AMOBES « Active MOBility Early after Stroke »
Quelle doit être la kinésithérapie dans les premiers jours après AVC?

A.Yelnik, pour le groupe AMOBES
Stroke 2017

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2 main goals for rehabilitation after stroke

To prevent immobility related events
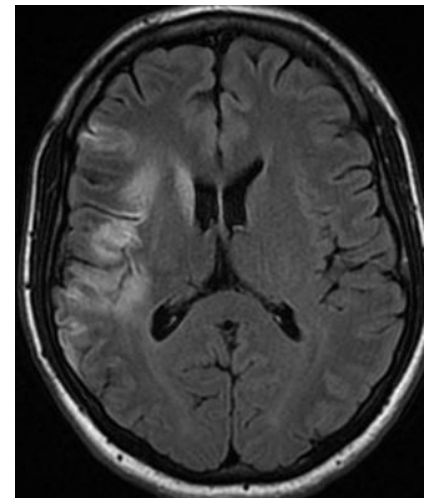
joint stiffness, deformities, cardiovascular events

body schema, neuromuscular abilities

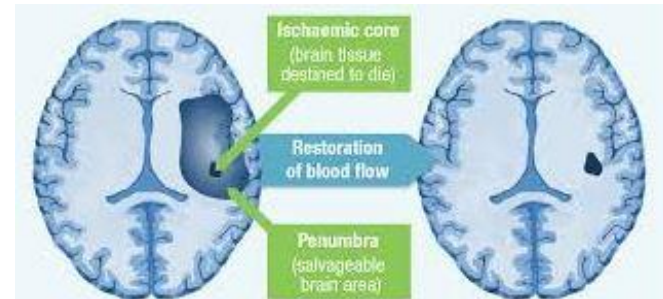**Stimulate recovery (mobility, cognition)**
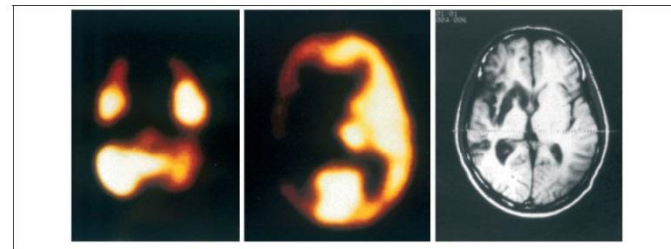
But

- When?

- How much?

Post-stroke recovery

Recovery of the penumbra zone


Release of diaschisis

Brain plasticity: new neural connections (synapses) → novel competencies of brain structures adjacent to the lesion

Major role of the rehabilitation to enhance and guide these tissular processes

The <u>early period</u> *(first weeks in animal models, first months in human?)* is a <u>crucial time for neural plasticity stimulation</u>

(Cramer 2000, Baron 2004, Biernaskie 2004, Carnichool ST 2006, Murphy 2009, Li S. 2010, Krakauer 2012…)
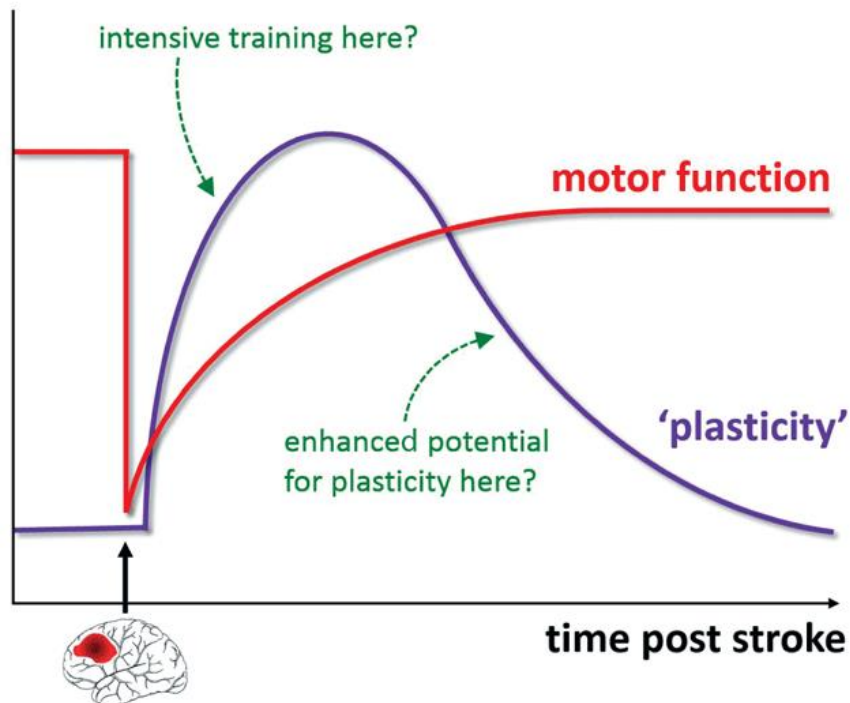
Animal models

