INDIVIDUAL BALANCE TRAINING VS. GROUP BALANCE TRAINING TO IMPROVE WALKING SPEED POST STROKE- A RANDOMIZED, CONTROLED PILOTSTUDY

Study type:	Other clinical trial
Study Category:	Category A
Study registration:	Swiss Clinical Trials Portal, ClinicalTrials.gov
Study identification:	Not yet known
Sponsor person and investigators persons:	Sponsor person - Prof. Dr. med. Peter Sandor Director Neurology RehaClinic RehaClinic Baden-Dättwil c/o Kantonsspital Baden, Im Ergel 1 5404 Baden, Switzerland Study director in RehaClinic Kilchberg - Dr. med. Caroline Jagella RehaClinic Kilchberg Grütstrasse 60, 8802 Kilchberg, Switzerland Study director Danube university Krems a.d. Donau - Ass.-Prof. Dr. Yvonne Teuchl Donauuniversität Krems Dr.-Karl-Dorrek-Straße 30, 3500 Krems an der Donau, Austria Principal Investigator: - Wiebke Weigert, BA Haldenstrasse 26 8134 Adliswil, Switzerland
Experimental intervention:	Individual and group balance training
Testplan-version and Date:	2.0 und Dezember 2019 20.11.2018

Confidential

The information in this test plan is strictly confidential and property of RehaClinic AG. They serve to inform the investigators, the other persons involved in the clinical trial and the ethics committees and the regulatory authorities. This test plan may not be duplicated - in whole or in part - without the consent of RehaClinic AG and may not be passed on to bystanders.

Contents

STUDY SYNOPSIS

Sponsor person	Prof. Dr. med. Peter Sandor
Study title:	***INDIVIDUAL BALANCE TRAINING VS. GROUP BALANCE TRAINING TO IMPROVE WALKING SPEED POST STROKE- A RANDOMIZED, CONTROLED PILOTSTUDY***
Protocol version and date:	Vers. 2.0, 20.11.2018
Registry:	Swiss Clinical Trials Portal Clinicaltrials.gov
Category:	Other clinical trial category A
Background and Ratio:	The RehaClinic Kilchberg is a neurological rehabilitation facility with the phases B-D (after Schönle 1996). Between February and the end of March, out of 78 patients, 71% had stroke patients. Therefore, my choice of topic for the Master's thesis fell on the stroke. The duration of the study is based on the timetable for the Master's thesis. Initially, 20 stroke patients will be recruited. When the number is reached, the study is completed to begin descriptive statistics and analyze potential BIAS. The primary goal of the study is to determine if there is a difference in effect size when comparing individual balance training to group balance training. Since only 7% of inpatient rehabilitation patients were able to climb stairs at discharge and had reached sufficient walking speed to be safe and independent in everyday mobility (Balasubramanian, Clark, & Fox, 2014), the primary outcome is walking speed. It is determined with the 10m walk test. The secondary outcome of balance is captured by the Berg Balance Scale. The ability to walk is determined by the functional ambulation categories (FAC). Deficits in the vestibular, visual, motor, and / or somatosensory systems lead to falls in the first 6 months after the stroke. This affects approximately 46% of patients (Mackintosh, Hill, Dodd, Goldie, & Culham, 2005). But also cognitive processes, such as attention and concentration. Therefore, the treatment must be adapted to the respective strategy of the patient. If the patient increasingly uses the visual system, the therapy has to work a lot with the eyes closed. In turn, if he uses more of the sensory motor system is increasingly trained with unstable documents (Mehrholz, Ada, Dean, Dettmers, & Dohle, 2011). After this system, the balance program was set up. It is the same for the intervention and control group to make a difference between individual and group training.
Goal:	Goal: A suitable sample size is to be determined for a larger follow-up study and the study design should be checked for feasibility. Question: In stroke patients, is there a difference between individual and group balance training in terms of improving walking speed? Hypothesis: individual balance training has a better impact on walking speed than group balance training. Primary outcome: gait speed → 10m walking tests Secondary outcome: Berg-Balance Scale, FAC

Participants:	It will recruit 20 patients after stroke at the RehaClinic Kilchberg.
Study design:	controled, randomized, open pilot study with paralell groups - monocentric
In/Exclusion criteria:	Inclusion: min. 18 years, stroke starting from rehabilitation phase B, ability to understand therapy instructions, walkable with aids Exclusion: Neurodegenerative disease, non-stroke dizziness, cardiopulmonary insufficiency, polyneuropathy, peripheral vascular disease
Experimental intervention:	individual balance training: after the initial assessments, the three week intervention time begins, which is completed with the reassessments. The patients receive 2x weekly individual balance training for 25 minutes each. This runs in addition to the normal, prescribed rehabilitation program. The rehabilitation program includes at least 3 therapies daily. These may be group therapies, speech therapy, occupational therapy, neuropsychology and physiotherapy adapted to the needs of the patient. In physiotherapy and occupational therapy no balance training may be performed during the intervention period.
Controle intervention:	The patients receive 2x weekly group balance training for 25 minutes each. This runs in addition to the normal, prescribed rehabilitation program. The rehabilitation program includes at least 3 therapies daily. These may be group therapies, speech therapy, occupational therapy, neuropsychology and physiotherapy adapted to the needs of the patient. In physiotherapy and occupational therapy no balance training may be performed during the intervention period. In group therapy are 3 to 6 patients with different neurological diagnoses. As it is usual in rehabilitation everyday life.
Number of participants:	In total, 20 patients should be recruited. 10 in the intervention group and the other half in the control group.
Study period:	It will start as soon as possible after the positive decision of the ethics committee. Expected on 07.01.2019. The last patient will complete the intervention on 26.04.2019. The positive decision of the ethics committee arrived at 19.12.2018.

