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Cardiac health in breast cancer (CHiB): protocol for a single-centre, randomised controlled trial

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ABSTRACT

The incidence of breast cancer has increased from 900 000 to 2.3 million new annual cases over the last 25 years. The 5-year survival rate has markedly risen to over 90% worldwide due to significant therapeutic advancements. Longer survival in patients with breast cancer means more patients may experience long-term effects of their treatments, including cancer therapy-related cardiac dysfunction (CTRCD). To date, there is no established primary prevention to minimise CTRCD. The Cardiac Health in Breast Cancer study is a two-arm, single-centre, randomised controlled trial investigating the impact of an exercise programme on cardiac changes in patients with breast cancer undergoing cardiotoxic cancer therapy. 48 females with breast cancer will be randomised to either a 12-month intervention group (IG) or a control group (CG). The IG will receive a combination of supervised high-intensity interval training (HIIT) and high-intensity resistance training (HIRT) for 6 months, while the CG will follow WHO guidelines for physical activity independently. All participants will undergo transthoracic echocardiography, cardiac magnetic resonance (CMR) imaging and cardiopulmonary exercise testing at baseline, after 6 months and after 12 months. The primary endpoint is the occurrence of symptomatic or asymptomatic CTRCD at the time points of examination, detected by cardiac imaging, which may be mitigated by structured physical exercise. Secondary endpoints include assessments of cardiac inflammation as detected by CMR, mitochondrial dysfunction, health-related quality of life, the occurrence of fatigue, depression and anxiety, as well as exercise capacity, average heart rate, heart rate variability and daily physical activity.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with breast cancer are at risk of developing cardiac damage and dysfunction as a long-term sequela of cardiotoxic cancer therapies.
⇒ Effective primary preventive strategies for cancer-therapy-related cardiac dysfunction (CTRCD) are currently lacking.

WHAT THIS STUDY ADDS

⇒ Cardiac Health in Breast Cancer is the first randomised clinical trial to investigate the long-term effects of structured high-intensity interval training and high-intensity resistance training on the occurrence of symptomatic and asymptomatic CTRCD and cardiac inflammation in patients with breast cancer.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND POLICY

⇒ The study may provide evidence for the primary preventive effects of a structured exercise program in mitigating cardiac dysfunction associated with cardiotoxic breast cancer therapies.
⇒ The clinical findings could be pivotal for CTRCD research, potentially informing the development of targeted exercise prescription guidelines during cardiotoxic cancer treatment.
⇒ As a single-centre study, the result could stimulate collaboration and pave the way for future multicentre studies in this area.

INTRODUCTION

Cancer-therapy-related cardiac dysfunction (CTRCD) and cardiovascular imaging

Female breast cancer, with an estimated 2.3 million new cases, is the most diagnosed cancer worldwide (11.7%).[1] Alongside the rising incidence of breast cancer, the 5-year survival rate has increased to over 90% currently, largely attributable to advances in early detection and treatment.[2] However, these therapeutic advances lead to more and more patients also experiencing long-term effects of their cancer therapy. CTRCD occurs in approximately 10% of patients with cancer.[3] It is characterised by either a decrease in left ventricular ejection fraction (LVEF) of more than 10% to an LVEF of below 55% or a decrease greater than 15% in global longitudinal strain (GLS) compared with baseline GLS as an indication of subclinical LV dysfunction.[4] In the 2022 European Society of Cardiology (ESC) guidelines on cardio-oncology, the definition of CTRCD is expanded by the inclusion of a new

significant rise in cardiac biomarkers (troponin T, 99th percentile, B-type natriuretic peptide (BNP) ≥35 pg/mL, N-terminal pro-BNP (NT-proBNP) ≥125 pg/mL).[5] Three-dimensional echocardiography (3DE) is superior to two-dimensional echocardiography (2DE) in terms of sensitivity and false negative rate for detecting an LVEF of less than 50% on cardiac magnetic resonance (CMR),[6] making it the preferred echocardiographic technique for monitoring the cardiac effects of chemotherapy and assessing LVEF.[7 8] Additionally, GLS can be determined and is crucial for predicting subclinical LV dysfunction at an earlier stage than LVEF measurement alone.[9 10] Moreover, GLS is essential for monitoring cardiotoxic effects after chemotherapy,[11 12] enabling the early detection of CTRCD.[13 14] CMR remains the gold standard for identifying early cardiac changes, including myocardial inflammation, oedema, alterations in LV strain and LV mass variations.[15] However, CMR is generally recommended as a second-line modality for screening and monitoring patients with cancer undergoing cardiotoxic therapy, primarily reserved for cases with poor echocardiographic image quality or inconclusive results. In our recent study on characterising cardiac changes during cardiotoxic cancer therapy, CMR identified subclinical CTRCD in 56.3% of a cohort of 34 patients with breast cancer.[16] Notably, follow-up CMR at 12 months indicated a regression of these subclinical cardiac abnormalities, suggesting potential reversibility of CTRCD with appropriate monitoring and management.