Effects of exercises on ischemia are still controversial

(review and meta analysis Egan KJ NNR 2014)

Intensive exercises too early after stroke

↑ Cerebral ischemia *(Kaslowski 1996, Humm 1998, Lee 2009)*

Moderated force exercises (30 mn/day 5 to 7 days/week) can be recommended *(Austin 2014 review of 47 studies)*

In human ?

Very few studies investigated the role of intensive PT within the first 2 weeks.

- Positive results   (*Peurala 2009*)

- Without advantage   (*Di Laura 2003, Boadke 2007, Kwakkel 2016*)

- Negative results   (*Dromerick 2009*)

Very early mobilization (VEM) AVERT group

< 24 h

6 days/week until discharge of stroke unit

Helping patient to be out of a bed, sitting or standing at least <u>twice a day</u> more than usual practice.

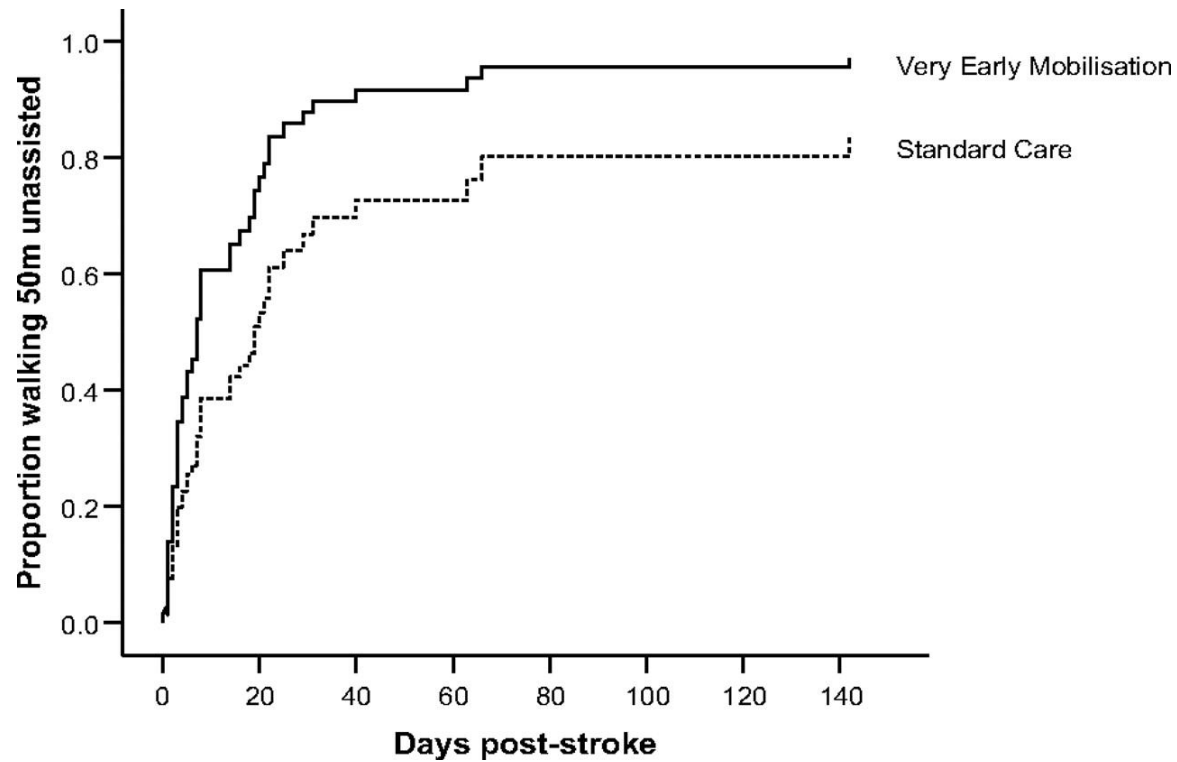|	
Safe and feasible	*(Bernhard 2008)*
even after severe stroke	*(Askin 2012)*
positive psychological effect	*(Cumming 2008)*
↓ of severe complications	*(Diserens 2012)*

