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Exercise Training in the Treatment of Paroxysmal Atrial Fibrillation: Study Protocol of the *Cologne ExAfib Trial*

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ABSTRACT

Introduction

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia and is associated with a number of comorbidities such as coronary artery disease and heart failure. While physical activity is already implemented in current international guidelines for the prevention and treatment of AF, the precise role of different types of exercise in the management of AF remains to be elucidated. The primary aim of the *Cologne ExAfib Trial* is to assess the feasibility and safety of different exercise modes in patients diagnosed with paroxysmal AF. Secondary outcomes include assessments of physical function, AF burden, quality of life and inflammation, as well as morphological and cardiac adaptations.

Methods and analysis

In the initial pilot phase of this 4-armed randomized controlled trial we aim to enroll 60 patients between 60 and 80 years of age with paroxysmal AF. After screening and pre-testing, patients will be randomized into one of the following groups: High-intensity-interval-training (4x4 minutes at 75-85% peak power output (PPO)), moderate-intensity continuous training (25 minutes at 55-65% PPO), strength training (whole body, 3 sets of 6-12 repetitions at 70-90% one repetition maximum (1RM)) or a usual-care control group. Training will be performed twice weekly for 12 weeks. If the feasibility and safety can be confirmed through the initial pilot phase, the recruitment will be continued and powered for a clinical endpoint.

Ethics and dissemination

Feasibility and safety will be assessed by measures of recruitment and completion, program tolerance and adherence as well as reported adverse events and including hospitalization rates. Secondary endpoints will be assessed by measures of VO_{2peak} and the 1RM of selected muscle groups, questionnaires concerning quality of life and AF burden, serum blood samples for the analysis of CRP, IL-6, TNF-α and NTproBNP concentrations and ultrasound for muscle and heart morphology as well as cardiac function.

Keywords: exercise medicine; cardiac arrhythmia; physical training; high intensity interval training (HIIT); strength training

STRENGTH AND LIMITATIONS

- First clinical trial to investigate the effects of HIIT, MICT and STR of patients with paroxysmal AF
- Single center: no deviations
- Limited detection of Afib due to “only” Holter 48hour
- Dropout quote maybe high
- Selection bias: patients interested in sports will join

INTRODUCTION

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia, with an estimated European prevalence of 2%. Although this may be significantly lower compared to other cardiovascular diseases such as arterial hypertension, the prevalence is age-dependent, reaching highly significant numbers amongst seniors. Thus, AF has been reported to affect ~ 8% of adults above 65 years of age, reaching levels of >15% in age-groups of over 80 years [1]. Due to the demographic transition towards an inverted age pyramid, by 2060 the number of patients will double amongst the > 65-year old and even triple amongst the > 80-year old adults, producing ~ 25 million seniors with AF in the European Union [1].

Based on the disease progression, AF may be classified into paroxysmal (i.e. self-terminating or cardioverted within 7 days), persistent (i. e. AF persisting for > 7 days), long-standing persistent (i.e. persisting for > 1 year) or permanent (i.e. arrhythmia is accepted and restoration of sinus rhythm is no longer pursued) [2]. Symptoms may include dyspnea, palpitations and angina pectoris, all of which can dramatically decrease overall quality of life. Moreover, AF is often accompanied by severe comorbidities, such as coronary artery disease, stroke and heart failure, making it a leading cause for hospitalization [3–6]. Thus, the treatment depends on the severity of symptoms and diagnosed comorbidities but may include stroke prevention via oral anti-coagulation (OAC), medical rate control and rhythm control via medication, cardioversion or ablation therapy [7]. However, despite recent advances in medical and interventional care, the socio-economic burden remains immense and is expected to increase even further with the demographic change in society.

In addition to conventional medical treatment, lifestyle interventions have recently gained scientific interest. These mainly include the management of risk factors, such as overweight, hypertension and hyperglycemia [8]. However, studies have shown that a sedentary lifestyle significantly increases the risk for AF, while already moderate levels of physical activity appear to be a promising countermeasure [9]. Surprisingly, studies specifically assessing the effects of structured exercise interventions with the aim of improving physical fitness and quality of life, while at the same time reducing AF burden are scarce and often limited to small pilot studies [10] .

In a previous large-scale randomized-controlled trial (RCT), Risom et al. showed an increase in aerobic capacity following 12 weeks of aerobic and strength training but effects on AF burden or hospitalization were not investigated [11]. In addition, in a study by Malmo et al. a significant reduction in AF burden and concomitant increase in VO_{2peak} and quality of life were

observed following 12 weeks of aerobic high-intensity interval training (HIIT) [12]. However, in subsequent meta-analyses it was concluded that the number of high-quality RCTs is insufficient to adequately deduce the effects of exercise-based interventions in the treatment of AF [13,14]. This concern was also confirmed in a recent systematic review including the safety aspects of physical training in AF patients, irrespective of whether patients were classified as paroxysmal, persistent or permanent [15].

While physical activity is already reflected in current international guidelines for the prevention and treatment of AF [7,16], specific recommendations concerning different exercise modes (i.e. aerobic vs. resistance training) and intensities (low-intensity continuous vs. HIIT) are lacking. The *Cologne ExAfib Trial* is a phase I clinical trial, that primarily aims at systematically assessing the effects of distinct exercise modes on the feasibility and safety of patients diagnosed with paroxysmal AF. Secondary outcomes will include assessments of the physical function, AF burden, quality of life (QoL), inflammation, muscle morphology as well as cardiac function. The outcomes of this trial will be used to further improve clinical knowledge pertaining to exercise prescription for AF patients. In addition, findings of this study will also be used do design phase II trials which will help to establish guidelines for exercise prescription.

MATERIALS AND METHODS

The current study will be carried out in accordance with the declaration of Helsinki and received ethical approval by the local ethics committee (175/2018, German Sports University Cologne, Germany). All participants will be comprehensively informed about the study procedures and are requested to provide a signed informed consent prior to participation. The study is registered both at the German and at the WHO trial registers (DRKS00016637).

Study design

The *Cologne ExAfib Trial* is a prospective 4-armed, randomized controlled trial (Fig. 1). Following recruitment and pre-screening, patients will be randomized into one of the four groups: aerobic moderate-intensity continuous training (MICT), HIIT, strength training (STR) or usual care (CON). After screening, patients that were randomized to the exercise groups will perform 12 weeks of supervised exercise training. Patients that were randomized to the usual care group will be asked to continue with daily habitual activities but will be offered to participate in supervised exercise training after completion of the study. All patients will be followed-up at 3 months after the completion of the intervention period.

Patient recruitment

Patients will be recruited by invitation of their treating practitioner. Local hospitals and practitioners will provide eligible patients with written information on the study procedures and will refer these patients to the study coordinator. The detailed inclusion- and exclusion criteria are presented in Table 1.

Table 1: In- and exclusion criteria

Inclusion criteria	Exclusion criteria
▪ Women and men with symptomatic paroxysmal atrial fibrillation (EHRA ≥ 2) ▪ Age of 60 to 80 years ▪ BMI ≤ 35 kg · m^{-2}	▪ Participation in regular aerobic or resistance exercise training in the last six months (> 60 minutes/week) or former high-performance athletes ▪ Left ventricular ejection fraction < 40% during sinus rhythm ▪ Significant valve disease ▪ Implanted cardiac pacemaker, ICD or resynchronization therapy ▪ Coronary artery disease without complete revascularization or unstable angina pectoris ▪ Uncontrolled limiting comorbidities (hypertension, diabetes mellitus, hyperthyroidism, etc.) ▪ Prior pulmonary vein ablation ▪ Any contraindication to strenuous exercise or testing

BMI: body mass index; EHRA: European Heart Rhythm Association; ICD: Implantable Cardioverter Defibrillator

Patient and public involvement

Patients and the public were not involved in any way.

Sample size calculation

Due to the novelty of this phase I clinical trial with the primary endpoint of safety and feasibility, the sample size was assessed based on previous studies investigating the effects of aerobic [11] or combined aerobic and strength training [12] on secondary outcomes, such as physical function. The sample size calculation was performed by G*power (version 3.1.9.2, Heinrich Heine University, Dusseldorf, Germany). For an effect size of 0.5, with a power (1-β) of 0.8 and an alpha level of 0.05 (two-tailed), a total of at least 40 patients would be needed. Since attrition is not known in this population and data on safety and feasibility are lacking for some of the exercise interventions utilized, we will initially include 60 patients (15 per group). Based on the initial findings, recruitment will then continue with distinct exercise regimens and will be powered based on a clinical endpoint.

Screening and randomization

This trial spans over a total duration of 14 weeks. After pre-screening and baseline testing, the patients will be randomly allocated in a ratio of 1:1:1:1 to the four study arms. A research officer

will perform randomization with no patient contact using a stratified minimization approach by RITA (Randomization In Treatment Arms, Evident, Germany). The stratification factors will include i) patients age, ii) gender and iii) BMI. Study investigators and exercise physiologists conducting testing procedures will be blinded to group allocation.

Interventions

Patients randomized into one of the training groups will perform supervised training twice weekly over a total duration of 12 weeks. All training sessions will be electronically recorded (Heart rate, workload, sets and repetitions; HUR Healthfitness Equipment; Kokkola, Finland; Ergoline ergoselect; Bitz, Germany). In addition, a one-lead ECG will continuously monitor cardiac function. Habitual physical activity will be assessed objectively in all groups (including the control group) by a wrist-worn activity tracker (ActiGraph GT9X, ActiGraph, LLC, Pensacola, FL). Assessment of habitual physical activity will be performed over 7 days at the following time-points: baseline, after 6 weeks (mid-point testing), after 12 weeks (end-point testing) as well as at the three-month follow-up.

All training sessions are time-matched (i.e. 40 minutes). Training sessions will include a standardized warm-up (5 minute cycling at 30% of peak power output [PPO]) and cool-down (10-minute cycling 30% PPO). Each training session will be concluded by an additional 10-minute recovery period, including a standardized stretching routine. Perceived exhaustion, pain and dyspnea will be assessed by visual analog scales ranging from 0 (no symptoms) to 10 (severe symptoms), prior to as well as immediately after each training session.

MICT: Training will be performed on a stationary cycle ergometer (Ergoline ergoselect; Bitz, Germany) at a target exercise intensity of 55 to 65% of PPO for 25 minutes. The training intensity will be initiated at 55% of PPO and will be progressively increased by 5% every 4 weeks.

HIIT: Training will be performed on a stationary cycle ergometer (Ergoline ergoselect; Bitz, Germany) and will consist of 4 × 4 minutes at 75 to 85% of PPO, separated by a 3-minute active rest at 30% of PPO. Initially, the intensity of high-intensity bouts will commence at 75% PPO and will progressively increase by 5% every four weeks.

