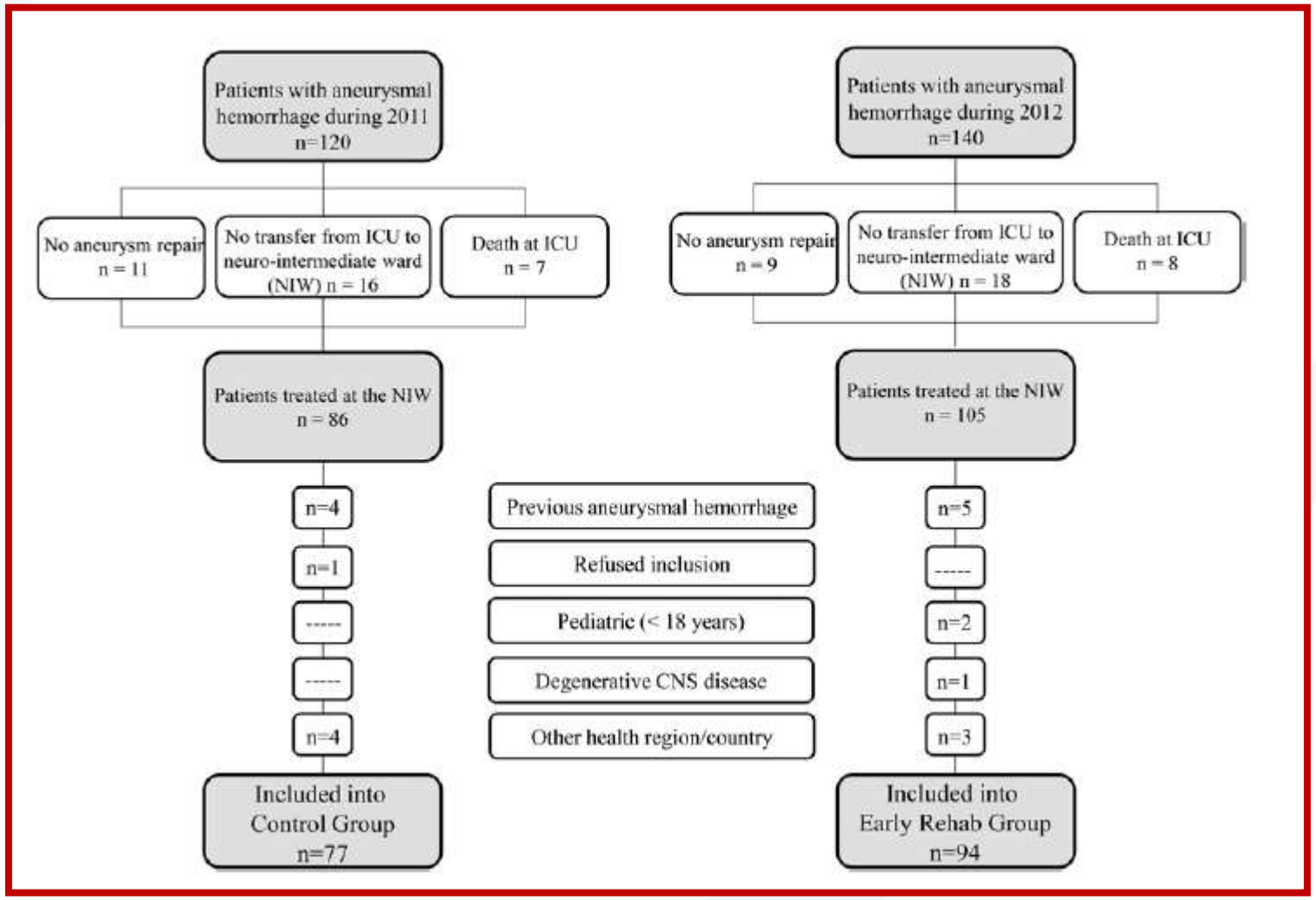
Karic T et al. J Rehabil Med.2016; 48:676-82

IMPACT OF EARLY MOBILIZATION AND REHABILITATION ON GLOBAL FUNCTIONAL OUTCOME ONE YEAR AFTER ANEURYSMAL SUBARACHNOID HAEMORRHAGE

	Adjacent-category logistic regression			
	Univariate		Multivariate	
Characteristics	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Patients in poor clinical status (WFNS 3,4,5) after aneurysm repair at arrival neuro-intermediate ward (n = 60) Good recovery = 19; Moderate disability = 23; Severe disability = 11; Dead = 7				
Early rehabilitation performed	1.007 (0.60–1.689)	0.979	2.33 (1.04–5.2)	**0.039**
Age (years)	0.942 (0.911–0.974)	0.000	0.93 (0.89–0.96)	**0.000**
Time to 12-month follow-up (days)	1.000 (–0.002–0.018)	0.137	1.00 (0.99–1.02)	0.064
Surgical aneurysm repair	0.964 (0.570–1.632)	0.894	1.07 (0.55–2.08)	0.843
Male sex	0.929 (0.530–1.628)	0.799	0.93 (0.44–1.97)	0.848
Patients in good clinical status (WFNS 1, 2) after aneurysm repair at arrival neuro-intermediate ward (n = 108) Good recovery=60; Moderate disability = 41; Severe disability = 3; Dead = 4				
Early rehabilitation performed	0.885 (0.52–1.507)	0.65	1.02 (0.57–1.85)	0.934
Age (years)	0.968 (0.942–0.995)	0.023	0.96 (0.93–0.99)	**0.012**
Time to 12 months follow-up	1.00 (–0.006–0.011)	0.558	1.00 (0.997–1.010)	0.265
Surgical aneurysm repair	1.365 (0.782–2.382)	0.273	1.56 (0.86–2.83)	0.145
Male sex	1.06 (0.617–1.829)	0.826	1.30 (0.71–2.36)	0.395

Karic T et al. J Rehabil Med.2016; 48:676-82

Effect of early mobilization and rehabilitation on complications in aneurysmal subarachnoid hemorrhage

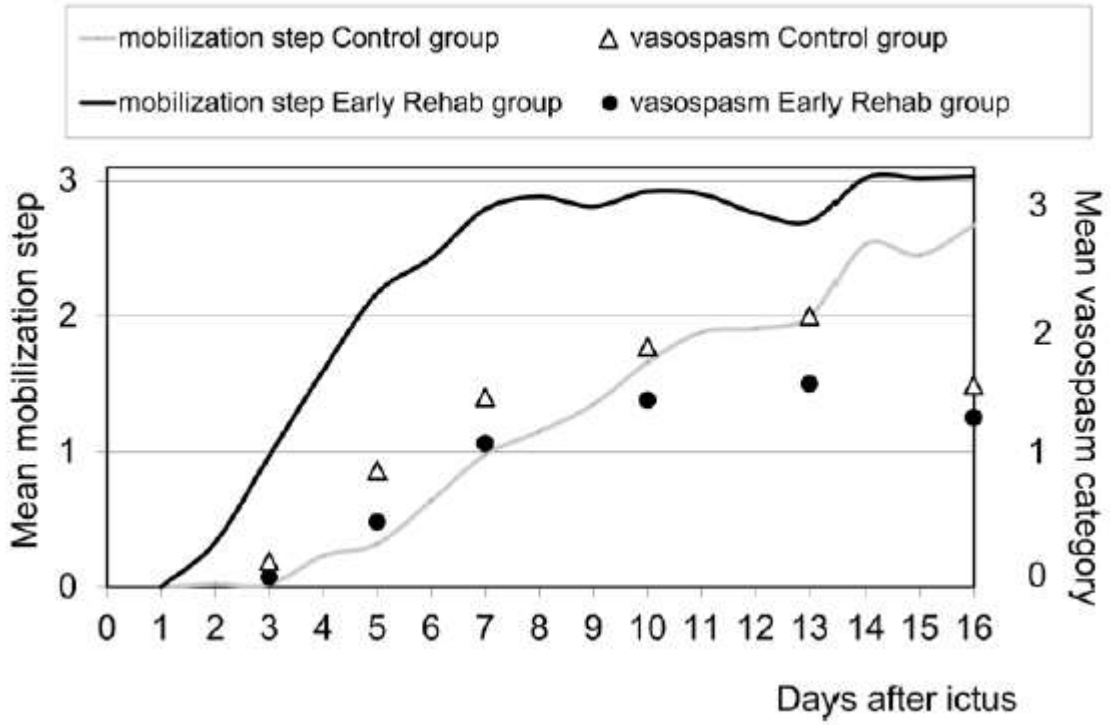


Karic T et al. J Neurosurg.2016; Apr 8: 1-9

Effect of early mobilization and rehabilitation on complications in aneurysmal subarachnoid hemorrhage