% of patients walking 50 m without assistance (N=71)

Cumming T B et al. Stroke 2011;42:153-158

2015 : le choc !

Very Early mobilisation within 24h of stroke onset (AVERT) *J.Bernhardt Lancet 2015*

RCT, **2104 patients**, 56 stroke units, 5 countries,

Primary criteria at 3 months :

« favourable outcome = modified Rankin Score 0-2 »

Very Early mobilisation within 24h of stroke onset (AVERT) *J.Bernhardt Lancet 2015*

	VEM 1038	Usual care 1045	OR – p value
Favourable outcome	480 (46%)	525 (50%)	0.73 (0.59-0.90) 0.004
Death	88 (8%)	72 (7%)	0.113 NS
Serious events			NS

Very Early mobilisation within 24h of stroke onset (AVERT) *J.Bernhardt Lancet 2015*

% of patients able to walk 50m without assistance = idem
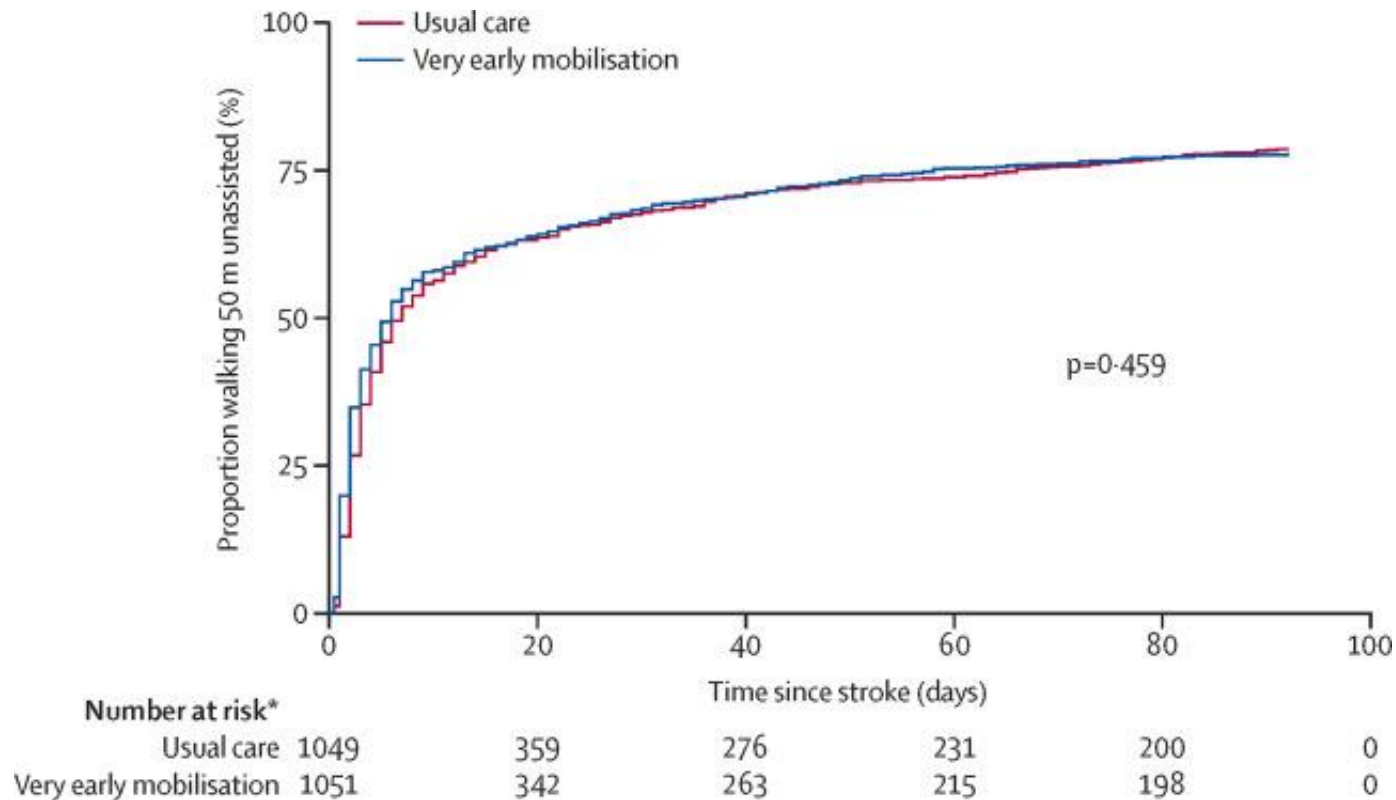
Very Early mobilisation within 24h of stroke onset (AVERT) *J.Bernhardt Lancet 2015*