STR: Strength training will consist of the following upper and lower body exercises, using pneumatic devices (HUR Healthfitness Equipment; Kokkola, Finland): Leg press, knee extension, hamstring curls, seated chest press, seated row, lat pull-down and shoulder press. Exercise load will be determined individually as percentage of the one-repetition maximum

(1RM). The exercises will be performed as a circuit with a 2-minute rest between sets. Every session includes leg press, seated row and chest press, while shoulder press or lat pull-down as well as knee extension or hamstring curls will be performed on alternating days.

The strength training intensity will be increased progressively every two weeks until week eight as follows: 3 sets of 12 reps at 70% 1RM, 3 sets of 12 reps at 75% 1RM, 3 sets of 10 reps at 80% 1RM, 3 sets of 10 reps at 85% 1RM. The intensity of the remaining four weeks will be 3 sets of 6 reps at 90% 1RM.

Measurements

All primary and secondary endpoints will be assessed at baseline (T0) as well as at end-point testing (T2) and the 3-months follow-up (Fig. 1). Venous blood samples will be additionally drawn at mid-point testing. Additional measures of feasibility and safety will be assessed throughout the study period (Table 2).

Primary endpoints

Feasibility of the exercise interventions will be quantified by measures of recruitment and completion, program tolerance and program adherence (Table 2). In order to calculate recruitment rates, the number of referrals will be compared to the number of patients who are deemed eligible after pre-screening. In addition, eligibility rates will be determined by the ratio of eligible patients and those actually enrolled in the trial. Program tolerance will be assessed by measures of perceived exhaustion, pain and dyspnea as well as continuous ECG recordings throughout each training session. The number of completed training sessions as well as the time and/or sets completed in each training session will determine program adherence.

Patient safety will be assessed by means of recorded adverse and severe adverse events as well as hospitalization rates (Table 2). Adverse events and severe adverse events will be graded as adapted from the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, including also events related to exercise training (such as muscular pain and fatigue).

Table 2: Assessment of safety and feasibility. Modified from Hart et al. (2018) [17].

Measures	Time of collection
Feasibility – recruitment and completion	
Referred patients	Trial completion

Eligible patients	Trial completion
Enrolled patients	Trial completion
Trial completion	Trial completion
Patient withdrawals	Trial completion
Patient drop-outs	Trial completion
Feasibility – program tolerance	
Pre- and post-sessional exhaustion, pain and dyspnea	At each exercise session
ECG-recordings	At each exercise session
Feasibility – program adherence	
Number of completed sessions	Trial completion
Time/sets completed in each session	At each exercise session
Patient Safety	
Number of adverse events	Once weekly and 3-months follow-up
Number of severe adverse events	Once weekly and 3-months follow-up
Hospital admissions/days of hospitalization	Once weekly and 3-months follow-up

Secondary endpoints

Physical function

Physical function will be determined by measures of aerobic capacity and maximal strength. Aerobic capacity defined as peak oxygen consumption (VO_{2peak}) will be determined by a cardiopulmonary exercise test on a cycle ergometer (Ergoline ergoselect; Bitz, Germany). In line with the guidelines provided by the WHO, the test will commence at a load of 25 Watts and will be increased by 25 Watts every 2 minutes until voluntary exhaustion. Patients will be requested to maintain a pedaling frequency of 70 ± 5 revolutions per minute (rpm). The test will be supervised by a cardiologist and ECG will be recorded consistently. Early termination due to acute clinical contraindications will be subject to further investigation. In addition, capillary blood samples will be collected from the earlobe at the end of each stage for the determination of blood lactate concentrations. Breathing gases, heart rate and subjective perceived exertion will be monitored throughout the test.

Maximal strength will be assessed by the 1RM for the following muscles, using pneumatic devices (HUR Health fitness Equipment; Kokkola, Finland): Leg press, seated chest press and seated row.

AF burden and quality of life

The AF burden will be assessed by means of ECG recordings at rest and during exercise as well as by questionnaires. Specifically, the total number and overall duration of AF episodes during a 48h ECG recording (Holter-ECG, Amedtec, Aue, Germany) as well as during each exercise and the post-exercise recovery period (Ergoline ergoselect; Bitz, Germany) will be assessed. In addition, patients are requested to complete the quality of life in patients with atrial fibrillation [IBL-VF]) questionnaire. Furthermore, the short Form (36) Health Survey (SF-36) will assess overall quality of life, the international Physical Activity Questionnaire (IPAQ) will determine physical activity levels and the Sleep Quality Index (PSQI) will assess quality of sleep.

Inflammatory profile

The following parameters will be analyzed to assess the inflammatory response through venous blood samples: C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) and collagen turnover markers, such as matrix metalloproteinases 1,2 and 9 (MMP-1, -2 and -9 respectively), carboxy-terminal telopeptide of collagen type I (CITP) and propeptide of procollagen type I (PICP).

Muscle morphology

Anatomical cross-sectional area of the vastus lateralis and rectus femoris muscles will be assessed by the extended field of view mode, using a Vivid iq ultrasound system equipped with a 5 cm 3-9 MHz linear-array probe (Vivid iq, GE Healthcare Systems, USA, 2018).

Cardiovascular morphology and function

Echocardiography will be performed by a Vivid iq with a M5Sc 1.5-4.6 transducer (GE Healthcare Systems, USA, 2018), with the participant in a semi-supine resting position. Conventional echocardiography will include standard measurements of cardiac dimensions, contractility and diastolic function. Speckle Tracking images for calculation of myocardial strain will be recorded in apical 3-chamber, 2-chamber and 4-chember views for longitudinal values and in the parasternal short-axis at the level of papillary muscles for circumferential and radial values. The analysis of all images will be performed using the EchoPac-Software (Version 203, GE Healthcare, USA). In addition, 48 h-ECG recordings will be performed (Holter-ECG, Amedtec, Aue, Germany), in order to assess heart rate, number of supraventricular and ventricular extra-systoles and heart rate variability. Further measures will include systolic and diastolic blood pressure and arterial stiffness (Mobil-O-Graph®, IEM, Stolberg, Germany) as well as the serum levels of N-terminal pro-brain natriuretic peptide (NTproBNP).

Data analysis

Within- and between-group analyses will be performed in order to investigate basal adaptations induced by the training interventions as well as the 3-months follow-up. Data will be checked for normality and log transformed prior to applying parametric statistics. Statistical analysis will include standard descriptive statistics and two way (group x time) repeated-measures analysis of variance (adjusted for baseline if necessary). Categorical variables will be assessed by Chi-square tests. Effect sizes will be calculated as partial et-squared. In order to account for missing or incomplete data, all results will be analyzed by the intention-to-treat approach.

DISCUSSION

Exercise interventions have previously been shown to be safe and effective for patients diagnosed with a variety of cardiovascular diseases, such as coronary heart disease, cerebral apoplexy, hypertension, heart failure and intermittent claudication [18]. Interestingly, the evidence for exercise interventions in the treatment of AF is scarce. To the best of our knowledge, previously only three randomized controlled trials have assessed the effects of exercise interventions in patients with paroxysmal AF, mainly focusing on physical capacity (VO_{2peak}) and AF burden [11,12,19]. However, feasibility as defined by recruitment and completion rates, program tolerance and program adherence was not thoroughly assessed in these studies. Moreover, the existing data are limited to aerobic training alone or combined aerobic and strength-training regimens, not allowing to directly assess and compare the feasibility and safety but also the efficacy of distinct exercise interventions.

The importance of this phase I clinical trial is further underlined by recent investigations that have provided evidence for an increased prevalence of AF in athletes, leaving it unclear as to whether regular strenuous exercise may actually be adverse for AF patients [20–22]. This may actually depend on the overall dose of exercise performed. On the one hand, a lifetime training volume at high-intensity levels of > 2000 hours was previously associated with an increase in the incidence of AF [23]. Regular high-intensity exercise at a recreational or preventive volume (< 2000 hours per lifetime), on the other hand, was strongly associated with a reduced AF-risk, as well as a reduction in cardiovascular, metabolic and neoplastic disease and overall mortality [24]. Validating this observational data in a randomized and controlled setting is among the primary aims of this trial.

In addition to feasibility and safety, the efficacy of distinct types of training will be assessed in this study. We do expect significant adaptations in physical function, such as VO_{2peak} and

maximal strength. VO_{2peak} as a marker of cardiorespiratory fitness (CRF) is a well established predictor of mortality in healthy adults [25], as well as cardiovascular patients, including heart failure [26,27] and coronary heart disease [28,29]. In fact, a reduced exercise tolerance has been associated with increased mortality in patients with AF [30]. Importantly, in previous large prospective longitudinal cohort studies changes in CRF were observed concomitantly with mortality outcomes, suggesting that improving VO_{2peak} through exercise may well reduce mortality [31]. In addition, in healthy elderly men (> 65 years) muscle strength appears to be directly related to all-cause mortality [32], even irrespective of muscle mass [33]. We hypothesize that the magnitude of the changes in VO_{2peak} and maximal strength will be dependent on the training mode. Thus, major improvements in cardiorespiratory function are expected in the aerobic training groups, while neuromuscular function is expected to increase to a larger extent in the STR-group.

In this trial we will also be able to document arrhythmia occurrences during exercise. Furthermore, we expect a reduction in AF-symptoms and -frequency measured by questionnaires, likely accompanied by an improvement in QoL. A reduction in AF-burden between the intervention groups and the control group may be documented in the 48-hour Holter-ECG recordings, collected before and after the intervention as well as at the 3-month follow-up. Considering that Malmo et al. reported an absolute reduction of AF duration following the HIIT-intervention of ~ 3% (from 8% to 5%) using implanted loop recorders, chances of detecting a change of this magnitude with only Holter-ECG recordings in the present study are slim [12]. However, after assessing safety and feasibility in the initial phase of this study, AF-burden may well be a relevant primary endpoint of the second phase of this trial.

One of the strengths of the current trial is the in depth mechanistic analysis of potential cardiac factors underlying changes in AF-burden and quality of life. Thus, echocardiographic data including atrial strain analysis may reveal mechanistic components of beneficial effects of exercise. While defining "*the* cause" of atrial fibrillation seems problematic, a host of evidence revealed etiological factors (i.e. hypertension, heart failure, diabetes mellitus, etc.) as well as structural aspects involved in the development of AF [7]. Thus, inflammatory processes associated with fibrotic restructuring as well as pathological changes in contractility and size of the left atrium seem to play key roles in atrial remodeling and the development of atrial fibrillation [34–42]. Exercise-induced reductions in inflammation and fibrosis may lead to therapeutic *reverse*-remodeling [43–46]. The data of the present trial may well document improved systemic inflammation (i.e. reductions in serum levels of CRP, IL6 and TNF-α),

potentially associated with measurable signs of atrial reverse-remodeling on a structural (i.e. reduced fibrotic restructuring) and functional (i.e. improved atrial diastolic and systolic function) level.