Variable	% Control, n = 72	% Early Rehab, n = 84
Radiological vasospasm		
None	35	41
Moderate (<50% narrowing), ≥1 vessel	46	43
Severe (≥50% narrowing), ≥1 vessel	19	16
Ultrasonic vasospasm		
None	34	48
Moderate (hemispheric ratio 3.5–<6), ≥1 vessel*	33	35
Severe (hemispheric ratio ≥6 or velocity >200 cm/sec), ≥1 vessel*	33	17
Clinical vasospasm†	29	14
Pts treated w/intraarterial nimodipine	4	10

* Lindegaard et al.
† p = 0.03.



Karic T et al. J Neurosurg.2016; Apr 8: 1-9

Effect of early mobilization and rehabilitation on complications in aneurysmal subarachnoid hemorrhage

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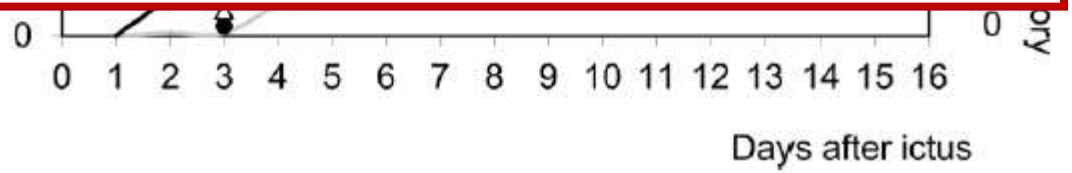
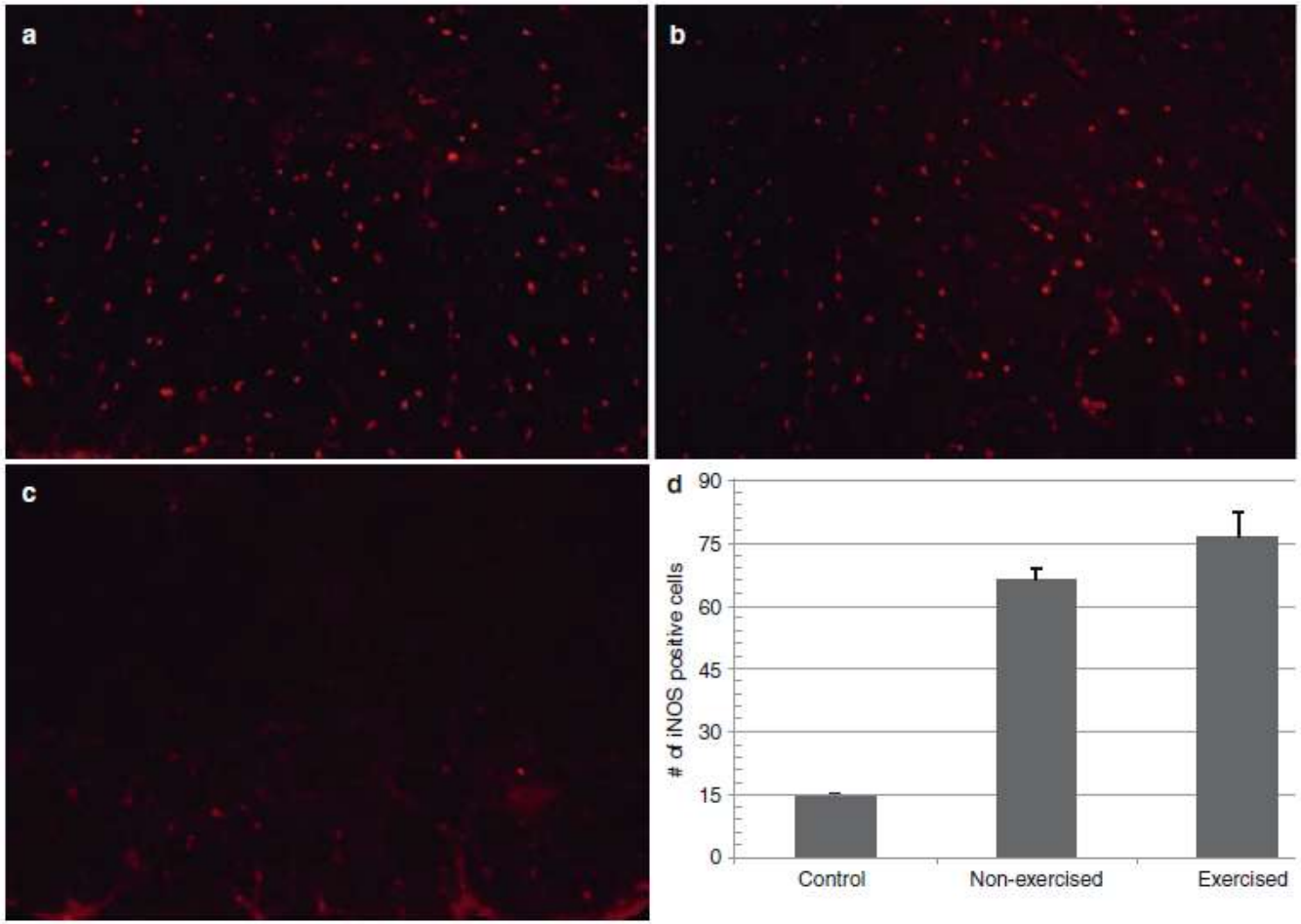
None	35	41
Moderate (<50% narrowing), ≥1 vessel	46	43
Severe (≥50% narrowing), ≥1 vessel	19	16

Variable	Univariate Analysis			Multivariate Forward/Backward Stepwise Logistic Regression		
	OR	95% CI	Significance	OR	95% CI	Significance
Clinical Hunt & Hess grade*	1.425	1.040–1.953	0.030			NS
Modified Fisher grade†	1.630	1.124–2.363	0.010	1.655	1.080–2.534	0.021
Intraventricular blood (LeRoux score)‡	1.101	0.991–1.225	NS (0.074)			NS
Max mobilization step w/in first 4 days after aneurysm repair	0.640	0.475–0.863	0.003	0.686	0.497–0.946	0.021
Age	0.966	0.933–1.001	0.056	0.949	0.911–0.989	0.012
If surgical aneurysm repair	0.599	0.271–1.321	NS			NS



Karic T et al. J Neurosurg.2016; Apr 8: 1-9

Mild Exercise Reduces Cerebral Vasospasm After Aneurysm Subarachnoid Hemorrhage: A Retrospective Clinical Study and Correlation with Laboratory Investigation



Riordan M et al. Acta Neurochir Suppl.2015; 120: 55-61

Mild Exercise Reduces Cerebral Vasospasm After Aneurysm Subarachnoid Hemorrhage: A Retrospective Clinical Study and Correlation with Laboratory Investigation

Table 2 Patient characteristics and outcome comparison by the timing of active physical therapy