A way to interpret these results
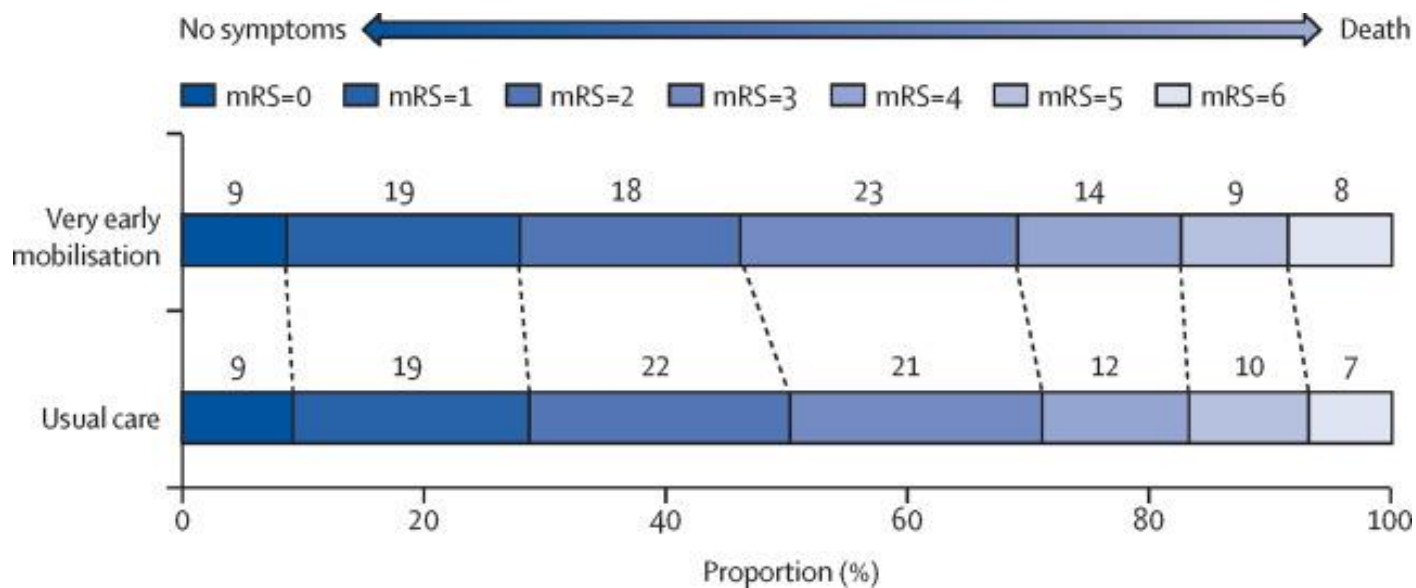
Significant differences between groups according to mobilisation.