The improvement of cardiac function may also be a key component in potentially beneficial effects of distinct exercise interventions for patients with AF. While the mechanisms of aerobic exercise leading to volume-dependent, pre-load associated cardiac adaptations are well-understood and are consistent throughout previous studies [47], the cardiac processes induced by strength training remain unclear [48]. The initial hypothesis that the increased vascular resistance and associated after-load elevation observed in strength-trained athletes will lead to concentric hypertrophy as seen in hypertensive patients was not confirmed consistently in previous trials [49]. Contrarily, strength training may actually reduce systolic and diastolic blood pressure in hypertensive patients [48]. However, the available literature is scarce and an in depth analysis of underlying cardiac processes and mechanisms is often lacking. Hypothetically, the intermittent pressure elevation in the cardiovascular system observed during strength training may induce similar structural cardiac benefits as intermittent increases of cardiac output in aerobic exercise. This remains conjecture due to the paucity of studies analyzing the underlying mechanisms of strength training on the cardiovascular system.

Ultimately, the present study aims to be the first randomized controlled trial to underline the feasibility and safety of distinct exercise modes including highly strenuous aerobic and strength exercise, while at the same time analyzing functional and mechanistic intervention effects with the goal of conducting follow-up studies powered for clinically relevant end-points.

No competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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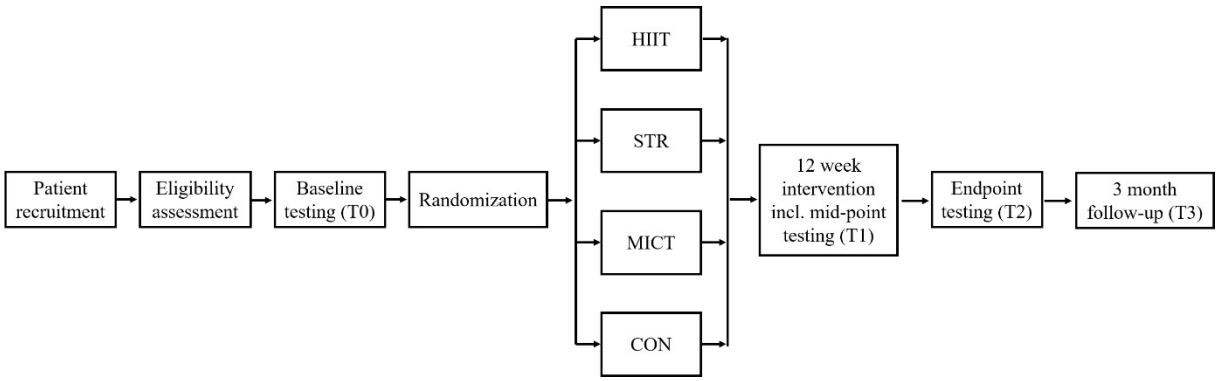

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Exercise Training in the Treatment of Paroxysmal Atrial Fibrillation: Study Protocol of the *Cologne ExAfib Trial*

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ABSTRACT

Introduction

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia and is associated with a number of comorbidities such as coronary artery disease and heart failure. While physical activity is already implemented in current international guidelines for the prevention and treatment of AF, the precise role of different types of exercise in the management of AF remains to be elucidated. The primary aim of the *Cologne ExAfib Trial* is to assess the feasibility and safety of different exercise modes in patients diagnosed with paroxysmal AF. Secondary outcomes include assessments of physical function, AF burden, quality of life and inflammation, as well as morphological and cardiac adaptations.

Methods and analysis

The study opened for recruitment in September 2019. In the initial pilot phase of this 4-armed randomized controlled trial we aim to enroll 60 patients between 60 and 80 years of age with paroxysmal AF. After screening and pre-testing, patients are randomized into one of the following groups: High-intensity-interval-training (4x4 minutes at 75-85% peak power output (PPO)), moderate-intensity continuous training (25 minutes at 55-65% PPO), strength training (whole body, 3 sets of 6-12 repetitions at 70-90% one repetition maximum (1RM)) or a usual-care control group. Training is performed twice weekly for 12 weeks. If the feasibility and safety can be confirmed through the initial pilot phase, the recruitment will be continued and powered for a clinical endpoint.

Feasibility and safety are assessed by measures of recruitment and completion, program tolerance and adherence as well as reported adverse events and including hospitalization rates. Secondary endpoints are assessed by measures of VO_{2peak} and the 1RM of selected muscle groups, questionnaires concerning quality of life and AF burden, serum blood samples for the analysis of CRP, IL-6, TNF-α and NTproBNP concentrations and ultrasound for muscle and heart morphology as well as cardiac function.

Ethics and dissemination

Ethics approval was obtained from the ethics committee of the German Sports University Cologne (No.: 175/2018). All procedures performed in studies involving human participants are in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Manuscripts will be written based on international authorship guidelines.

No professional writers will be commissioned for manuscript drafting. The findings of this study will be published in peer-reviewed Journals and presented at leading exercise and medicine conferences.

Keywords: exercise medicine; cardiac arrhythmia; physical training; high intensity interval training (HIIT); strength training

STRENGTH AND LIMITATION

- First clinical trial to investigate the effects of HIIT, MICT and STR of patients with paroxysmal AF
- Due to the single center design, we do not expect protocol deviations
- An initial pilot phase allows for refining of the clinical endpoint and/or study arms after initial safety and feasibility assessment
- Due to the nature of the disease, detection of the disease burden may be limited by a 48 h Holter ECG recording
- A selection bias is expected in this population, since individuals who are more prone to exercise are more likely to participate in the study

INTRODUCTION

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia, with an estimated European prevalence of ~ 2% [1]. Although this may be significantly lower compared to other cardiovascular diseases such as arterial hypertension, the prevalence is age-dependent, reaching highly significant numbers amongst seniors. Thus, AF has been reported to affect ~ 8% of adults above 65 years of age, reaching levels of >15% in age-groups of over 80 years [1]. Due to the demographic transition towards an inverted age pyramid, by 2060 the number of patients will double amongst the > 65-year old and even triple amongst the > 80-year old adults, producing ~ 25 million seniors with AF in the European Union [1].

Based on the disease progression, AF may be classified into paroxysmal (i.e. self-terminating or cardioverted within 7 days), persistent (i. e. AF persisting for > 7 days), long-standing persistent (i.e. persisting for > 1 year) or permanent (i.e. arrhythmia is accepted and restoration of sinus rhythm is no longer pursued) [2]. Symptoms may include dyspnea, palpitations and angina pectoris, all of which can dramatically decrease overall quality of life. Moreover, AF is often accompanied by severe comorbidities, such as coronary artery disease, stroke and heart failure, making it a leading cause for hospitalization [3–6]. Thus, the treatment depends on the severity of symptoms and diagnosed comorbidities but may include stroke prevention via oral anti-coagulation (OAC), medical rate control and rhythm control via medication, cardioversion or ablation therapy [7]. However, despite recent advances in medical and interventional care, the socio-economic burden remains immense and is expected to increase even further with the demographic change in society.

In addition to conventional medical treatment, lifestyle interventions have recently gained scientific interest. These mainly include the management of risk factors, such as overweight, hypertension and hyperglycemia [8]. However, studies have shown that a sedentary lifestyle significantly increases the risk for AF, while already moderate levels of physical activity appear to be a promising countermeasure [9]. Surprisingly, studies specifically assessing the effects of structured exercise interventions with the aim of improving physical fitness and quality of life, while at the same time reducing AF burden are scarce and often limited to small pilot studies [10] .

In a previous large-scale randomized-controlled trial (RCT), Risom et al. showed an increase in aerobic capacity following 12 weeks of aerobic and strength training but effects on AF burden or hospitalization were not investigated [11]. In addition, in a study by Malmo et al. a significant reduction in AF burden and concomitant increase in VO_{2peak} and quality of life

were observed following 12 weeks of aerobic high-intensity interval training (HIIT) [12]. However, in subsequent meta-analyses it was concluded that the number of high-quality RCTs is insufficient to adequately deduce the effects of exercise-based interventions in the treatment of AF [13,14]. This concern was also confirmed in a recent systematic review including the safety aspects of physical training in AF patients, irrespective of whether patients were classified as paroxysmal, persistent or permanent [15].

While physical activity is already reflected in current international guidelines for the prevention and treatment of AF [7,16], specific recommendations concerning different exercise modes (i.e. aerobic vs. resistance training) and intensities (low-intensity continuous vs. HIIT) are lacking. The *Cologne ExAfib Trial* is a phase I clinical trial, that primarily aims at systematically assessing the effects of distinct exercise modes on the feasibility and safety of patients diagnosed with paroxysmal AF. Secondary outcomes include assessments of the physical function, AF burden, quality of life (QoL), inflammation, muscle morphology as well as cardiac function. The outcomes of this trial will be used to further improve clinical knowledge pertaining to exercise prescription for AF patients. In addition, findings of this study will also be used to design phase II trials which will help to establish guidelines for exercise prescription.

MATERIALS AND METHODS

The current study is carried out in accordance with the declaration of Helsinki and received ethical approval by the local ethics committee (175/2018, German Sports University Cologne, Germany). All participants are comprehensively informed about the study procedures and are requested to provide a signed informed consent prior to participation by the authorized study personnel. Personal information about potential and enrolled participants will be collected, shared, and maintained according to European regulations in order to protect confidentiality. The study is registered both at the German and at the WHO trial registers (DRKS00016637). The presented protocol is version 2.0. Protocol modifications, if any, will be entered into the trial registry.

Study design

The *Cologne ExAfib Trial* is a prospective 4-armed, randomized controlled single-center trial (Fig. 1). The study opened for recruitment in September 2019 and is still ongoing. Testing and interventions take place at the German Sports University Cologne, Germany. The study

coordinator is responsible for data handling and storing and is the solely be able to access the final data set.

Following recruitment and pre-screening, patients are randomized into one of the four groups: aerobic moderate-intensity continuous training (MICT), HIIT, strength training (STR) or usual care (CON). After screening, patients that were randomized to the exercise groups perform 12 weeks of supervised exercise training. Patients that were randomized to the usual care group are asked to continue with daily habitual activities but are also offered to participate in supervised exercise training after completion of the study. All patients are followed-up at 3 months after the completion of the intervention period.

Patient recruitment

Patients are recruited by invitation of their treating practitioner. Local hospitals and practitioners provide eligible patients with written information on the study procedures and refer these patients to the study coordinator. The inclusion- and exclusion criteria are presented in Table 1. For detailed information see *Appendix 1*.