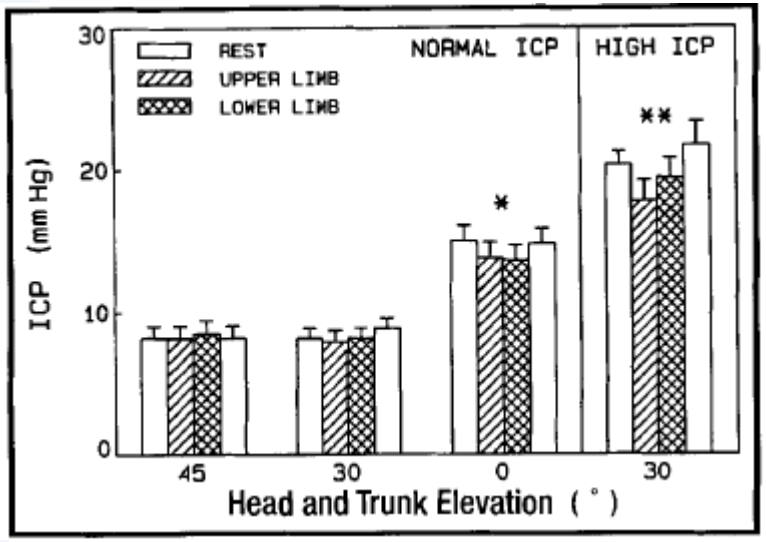
	Day of active exercise initiation				
	≤3 (n=22)	4–9 (n=20)	10–19 (n=9)	≥20/none (n=29)	P
Male	6 (27.3 %)	9 (45.0 %)	5 (55.6 %)	9 (31.0 %)	0.366
Hunt-Hess ≥ 3	7 (31.8 %)	7 (35.0 %)	4 (44.4 %)	22 (75.9 %)	0.005[a]
Fisher grade ≥ 3	19 (86.4 %)	14 (70.0 %)	9 (100 %)	26 (89.7 %)	0.179
Endovascular aneurysm securement	18 (81.8 %)	12 (60.0 %)	6 (66.7 %)	15 (51.7 %)	0.158
Symptomatic cerebral vasospasm	3 (13.6 %)	7 (35.0 %)	4 (44.4 %)	16 (55.2 %)	0.019[b]
Radiographic cerebral vasospasm	14 (63.6 %)	11 (55.0 %)	6 (66.7 %)	18 (62.1 %)	0.917
Complications	8 (36.4 %)	9 (45.0 %)	5 (55.6 %)	12 (41.4 %)	0.795
Discharge disposition					
Home	17 (77.3 %)	10 (50.0 %)	4 (44.4 %)	8 (27.6 %)	0.005[c]
Rehabilitation	3 (13.6 %)	9 (45.0 %)	5 (55.6 %)	12 (41.4 %)	0.050[d]
Deceased	2 (9.1 %)	1 (5.0 %)	0 (0 %)	9 (31.0 %)	0.035[e]

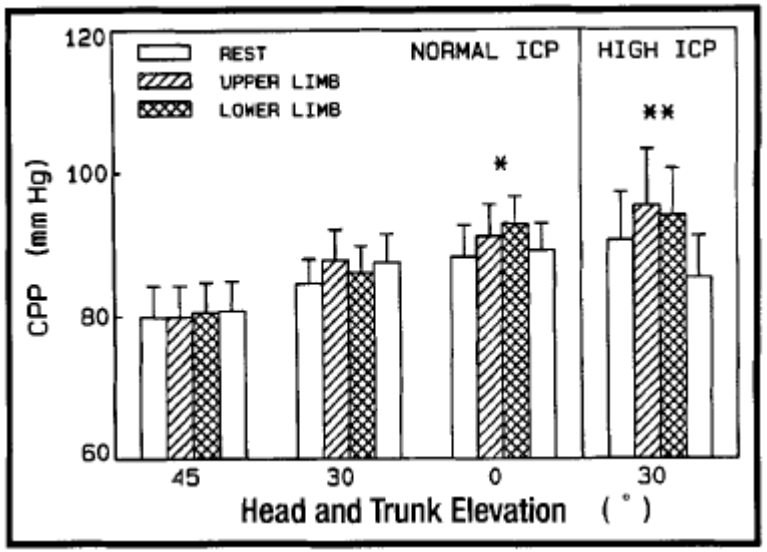
Riordan M et al. Acta Neurochir Suppl.2015; 120: 55-61

EARLY MOBILIZATION and T.B.I.

Effects of Positioning and Exercise on Intracranial Pressure in a Neurosurgical Intensive Care Unit

65 patients
Various brain injuries
Various Head Position/ Passive Range of Motion (PROM) / Exercise



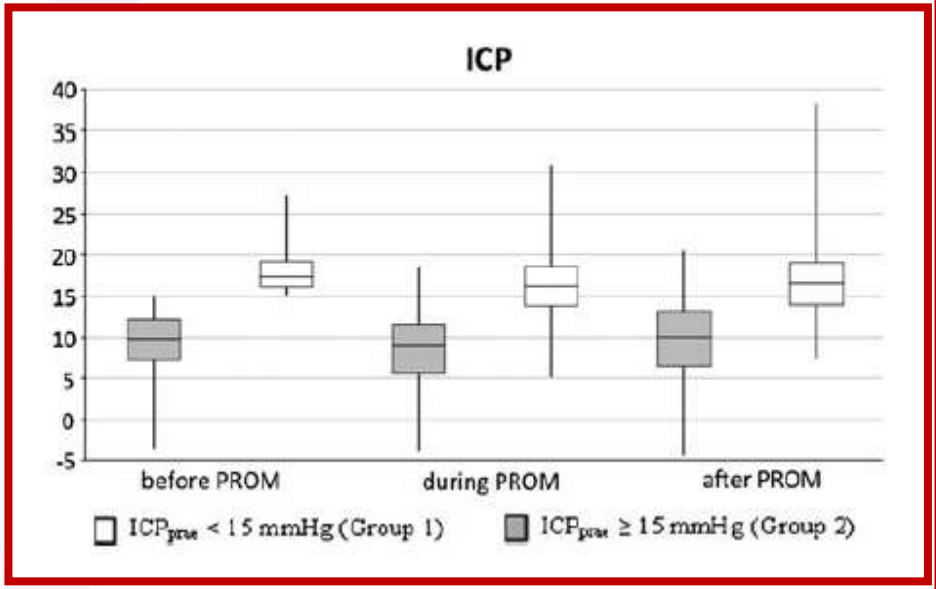


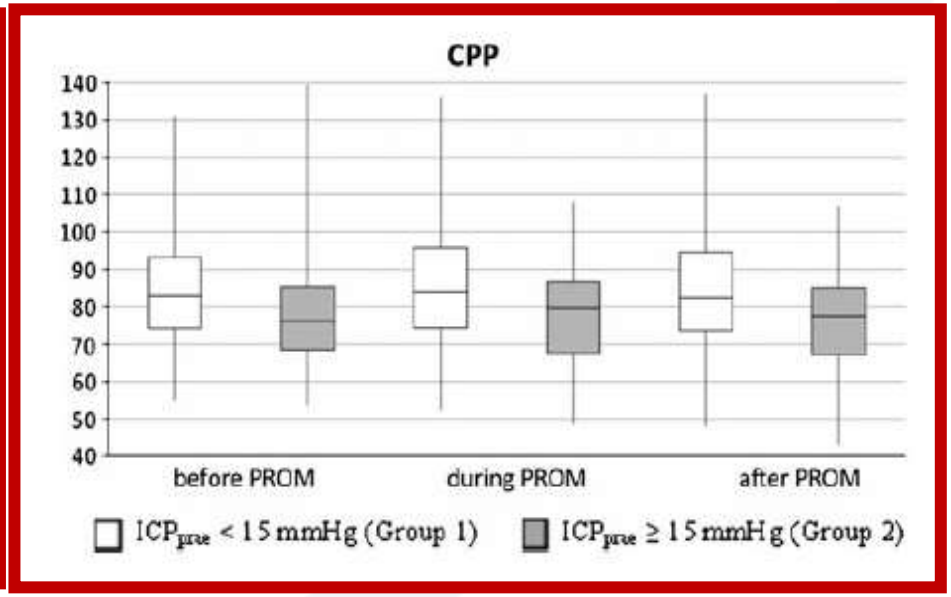
Be careful for Valsalva-like maneuver

Brimioulle S et al. Phys Ther.1997;77(12):1682-9

Effect of Early Physiotherapy on Intracranial Pressure and Cerebral Perfusion Pressure