« Usual Care » group is very different than the one of the first study++

	VEM	Usual care	p
Time to 1st mob.	18.5 hours	22.4 h	<0.0001
Freq / person	**6.5**	**3**	<0.0001
Daily amount / person	31	10	<0.0001
Total amount / person	201	70	<0.0001

Very Early mobilisation within 24h of stroke onset
(J.Bernhardt Lancet 2015)

Clear conclusion for VEM

  - beneficial when provided 3/day

  - there is no need to increase this frequency

(unfavorable outcome and trend to increase number of death)

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« Active MOBility Early after Stroke »

Multicentre RCT

A.P. Yelnik Stroke 2017

addresses the question of the amount of exercises

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Hypothesis: an active and intensive Physical Therapy (PT) conducted within the first 2 weeks after a stroke

could improve recovery of the motor control

compared to a "soft" PT devoted to the only prevention of immobility related events.

Method:

Multicenter Randomized Controled Trial

Blind assessment

Zelen design (patient unaware of the hypothesis)

Analysis in intention to treat

Stratification: centre
               severity according to NIH : <8 ; 8-15 ; >15
               age

Inclusions

1rst ischemic/haemorrhagic
            hemispheric, unilateral stroke

Age ≥ 18 years

Motor control deficiency ≥ 2 upper or lower limb (NIHSS)

From 24 to 72 hours after stroke

Intervention

The control group: received <u>"soft" PT</u> aiming at preventing immobility related events, 15-20 minutes/day apart from respiratory needs, at least 5 days a week.

Physical therapist had <u>to accompany the patient</u> without anticipation of its ability: passive limb mobilizations, sitting posture when allowed, help to walking if it seems possible...

Apart from the PT intervention, the patient' mobilization (sitting up in bed or chair, ambulation) was conducted by the nurse staff and the relatives according to the medical prescriptions and the usual rules of the stroke unit.

Intervention

The experimental group: received "intensive" PT defined as the same treatment than the control group added with 45 minutes of intensive exercises/day applied to the limbs and the trunk.

Active intensive physical therapy was made of: repetition of the movements, resistance applied by the PT at the limit of the patient' performance, length of each exercise, oral stimulation.

PT was free for the use of all technics.

Main Criterion:

Motor control assessed with the <u>Fugl Meyer score at D90</u>

Secondary criteria:

* Motor control: Fugl Meyer score (D15, D30 and D45)

* Number of days to walk 10 m. without human assistance

* Balance: Postural Assessment Scale for Stroke (M1, M3)

* Total length of stay in hospital (Stroke unit + PRM)

* Autonomy: mRS and FIM (M1, M3)

* Unexpected events (M1, M3)

* Quality of life (SIS)

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Population (1)

° Included 104   analysed **103**   *July 2012 to december 2014*

° 51 Control / 52 experimental group

° Median age: 65 [58;78] / 67 [61;75.5]

° Etiology: **ischemic**   **80**

                hemorragic   23

° Side: **right**   **67 (35/32)**

                left   36 (16/20)

° Thrombolysis: 41 (21/20)

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Population (2)

° <u>Initial NIHSS</u> < 8 = 19 (9/10) 18%

8-15 = 42 (21/21)	41%
> 15 = 42 (21/21)	41%

° <u>Initial Fugl Meyer</u> (max 98) median

  7 [1;18] / 9.5 [2;8.5]