Table 1: In- and exclusion criteria

Inclusion criteria	Exclusion criteria
▪ Women and men with symptomatic paroxysmal atrial fibrillation (EHRA ≥ 2) ▪ Age of 60 to 80 years ▪ BMI ≤ 35 kg · m^{-2}	▪ Participation in regular aerobic or resistance exercise training in the last six months (> 60 minutes/week) or former high-performance athletes ▪ Left ventricular ejection fraction < 40% during sinus rhythm ▪ Significant valve disease ▪ Implanted cardiac pacemaker, ICD or resynchronization therapy ▪ Coronary artery disease without complete revascularization or unstable angina pectoris ▪ Uncontrolled limiting comorbidities (hypertension, diabetes mellitus, hyperthyroidism, etc.) ▪ Prior pulmonary vein ablation ▪ Any contraindication to strenuous exercise or testing

BMI: body mass index; EHRA: European Heart Rhythm Association; ICD: Implantable Cardioverter Defibrillator

Patient and public involvement

Patients and the public were not involved in any way.

Sample size calculation

Due to the novelty of this phase I clinical trial with the primary endpoint of safety and feasibility, the sample size was assessed based on previous studies investigating the effects of aerobic [11] or combined aerobic and strength training [12] on secondary outcomes, such as

physical function. The sample size calculation was performed by G*power (version 3.1.9.2, Heinrich Heine University, Dusseldorf, Germany). For an effect size of 0.5, with a power (1-β) of 0.8 and an alpha level of 0.05 (two-tailed), a total of at least 40 patients would be needed. Since attrition is not known in this population and data on safety and feasibility are lacking for some of the exercise interventions utilized, we will initially include 60 patients (15 per group). Based on the initial findings, recruitment will then continue with distinct exercise regimens and will be powered based on a clinical endpoint.

Screening and randomization

This trial spans over a total duration of 14 weeks. After pre-screening and baseline testing, the patients are randomly allocated in a ratio of 1:1:1:1 to the four study arms. Randomization is performed by a research officer with no patient contact using a stratified minimization approach by RITA (Randomization In Treatment Arms, Evident, Germany). The stratification factors include i) patients age, ii) gender and iii) BMI. Study investigators and exercise physiologists conducting testing procedures are blinded to group allocation.

Interventions

Patients randomized into one of the training groups perform supervised training twice weekly over a total duration of 12 weeks. All training sessions are electronically recorded (Heart rate, workload, sets and repetitions; HUR Healthfitness Equipment; Kokkola, Finland; Ergoline ergoselect; Bitz, Germany). In addition, a one-lead ECG is used in order to continuously monitor cardiac function throughout each training session by means of beat-to-beat recordings with a amplitude frequency of 0.05 – 125 Hz. Habitual physical activity is assessed objectively in all groups (including the control group) by a wrist-worn activity tracker (ActiGraph GT9X, ActiGraph, LLC, Pensacola, FL). Assessment of habitual physical activity takes place over 7 days at the following time-points: baseline, after 6 weeks (mid-point testing), after 12 weeks (end-point testing) as well as at the three-month follow-up.

All training sessions are time-matched (i.e. 40 minutes). Training sessions include a standardized warm-up (5 minute cycling at 30% of peak power output [PPO]) and cool-down (10-minute cycling 30% PPO). Each training session is concluded by an additional 10-minute recovery period, including a standardized stretching routine. Perceived exhaustion, pain and dyspnea are assessed by visual analog scales ranging from 0 (no symptoms) to 10 (severe symptoms), prior to as well as immediately after each training session.

MICT: Training is performed on a stationary cycle ergometer (Ergoline ergoselect; Bitz, Germany) at a target exercise intensity of 55 to 65% of PPO for 25 minutes. Initially, the training intensity is 55% of PPO and is progressively increased by 5% every 4 weeks.

HIIT: Training is performed on a stationary cycle ergometer (Ergoline ergoselect; Bitz, Germany) and consists of 4 × 4 minutes at 75 to 85% of PPO, separated by a 3-minute active rest at 30% of PPO. Initially, the intensity of high-intensity commences at 75% PPO and progressively increases by 5% every four weeks.

STR: Strength training consists of the following upper and lower body exercises, using pneumatic devices (HUR Healthfitness Equipment; Kokkola, Finland): Leg press, knee extension, hamstring curls, seated chest press, seated row, lat pull-down and shoulder press. Exercise loads are determined individually as percentage of the one-repetition maximum (1RM). The exercises are performed as a circuit with a 2-minute rest between sets. Every session includes leg press, seated row and chest press, while shoulder press or lat pull-down as well as knee extension or hamstring curls are performed on alternating days.

The strength training intensity is progressively increasing every two weeks until week eight as follows: 3 sets of 12 reps at 70% 1RM, 3 sets of 12 reps at 75% 1RM, 3 sets of 10 reps at 80% 1RM, 3 sets of 10 reps at 85% 1RM. The sessions of the remaining four weeks are consisting of 3 sets of 6 reps at 90% 1RM.

Measurements

All primary and secondary endpoints are assessed at baseline (T0) as well as at end-point testing (T2) and the 3-months follow-up (Fig. 1 and Table 2). Venous blood samples are additionally drawn at mid-point testing (T1). Additional measures of feasibility and safety are assessed throughout the study period (Table 3).

Table 2: Measurements

T0 (baseline testing)	T1 (midpoint testing, after 6 weeks)	T2 (endpoint testing)	T3 (3-months follow-
▪ Venous blood sampling ▪ Bio-impedance-analysis ▪ Echocardiography ▪ Cardiopulmonary exercise test ▪ Maximal strength test ▪ Resting ECG (48 h) ▪ Resting blood pressure and Arteriography ▪ Panoramic ultrasound of vastus lateralis and rectus femoris ▪ Questionnaires (SF-36, IBL-VF, PSQI)	▪ Venous blood sampling	idem T0	idem T0

Primary endpoints

Feasibility of the exercise interventions will be quantified by measures of recruitment and completion, program tolerance and program adherence (Table 3). In order to calculate recruitment rates, the number of referrals will be compared to the number of patients who are deemed eligible after pre-screening. In addition, eligibility rates will be determined by the ratio of eligible patients and those actually enrolled in the trial. Program tolerance will be assessed by measures of perceived exhaustion, pain and dyspnea as well as continuous ECG recordings throughout each training session. The number of completed training sessions as well as the time and/or sets completed in each training session will determine program adherence.

Patient safety will be assessed by means of recorded adverse and severe adverse events as well as hospitalization rates (Table 3, modified from Hart et al. (2018) [17]). Adverse events and severe adverse events will be graded as adapted from the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, including also events related to exercise training (such as muscular pain and fatigue).

Table 3: Assessment of safety and feasibility.

Measures	Time of collection
Feasibility – recruitment and completion	
Referred patients	Trial completion
Eligible patients	Trial completion
Enrolled patients	Trial completion
Trial completion	Trial completion

Patient withdrawals	Trial completion
Patient drop-outs	Trial completion
Feasibility – program tolerance	
Pre- and post-sessional exhaustion, pain and dyspnea	At each exercise session
ECG-recordings	At each exercise session
Feasibility – program adherence	
Number of completed sessions	Trial completion
Time/sets completed in each session	At each exercise session
Patient Safety	
Number of adverse events	Once weekly and 3-months follow-up
Number of severe adverse events	Once weekly and 3-months follow-up
Hospital admissions/days of hospitalization	Once weekly and 3-months follow-up

Secondary endpoints

Physical function

Physical function will be determined by measures of aerobic capacity and maximal strength. Aerobic capacity defined as peak oxygen consumption (VO_{2peak}) will be determined by a cardiopulmonary exercise test on a cycle ergometer (Ergoline ergoselect; Bitz, Germany). In line with the guidelines provided by the WHO, the test is commencing at a load of 25 Watts and the load is increased by 25 Watts every 2 minutes until voluntary exhaustion. Patients are requested to maintain a pedaling frequency of 70 ± 5 revolutions per minute (rpm). The test is supervised by a cardiologist and ECG is recorded consistently. Early termination due to acute clinical contraindications will be subject to further investigation. In addition, capillary blood samples are collected from the earlobe at the end of each stage for the determination of blood lactate concentrations. Breathing gases, heart rate and subjective perceived exertion are monitored throughout the test.

Maximal strength is assessed by the 1RM for the following muscles, using pneumatic devices (HUR Health fitness Equipment; Kokkola, Finland): Leg press, seated chest press and seated row.

AF burden and quality of life

The AF burden is assessed by means of ECG recordings at rest and during exercise as well as by questionnaires. Specifically, the total number and overall duration of AF episodes during a

3-lead 48 h ECG recording (Holter-ECG, Amedtec, Aue, Germany) as well as during each exercise and the post-exercise recovery period (Ergoline ergoselect; Bitz, Germany) is assessed. In addition, patients are requested to complete the quality of life in patients with atrial fibrillation [IBL-VF]) questionnaire. Furthermore, the short Form (36) Health Survey (SF-36) is used to assess overall quality of life, the international Physical Activity Questionnaire (IPAQ) is used to determine physical activity levels, while quality of sleep is assessed by the Sleep Quality Index (PSQI).

Inflammatory profile

The following parameters will be analyzed to assess the inflammatory response through venous blood samples: C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) and collagen turnover markers, such as matrix metalloproteinases 1,2 and 9 (MMP-1, -2 and -9 respectively), carboxy-terminal telopeptide of collagen type I (CITP) and propeptide of procollagen type I (PICP).

Muscle morphology

Anatomical cross-sectional area of the vastus lateralis and rectus femoris muscles is assessed by the extended field of view mode, using a Vivid iq ultrasound system equipped with a 5 cm 3-9 MHz linear-array probe (Vivid iq, GE Healthcare Systems, USA, 2018).

Cardiovascular morphology and function

Echocardiography is carried out by a Vivid iq with a M5Sc 1.5-4.6 transducer (GE Healthcare Systems, USA, 2018), with the participant in a semi-supine resting position. Conventional echocardiography includes standard measurements of cardiac dimensions, contractility and diastolic function. Speckle Tracking images for calculation of myocardial strain are recorded in apical 3-chamber, 2-chamber and 4-chamber views for longitudinal values and in the parasternal short-axis at the level of papillary muscles for circumferential and radial values. The analysis of all images will be performed using the EchoPac-Software (Version 203, GE Healthcare, USA). In addition, 48 h-ECG recordings are performed (Holter-ECG, Amedtec, Aue, Germany), in order to assess heart rate, number of supraventricular and ventricular extra-systoles and heart rate variability (starting immediately after the testing at T0, T2 and T3). Further measures include systolic and diastolic blood pressure and arterial stiffness (Mobil-O-Graph®, IEM, Stolberg, Germany) as well as the serum levels of N-terminal pro-brain natriuretic peptide (NTproBNP).