Timeplan:	▪ I check the submitted reports one day before arrival, if the patient is suitable and inform the doctors (head doctor, senior physician and assistant doctors of the ward) ▪ The doctors check this again on the admission day and give me feedback ▪ I go to the patient on the second day and inform him / her about the ongoing study and give him / her the consent ▪ If the patient has signed, the berg balance scale and the 10m walk test will be performed on the same or the next day and the envelope will be drawn for randomization. ▪ Then he will be assigned at the next opportunity so that he gets the balance training twice a week
Investigator:	Wiebke Weigert, Physiotherapist, BA Haldenstrasse 26, 8134 Adliswil, Switzerland w.weigert@rehaclinic.ch +41774461693
Study location:	RehaClinic Kilchberg, Grütstrasse 60, 8802 Kilchberg, Switzerland
Statistic Analyses:	It is applied by the low descriptive statistics record and the SampleSize is determined. It uses SPPS version 25 and G * Power Vers. 3.1.9.2
GCP:	This clinical trial will be conducted in compliance with the protocol, the current version of the Helsinki Declaration and ICH-GCP, as well as national guidelines and legislation.

LIST OF ABBREVIATIONS

BBS	Berg Balance Scale
CRF	Case Report Form (Prüfbogen)
IB	Individual balance
eCRF	Electronic Case Report Form (elektronischer Prüfbogen)
FAC	Functional ambulation categories
GB	Groupbalance
GCP	Good Clinical Practice (Gute Klinische Praxis)
ICH	International Council on Harmonization
ISF	Investigator Site File/Prüfzentrums-Ordner
SAE	Serious Adverse Event
SDV	Source Data Verification
SNCTP	Swiss National Clinical Trial Portal
SOP	Standard Operating Procedure
TMF	Trial Master File

VISITATION PLAN

Testplan periode	**Screening**	**Treatment periode**							**Follow-up**
week	**-1 bis 1**	**1**	**1-2**	**2**	**2**	**2-3**	**3**	**3**	**3 until rehabilitation ends**
Visitation	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Participant information and consent	x								
Demografic Data	x								
Anamnese	x								
In-/Exclusion	x								
Physical examinaton	x								x
Vital signs	x	x	x	x	x	x	x	x	x
Laboratory	x								x
Randomisation	x								
Assessments	x								x
Testintervention	(x) Je nach Anreisetag	x	(x)	x	x		x	x	
Medication	x	x	x				x	x	x

1 TESTPERSONS AND ADMINISTRATIVE STRUCTURE OF THE STUDY

1.1 Sponsor person

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1.2 Leading Persons at the location

Leading doctor RehaClinic Kilchberg
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1.3 Statistics/Biometrics

It is applied by the low descriptive statistics record and the SampleSize is determined. It will be use SPPS version 25 and G * Power Vers. 3.1.9.2

2 ETHICS UND REGULATORY ASPECTS

Before proceeding with this study, in accordance with local regulatory requirements, the protocol, the patient information draft and consent form, together with the other study-specific documents, should be sent to a properly composed, competent ethics committee for formal trial approval.

The decision of the competent ethics committee regarding the conduct of the study will be communicated to the sponsor examiner in writing before the beginning of the experiment. The clinical trial may begin only after approval by the EC has been obtained. Registrierung

Die Pilotstudie wird im Swiss Clinical Trials Portal registriert.

2.1 Study category

Category A: *The examined health-related intervention is associated with only minimal risks and burdens.*

2.2 competent Ethic commission (EC)

For the clinical trial, the approval of the properly composed competent ethics committee will be obtained. The reporting obligations and the prescribed time windows are adhered to. No significant changes will be made to the protocol without the prior approval of the sponsor and the Competent Ethics Committee. Excluded are situations in which immediate danger is to be averted from the participating persons.

A planned termination of the trial must be reported to the EC within 90 days, premature termination or interruption within 15 days. The final report must be submitted within one year after the end of the clinical trial. Amendments are to be reported according to chapter 2.9.

2.3 Conduct the studies according to ethical guidelines

This study is conducted in compliance with the principles outlined in the current version of the Helsinki Declaration, in accordance with Good Clinical Practice (GCP) issued by the International Committee for Harmonization (ICH), as well as Swiss legislation.

The Ethics Committee will be informed in accordance with local requirements with annual safety reports and interim reports of any other changes, the course of the clinical trial, and the end / stop of the trial.

2.4 Declaration of Interest

It states that there are no competing interests and intellectual, financial and copyright independence is respected.

2.5 Participant information and consent

The investigator must explain to each participant the nature and purpose of the clinical trial, the intended actions, the likely duration, the benefits and possible risks, and any inconvenience this may cause. Each participant must be informed that participation in a clinical trial is voluntary, that he / she may terminate the activity at any time, and that withdrawal of the consent will not interfere with his / her subsequent medical treatment / care.

The study participant must be informed that his / her medical records can be inspected by other, authorized persons in addition to the attending physician.

All study participants will be provided with participant information and a declaration of consent, which describes the study and contains sufficient information so that the participants can make an informed decision about their study participation.

The participant information and informed consent will be presented together with the study protocol for review and approval by the Competent Ethics Committee and Swissmedic. The formal consent of a participant must be obtained before the participant participates in any study activity. The approved consent form must be used for this purpose.

The participant should read and rethink the information before signing and dating the consent form. The consent form must also be signed and dated by the investigator or his deputy and kept as part of the study documentation.

2.6 Confidentiality of the subscriber data

The investigators are responsible for ensuring that all study-related information and data collected are kept strictly confidential. Any transfer of information to persons who are not directly involved in the study must be approved by the owner of the data.