° <u>Previous history</u>

HTA	72	(35/37)
Diabetus	20	(9/11)
Myocardial infarctus	8	(2/6)

  ………

Results

No difference at all

* Primary criteria (median)

Fugl Meyer	Control	Exp	
D0	7 [1;18]	9.5 [2;28.5]	NS
D30	15.5 [4;62]	28 [9;67]	NS
M3	41.5 [14;76]	54 [22;80]	0.32 NS
M3/D0	27.5 [12;40]	22 [12;56]	0.69 NS

No difference according to: side, NIH, thrombolysis, aetiology

Mean Fugl Meyer
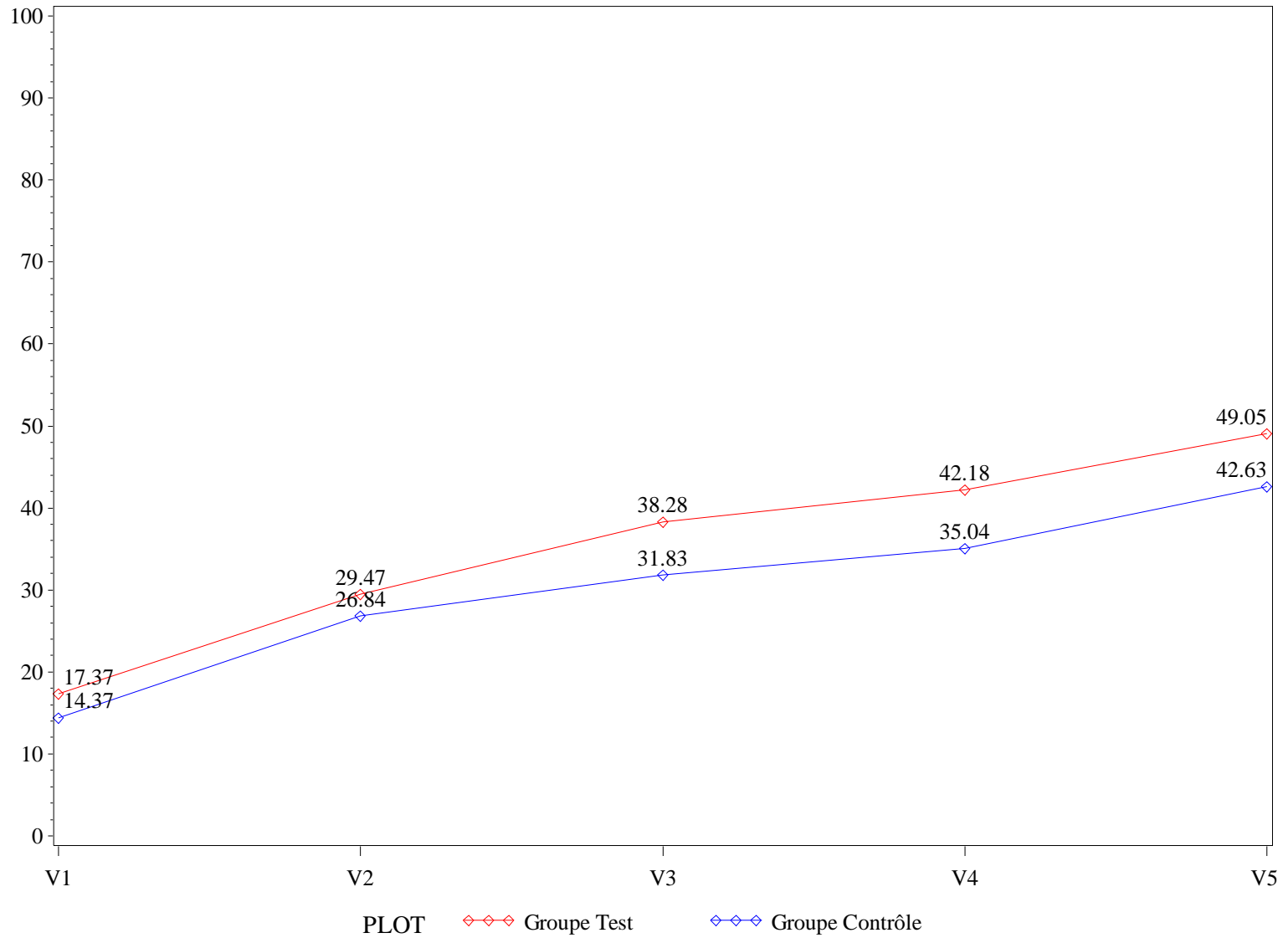
* PASS (median)