Data analysis

Data will be collected digitally and will be cross-checked for accuracy. Within- and between-group analyses will be performed in order to investigate basal adaptations induced by the training interventions as well as the 3-months follow-up. Data will be checked for normality and log transformed prior to applying parametric statistics. All statistics will be performed using an intention to treat approach. Missing data will be accounted for by multiple imputation. Statistical analysis will include standard descriptive statistics and two way (group x time) repeated-measures analysis of variance (adjusted for baseline if necessary). Categorical variables will be assessed by Chi-square tests. Effect sizes will be calculated as partial et-squared. In order to account for missing or incomplete data, all results will be analyzed by the intention-to-treat approach. All included patients will be invited to an informative meeting on the study results following completion of the study.

Data sharing

Data generated by our research will be made available as soon as possible, if legally and ethically allowed and upon reasonable request.

DISCUSSION

Exercise interventions have previously been shown to be safe and effective for patients diagnosed with a variety of cardiovascular diseases, such as coronary heart disease, cerebral apoplexy, hypertension, heart failure and intermittent claudication [18]. Interestingly, the evidence for exercise interventions in the treatment of AF is scarce. To the best of our knowledge, previously only three randomized controlled trials have assessed the effects of exercise interventions in patients with paroxysmal AF, mainly focusing on physical capacity (VO_{2peak}) and AF burden [11,12,19]. However, feasibility as defined by recruitment and completion rates, program tolerance and program adherence was not thoroughly assessed in these studies. Moreover, the existing data are limited to aerobic training alone or combined aerobic and strength-training regimens, not allowing to directly assess and compare the feasibility and safety but also the efficacy of distinct exercise interventions.

The importance of this phase I clinical trial is further underlined by recent investigations that have provided evidence for an increased prevalence of AF in athletes, leaving it unclear as to whether regular strenuous exercise may actually be adverse for AF patients [20–22]. This may possibly depend on the overall dose of exercise performed. On the one hand, a lifetime training volume at high-intensity levels of > 2000 hours was previously associated with an

increase in the incidence of AF [23]. Regular high-intensity exercise at a recreational or preventive volume (< 2000 hours per lifetime), on the other hand, was strongly associated with a reduced AF-risk, as well as a reduction in cardiovascular, metabolic and neoplastic disease and overall mortality [24]. Validating this observational data in a randomized and controlled setting is among the primary aims of this trial.

In addition to feasibility and safety, the efficacy of distinct types of training will be assessed in this study. We do expect significant adaptations in physical function, such as VO_{2peak} and maximal strength. VO_{2peak} as a marker of cardiorespiratory fitness (CRF) is a well-established predictor of mortality in healthy adults [25], as well as cardiovascular patients, including heart failure [26,27] and coronary heart disease [28,29]. In fact, a reduced exercise tolerance has been associated with increased mortality in patients with AF [30]. Importantly, large previous prospective longitudinal cohort studies observed changes in CRF concomitantly with mortality outcomes, suggesting that improving VO_{2peak} through exercise may well reduce mortality [31]. In addition, in healthy elderly men (> 65 years) muscle strength appears to be directly related to all-cause mortality [32], even irrespective of muscle mass [33]. We hypothesize that the magnitude of the changes in VO_{2peak} and maximal strength will be dependent on the training mode. Thus, major improvements in cardiorespiratory function are expected in the aerobic training groups, while neuromuscular function is expected to increase to a larger extent in the STR-group.

In this trial, we will also be able to document arrhythmia occurrences during exercise. Furthermore, we have included questionnaires that will allow us to determine possible effects of the exercise interventions on AF symptoms and –frequencies. However, while we also include 48h Holter ECG recordings, it has to be acknowledged that the chances to detect objective changes in AF burden of patients with paroxysmal AF are slim. This is especially true in light of a previous study reporting an absolute reduction of AF duration following the HIIT-intervention of ~ 3% (from 8% to 5%) using implanted loop recorders [12]. However, after assessing safety and feasibility in the initial phase of this study, AF-burden may well be a relevant primary endpoint of the second phase of this trial. Implantable loop recording or constant rhythm assessment via wearable are currently being considered.

One of the strengths of the current trial is the in depth mechanistic analysis of potential cardiac factors underlying changes in AF-burden and quality of life. Thus, echocardiographic data including atrial strain analysis may reveal mechanistic components of beneficial effects of exercise. While defining "*the* cause" of atrial fibrillation seems problematic, a host of

evidence revealed etiological factors (i.e. hypertension, heart failure, diabetes mellitus, etc.) as well as structural aspects involved in the development of AF [7]. Thus, inflammatory processes associated with fibrotic restructuring as well as pathological changes in contractility and size of the left atrium seem to play key roles in atrial remodeling and the development of atrial fibrillation [34–42]. Exercise-induced reductions in inflammation and fibrosis may lead to therapeutic *reverse*-remodeling [43–46]. The data of the present trial may well document improved systemic inflammation (i.e. reductions in serum levels of CRP, IL6 and TNF-α), potentially associated with measurable signs of atrial reverse-remodeling on a structural (i.e. reduced fibrotic restructuring) and functional (i.e. improved atrial diastolic and systolic function) level.

The improvement of cardiac function may also be a key component in potentially beneficial effects of distinct exercise interventions for patients with AF. While the mechanisms of aerobic exercise leading to volume-dependent, pre-load associated cardiac adaptations are well-understood and are consistent throughout previous studies [47], the cardiac processes induced by strength training remain unclear [48]. The initial hypothesis that the increased vascular resistance and associated after-load elevation observed in strength-trained athletes will lead to concentric hypertrophy as seen in hypertensive patients was not confirmed consistently in previous trials [49]. Contrarily, strength training may actually reduce systolic and diastolic blood pressure in hypertensive patients [48]. However, the available literature is scarce and an in depth analysis of underlying cardiac processes and mechanisms is often lacking. Hypothetically, the intermittent pressure elevation in the cardiovascular system observed during strength training may induce similar structural cardiac benefits as intermittent increases of cardiac output in aerobic exercise. This remains conjecture due to the paucity of studies analyzing the underlying mechanisms of strength training on the cardiovascular system.

Ultimately, the present study aims to be the first randomized controlled trial to underline the feasibility and safety of distinct exercise modes including highly strenuous aerobic and strength exercise, while at the same time analyzing functional and mechanistic intervention effects with the goal of conducting follow-up studies powered for clinically relevant end-points.

ETHICS AND DISSEMINATION

Ethics approval was obtained from the ethics committee of the German Sports University Cologne (No.: 175/2018). All procedures performed in studies involving human participants

were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Manuscripts will be written based on international authorship guidelines. No professional writers will be commissioned for manuscript drafting. The findings of this study will be published in peer-reviewed Journals and presented at leading exercise and medicine conferences.

No competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Informed consent

Informed consent was obtained from all individual participants included in the study.

Author Contributions

JZ, KD, NF, TK, BB, WB, HGP MS contributed to planning, conduct and reporting of the study. JZ, KD, NF, TK, BB and MS conceptualized and designed the study. JZ, KD, NF, TK, BB, WB, HGP MS are involved in data analysis and interpretation. JZ, KD, NF and MS have drafted the manuscript. TK, BB, WB, HGP have edited the manuscript. All authors have approved the final version of the manuscript.

FIGURE LEGEND

Figure 1: Timeline p. 5

Table 1: In- and exclusion criteria p. 6

Table 2: Measurements p. 9

Table 3: Assessment of safety and feasibility p. 9

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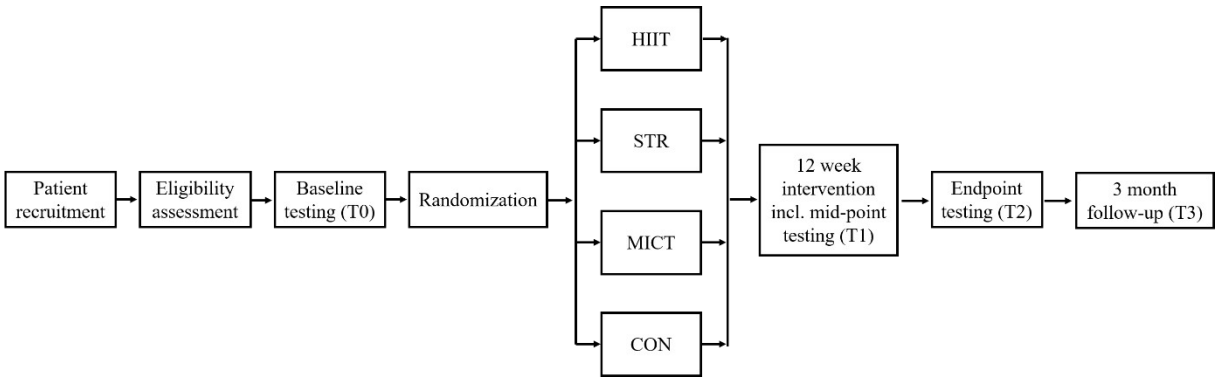

Patienteninformation zur Studie

„Vorhofflimmern und Sport."

Name _____ Geburtsdatum _____

An der Deutschen Sporthochschule Köln wird im Institut für Kreislaufforschung und Sportmedizin eine Studie vorbereitet, welche den Einfluss von körperlicher Belastung in Form von Ausdauertraining, Intervalltraining und Krafttraining auf Patienten mit Vorhofflimmern untersucht. Hintergrund der Studie ist die Beobachtung, dass Vorhofflimmern in der Bevölkerung immer mehr zunimmt und dass sportliche Interventionen bisher positive Effekte auf Häufigkeit und Intensität der Vorhofflimmerepisoden zeigen konnten. Die gewonnenen Ergebnisse aus der Studie sollen mit dazu beitragen, neue Konzepte für die Therapie des Vorhofflimmerns zu entwickeln.

Studieninhalte

Im Rahmen der Studie wird ein 12-wöchiges Trainingsprogramm à 2 Trainingseinheiten pro Woche durchgeführt. Vor und nach dem 12-Wochen-Zeitraum werden medizinische Untersuchungen und Testungen zu Ausdauer und Kraft durchgeführt. Ein Viertel der Teilnehmer wird der Kontrollgruppe zugelost, die kein Training durchführt. Dies ist wichtig, um die Effekte des Trainings vergleichen zu können. Nachdem der 12-wöchige Interventionszeitraum abgeschlossen ist, wird auch den Patientend er Kontrollgruppe das gleiche Sportprogramm angeboten, das die anderen Gruppen durchliefen, um auch von den (mutmaßlich) positiven Aspekten zu profitieren.

Untersuchung

An der Studie können Menschen im Alter zwischen 50 und 80 Jahren mit anfallsartigem (paroxysmalem) Vorhofflimmern teilnehmen.

Alle Untersuchungen finden in der Deutschen Sporthochschule Köln, Institut für Kreislaufforschung und Sportmedizin, statt (NawiMedi, 1. Stock).

Im Rahmen einer Voruntersuchung werden Sie über den Inhalt, den Ablauf und mögliche Risiken der Studie aufgeklärt. Es werden Ihnen formale Dokumente ausgeteilt, Sie füllen einen Fragebogen aus und unterschreiben die Einverständniserklärung. Des Weiteren vereinbaren wir nach Einschluss in die Studie die weiteren Termine für die nächsten Untersuchungen.