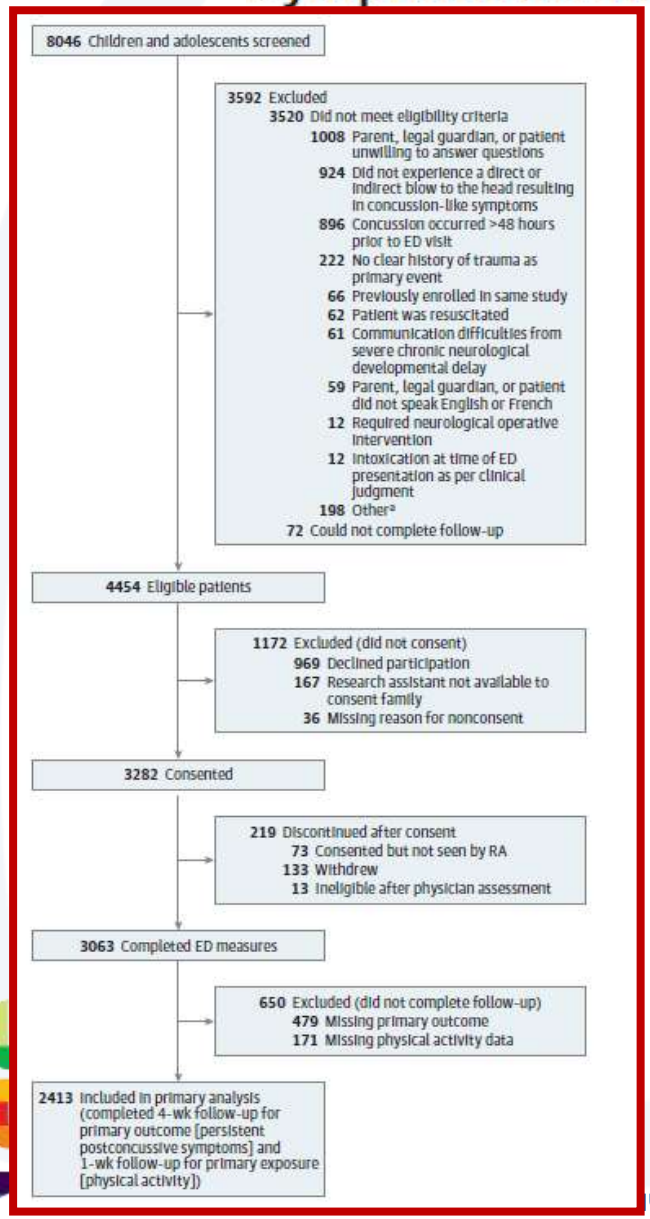
84 patients
Various brain injuries
Head 30° / Passive Range of Motion (PROM)





Roth C et al. Neurocrit Care.2013;18:33-8

Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents



- Prospective MultiCenter Cohort Study
- August 203 – June 2015
- 9 Paediatric ED in Canada
- 3063 children (<18) with acute concussion (according to the Zurich consensus statement)

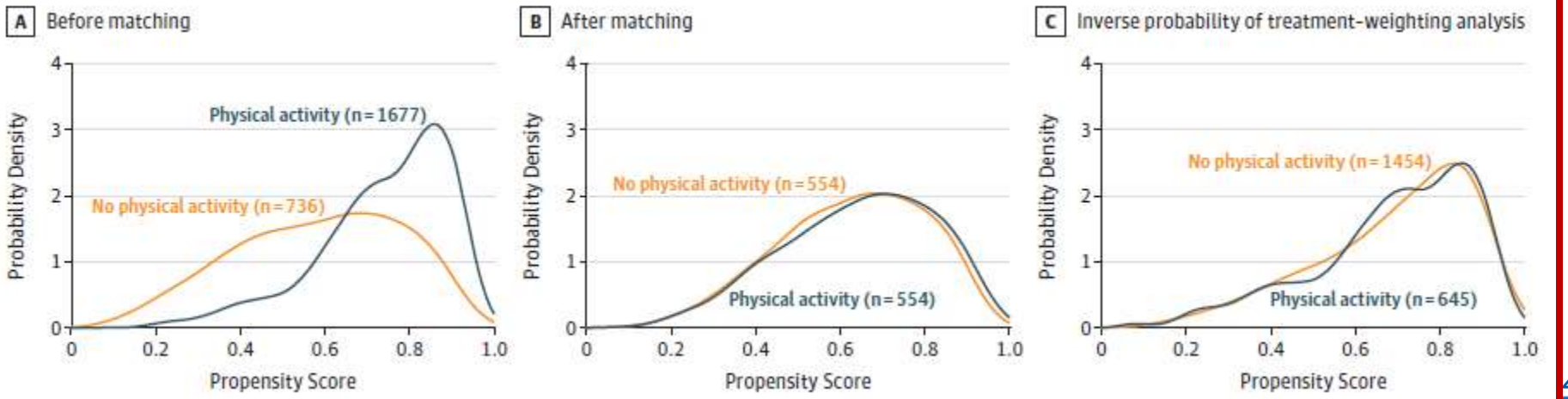
- Physical activity participation and concussive symptoms severity (questionnaire)

- Unadjusted analysis
  1/1 Propensity Score Matching
  Inverse probability of treatment weighting

Grool AL et al. JAMA.2016;316(23):2504-14

Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents

Type Analysis	No. (Absolute Risk, %)		Absolute Risk Difference, % (95% CI)	Relative Risk (95%CI)
	Physical Activity	No Physical Activity		
Unweighted sample	1677 (24.6)	736 (43.5)	18.9 (14.7-23.0)	0.75 (0.70-0.80)
Light activity vs none (subgroup 1)	795 (31.4)	736 (43.5)	12.0 (7.2-16.8)	0.82 (0.76-0.89)
Moderate activity vs none (subgroup 2)	357 (24.4)	736 (43.5)	19.1 (13.2-24.6)	0.75 (0.69-0.81)
Full-contact activity vs none (subgroup 3)	525 (14.5)	736 (43.5)	29.0 (24.2-33.5)	0.66 (0.61-0.71)
Matched	554 (28.7)	554 (40.1)	11.4 (5.8-16.9)	0.84 (0.77-0.92)
Inverse probability of treatment weighting	1454	645	9.7 (5.7-13.5)	0.74 (0.65-0.84)



4

Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents

2413 participants:

- ***UNADJUSTED ANALYSIS:***

PPCS occured in 24% of the early physical therapy (versus 43%)

- ***PROPENSITY MATCHING ANALYSIS:***

PPCS occured in 28,7% of the early physical therapy (versus 41,1%)

- ***INVERSE PROBABILITY of TREATMENT WEIGHTING:***

Relative Risk for PPCS: 0,74 (C I: 0,65 - ,84)

- **MORE EXERCISE IS ASSOCIATED WITH LESS PPCS**

Grool AL et al. JAMA.2016;316(23):2504-14

Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents

Key Points

Question Is participation in physical activity within 7 days following acute concussion associated with lower rates of persistent postconcussive symptoms in children and adolescents compared with conservative rest?

Findings In this prospective, multicenter cohort study of 3063 children and adolescents aged 5.00 to 17.99 years after propensity matching, the proportion with postconcussive symptoms at 28 days was 28.7% with participation in early physical activity vs 40.1% with conservative rest, a significant difference.