Data collection, dissemination, archiving and analysis of personal data within the study are strictly based on the valid Swiss data protection regulations. The prerequisite for this is the voluntary approval of the test participants, which is given by signing the declaration of consent before participating in the clinical trial.

Personal medical information of a participant obtained in the study should be considered confidential and disclosure to third parties is prohibited. Confidentiality is further ensured through the use of subscriber identification numbers (IDs) associated with the electronically stored treatment data.

If the participant has given their written consent, this medical information may be passed on to the family doctor or other treating physicians to ensure the well-being of the subject.

The data collected during this clinical trial are available for review or inspection by monitors and the independent EC.

2.7 *Premature termination of the experiment*

Under the following conditions, the sponsor investigator may terminate the clinical trial prematurely:

• ethical concerns,

• insufficient patient recruitment,

• if the safety of the participants is doubtful or endangered,

• Change in accepted clinical practice, which would make it unwise to continue the experiment

• Achieving a positive or negative result earlier than expected.

2.8 Protocol amendements

Significant amendements are only to be implemented after approval by the competent Ethics Committee.

For the competent ethics committee are considered substantial changes:

- changes affecting the safety and health of the participants or their rights and obligations;
- Amendments to the control plan, including changes due to new scientific knowledge, including the experimental design, the test method,
- concern the target criteria or the statistical evaluation concept;
- the change of the place of performance or the conduct of the clinical trial at an additional site; or
- the change of the sponsor, the coordinating investigator or the investigator responsible at a place of performance.

In emergency situations, without the consent of the sponsor, the ethics committee may be waived from the protocol to ensure the rights, safety and well-being of the participants. These deviations must be documented as soon as possible and reported to the sponsor and the ethics committee. All non-essential Amendements are to be notified to the Ethics Committee with the annual safety report.

3 INTRODUCTION

Every year, around 16,000 Swiss people a stroke (Meyer, Simmet, Arnold, Mattle, & Nedeltchev, 2009). This leads to the interruption of the blood supply in the brain. This can be caused on the one hand by an ischemia, or by a rupture of a blood vessel (World Health Organization, 2016). This often leads to limitations in everyday activities (Busch & Kuhnert, 2017). This is the main goal of the patient's treatment goals (Bohannon, Andrews, & Smith, 1988).

A 2014 review found that as many as 7% of inpatient rehabilitation patients were able to go upstairs on discharge and had reached sufficient walking speed to be safe and independent in everyday mobility (Balasubramanian, Clark, & Fox, 2014). In another study, 39% of stroke survivors fell (Nyberg & Gustafson, 1995).

Strokes often affect the exact systems we need for standing and aisle safety. According to Mehrholz et al. (2011) these are the vestibular, the visual, the motor and the somatosensory system. But also cognitive processes, such as attention and concentration play an important role here. Therefore, it seems likely that single-balance training is more efficient to improve walking speed. There is less distraction, with 55% of stroke patients complaining of lack of concentration (Hochstenbach, Prigatano, & Mulder, 2005), and individual instruction and external feedback promoting and supporting patient autonomy (Wulf, 2011)

In the reviews by Pollock et al (2014) or also by Dohle et al. (2016), different treatment approaches are analyzed and compared. So far, however, it has not been examined whether there is an effect difference in the intervention itself, whether this is done in individual or group settings. Therefore, in this pilot study, group balance training will be compared to single-weight training (Dohle, et al., 2016).
Therefore, a pilot study will be carried out to determine the feasibility of an RCT. This will reveal BIAS and determine the SampleSize needed to get a meaningful result.

3.1 Background and Ratio

The RehaClinic Kilchberg is a neurological rehabilitation facility with phases B-D. Between February and the end of March, out of 78 patients, 71% were stroke patients. Therefore, my choice of topic for the Master's thesis fell on the stroke. Sufficient patients should be recruited for the study period from July to the end of September. The duration of the study is based on the timetable for the Master's thesis. Initially, 20 stroke patients will be recruited. Once the number has been reached, the study is completed in order to be able to start with the descriptive statistics and to analyze potential BIAS.

The main purpose of the study is to determine if there is a difference in effect size when comparing single-balance training to group-balance training. Since only 7% of inpatient rehabilitation patients were able to climb stairs at discharge and had reached sufficient walking speed to be safe and independent in everyday mobility (Balasubramanian, Clark, & Fox, 2014), the primary outcome is walking speed. It is determined with the 10m walk test. The secondary outcome of balance is captured by the Berg Balance Scale. The ability to walk is determined by the FAC.

Deficits in the vestibular, visual, motor, and / or somatosensory systems lead to falls in the first 6 months after the stroke. This affects approximately 46% of patients (Mackintosh, Hill, Dodd, Goldie, & Culham, 2005). But also cognitive processes such as attention and concentration play an important role. Therefore, the treatment must be adapted to the respective strategy of the patient. If the patient increasingly uses the visual system, the therapy has to work a lot with the

eyes closed. In turn, if he uses more of the sensorimotor system is increasingly trained with unstable documents (Mehrholz, Ada, Dean, Dettmers, & Dohle, 2011). After this system, the balance program was set up. It is the same for the intervention and control group to make a difference between individual and group training. The group size results from the specification of the RehaClinic Kilchberg with a number of participants between 3-6 patients. The group will not exclusively include stroke patients, since the participants in rehabilitation routine are otherwise mixed up by the diagnoses. In most cases, stroke, Parkinson's, craniocerebral trauma and also tumor patients participate.