Hauptuntersuchung (Durchführung einmal vor der Trainingsintervention und einmal nach der Trainingsintervention)

Es werden folgende Untersuchungen durchgeführt:

- Anthropometrische Daten:
  - Körpergewicht, Körpergröße, Körperzusammensetzung, Bauchumfang

- Ruhe-EKG
- Ruhe Blutdruckmessung
- Arteriographie
- Herzfrequenzvariabilitätsmessung
- Blutabnahme (nüchtern)
- Echokardiografie
- Ultraschall der Beinmuskulatur
- Spiroergometrie mit Laktatmessung auf dem Fahrradergometer
- 24-Stunden-Blutdruckmessung und -EKG

Training

Das Training findet in den Räumlichkeiten der Deutschen Sporthochschule statt (NawiMedi, 1. Stock, Trainingsraum).

Die TeilnehmerInnen werden in vier Gruppen zufällig eingeteilt (**randomisiert**).

Gruppe A: submaximales Krafttraining

Gruppe B: moderates Ausdauertraining

Gruppe C: intensives Intervall-Ausdauertraining (HIIT)

Gruppe D: Kontrollgruppe (kein Training)

Die Trainingseinheiten werden unter Anleitung und kontinuierlicher Betreuung durchgeführt.

Das Gruppentraining findet 2x wöchentlich à 60 Minuten statt.

Die Trainingseinheiten sind auf Ihre individuelle Leistungsfähigkeit zugeschnitten. Die individuelle Belastungsintensität wird aus dem Fahrradbelastungstest und durch standardisierte Krafttestungen am Gerät ermittelt.

Nach dem Ende der Trainingsintervention und absolvierter Untersuchung ist die empirische Phase der Studie beendet.

Es fallen bei Teilnahme an der Studie für Sie keinerlei Kosten an. Die Anfahrt zu den Untersuchungen und Trainingseinheiten müssen Sie jedoch selber tragen. Es werden keine Reisekosten erstattet.

Mögliche gesundheitliche Risiken

Zur Vermeidung eines erhöhten Risikos bei einer Teilnahme an körperlichen Belastungstests und sportlichem Training, werden mögliche gesundheitliche Risiken mittels Fragebogen, Untersuchung und eines Belastungstests des Herz-Kreislauf-Systems unter ärztlicher Aufsicht beurteilt.

Die TeilnehmerInnen werden während des Trainings von ausgebildeten Fachkräften betreut.

Trotzdem können natürlich bei intensiver oder ungewohnter Belastung Beschwerden auftreten (z.B. Muskelkater durch Krafttraining, Bluthochdruck durch Belastung, etc.). Die Wahrscheinlichkeit für Komplikationen ist sehr gering. Das erfahrene Team aus Sportwissenschaftlern und Sportmedizinern wird Sie diesbezüglich kontrollieren, informieren und Ihnen stets zur Seite stehen.

Blutentnahme

Mit der Ausnahme der Blutentnahmen und Laktatmessungen beinhaltet diese Studie kein weiteres invasives Verfahren.

Falls Sie krank sind oder sich nicht wohl fühlen, informieren Sie bitte das Studienpersonal.

Ihr persönlicher Nutzen bei Studienteilnahme

- kostenfreie, umfangreiche sportmedizinische Untersuchungen mit Bestimmung der körperlichen Leistungsfähigkeit und der Laborparameter
- individuelle Empfehlungen für ein sportliches Training
- kostenfreies gesundheitsorientiertes und strukturiertes Trainingsprogramm
- mutmaßlich Verbesserung Ihrer Vorhofflimmer-Beschwerden
- beitrag zur konzeptionellen Entwicklung der Therapie bei Vorhofflimmern.

Nur durch Ihr Engagement, Ihre ermittelten Körperdaten und Ihre Meinung kann unser wissenschaftliches Projekt gelingen und ein wichtiger Beitrag zur Vorhofflimmerbehandlung geleistet werden!

Wir würden uns freuen, Sie als TeilnehmerIn unserer Studie begrüßen zu dürfen!

Mit freundlichen Grüßen

Studienarzt Sportwissenschaftlerin wissenschaftliche Assistenz

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Anhang C: Patienteneinverständniserklärung Studie

„Vorhofflimmern und Sport."

Name _____ **Geburtsdatum** _____

Probanden- Einverständniserklärung

1. Hiermit erkläre ich mich freiwillig bereit, an der oben genannten Studie teilzunehmen.

2. Mir ist bekannt, dass ich jederzeit meine Zustimmung zur Teilnahme an der Studie widerrufen kann, ohne mich hierfür rechtfertigen zu müssen.

3. Die zuständigen Personen des Instituts für Kreislaufforschung und Sportmedizin der Deutschen Sporthochschule Köln haben mich über Wesen, Bedeutung und Tragweite dieser Studie in verständlicher Form aufgeklärt.

4. Ich habe die Patienteninformation erhalten, gelesen und verstanden.

5. Mir wurde die Möglichkeit eingeräumt, Fragen zur Probandenaufklärung und zu meiner Teilnahme an der Studie zu stellen. Auf meine Fragen habe ich ausreichend Antworten erhalten.

6. Ich bin einverstanden, dass meine Daten – im Rahmen der Studie – gespeichert sowie wissenschaftlich ausgewertet werden. Dies geschieht ohne Angabe von Name und Anschrift meiner Person.

Eine Kopie dieser Einverständniserklärung habe ich erhalten.

_____ _____

Unterschrift Studienteilnehmerin Unterschrift der aufklärenden Person

_____ _____

Ort, Datum Ort, Datum

Deutsche Sporthochschule Köln
German Sport University Cologne

ExAfib-Studie - Datenschutzinformationen

Das Institut für Kreislaufforschung und Sportmedizin der Deutschen Sporthochschule Köln (nachfolgend bezeichnet als „DSHS“) erhebt von Ihnen personenbezogene Daten zum Zwecke der **sportmedizinischen Untersuchung und Behandlung**. Der Schutz Ihrer personenbezogenen Daten ist für die DSHS dabei ein zentrales Anliegen. Dementsprechend fühlen wir uns den gesetzlichen Vorgaben, insbesondere der europäischen Datenschutz-Grundverordnung (nachfolgend bezeichnet als „DS-GVO“), dem Datenschutzgesetz des Landes Nordrhein-Westfalen und dem Hochschulgesetz des Landes Nordrhein-Westfalen verpflichtet.

Mit diesen Datenschutzbestimmungen informieren wir Sie gemäß Art. 13 und 14 DS-GVO über den Umgang mit Ihren personenbezogenen Daten und Ihre Rechte nach der DS-GVO.

1. Wer ist für die Datenverarbeitung verantwortlich?

Verantwortliche Stelle im Sinne der Datenschutzgesetze ist die

Deutsche Sporthochschule Köln,
Institut für Kreislaufforschung und Sportmedizin
Am Sportpark Müngersdorf 6
50933 Köln
Deutschland
Tel.: 0221 4982 5270
E-Mail: sportmedizin@dshs-koeln.de

2. Wie kann der Datenschutzbeauftragte kontaktiert werden?

Der Datenschutzbeauftragte der verantwortlichen Stelle kann wie folgt kontaktiert werden:

Deutsche Sporthochschule Köln
Der Datenschutzbeauftragte
- persönlich -
Am Sportpark Müngersdorf 6
50933 Köln
Deutschland
E-Mail: datenschutz@dshs-koeln.de

3. Für welche Zwecke und auf welchen Rechtsgrundlagen werden Ihre Daten verarbeitet?

Die DSHS erhebt von Ihnen im Rahmen der sportmedizinischen Betreuung folgende personenbezogene Daten: Geburtsdatum, Adresse und weitere Kontaktdaten, Krankengeschichte inkl. akuter Beschwerden, Sport- und Leistungshistorie, sowie weitere sportmedizinisch relevante Informationen je nach Fall und spezifischer Fragestellung: Hierzu können zählen Körpermaße und -zusammensetzung, Leistungsparameter (z.B. Ergometriedaten,

Laktatwerte, etc.), Funktionsparameter diverser Organe (z.B. EKG, Lungenfunktionsprüfung, Herzleistung, etc.), Laborwerte (ausmaß je nach Untersuchungsziel variabel).

Rechtsgrundlage der Datenverarbeitung ist Art. 6 Abs. 1 S. 1 a) und Art. 9 Abs. 2 a) DS-GVO.

Um die sportmedizinische Athleten- und Patientenbetreuung stets zu optimieren werden die erhobenen Daten anonymisiert für Forschungsprojekte verwendet. Eine Veröffentlichung Ihrer personenbezogenen Daten erfolgt grundsätzlich nur in anonymisierter Form, also ohne die Möglichkeit einen Rückschluss auf Ihre Person zu ziehen.

4. An wen werden Ihre Daten weitergeleitet?

Eine Weitergabe Ihrer persönlichen Daten an Dritte erfolgt ohne Ihre ausdrückliche Einwilligung nicht. Auch die Übermittlung an auskunftsberechtigte staatliche Institution und Behörden erfolgt nur im Rahmen der gesetzlichen Auskunftspflichten oder wenn wir durch eine gerichtliche Entscheidung zur Auskunft verpflichtet werden. Sofern wir zur Zweckerfüllung auf vertraglich verbundene Fremdunternehmen und externe Dienstleister angewiesen sind, wurden diese von uns sorgfältig ausgewählt und beauftragt, sind an unsere Weisungen gebunden und werden regelmäßig kontrolliert.
Im Ramen der sportmedizinischen Untersuchung werden entnommene Blutproben inklusive personenbezogener Daten an externe Labore übergeben, um Werte zu erheben, die die hausinterne Diagnostikmöglichkeit überschreiten.

5. Wie lange werden Ihre Daten gespeichert?

Ihre Daten werden 10 Jahre in den Archiven des Institutes für Kreislaufforschung und Sportmedizin aufbewahrt. Nach Ablauf der Aufbewahrungsfrist werden Ihre Daten gelöscht/vernichtet.

Ihre Daten werden anonymisiert, sobald dies nach dem Forschungs- oder Statistikzweck möglich ist.

6. Welche Rechte haben Sie?

Aufgrund der Erhebung und Verarbeitung Ihrer personenbezogenen Daten haben Sie uns gegenüber folgende Rechte hinsichtlich der Sie betreffenden personenbezogenen Daten:

- Recht auf Auskunft nach Art. 15 DS-GVO,
- Recht auf Berichtigung Ihrer Daten nach Art. 16 DS-GVO oder Löschung Ihrer Daten nach Art. 17 DS-GVO,
- Recht auf Einschränkung der Verarbeitung nach Art. 18 DS-GVO,
- Recht auf Datenübertragbarkeit nach Art. 20 DS-GVO.
- Sofern die Datenverarbeitung auf Grundlage einer Einwilligung (Art. 6 Abs. 1 S. 1 a) oder Art. 9 Abs. 2 a) DS-GVO) erfolgt, haben Sie gemäß Art. 7 Abs. 3 DS-GVO das Recht auf jederzeitigen Widerruf Ihrer Einwilligung, ohne dass die Rechtmäßigkeit der aufgrund der Einwilligung bis zum Widerruf erfolgten Verarbeitung berührt wird.