Meaning Participation in physical activity within 1 week after injury may benefit symptom recovery following acute concussion in children and adolescents.

Grool AL et al. JAMA.2016;316(23):2504-14

PRONE POSITION and BRAIN

Prone position in subarachnoid hemorrhage patients with acute respiratory distress syndrome: Effects on cerebral tissue oxygenation and intracranial pressure*

- Retrospective data analysis
- 16 patients treated for SAH – H&H 3 or more – ARDS

Variable	Supine	Prone	*P* Value[a]
Pao_2	92.8 ± 11.9 torr	129.2 ± 24.4 torr	<.0001
MAP	82.6 ± 7.6 mm Hg	83.0 ± 7.0 mm Hg	.217 NS
ICP	9.6 ± 3.5 mm Hg	15.8 ± 3.5 mm Hg	<.0001
CPP	74.4 ± 8.4 mm Hg	67.0 ± 7.1 mm Hg	<.0001
$ptiO_2$	27.2 ± 4.19 torr	33.5 ± 5.26 torr	<.001

		Supine, %	Prone, %	*P* Value[a]
ICP	>20 mm Hg	2.24	17.96	.0338
	>25 mm Hg	—	10.68	NS
CPP	<60 mm Hg	7.57	21.8	.0188
	<55 mm Hg	1.61	8.05	.0191
$ptiO_2$	<20 torr	32.7	10	.0473
	<15 torr	11.3	2	NS

Reinprecht A et al. Crit Care Med.2003;31:1831-8

Prone ventilation for refractory hypoxaemia in a patient with severe chest wall disruption and traumatic brain injury

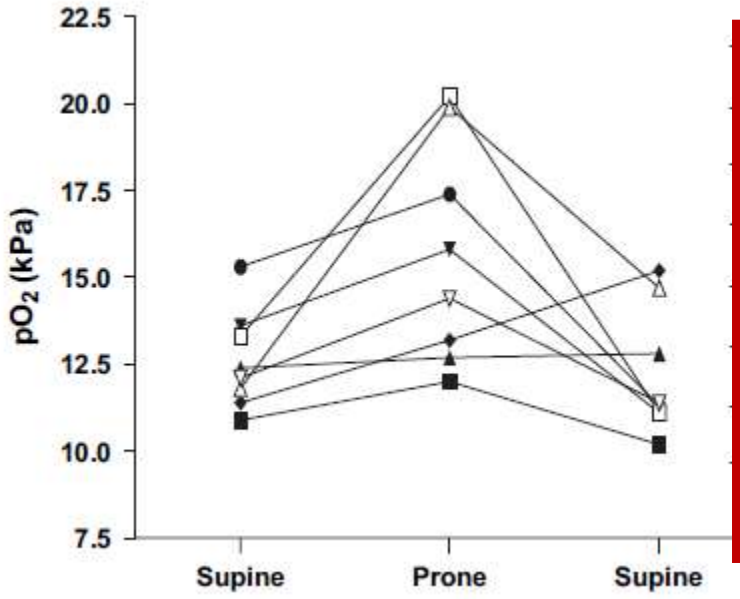
Table 1 Trend in arterial blood gas, ICP, and ventilator parameters before and after prone positioning. Pa_{O_2}, partial pressure of oxygen (arterial); Pa_{CO_2}, partial pressure of carbon dioxide (arterial); BE, base excess, HCO_3^-, standard bicarbonate; F_{IO_2}, fractional inspired oxygen concentration; V_T, tidal volume; IBW, ideal body weight; PEEP, positive end-expiratory pressure; P_{Peak}, peak inspiratory pressure; ICP, intracranial pressure

	Admission	24 h pre-prone	2 h pre-prone	1 h post-prone	7 h post-prone	12 h post-prone	24 h post-prone	48 h post-prone
pH	7.337	7.462	7.276	7.270	7.444	7.490	7.498	7.504
Pa_{O_2} (kPa)	23.0	6.11	5.29	7.78	9.73	10.1	13.4	10.4
Pa_{CO_2} (kPa)	4.90	5.97	10.5	10.2	6.8	6.18	5.66	5.27
BE (mmol litre^{-1})	−5.6	7.6	8.6	7.4	9.9	10.9	8.9	7.4
HCO_3^- (mmol litre^{-1})	19.2	31.6	35.3	34.1	34.4	35.0	32.7	30.9
F_{IO_2}	0.50	1.0	1.0	1.0	0.85	0.7	0.55	0.35
V_T (ml) (ml kg^{-1} for IBW)	611 (6.8)	805 (8.9)	451 (5.0)	415 (4.6)	611 (6.8)	612 (6.8)	572 (6.4)	605 (6.7)
PEEP (cm H_2O)	8	5	15	15	15	15	15	12
$Pa_{O_2}F_{IO_2}$ ratio (mm Hg)	345.0	45.8	39.6	58.4	85.9	108.2	182.7	222.9
ICP (mm Hg)	—	23	17	30	22	18	2	—

Ashton-Cleary et al. Br J Anaesth.2011;107(6):1009-10

Oxygenation and cerebral perfusion pressure improved in the prone position

- 8 patients
- TBI or SAH



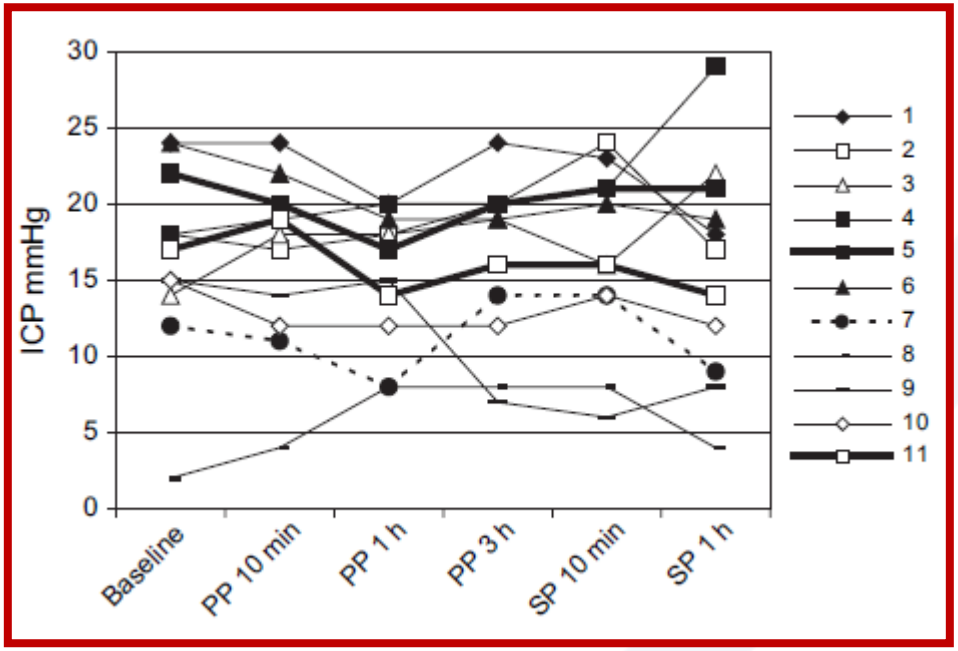
Intracranial pressure, cerebral perfusion pressure, and mean arterial pressure.