3.2 Experimental intervention und Indication

The intervention is the balance training. It is carried out by me, or by a trained employee, in the case of my absence. There is a schedule for this, which I attach with. It is standing balance training in a safe setting. So nearby a bar. It is worked with different sized support surfaces. In each position you work with closed eyes and also with head rotation. Patients should be encouraged to take a protective step if they feel they are unbalanced. This balance program is standard in our rehabilitation clinic.

3.3 Clinical data and experience

My Master's thesis is mainly about a feasibility study in order to be able to conduct an RCT on the subject. The required number of patients should be determined in order to obtain a meaningful result. Any occurring BIAS should be discussed and solutions found.

The walking speed and fall risk of stroke patients are determined from the moment of walking in a neurological rehabilitation clinic.

3.4 Justification oft he experimental intervention

The individual balance training will take place twice a week. This is sufficient to improve the balance (Mehrholz, Ada, Dean, Dettmers, & Dohle, 2011). The time is determined by the hospital setting. The effective practice time will be 25 minutes per balance unit, with a 30 minute clocking. Before the first intervention and after the 6th (last) the assessments are tested. During the intervention period, no balance training will be carried out in the other individual therapies or even in the group. The intervention takes place in addition to the normal therapy sessions.

3.5 Justification for the choice of the comparison intervention

In the reviews by Pollock et al (2014) or also by Dohle et al. (2016), different treatment approaches are analyzed and compared. So far, however, it has not been examined whether there is an effect difference in the intervention itself, whether this is done in individual or group settings. Therefore, the control group will participate in the group balance. The process will take place exactly the same as in single-balance training. Again, may be performed in the other individual therapies and not in the group. The group balance training takes place in addition to the normal therapy sessions.

3.6 Risk / benefit analysis

There is hardly an additional risk, because the balance training in the RehaClinic Kilchberg is always carried out in this way. Patients are assigned, after routine analysis, fitness for training, assessments and clinical observation of the balance group. Eventually, the additional therapy unit could cause fatigue. In order to reduce the risk of falling is trained nearby the bar, where the participants can hold if necessary.

The participants could be further promoted as they receive more therapy than intended.

Randomization does not disadvantage anyone in one of the groups (intervention / control).

At least three times a week the medical visit takes place during which patients can address questions or problems.

3.7 Participants

Stroke patients who are at least 18 years of age, are capable of judgment and do not need a legal representative are recruited.

4 GOAL OF THE STUDY

4.1 maingoal

The study is part of my master thesis. But it has found so much interest in my superiors that they would possibly perform as a larger-scale RCT. Therefore, it is designed as a pilot study to detect any occurring BIAS and to be able to calculate a sample size, which will be necessary to be able to make a statement.

4.2 Primary goal

Improvement of walking speed in stroke patients in inpatient rehabilitation through balance training. Determine if there is a difference in effect size between individual and group balance training.

4.3 Secondary goal

Determination of the improvement of the balance by means of the berg balance scale.

4.4 Safety goals

A safety goal is the fall prophylaxis. The safety is to be ensured by the bar, on which the patients can hold on, if they lose the balance. In addition, the patients should as far as possible achieve a walking speed with which they can safely cross a street.

5 TARGETS OF THE STUDY

5.1 Primary target

Improving walking speed by 18 cm/sec would be a successful outcome (Fulk et al, 2011). Whether there is a difference between individual balance training and group balance training is to be determined. To be able to cross a pedestrian traffic light, a walking speed of 1.0-1.2 m/sec would be necessary (Hüter-Becker, et al., 2005). This would be the ideal value.

5.2 Secondary target

If not already achieved in the initial assessment, a score of 45/56 points should be achieved for reassessment in the berg balance scale (BBS). That's the cut-off value (Schädler, et al., 2012).

5.3 Safety targets

The risk of falling should be reduced. In order to be able to prove this, patients should achieve a score of at least 45 in the reassessment of the BBS. In addition, a walking speed of 0.8 m/sec in a 10m walk test should be achieved.

6 DESIGN AND EXPIRATION OF THE STUDY

6.1 General design and justification of the design

A controlled, randomized, open pilot study with parallel group design will be conducted.

In each case, ten patients are recruited randomly into the intervention group or control group. It does not pay attention to gender distribution. Each patient takes about three to four weeks to participate in the study. There are three weeks of intervention time.

The screening begins with the registration of the patient, because then usually already a preliminary discharge report, or referral report exists. On the day of arrival the medical admission takes place and the screening is checked. On the second day the Investigator visit the patient and explain to him about the possible participation in the study. He receives the consent form with the explanations from me and is informed that he will answer further questions, e.g. for medical safety to the attending physician could turn. With the signed consent, the randomization and accordingly the planning of the therapies, including initial and reassessment. Depending on the day of arrival, the intervention may begin in the first or second week. With the allocation, the therapists will also be informed, since they are not allowed to do any additional balance training in the therapy. When the sixth balance training is done, the reassessment takes place the next day.

This is an ongoing process for each patient.

6.2 Study duration and time planning

It will start as soon as possible after the positive decision of the ethics committee. Expected on 07.01.2019. Respectively as soon as possible after the positive decision of the ethics committee. The last patient will complete the intervention on 26.04.2019.
Thereafter, the data is evaluated.

The positive decision of the ethics committee arrived at 19.12.2018.
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6.3 Methods to minimize bias

All physiotherapists were trained twice in the scheduled assessments. The colleague, who is to represent me in the balance training, was enrolled and the program already included by default in the balance group. If necessary, it will be retrained.

All colleagues, including nurses and doctors have received detailed information on the planned pilot study in the course of an information event and will be informed shortly before the start, if there are changes due to the ethics application.

The randomization was prepared and the sealed envelopes numbered in order.