- Soweit Sie der Ansicht sind, dass Ihre vorstehend aufgeführten Rechte im Sinne des geltenden Datenschutzrechts verletzt sind, haben Sie zudem nach Art. 77 DS-GVO das Recht sich bei der zuständigen Aufsichtsbehörde zu beschweren. Hierzu können Sie sich an

  die Landesbeauftragte für Datenschutz und Informationsfreiheit Nordrhein-Westfalen,
  Kavalleriestraße 2-4, 40213 Düsseldorf
  Postfach 20 04 44, 40102 Düsseldorf,
  Telefon: 0211 38424 – 0
  E-Mail unter poststelle@ldi.nrw.de

  wenden. Weitere Informationen erhalten Sie unter http://www.ldi.nrw.de.

Sofern die Datenverarbeitung gemäß Art. 6 Abs. 1 S. 1 e) DS-GVO erfolgt, haben Sie nach Art. 21 DS-GVO das Recht, dieser Verarbeitung jederzeit unter der oben unter Ziff. 1 genannten Adresse zu widersprechen, sofern sich aus Ihrer besonderen Situation Gründe ergeben, die dieser Datenverarbeitung entgegenstehen. Die Datenverarbeitung wird dann beendet, es sei denn, die DSHS kann zwingende schutzwürdige Gründe für die Verarbeitung nachweisen, die Ihre Interessen, Rechte und Freiheiten überwiegen, oder sofern die Verarbeitung der Geltendmachung, Ausübung oder Verteidigung von Rechtsansprüchen dient.

Ich habe die Datenschutzinformation gelesen, zur Kenntnis genommen und bin einverstanden.

Vor- und Nachname

Ort, Datum, Unterschrift

ExAfib-Studie - Einwilligungserklärung zur Datenverarbeitung:

Im Rahmen der sportmedizinischen Untersuchung werden folgende personenbezogene Daten von Ihnen erhoben und verarbeitet: Vor- und Zuname, Geburtsdatum, Adresse und weitere Kontaktdaten, Krankengeschichte inkl. akuter Beschwerden, Sport- und Leistungshistorie, sowie weitere sportmedizinisch relevante Informationen je nach Fall und spezifischer Fragestellung: Hierzu können zählen Körpermaße und -zusammensetzung, Leistungsparameter (z.B. Ergometriedaten, Laktatwerte, etc.), Funktionsparameter diverser Organe (z.B. EKG, Lungenfunktionsprüfung, Herzleistung, etc.), Laborwerte (ausmaß je nach Untersuchungsziel variabel).

Hierfür benötigen wir Ihre Einwilligungserklärung. Rechtsgrundlage der Datenverarbeitung ist Art. 6 Abs. 1 S. 1 a) sowie Art. 9 Abs. 2 a) DS-GVO. Ihre Einwilligungserklärung ist freiwillig, jedoch ist eine Studienteilnahme ohne Einwilligung nicht möglich. Sie können Ihre Einwilligungserklärung jederzeit mit Wirkung für die Zukunft widerrufen. Ihre personenbezogenen Daten werden dann unverzüglich gelöscht, soweit die weitere Speicherung nicht auf Grundlage einer gesetzlichen Vorschrift gestattet und geboten ist. Durch den Widerruf der Einwilligungserklärung wird die Rechtmäßigkeit der aufgrund der Einwilligungserklärung bis zum Widerruf erfolgten Datenverarbeitung nicht berührt.

Ich willige in die Verarbeitung meiner personenbezogenen Daten ein.

Vor- und Nachname

Ort, Datum, Unterschrift

„Vorhofflimmern und Sport.“

Name der/des Patienten/in_____

An der Deutschen Sporthochschule Köln wird im Institut für Kreislaufforschung und Sportmedizin eine Studie vorbereitet, welche den Einfluss von körperlicher Belastung in Form von Ausdauertraining, Intervalltraining und Krafttraining auf Patienten mit Vorhofflimmern untersucht. Hintergrund der Studie ist die Beobachtung, dass Vorhofflimmern in der Bevölkerung immer mehr zunimmt und dass sportliche Interventionen bisher positive Effekte auf diverse Parameter aufzeigen konnten. Die gewonnenen Ergebnisse aus der Studie sollen mit dazu beitragen, neue Konzepte für die Therapie des Vorhofflimmerns zu entwickeln.

Studieninhalte

Im Rahmen der Studie wird ein 12-wöchiges Trainingsprogramm á 2 Trainingseinheiten pro Woche durchgeführt. Vor und nach dem 12-Wochen-Zeitraum werden medizinische Untersuchungen und Testungen zu Ausdauer und Kraft durchgeführt.

Untersuchung

An der Studie können Menschen im Alter zwischen 50 und 80 Jahren mit anfallsartigem (paroxysmalem) Vorhofflimmern teilnehmen.

Alle Untersuchungen finden in der Deutschen Sporthochschule Köln, Institut für Kreislaufforschung und Sportmedizin, statt (NawiMedi, 1. Stock).

Im Rahmen einer Voruntersuchung werden Sie über den Inhalt, den Ablauf und mögliche Risiken der Studie aufgeklärt. Es werden Ihnen formale Dokumente ausgeteilt, Sie füllen einen Fragebogen aus und unterschreiben die Einverständniserklärung. Des Weiteren vereinbaren wir nach Einschluss in die Studie die weiteren Termine für die nächsten Untersuchungen.

Hauptuntersuchung (Durchführung einmal vor der Trainingsintervention und einmal nach der Trainingsintervention)

Es werden folgende Untersuchungen durchgeführt:

- Anthropometrische Daten:
  - Körpergewicht, Körpergröße, Körperzusammensetzung, Bauchumfang
- Ruhe-EKG
- Ruhe Blutdruckmessung
- Arteriographie
- Herzfrequenzvariabilitätsmessung
- Blutabnahme (nüchtern)
- Echokardiografie
- Ultraschall der Beinmuskulatur
- Spiroergometrie mit Laktatmessung auf dem Fahrradergometer
- 24-Stunden-Blutdruckmessung und -EKG

Training

Das Training findet in den Räumlichkeiten der Deutschen Sporthochschule statt (NawiMedi, 1. Stock, Trainingsraum).

Die TeilnehmerInnen werden in vier Gruppen zufällig eingeteilt (**randomisiert**).

Gruppe A: submaximales Krafttraining

Gruppe B: moderates Ausdauertraining

Gruppe C: intensives Ausdauertraining (HIIT)

Gruppe D: Kontrollgruppe

Die Trainingseinheiten werden unter Anleitung und kontinuierlicher Betreuung durchgeführt.

Das Gruppentraining findet 2x wöchentlich à 60 Minuten statt.

Die Trainingseinheiten sind auf Ihre individuelle Leistungsfähigkeit zugeschnitten. Die individuelle Belastungsintensität wird aus dem Fahrradbelastungstest und durch standardisierte Krafttestungen am Gerät ermittelt.

Nach dem Ende der Trainingsintervention und absolvierter Untersuchung ist die empirische Phase der Studie beendet.

Es fallen bei Teilnahme an der Studie für Sie keinerlei Kosten an. Die Anfahrt zu den Untersuchungen und Trainingseinheiten müssen Sie jedoch selber tragen. Es werden keine Reisekosten erstattet.

Mögliche gesundheitliche Risiken

Zur Vermeidung eines erhöhten Risikos bei einer Teilnahme an körperlichen Belastungstests und sportlichem Training, werden mögliche gesundheitliche Risiken mittels Fragebogen, Untersuchung und eines Belastungstests des Herz-Kreislauf-Systems unter ärztlicher Aufsicht ausgeschlossen.

Die TeilnehmerInnen werden während des Trainings von ausgebildeten Fachkräften betreut.

Trotzdem können natürlich bei intensiver oder ungewohnter Belastung Beschwerden auftreten (z.B. Muskelkater durch Krafttraining, Bluthochdruck durch Belastung, etc.). Die Wahrscheinlichkeit für Komplikationen ist sehr gering. Das erfahrene Team aus Sportwissenschaftlern und Sportmedizinern wird Sie diesbezüglich kontrollieren und informieren und stets zur Seite stehen.

Blutentnahme

Mit der Ausnahme der Blutentnahmen und Laktatmessungen beinhaltet diese Studie kein weiteres invasives Verfahren.

Falls Sie krank sind oder sich nicht wohl fühlen, informieren Sie das Studienpersonal.

Ihr persönlicher Nutzen bei Studienteilnahme

- Kostenfreie, umfangreiche Untersuchungen mit Bestimmung der körperlichen Leistungsfähigkeit und der Laborparameter
- Individuelle Empfehlungen für ein sportliches Training
- Kostenfreies gesundheitsorientiertes und strukturiertes Trainingsprogramm
- Bewusster Beitrag für Ihre Gesundheit
- Beitrag zur konzeptionellen Entwicklung der Therapie bei Vorhofflimmern.

Aus diesen Gründen werden Sie auf jeden Fall von der Studienteilnahme profitieren.

Nur durch Ihr Engagement, Ihre ermittelten Körperdaten und Ihre Meinung kann unser wissenschaftliches Projekt gelingen.

Wir würden uns freuen, Sie als Teilnehmerin an unserer Studie begrüßen zu dürfen.

Mit freundlichen Grüßen

Studienarzt Sportwissenschaftlerin wissenschaftliche Assistentin

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Anhang C: Patienteneinverständniserklärung Studie

„Vorhofflimmern und Sport."

Name der/des Patienten/in_____

Probanden- Einverständniserklärung

1. Hiermit erkläre ich mich freiwillig bereit, an der oben genannten Studie teilzunehmen.

2. Mir ist bekannt, dass ich jederzeit meine Zustimmung zur Teilnahme an der Studie widerrufen kann, ohne mich hierfür rechtfertigen zu müssen.

3. Die zuständigen Personen des Instituts für Kreislaufforschung und Sportmedizin der Deutschen Sporthochschule Köln haben mich über Wesen, Bedeutung und Tragweite dieser Studie in verständlicher Form aufgeklärt.

4. Ich habe die Patienteninformation erhalten, gelesen und verstanden.

5. Mir wurde die Möglichkeit eingeräumt, Fragen zur Probandenaufklärung und zu meiner Teilnahme an der Studie zu stellen. Auf meine Fragen habe ich ausreichend Antworten erhalten.