	Baseline (start)	Prone position	Baseline (end)
ICP (mmHg)	12 ± 6	15 ± 4* $P = 0.03$	14 ± 5
CPP (mmHg)	66 ± 7	73 ± 8* $P = 0.03$	66 ± 8
MAP (mmHg)	78 ± 8	88 ± 8** $P = 0.005$	80 ± 10

Nekludov et al. Acta Anaesthesiol Scand.2006;50:932-6

Prone position in mechanically ventilated patients with reduced intracranial compliance

- Consecutive, prospective, pilot study
- 11 patients with TBI or IC haemorrhage



Thelandersson A et al. Acta Anaesthesiol Scand.2006;50:937-41

Prone position in mechanically ventilated patients with reduced intracranial compliance

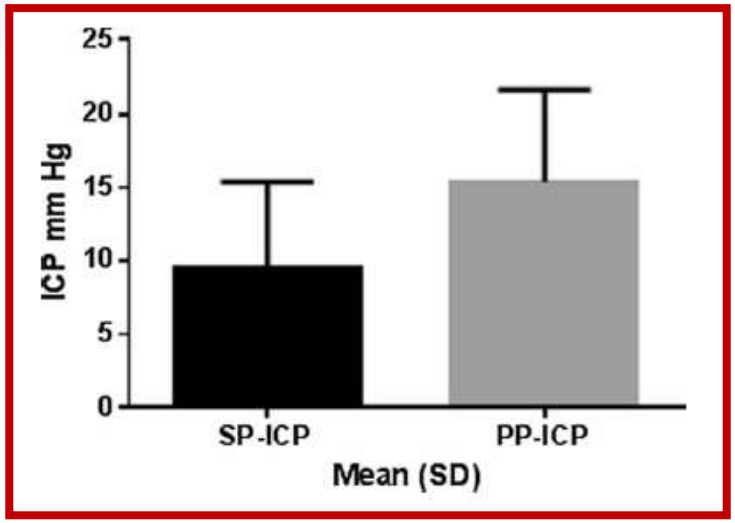
Intracranial and circulatory results in the supine position at baseline, in the prone position after 10 min, 1 and 3 h and in the supine post-pone position after 10 min and 1 h.

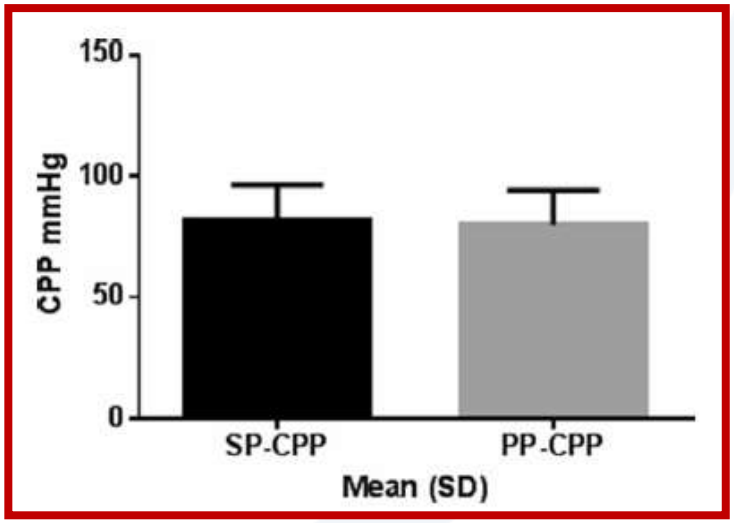
	Supine position	Prone position			Supine post-prone position	
	Baseline	10 min	1 h	3 h	10 min	1 h
ICP	16 ± 6	16 ± 5	15 ± 4	16 ± 5	17 ± 6	16 ± 7
CPP	78 ± 12	75 ± 13	78 ± 13	79 ± 10	75 ± 17	72 ± 13†
MABP	94 ± 15	91 ± 13	93 ± 13	95 ± 10	88 ± 17	88 ± 13†
HR	67 ± 15	72 ± 15*	73 ± 15*	76 ± 18*	74 ± 18*	69 ± 14

Thelandersson A et al. Acta Anaesthesiol Scand.2006;50:937-41

Does Prone Positioning Increase Intracranial Pressure? A Retrospective Analysis of Patients with Acute Brain Injury and Acute Respiratory Failure

- 115 patients treated in prone between 2007 and 2013
- 29 patients with ICP monitoring





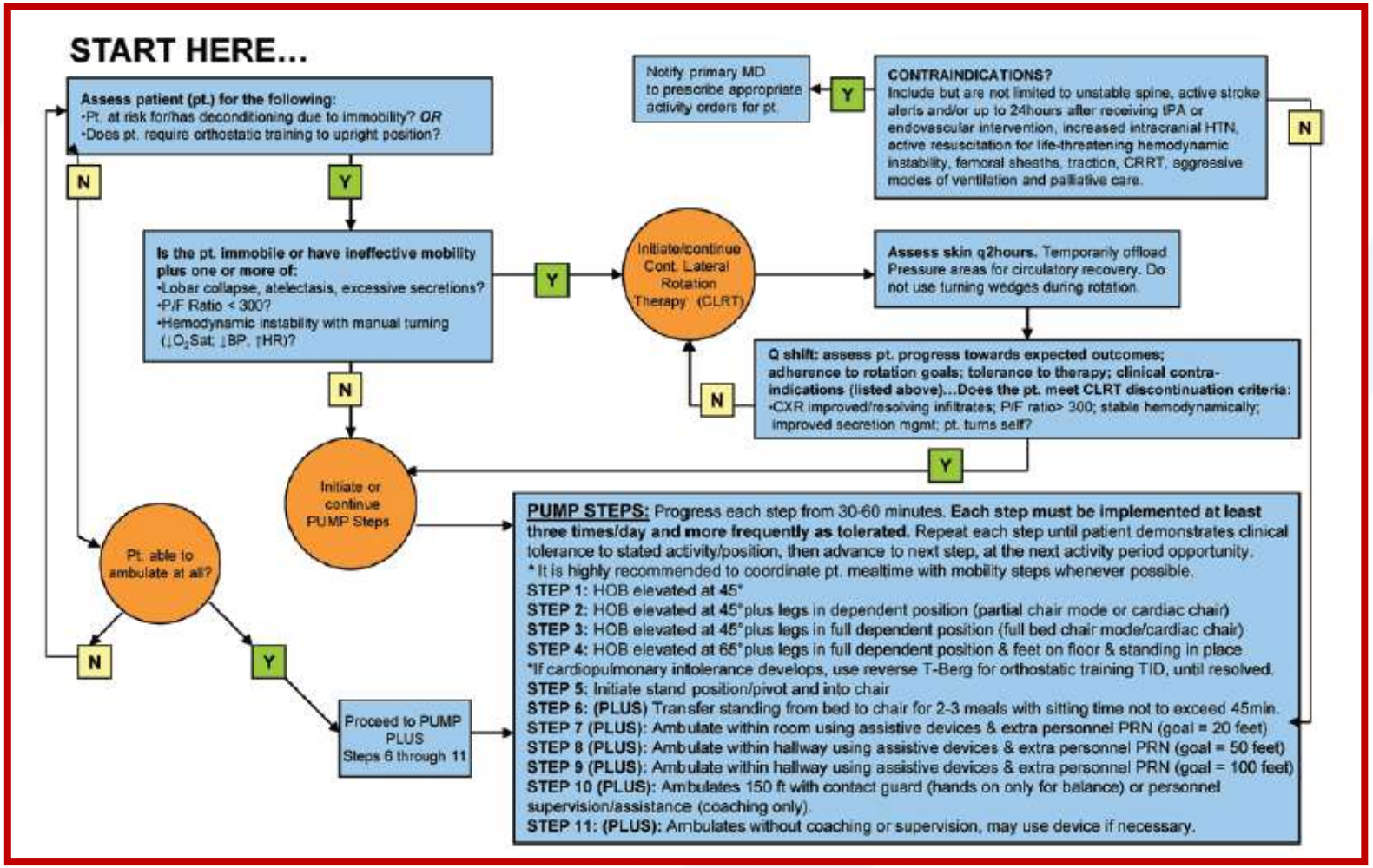
	Before	During	After	*p* value
PEEP (mbar)	11	11.1	10.6	0.1714
pCO_2 (mmHg)	43.1	38.1	35.9	0.003
PaO_2/FiO_2 ratio	135.4	339.8	345.8	<0.0001

Roth C et al. Neurocrit Care.2014;21:186-91

EARLY MOBILIZATION and NEURO - ICU

From an Italian, observational study *(Bartolo et al. Eur J Phys Rehab Med.2016)*, we know early rehabilitation is not diffusely performed in sABI in ICU/NICU.
Furthermore, rehabilitative interventions are very variable.