6.4 Randomization

The randomization was prepared and the sealed envelopes numbered in order.
Randomization was done using a list randomizer (https://www.random.org/lists/). The list is not publicly available.

6.5 Mask, Blinding

There is no blinding. Compliance with the blinding is hardly feasible in this setting. The patients recognize which group they are in and the group room is freely accessible and accessible by my colleagues.

7 PARTICIPANTS

Adult patients with strokes from rehabilitation phase B are recruited as long as they are able to walk with aids. It is a monocentric study in the RehaClinic Kilchberg. There, a total of 20 patients will be recruited over a 3-month period. Since it is a pilot study, I would look for a solution in the discussion, if the number of participants would not be reached. The patients who are already inpatients are recruited insofar as the discharge date is far enough in the future and the patients who have recently arrived there.

7.1 Eligibility criteria

7.1.1 Inclusion criteria

Patients who meet all of the following inclusion criteria may be included in the clinical trial.

- min. 18 years
- stroke starting from Rehaphase B
- ability to understand therapy instructions
- walkable with aids

7.1.2 Ausschlusskriterien

If one or more of the following exclusion criteria is met, the individual can not be included in the clinical trial.

- Neurodegenerative disease
- non-stroke dizziness
- cardiopulmonary insufficiency
- polyneuropathy
- peripheral vascular diseasemännliche
- Known or suspected non-compliance with the protocol, drug or alcohol use
- Inability of the patient to follow the experimental procedure, e.g. because of language problems, mental illness, dementia etc.

7.2 Recruiting and screening

The screening begins with the registration of the patient, because then usually already a preliminary discharge report, or referral report exists. On the day of arrival the medical admission takes place and the screening is checked. On the second day I visit the patient and explain to him about the possible participation in the study. He receives the informed consent with explanations from me.

There is no compensation for participation in this pilot study.

7.3 Assignment to study groups

The randomization was prepared and the sealed, opaque envelopes numbered in order. The randomization list is not public. Only I have access to it. The procedure is based on the order of consent, so that the allocation can not be manipulated.
After signing the consent form, I go with this to one of my direct supervisor (Nicole Herzig-Ahrendt) show her the consent and give them access to the envelopes (in a lockable closet). You open the envelope and show me which group has been assigned. I label the envelope and lock it again and lock it into my spint.

7.4 Premature attempt abort of a participant

- The participant withdraws his consent
- Death of the participant
- The participant does not follow the study protocol (trains balance outside the intervention)
- The participant has one of the exclusion

If possible, the participant still receives the final medical examination and the reassessments are carried out.

If possible, the participant will be replaced. This means that the next signed declaration of consent takes this place.

Regular visits are always Monday, Wednesday and Friday. If an appointment is missed, the doctor's contact can be made up at any time. If I or the patient sees a requirement for an additional doctor contact, it will be arranged promptly (preferably on the same day). STudieninterventionen

7.5 General

Standard therapy

According to the payer, the therapy is individually composed of the following therapies:

Individual Therapies: Speech Therapy (45min), Physiotherapy (30-45), Occupational Therapy (30-45), Neuropsychology (30-180), Physical Therapy (30-60)

Group therapies: Seating group (30), MTT (60), endurance group (45), self-training (30), water aerobics (30), fine motor skills (45), memory group (45), public transport group (135), cooking group (150), arm-hand Group (45), Household Group (45)

Of these, 3-4 therapies are selected Monday-Friday.

7.5.1 Experimental intervention

Individual balance training (IB)

Standard course of balance exercises

1. Stand with a narrow track
    a. Head rotation (30 sec)
    b. Closed eyes (3x10 sec)
    c. Turn head with closed eyes (3x10 sec)

2nd Stand narrow track set half a foot, "load both feet evenly"
    a. Head rotation (30 sec)
    b. Closed eyes (3x10 sec)
    c. Turn head with closed eyes (3x10 sec)
    d. Change of feet: a-c

3rd step, "at least the toes are behind the heel and strain both feet evenly", Spurbreit depending on the level of the patient, very good patients go into tandem
    a. Head rotation (30 sec)

b. Closed eyes
c. Turn head with closed eyes (10 sec)
d. Change of feet: a-c

4. Toe stance, "big toe ball stays on the ground and can not take off"
   a. Head rotation (30 sec)
   b. Closed eyes (10 sec)
   c. Turn head with closed eyes (10 sec)
5. Stretching calves in step position with hold (2x per side, each 30 sec. Per leg)
6. Labile underlay (AirexPad, air cushion)
   Repeat exercises 1-5
7. Patients receive a disinfectant wipe with instructions to wipe the ingot and then the AirexPad.

→ Exercises keeping balance after bending over the pillow

7.5.2 Controle intervention

Group balance training (GB)

The exercise sequence is the same as IB training.

There will be between 3-6 patients. These may have different diagnoses and will not all have a stroke as a basic diagnosis.

7.6 Administration oft he experimental intervention and the controle intervention

7.6.1 Experimental intervention

Individual balance training

After the assessments, the intervention starts the next day. Twice a week the participants receive individual balance training with an effective training time of 25 minutes. Between the two days should be at least 1 day break. In total there will be six units. There must be no balance training in the other therapies. Completed with the reassessments, one day after the last IB. To exclude a training effect before the reassement.

7.6.2 Controle intervention

Group balance training

After the assessments the balance group starts the next day. The exercise sequence corresponds to the single-balance training.

For the study participants, the group will be held twice a week with 25 minutes each of effective training time. There are six units in total. It concludes with the reassessments, one day after the last GB, to exclude a training effect before the Reassment.

In the individual therapies no balance training may take place.