	Control	**Exp**	
D30	25 [8;33]	25 [16;32]	NS
D90	31 [21;35]	32 [27;34]	NS
D90/D30	3 [1;8]	4 [0;10]	NS

No difference according to: side, NIH, thrombolysis, aetiology

* Walk 10m. without human assistance at D90

	Control	**Exp**	**p**
Acquired walk	28 (55 %)	33 (63.5 %)	0.36 NS
Delay (days/median)	41 (25;93)	42.5 (23.5;87)	0.76 NS
DC	2	4	

* Length of stay (median)

	control	exp	
Still hospit.	35 (68.6%)	28 (53.8%)	0.34 NS
Dead	2 (3.9%)	4 (7.7%)	

No difference according to: side, NIH, thrombolysis, aetiology

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* FIM (Median) (motor sub-score 18-91)

FIM	Control	Exp	
D30	48 [23;71]	55.5 [31;69]	NS
D90	73.5 [36;87]	77.5 [59;87]	NS

No difference according to: side, NIH, thrombolysis, aetiology

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* Modified Rankin score

	D30 Control/Exp.	D90 Control/Exp.
1	2 (4.5%) /0	4 (9 %) / 3 (7 %)
2	2 (4.5%) /5 (11 %)	10 (21 %) / 12 (27 %)
3	11 (22 %) / 8 (17 %)	11 (24 %) / 15 (34 %)
4	24(49 %) / 27 (59 %)	17 (37 %) / 13 (30%)
5	10 (20 %) / 6 (13 %)	4 (9 %) / 1 (2%)
Total	*49/ 46*	*46/ 44*
p	0.34 NS	0.55 NS

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* Stroke Impact Scale at D90

-   Each of the 8 Questions

no difference

-   Visual analogic scale

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- **Unexpected events**

  Falls: 74 in 37 patients (13/24)

  Epilepsy: 8 in 5 patients (5/0)

  Cardiac or neurologic vascular event: 26 in 20 patients

	Control	Exp	Total subjects / events
D30	25	25	50/98
D90	36	39	75/142

No difference according to NIH

Results among the followed cohort at 12 months

61 patients

      40 males,

      45 right hemispheric lesions,

      47 ischemic lesions,

      age 63.1 ± 12.1

Nb of patients with <u>moderate stroke</u> (NIHSS<8)

      was higher (25%) than in the initial group (10%).

Results among the followed cohort at 12 months

No significant differences

but <u>interresting trend</u> to better results in the experimental group

	Control	Exp	
Fugl Meyer M12/D0	36.7	36.1	
FIM at M12	73.4	78.5	NS
length of stay (days)	127.6	92.8	NS
time to walk 10 meters alone	43.2	35.4	NS

Could be in favour of intensive physical rehabilitation among patients with <u>less severe stroke</u>

<u>Discussion</u>

Small population

But strength of the results as, calculated on the basis of these data:

the needed population in order to observe a possible difference between groups at 3 months should be at least 4000 subjects!

Conclusion

Dans les suites d'un AVC de gravité modérée ou sévère,
il ne semble pas nécessaire, voire délétère, de débuter une
kinésithérapie intense très précocément.

Il pourrait en être différemment après AVC plus léger.

Merci de votre attention
Et n'oubliez pas :