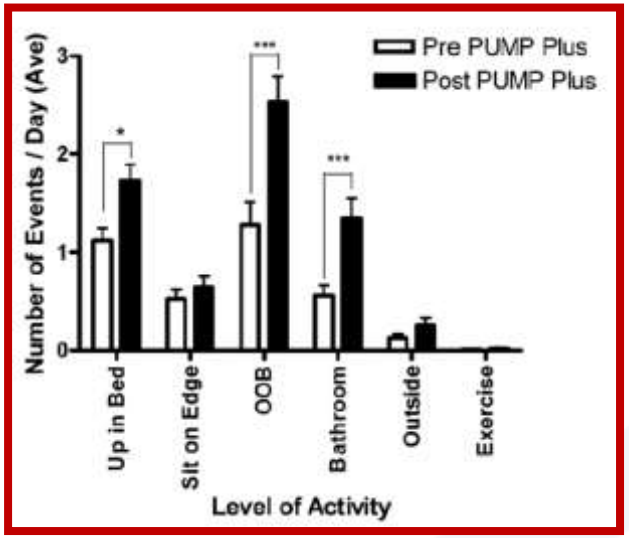
The effect of increased mobility on morbidity in the neurointensive care unit



Titsworth WL et al. J Neurosurg.2012; 116:1379-88

The effect of increased mobility on morbidity in the neurointensive care unit

Variable	Before the Initiative	After the Initiative	p Value
dates	Jan 18–Jan 31, 2011	May 31–June 14, 2011	
no. of patients	77	93	
mean corrected I-MOVE mobility score (95% CI)	14.5 (9.1–22.9)	44.7 (27.9–71.3)	<0.0001
mean hospital LOS in days (95% CI)	12.0 (9.87–14.7)	8.6 (6.93–10.8)	<0.01



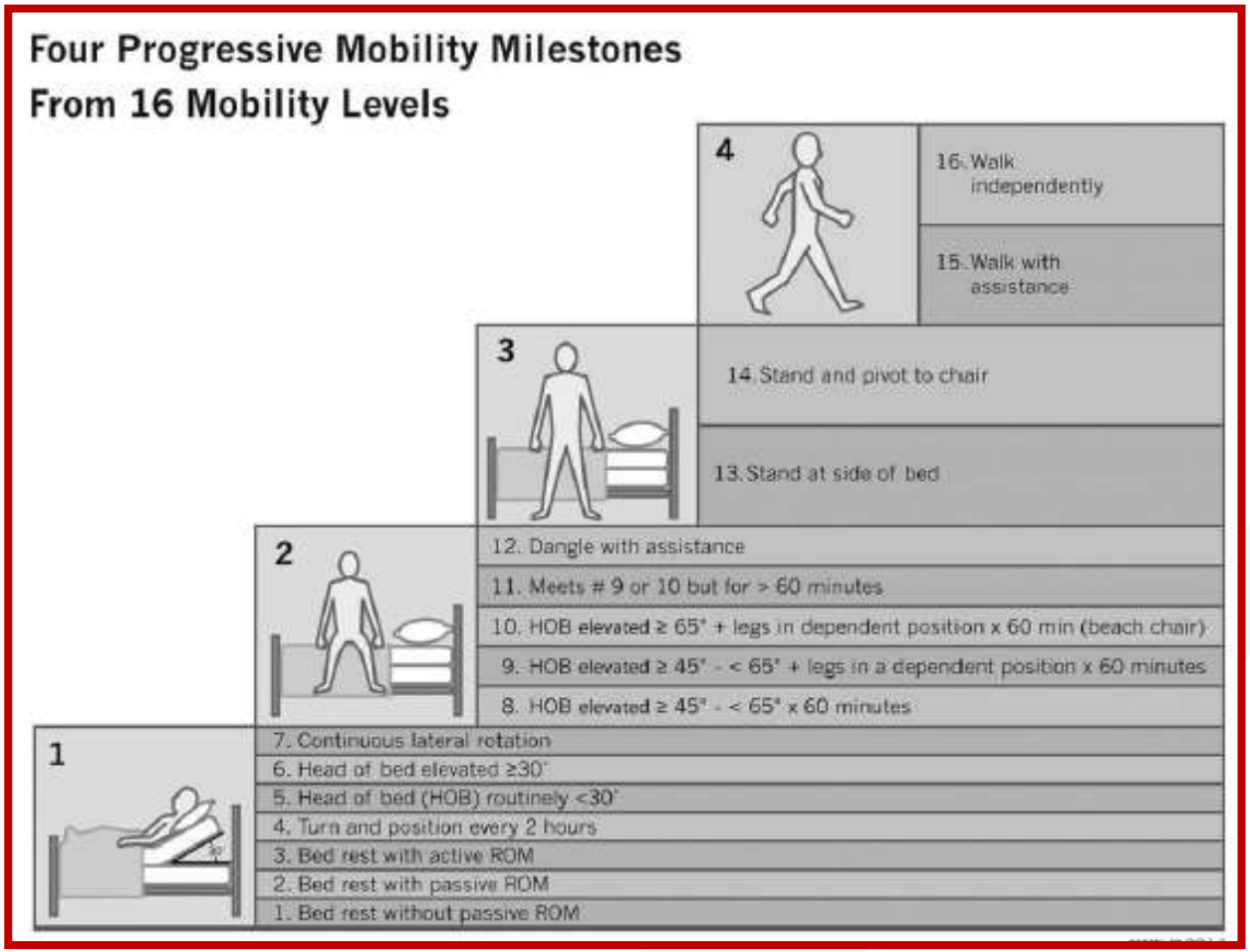
Titsworth WL et al. J Neurosurg.2012; 116:1379-88

The effect of increased mobility on morbidity in the neurointensive care unit

Outcome Measure	Before Mobility	After Mobility	p Value
dates	April 1, 2010–Jan 31, 2011	Feb 11–June 31, 2011	
patient days	802 ± 71	742 ± 75	0.12
neurointensive care unit LOS (days)	4.00 ± 0.31	3.46 ± 0.31	<0.004
acquired pressure ulcer prevalence	2.6% ± 0.03	4.6% ± 0.02	0.22
days in restraints	368.57 ± 46.8	301.2 ± 55.3	<0.05
hospital-acquired infections	5.5 ± 0.9	2.2 ± 1.0	<0.05
VAP rate†	2.14 ± 0.95	0 ± 0	<0.001
% of patients ventilated	32.0 ± 0.03	30.6 ± 0.07	0.66
ventilator days	255 ± 27.9	231 ± 70.7	0.39
VAP bundle compliance (%)	98.5 ± 0.02	95.6 ± 0.07	0.23
UTI rate†	2.72 ± 1.17	1.07 ± 1.67	0.11
urinary catheter days	581.6 ± 30	463 ± 145	<0.05
central venous line infections	0.35 ± 0.78	1.0 ± 0.93	0.24
total falls†	1.00 ± 0.35	1.0 ± 0.63	1.00
fall rate per 1000 patient days	1.39 ± 0.57	1.31 ± 0.85	0.867
critical line pulls	0.90 ± 0.53	0.67 ± 0.81	0.63
line pull rate†	1.10 ± 0.67	0.91 ± 1.12	0.766

Titsworth WL et al. J Neurosurg.2012; 116:1379-88

Clinical and Psychological Effects of Early Mobilization in Patients Treated in a Neurologic ICU: A Comparative Study*