7.6.3 Modificationen of the intervention

All patients are made aware that their safety is paramount and they should open their eyes if they feel they are losing their balance. They are encouraged to react with a protective step, but may also be able to hold on to the bar.

Therapy is discontinued if the patient wishes he has a fever or has other contraindications to active therapy.

7.7 Compliance

Noncompliant is the patient when performing additional balance exercises during leisure time. This is actively being asked by me and the treating therapist. If this is the case he must be excluded from the study because it might affect the results.

7.8 Data collection / follow-up examinations in case of premature termination of studies

If a patient has to stop, he will be examined by a doctor on the same day. The reassessments of the physiotherapy (BBS and 10m walk test) will take place on the following treatment day if the patient has not been relocated.

7.9 accompanying interventions

There will be no rules for the medications because they are not a contraindication to balance training.

If the patients are in individual balance training, they should not receive a group balance and in the free time also not to train balance.

If the patients are in group balance training, they should not receive any balance training in the individual therapy and in the free time also do not train balance.

During the study period, therefore, the seat-and-stand group will be dropped for both groups, as this is where the balance is trained.

8 TEST METHODS

8.1 Schedule of study, Table of study measures

one day before arrival	• Screening of the remittance findings
Day of arrival	•Admission by the doctors, nursing and physiotherapy --> Screening Inclusion / Exclusion
2nd Day	•Discussion and presentation of the consent form •Information to the therapist that the patient may be eligible •in physiotherapy only BBS and 10 m walk test if patient has already signed
from the 2nd day	•Signing of consent (SC)
Day of SC	•Envelopes draw IB or GB for the allocation •Report to the scheduling about allocation and notification of the patient
SC +1d	•Assessment Primary target: Gait speed through 10 m walk test •Assessment secondary target: Fall risk due to BBS, walkabilitay due to FAC
SC +2d	• IB or GB so that it can be found twice a week (see point 8.2)
6. IB/GB	•next day reassessments •10 m walk test, BBS, FAC
Visitation	•see point visitation plan

8.2 Recording of the target values

The first introduction and training of the assessments took place in January 2018. Therefore, all physiotherapists have at least half a year of practical experience with the tests. A second training took place in February 2018 to discuss questions and to review the standardized procedure. A third review took place in November 2018.

Walking speed
The walking speed is measured using the 10m walk test. This has a high reliability for stroke patients (Flansbjer, Holback, Downham, Patten, & Lexell, 2005).
The patient walks a distance of 20m. The start and end points are each marked with a cone. The patient is asked to walk this route as fast as possible, but so that he feels safe. The measurement begins as soon as one of the lower extremities crosses the 5m mark and stops when one of the lower extremities crosses the 15m mark. The therapist goes with the patient to see this. This is to exclude the startup and stopping delays (Schädler, et al., 2012). Three consecutive passes are taken to calculate the mean.

This gives you the walking speed in m / sec if you calculate 10m divided by the seconds. If an aid was needed to go, this will be noted.
This test has high reliability with an ICC of 0.94-0.97 (Flansbjer, Holmback, Downham, Patten, & Lexell, 2005).
In addition, stroke abilities were classified as having everyday abilities (Perry, Garrett, Gronley, & Mulroy, 1995).

Falling risk
The Berg Balance Scale is used to determine the risk of falling. The BBS detects deficits at both activity and body function levels. It consists of 14 items. Scaling takes place from 0 points (not possible) to 4 points (independently possible). This results in a total score of 56 points. The individual items are shown in the template in the appendix.
Very good intertester reliability was found in a study of 112 stroke patients (Mao, Hsueh, Tang, Sheu, & Hsieh, 2002).

The best values in terms of validity resulted from the combination of the BBS with the walking speed. This gave a specificity of 70% and 91% sensitivity (Schädler, et al., 2012).

8.2.1 Recording oft he primary target

The walking speed is tested one day before the first IB or GB and one day after the last IB / GB. So a training effect that could falsify the result should be avoided. It is measured by a physiotherapist.

8.2.2 Recording secondary target

The risk of falling is tested one day before the first IB or GB and one day after the last IB / GB. So a training effect that could falsify the result should be avoided. It is measured by a physiotherapist.

8.2.3 Recording safety targets

8.2.3.1 Serious Adverse Event (SAE)

A SAE would be a fall of the patient. If this has happened, a fall protocol will be created on the RehaClinic intranet. It records how the fall came about and under what circumstances, when the fall took place, and which people were present. The patient is examined by the ward physician and, where appropriate, measures for further examination or treatment are initiated. If the patient later describes the fall, as unobserved, the same procedure nevertheless takes place.

8.2.3.2 Laboratory

For the study itself, no laboratory parameters have to be taken. They are supervised as part of the rehabilitation stay. These are mainly blood samples. See visit plan.

8.2.3.3 Vitality parameters

Blood pressure and pulse are measured at least once daily. Also several times daily measurements are possible, depending on the regulation. It is measured by the caregiver. The patient sits during the measurement.

The body temperature is monitored by an ear thermometer only after extra prescription.

Body weight is checked at least twice a week. This can also be prescribed more often, if appropriate comorbidities cause this..

8.2.4 Investigations in case of premature termination of studies

In the event of premature termination of the study which was not caused by normal termination of the stay, a new medical examination will be carried out according to the initial examination. At the discretion of the physician, additional examinations may be arranged.

8.3 Study measures during the visits

8.3.1 Visit 1 or screening Visit

The first doctor contact takes place on the day of arrival. The inclusion and exclusion criteria are examined by file review and, if necessary, by taking anamnesis and testing. The examination complies with the standard of an initial medical examination with anamnesis, inspection, palpation and complete neurological status. If necessary, special tests such as coordination and reflexes are performed.

