A HEART FOR RUNNING – SAFETY CONSIDERATIONS ON AEROBIC EXERCISE IN THE SUBACUTE PHASE OF STROKE – DATA FROM THE PHYS-STROKE TRIAL

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Introduction

Within the subacute phase of stroke aerobic exercise including treadmill training is a promising rehabilitative therapy (Saunders et al, 2016) to improve walking abilities and minimize physical deterioration but its safety still needs to be further analyzed. Our aim was to identify patients from the trial “Physical fitness in subacute stroke – PHYS-Stroke” with an increased risk of encountering a serious adverse event (SAE) during or after an aerobic exercise intervention in the subacute phase of stroke.

Methods

Data are drawn from the German endpoint-blinded, multicenter, randomized clinical trial ‘Physical Activity in Subacute Stroke (PHYS-Stroke)’ (Flöel et al, 2014). In this trial patients in the early subacute phase of stroke (day 5-45 after stroke) were recruited from seven rehabilitation clinics in and around Berlin. Patients were randomized to receive 25 minutes of either treadmill-based, aerobic physical exercise (PHYS) or relaxation sessions (RELAX) five times per week for four weeks, in addition to standard rehabilitative therapy.

Study design

Safety Assessment

Safety endpoints were recorded until 6 months post stroke and comprised recurrent fatal or no-fatal cardiovascular event including stroke, hospital re-admissions, and death.

Results

Safety analyzes are on the basis of 200 patients who were randomized in the trial (end of recruitment: April 30th, 2017; Database closed: Nov 10th, 2017)

	All n = 200	PHYS n = 105	RELAX n = 95	Odds Ratio (95% CI)	p
Stroke, n [%]	14 [7%]	10 [10%]	4 [4%]	2.40 (0.73 – 7,91)	0.15
Myocardial infarction	0	0	0		
Admission to hospital, n [%]	26 [13%]	19 [18%]	7 [7%]	2.78 (1.11 – 6.94)	0.03
Death, n [%]	5 [3%]	1 [1%]	4 [4%]	0.22 (0.02 – 1.99)	0.18

- 57% (n = 8) of recurrent strokes and 35 % (n = 9) of readmission to hospital happened during intervention phase
- SAEs happening in the PHYS group lead to a worse health status in 34% compared to 23% in the RELAX group (PHYS n = 32, RELAX n = 13, not significant)
- Patients with recurrent strokes were more often older, females with an early intervention start compared to the entire trial population
- Recurrent strokes within the intervention phase happend in the PHYS group (p = 0.01) and were older than 75 years of age and predominantly female (75%)
- Patients with readmission to hospital during intervention phase were more likely to have atrial fibrillation (56%, p = 0.03) and/or a stroke form with a cardioembolic aetiology (56%, p = 0.03)
- No myocardial infarction were reported
- Death happened more often in the RELAX group but none were regarded as related to the intervention by the data safety monitoring board
- Self-reported falls occurred more often in the PHYS group (n = 36) than in the RELAX group (n = 14, p = 0.01) but had no serious consequences

Event	All N = 200	Stroke N = 14	Readmission N = 26	Death N = 5
Female sex, n [%]	81 [41]	10 [71]*	14 [54]	3 [60]
Age in years, Mean [SD]	69 [12]	76 [8]*	71 [9]	71 [4]
NIHSS, Median [IQR]	9 [5 – 12]	5 [4 – 9]*	10 [4 – 14]	5 [4 – 11]
Time until intervention in days, Median [IQR]	28 [17 – 40]	18 [11 – 29]*	24 [13 – 40]	21 [11 – 26]
Right hemisphere, n [%]	110 [55]	11 [79]	19 [74]	3 [60]
Ischemic Stroke, n [%]	181 [91]	14 [100]	25 [96]	5 [100]
LAA, n [%]	36 [20]	3 [21]	7 [27]	2 [40]
Cardioembolism, n [%]	36 [20]	1 [7]	9 [35]	1 [20]
Small vessel occlusion, n [%]	31 [17]	4 [29]	0 [0]	1 [20]
Other etiology, n [%]	7 [4]	0 [0]	1 [4]	0 [0]
Undetermined etiology, n [%]	62 [34]	4 [29]	8 [31]	1 [0]
Competing etiologies, n [%]	9 [5]	2 [14]	1 [4]	1 [20]
Atrial fibrillation, n [%]	46 [23]	3 [21]	9 [35]	0 [0]
Arterial hypertension, n [%]	166 [83]	14 [100]	21 [81]	4 [80]
Coronary artery disease, n [%]	29 [15]	4 [29]	4 [15]	3 [60]*
Previous stroke, n [%]	38 [19]	4 [29]	6 [13]	0 [0]

* Statistical significant with p < 0.05; tests performed using χ² statistics

Discussion

Despite its many advantages to prevent from secondary events an aerobic fitness intervention might provoke further complications in older females or in patients with cardiac comorbidities in the subacute phase of stroke and should be administered with caution or in the later phase of recovery. An increased occurrence of falls has been reported by other trials and warrants further assessment to prevent from fractures or trauma.

Saunders DH, Sanderson M, Brazzelli M, et al. Physical fitness training for stroke patients. *Cochrane Database Syst Rev.* 2016;10(3)

Flöel A, Werner C, Grittner U, et al. Physical fitness training in Subacute Stroke (PHYS-STROKE)--study protocol for a randomised controlled trial. *Trials.* 2014;15:45

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