Klein K et al. Crit Care Med.2015; 43:865-73

TABLE 2. Clinical Outcome Differences Between Pre- and Postintervention Groups

Outcome Factors	Intervention Group		p
	Pre ($n = 260$)	Post ($n = 377$)	
Maximum mobility by mobility groupings			< 0.001
Levels 1–7, *n* (%)	101 (38.8)	102 (27.1)	
Levels 8–12, *n* (%)	104 (40.0)	114 (30.2)	
Levels 13–14, *n* (%)	30 (11.5)	117 (31.0)	
Levels 15–16, *n* (%)	25 (9.6)	44 (11.7)	
Length of stay, mean (SD)			
Hospital	15.2 (16.0)	10.2 (8.2)	< 0.001
Neuroscience ICU	7.8 (9.6)	4.3 (5.1)	< 0.001
Mortality, 30 d, *n* (%)	43 (16.5)	45 (12.0)	0.12
Disposition home, *n* (%)	67 (25.8)	139 (37.1)	0.002
Ventilator-associated pneumonia, *n* (%)	4 (1.5)	1 (0.3)	0.11
Blood stream infection, *n* (%)	10 (3.8)	3 (0.8)	0.015
Deep vein thrombosis ≥ 1, *n* (%)	17 (6.5)	42 (11.1)	0.12
Hospital-acquired pressure ulcers (%)	10 (3.8)	4 (1.1)	0.026
Psychological profile score, mean (SD)			
Overall	2.4 ± 2.4	1.7 ± 2.0	0.13
Depression	0.90 ± 1.09	0.59 ± 0.86	0.055
Anxiety	1.03 ± 1.05	0.74 ± 0.82	0.029
Hostility	0.48 ± 0.71	0.35 ± 0.51	0.18

Klein K et al. Crit Care Med.2015; 43:865-73

CO0343

Early in-bed tilting in neurological intensive care unit: Feasibility and interest

Discussion - conclusion The in-bed verticalization for brain-damaged patients in ICU can be very early, with a low rate of reversible side effects. It requires a good definition of indications and contraindications. Some of the patients improve their wakefulness status during the verticalization. The data collection will be continued for a 6 months period.

Fazilleau S. Ann Phys Rehab Med.2016; 59S:e153

Effectiveness of a Very Early Stepping Verticalization Protocol in Severe Acquired Brain Injured Patients: A Randomized Pilot Study in ICU

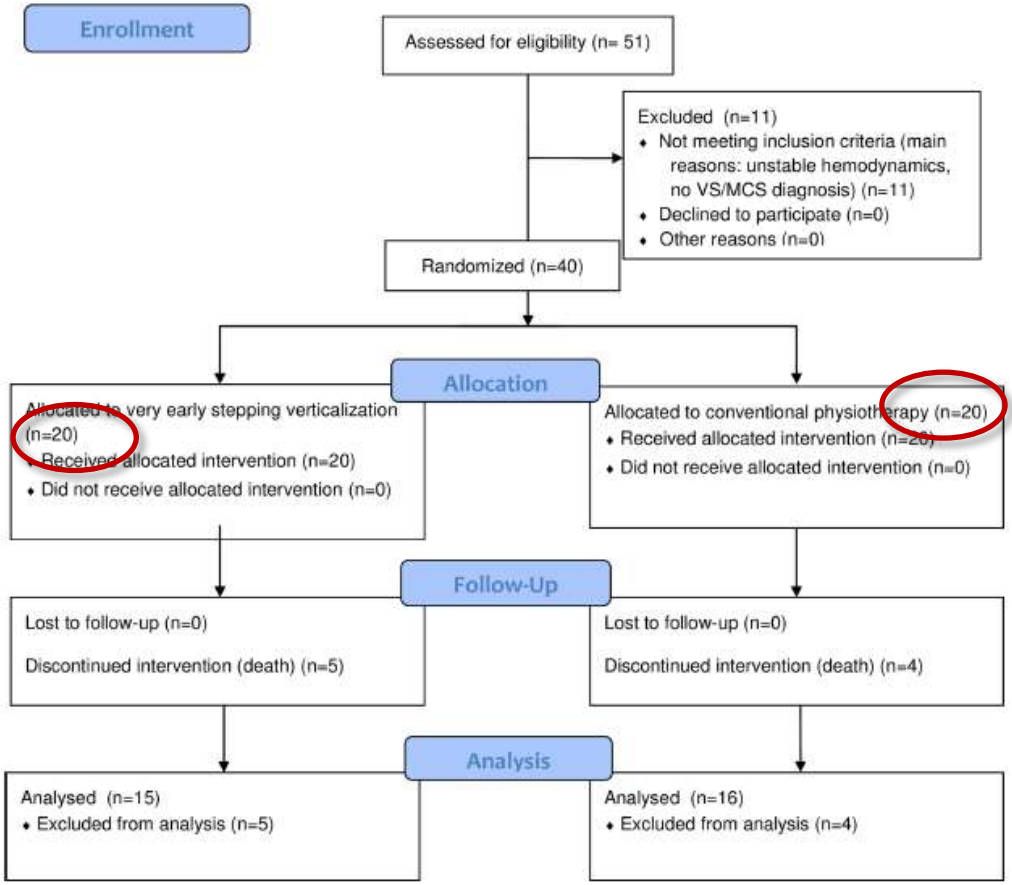


Fig 2. "Erigo" setting in the ICU room.

Effectiveness of a Very Early Stepping Verticalization Protocol in Severe Acquired Brain Injured Patients: A Randomized Pilot Study in ICU

Conclusions

A stepping verticalization protocol, started since the acute stages, improves the short-term and long-term functional and neurological outcome of ABI patients.

BUT:

- Type of injury
- Patient younger in the verticalization group
- Verticalization started 12,4 ± 7,3 days after TBI
- ICU LOS longer for the verticalized patients

Frazzitta G et al. PLoS One.2016; e0158030

Patients with severe acquired brain injury show increased arousal in tilt-table training

16 patients enrolled (out of 56 admitted in the unit/ward)
Mainly TBI but also anoxia and stroke
40 ± 22 days after surgery

Tilt Table
Orthostatic tolerance ?

- **15/16 patients were unable to complete 20 minutes of training bc of orthostatic symptoms.**
- Increased arousal (eyes opened)

Riberholt CG et al. Dan Med J.2013;

TAKE HOME MESSAGE

Exercise is the best medicine—even in the Neuro ICU.

Creutzfeld CJ et al. Crit Care Med.2015; 43(4):926-7

- Implement a mobilisation program
- Monitor the patient
- Avoid complications (hypotension, …)

TAKE HOME MESSAGE

Exercise is the best medicine—even in the Neuro ICU.

Creutzfeld CJ et al. Crit Care Med.2015; 43(4):926-7

- Implement a mobilisation program / Check list
- Monitor the patient
- Avoid complications (hypotension, …)

HOWEVER:

- Interpret the reported data with caution
- Compare what is comparable

Table 3 Safety checklist specific to early mobilization in the NICU

Yes	No	N/A	Inclusion criteria
☐	☐	☐	If there is an EVD, is the EVD closed and secure for patient mobilization?
☐	☐	☐	Have ICPs been well controlled for 24 h with no administration of mannitol or hypertonic saline?
☐	☐	☐	Is there no *active* titration of parenteral vasopressors or antihypertensives?
☐	☐	☐	Is the CAM-ICU negative for delirium?
☐	☐	☐	Does the patient have a stable neurologic exam?
☐	☐	☐	If patient has an AIS, has it been 24 h after the onset of symptoms?
☐	☐	☐	If patient has an aSAH, has the aneurysm been treated?
☐	☐	☐	If patient has a spontaneous ICH, has the hemorrhage volume been stable for 24 h?

If all above questions are answered "Yes" or "N/A," proceed with early mobilization

Olkowski BF et al. Neurocrit Care.2016: in press