8.3.2 Visit 2 until 8 (see visitation plan)

At each visit the condition of the patient is inquired. If abnormalities show up, further examinations such as clinical examination, ECG, EEG, X-ray, blood sample, stool sample, etc. will be available. causes. In addition, he is asked how he is doing with the study participation.

8.3.3 final visitation

During the final visit, the patient's condition is also inquired and whether he is satisfied with the participation in the study. For the last medical examination, an overall examination is again carried out as for the initial visit. This takes place according to the standard at the end of the rehabilitation stay.

9 SAFETY

Further details on the security messages can be found in the SOPs of the sponsor.

According to KlinV, SAEs are recorded throughout the study, documented in full and in a standardized manner in the source data and the test sheet, and comprehensively clarified, in which a causal relationship with the investigated intervention can not be ruled out.

The duration of the study starts with the signing of the participant's consent and ends with the last protocol-specific activity, including the safety follow-up examinations.

9.1 Definition Serious Adverse Event (SAE)

Adverse Event (AE)

An AE is any adverse medical event that occurs in a patient or participant in a clinical trial following a health-related intervention and that is not necessarily causally related to that intervention.

An adverse event (AE) may therefore be any adverse or unintentional reaction (including an abnormal laboratory finding), any symptom or disease associated with the intervention, whether causally related to the investigational medicinal product or not. An AE may also be the onset of a new disease, the worsening of a pre-existing disease, or the recurrence of an episodic disease; These may be multiple or individual complaints or symptoms.

Serious Adverse Event (SAE)

A SAE is any event that:

- requires inpatient treatment or its extension not provided for in the research plan;
- leads to permanent or severe disability or disability;
- is life threatening or leads to death; or
- results in a congenital anomaly or birth defect.

9.2 Documentation / Assessment of Serious Adverse Events

The investigator has the responsibility to identify, document and determine the causal relationship to intervention.

All SAEs are fully documented on the corresponding SAE page in the CRF. For each SAE, the investigator indicates the beginning, duration, required treatment and outcome of the SAE, as well as changes in the implementation of the intervention.

The causal relationship of the (S) AE with the study intervention is determined by the investigator according to the following definitions:

No correlation	• The event did not begin in any temporal context with the study measure and • The event can be clearly explained by the underlying disease or other factors.
Possible correlation	• The event did not begin in any temporal context with the study measure and • The event can not be explained clearly by the underlying disease or other factors.

9.3 Report of Serious Adverse Events

If SAEs occur during the conduct of a clinical trial of participating individuals in Switzerland that can not be ruled out to be due to the intervention being studied, the investigator must report these events::

- If the responsible investigator and sponsor examiner are not the same person: to the sponsor within 24 hours of becoming aware, and
  - the responsible EC within 15 calendar days.

Safety and protective measures
If prompt safety and protection measures are to be taken while conducting a clinical trial, the investigator shall notify these measures and the circumstances in which they became necessary to the EC within 7 days.

Annual safety report

The investigator submits an annual safety report to the Competent Ethics Committee.

All SAEs are summarily listed in the annual safety report to the Ethics Committee, with the following contents:
- A short, critical summary, taking into account the safety aspects;
- In the cover letter to the annual safety report, the status of the clinical trial in Switzerland should be briefly summarized (number of centers open / closed, number of patients recruited / completed, number of SAEs).

9.4 Tracking Serious Adverse Events

Participants terminating the clinical trial (regular or premature) because of

• reported, ongoing SAE, or

• sustained SAE, e.g. laboratory values or alarming vital signs,

are examined during a follow-up visit. This visit will take place until 30 days after completion of the study treatment phase. Information from this follow-up visit will be recorded in the CRF.

Follow-up visits may also be necessary at the discretion of the investigator, even if the subject does not suffer from SAE at the end of the experiment. The information of such visits must be documented only in the source data (e.g., medical records), not in the CRF..

10 STATISTICS

One aim of this pilot study is to determine an appropriate number of cases. Therefore, with the obtained data set using G * Power Ver. 3.1.9.2 the SampleSize is calculated.

Further descriptive statistics are done with SPPS version 25. The mean values for each assessment are calculated. The absolute and relative frequencies are calculated. To determine the scattering parameters, the standard deviation is determined.

To determine if there is a difference between intervention and control group, first the odds ratio is shown.

10.1 Hypothesis

Zero Hypothesis: individual balance training is more effective in stroke patients to improve walking speed than group balance training.

Alternative Hypothesis: individual balance training is not more effective.

Due to the limited number of cases, however, only one guess can be made. The number of cases is limited by the time factor of the deadline for the Master thesis. I think a realistic number for recruiting is 20 patients.

10.2 Sample size calculation

It is planned to recruit 20 patients to RehaClinic Kilchberg. This results in 10 patients each for the experimental group and the control group. This number is based more on the temporal than on the statistical factor. It serves only for the descriptive statistics in order to be able to make already first assumptions and to be able to carry out a SampleSize calculation. If this number is not reached by the end of April, the pilot study will nevertheless end. This should ensure the writing of the master thesis, so that it can be delivered on time.

10.3 plannend analysis

For the pilot study mainly the BIAS (systemic errors) should be analyzed.
These could turn out to be selective or during the test procedure. But of course also in the amount of data collected.
The collected records are also discussed.

10.3.1 Analysis of datasets and study groups

The walking speed and fall risk of stroke patients during inpatient rehabilitation is analyzed. All data is logged and merged into a table. The records are encrypted to preserve the anonymity of the patients.

10.3.2 Primary analysis

The analysis will be carried out by the investigator after completion of the entire intervention.

10.3.3 Safety analysis

The physiotherapists will be trained by the examiner in the assessments and the balance training before starting the pilot study.