6. Ich bin einverstanden, dass meine Daten – im Rahmen der Studie –gespeichert sowie wissenschaftlich ausgewertet werden. Dies geschieht ohne Angabe von Name und Anschrift meiner Person.

7. Die Bestimmungen des Bundesdatenschutzgesetztes sowie des SGB (Sozial-Gesetzbuches) 5 und SGB 10 werden erfüllt.

Eine Kopie dieser Einverständniserklärung habe ich erhalten

_ _

Unterschrift Studienteilnehmerin Unterschrift der aufklärenden Person

_ _

Ort, Datum Ort, Datum

Deutsche Sporthochschule Köln
German Sport University Cologne

Datenschutzinformationen

Das Institut für Kreislaufforschung und Sportmedizin der Deutschen Sporthochschule Köln (nachfolgend bezeichnet als „DSHS“) erhebt von Ihnen personenbezogene Daten zum Zwecke der **sportmedizinischen Untersuchung und Behandlung**. Der Schutz Ihrer personenbezogenen Daten ist für die DSHS dabei ein zentrales Anliegen. Dementsprechend fühlen wir uns den gesetzlichen Vorgaben, insbesondere der europäischen Datenschutz-Grundverordnung (nachfolgend bezeichnet als „DS-GVO“), dem Datenschutzgesetz des Landes Nordrhein-Westfalen und dem Hochschulgesetz des Landes Nordrhein-Westfalen verpflichtet.

Mit diesen Datenschutzbestimmungen informieren wir Sie gemäß Art. 13 und 14 DS-GVO über den Umgang mit Ihren personenbezogenen Daten und Ihre Rechte nach der DS-GVO.

1. Wer ist für die Datenverarbeitung verantwortlich?

Verantwortliche Stelle im Sinne der Datenschutzgesetze ist die

Deutsche Sporthochschule Köln,
Institut für Kreislaufforschung und Sportmedizin
Am Sportpark Müngersdorf 6
50933 Köln
Deutschland
Tel.: 0221 4982 5270
E-Mail: sportmedizin@dshs-koeln.de

2. Wie kann der Datenschutzbeauftragte kontaktiert werden?

Der Datenschutzbeauftragte der verantwortlichen Stelle kann wie folgt kontaktiert werden:

Deutsche Sporthochschule Köln
Der Datenschutzbeauftragte
- persönlich -
Am Sportpark Müngersdorf 6
50933 Köln
Deutschland
E-Mail: datenschutz@dshs-koeln.de

3. Für welche Zwecke und auf welchen Rechtsgrundlagen werden Ihre Daten verarbeitet?

Die DSHS erhebt von Ihnen im Rahmen der sportmedizinischen Betreuung folgende personenbezogene Daten: Geburtsdatum, Adresse und weitere Kontaktdaten, Krankengeschichte inkl. akuter Beschwerden, Sport- und Leistungshistorie, sowie weitere sportmedizinisch relevante Informationen je nach Fall und spezifischer Fragestellung: Hierzu können zählen Körpermaße und -zusammensetzung, Leistungsparameter (z.B. Ergometriedaten, Laktatwerte, etc.), Funktionsparameter diverser Organe (z.B. EKG, Lungenfunktionsprüfung, Herzleistung, etc.), Laborwerte (ausmaß je nach Untersuchungsziel variabel).

Rechtsgrundlage der Datenverarbeitung ist Art. 6 Abs. 1 S. 1 a) und Art. 9 Abs. 2 a) DS-GVO.

Um die sportmedizinische Athleten- und Patientenbetreuung stets zu optimieren werden die erhobenen Daten anonymisiert für Forschungsprojekte verwendet. Eine Veröffentlichung Ihrer personenbezogenen Daten erfolgt grundsätzlich nur in anonymisierter Form, also ohne die Möglichkeit einen Rückschluss auf Ihre Person zu ziehen.

4. An wen werden Ihre Daten weitergeleitet?

Eine Weitergabe Ihrer persönlichen Daten an Dritte erfolgt ohne Ihre ausdrückliche Einwilligung nicht. Auch die Übermittlung an auskunftsberechtigte staatliche Institution und Behörden erfolgt nur im Rahmen der gesetzlichen Auskunftspflichten oder wenn wir durch eine gerichtliche Entscheidung zur Auskunft verpflichtet werden. Sofern wir zur Zweckerfüllung auf vertraglich verbundene Fremdunternehmen und externe Dienstleister angewiesen sind, wurden diese von uns sorgfältig ausgewählt und beauftragt, sind an unsere Weisungen gebunden und werden regelmäßig kontrolliert.
Im Ramen der sportmedizinischen Untersuchung werden entnommene Blutproben inklusive personenbezogener Daten an externe Labore übergeben, um Werte zu erheben, die die hausinterne Diagnostikmöglichkeit überschreiten.

5. Wie lange werden Ihre Daten gespeichert?

Ihre Daten werden 10 Jahre in den Archiven des Institutes für Kreislaufforschung und Sportmedizin aufbewahrt. Nach Ablauf der Aufbewahrungsfrist werden Ihre Daten gelöscht/vernichtet.

Ihre Daten werden anonymisiert, sobald dies nach dem Forschungs- oder Statistikzweck möglich ist.

6. Welche Rechte haben Sie?

Aufgrund der Erhebung und Verarbeitung Ihrer personenbezogenen Daten haben Sie uns gegenüber folgende Rechte hinsichtlich der Sie betreffenden personenbezogenen Daten:

- Recht auf Auskunft nach Art. 15 DS-GVO,
- Recht auf Berichtigung Ihrer Daten nach Art. 16 DS-GVO oder Löschung Ihrer Daten nach Art. 17 DS-GVO,
- Recht auf Einschränkung der Verarbeitung nach Art. 18 DS-GVO,
- Recht auf Datenübertragbarkeit nach Art. 20 DS-GVO.
- Sofern die Datenverarbeitung auf Grundlage einer Einwilligung (Art. 6 Abs. 1 S. 1 a) oder Art. 9 Abs. 2 a) DS-GVO) erfolgt, haben Sie gemäß Art. 7 Abs. 3 DS-GVO das Recht auf

jederzeitigen Widerruf Ihrer Einwilligung, ohne dass die Rechtmäßigkeit der aufgrund der Einwilligung bis zum Widerruf erfolgten Verarbeitung berührt wird.

- Soweit Sie der Ansicht sind, dass Ihre vorstehend aufgeführten Rechte im Sinne des geltenden Datenschutzrechts verletzt sind, haben Sie zudem nach Art. 77 DS-GVO das Recht sich bei der zuständigen Aufsichtsbehörde zu beschweren. Hierzu können Sie sich an die Landesbeauftragte für Datenschutz und Informationsfreiheit Nordrhein-Westfalen,
  Kavalleriestraße 2-4, 40213 Düsseldorf
  Postfach 20 04 44, 40102 Düsseldorf,
  Telefon: 0211 38424 – 0
  E-Mail unter poststelle@ldi.nrw.de

  wenden. Weitere Informationen erhalten Sie unter http://www.ldi.nrw.de.

Sofern die Datenverarbeitung gemäß Art. 6 Abs. 1 S. 1 e) DS-GVO erfolgt, haben Sie nach Art. 21 DS-GVO das Recht, dieser Verarbeitung jederzeit unter der oben unter Ziff. 1 genannten Adresse zu widersprechen, sofern sich aus Ihrer besonderen Situation Gründe ergeben, die dieser Datenverarbeitung entgegenstehen. Die Datenverarbeitung wird dann beendet, es sei denn, die DSHS kann zwingende schutzwürdige Gründe für die Verarbeitung nachweisen, die Ihre Interessen, Rechte und Freiheiten überwiegen, oder sofern die Verarbeitung der Geltendmachung, Ausübung oder Verteidigung von Rechtsansprüchen dient.

Ich habe die Datenschutzinformation gelesen, zur Kenntnis genommen und bin einverstanden.

Vor- und Nachname

Ort, Datum, Unterschrift

Einwilligungserklärung zur Datenverarbeitung:

Im Rahmen der sportmedizinischen Untersuchung, ggf. im Sinne einer Sporttauglichkeitsuntersuchung, werden folgende personenbezogene Daten von Ihnen erhoben und verarbeitet: Vor- und Zuname, Geburtsdatum, Adresse und weitere Kontaktdaten, Krankengeschichte inkl. akuter Beschwerden, Sport- und Leistungshistorie, sowie weitere sportmedizinisch relevante Informationen je nach Fall und spezifischer Fragestellung: Hierzu können zählen Körpermaße und -zusammensetzung, Leistungsparameter (z.B. Ergometriedaten, Laktatwerte, etc.), Funktionsparameter diverser Organe (z.B. EKG, Lungenfunktionsprüfung, Herzleistung, etc.), Laborwerte (ausmaß je nach Untersuchungsziel variabel).

Hierfür benötigen wir Ihre Einwilligungserklärung. Rechtsgrundlage der Datenverarbeitung ist Art. 6 Abs. 1 S. 1 a) sowie Art. 9 Abs. 2 a) DS-GVO. Ihre Einwilligungserklärung ist freiwillig, jedoch ist ohne diese eine sportärztliche Beurteilung und Ausstellung einer Sporttauglichkeit nicht möglich, was je nach Regelwerk des jeweiligen Sportverbandes eine regelrechte Teilnahme an Training und Wettkämpfen unmöglich machen könnte und in speziellen Fällen auch eine Einschränkung von Förderung nach sich ziehen kann. Sie können Ihre Einwilligungserklärung jederzeit mit Wirkung für die Zukunft widerrufen. Ihre personenbezogenen Daten werden dann unverzüglich gelöscht, soweit die weitere Speicherung nicht auf Grundlage einer gesetzlichen Vorschrift gestattet und geboten ist. Durch den Widerruf der Einwilligungserklärung wird die Rechtmäßigkeit der aufgrund der Einwilligungserklärung bis zum Widerruf erfolgten Datenverarbeitung nicht berührt.

Ich willige in die Verarbeitung meiner personenbezogenen Daten ein.

Vor- und Nachname

Ort, Datum, Unterschrift

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	5
	2b	All items from the World Health Organization Trial Registration Data Set	5
Protocol version	3	Date and version identifier	5
Funding	4	Sources and types of financial, material, and other support	14
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1
	5b	Name and contact information for the trial sponsor	NA
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	5
Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
	6b	Explanation for choice of comparators	4-5
Objectives	7	Specific objectives or hypotheses	4-5

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	5-6
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	7
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6/7
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8-9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	8 (see fig. 1)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	6-7
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7

Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	7
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	7-8
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9/10
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	12
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	6/7
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	9/10
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA

Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	14
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	5
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	5
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	14
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	5
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	12
	31b	Authorship eligibility guidelines and any intended use of professional writers	15
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	14+appendix 1
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.