10.3.4 Deviations from the original statistics plan

Should changes occur, the EC will be informed in writing and the decision substantiated.

10.4 Dealing with missing data and drop-outs

If the data can not be completed, the patient is excluded so as to avoid falsification of the results. The existing data and also the drop-outs will be archived anyway.

11 SUITABILITY TEST CENTER

The RehaClinic Kilchberg is a neurological rehabilitation facility with phases B-D. Between February and the end of March 2018, 78% of patients were 71% stroke patients. It is integrated in the Seepital Kilchberg.

The patients stay stationary between four weeks and about 5 months (with early rehabilitation).

RehaClinic AG has its own research department, which receives awards at regular intervals.

There are no other studies taking place at the same time in the RehaClinic Kilchberg.

12 QUALITY ASSURANCE AND CONTROL

The sponsor examiner is responsible for implementing and maintaining a quality system with written SOPs and Working Instructions (WI). This ensures that the clinical trial and trial data are treated according to protocol, GCP and valid law.

12.1 DOCUMENTATION AND STORAGE OF THE DATA

The clinical trial is strictly conducted according to the protocol. If changes are necessary, they must be recorded in a protocol amendment. All inspection plan changes must be signed by the sponsor investigator and submitted to the competent ethics committee for approval.

12.1.1 case report forms

For each test participant, the examiner performs a paper case report form (CRF) in which all test-relevant data of a participant are entered. All participants (subjects enrolled in the study, non-clinical subjects, or non-admitted individuals eligible for the clinical trial) will be documented in a screening log. The investigator notes a person's participation in a special enrollment log.

CRFs need to be kept up-to-date to reflect the status of a participant at each stage of the study. The name of the test participant may not be visible in the CRF. Use appropriate coding (e.g., subscriber number).

It must also be ensured that anyone who can make entries and corrections in the CRF can be identified. A list with the signature and abbreviation of all authorized persons is stored in the Investigator Site File and the central reviewer.

The documented medical history and written statements on the status of the participant during the clinical trial should be kept together with the CRF of the participant concerned. These records may also include: originals or copies of laboratory results, other medical tests (e.g., ECG), etc.

The test persons ensure complete and correct documentation of the participant data in the CRF. All data entered into the CRF must also be included in the patient record, either as printouts or as notes by the investigator or by another person delegated by the investigator.

All essential clinical trial documents must be kept for a minimum of 10 years after the end or termination of the clinical trial.

The medical records and other original data must be kept for the longest possible period of time allowed by the hospital, institution or private practice.

12.1.2 Specification oft he sources

The following documents are considered source data:

- SAE forms
- Notes from nursing staff, experimental coordinators
- Medical records from other departments or other hospitals, or discharge reports (findings, medical reports) or correspondence with other departments / hospitals if the subject was treated there during the clinical trial or during the follow-up phaseFolgende Dokumente werden als Quelldaten betrachtet:

The following information should at least be contained in the source data:

• Demographic data (age, gender)

• Details of inclusion and exclusion criteria

• Dated and signed consent letters from the participants

• Data of the visits

• Intervention details

• Details of the medical history and physical examinations

• The efficacy and safety data specified in the test plan

• SAEs and concomitant medication

• Results of relevant investigations

• Laboratory printouts

• Details on submission and return of intervention materials related to the intervention

• Reasons for early withdrawal

• randomisation

12.1.3 Recordings / Archiving

All study data must be retained for at least 10 years after termination or premature termination of the study.
They are deposited in a lockable cabinet.

12.2 Data management

All data is recorded in paper form. To encode the patients, the trial version of the eCRF of the University of Zurich is used. In order to be able to use the data for the statistics, the SPPS and G * Power are used as mentioned above. These data are stored on my account in the RehaClinic Kilchberg. This account is password-protected and access is only possible through investigator.

12.3 Routine Monitoring

Since this pilot study is a feasibility study to determine the number of patients for an RCT, independent monitoring is not organized. But considered in a possible follow-up study.

12.4 Audits and inspections

To review the conduct of the clinical trial in accordance with GCP guidelines, audits or inspections may be performed by the independent EC. The auditor / inspector receives access to all medical records, examination-relevant documents and correspondence, as well as informed consent of the test participants.

The investigator ensures that the persons responsible for the audit / inspection have access to medical records and that all arising questions are answered. All persons involved treat the data of the participants strictly confidentially.

12.5 Confidentiality and privacy

Direct access to the source documents of the clinical trial is granted during audits and inspections.

13 PUBLICATION

The pilot study will be published as part of the master thesis by Danube University Krems.

14 FINANCING AND SUPPORT

The RehaClinic Kilchberg provides me with the necessary time to supervise and / or check all processes. Dr. med. Jagella will provide expert support to the investigator and Prof. Sandor will contribute his research expertise in the form of GCP modules.

14.1 Financing

Ther will be no financing.

14.2 Other support

Mrs. Ass.-Prof. Teuchl supervises the master thesis for the Danube University Krems and will support me in the methodology.

15 INSURANCE

The insurance is covered by AXA Versicherungs AG with the policy no. 14.734.457.
This covers all damage related to the clinical trial. Participants must adhere strictly to the instructions of the trial staff in order not to jeopardize the insurance cover. Furthermore, they must not undergo any other medical treatment during the clinical trial without the consent of the investigator (except emergencies). You must inform the examiner immediately about an emergency treatment. In the event of health problems or other damage during or after the trial, the investigator should be informed.
In the event of a claim, representatives of the insurance also receive access to the medical data via the examiner, but only to the extent necessary to settle the claim.
A copy of the insurance certificate is stored in the test center folder.

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