Effects of training intervention on cardiac function in patients with breast cancer

Regular physical activity is a fundamental component in primary and secondary prevention of cardiovascular disease.[17] Evidence indicates that exercise training significantly reduces the risk of cardiovascular events,[18 19] as well as overall morbidity and mortality,[20] in breast cancer survivors. Preclinical studies have shown that exercise offers cardioprotective effects during doxorubicin treatment by upregulating cardiac telomere-stabilising proteins[21] and enhancing cardiac mitochondrial antioxidant enzymes.[22] Previous studies assessing the impact of exercise training on LVEF and GLS in patients with breast cancer undergoing cardiotoxic chemotherapy revealed no significant differences for both parameters between the exercise and non-exercise groups.[23 24] However, one study reported that exercise mitigated the adverse effects of anthracyclines (AC) on GLS, indicating potential cardioprotective benefits.[25] This study was CMR-based and observed a significant increase in native T1 time post-AC chemotherapy in all participants and reduced GLS in the non-exercise group, indicating early myocardial inflammation and dysfunction, respectively. In our previous research on patients with breast cancer gene mutations, high-intensity interval training (HIIT) and high-intensity resistance training (HIRT) were found to positively influence subjective well-being and physical performance while also temporarily reducing inflammatory markers.[26 27] This aligns with other studies demonstrating improved maximum oxygen uptake (VO_2peak) in exercise intervention groups (IGs), in contrast to a decline in VO_2peak observed in usual care groups among patients with breast cancer.[24 28] Furthermore, physical exercise has been shown to enhance psychosocial functioning and health-related quality of life in patients with breast cancer and survivors,[29] while significantly reducing cancer-related fatigue.[30]

The field of research on the effects of exercise on GLS and LVEF in patients with breast cancer is significantly underserved and suffers from a lack of quality in methodological design. The current data on the impact of exercise on cardiac function in patients with breast cancer does not allow for definitive recommendations due to the lack of randomised trials, studies with large sample sizes and comparable training programmes and durations. This study aims to investigate the long-term effects of structured HIIT and HIRT on symptomatic and asymptomatic CTRCD and cardiac inflammation in patients with breast cancer. The findings have the potential to significantly advance CTRCD research and contribute to the development of targeted exercise prescription guidelines for patients undergoing cardiotoxic cancer treatments.

METHODS AND ANALYSIS

Study design

The Cardiac Health in Breast Cancer (CHiB) study is a single-centre, two-armed, randomised controlled

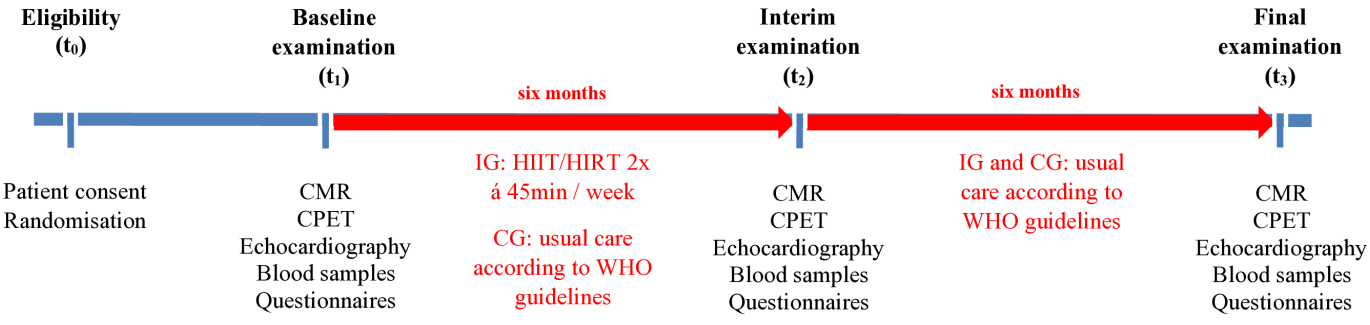

Figure 1 Schedule for study visits and procedures in the Cardiac Health in Breast Cancer study. CG, control group; CMR, cardiac magnetic resonance; CPET, cardiopulmonary exercise testing; IG, intervention group; HIIT, high-intensity interval training; HIRT, high-intensity resistance training.

trial. The study protocol (V.2.1, 9 August 2024) follows the[31] Standard Protocol Items: Recommendations for Interventional Trials 2013 statement, defining standard protocol items for clinical trials.[31] All participants will be recruited from the Sports and Rehabilitation Medicine at the University Hospital of Ulm in Germany. The study aims to randomly assign 48 patients with breast cancer undergoing adjuvant or neoadjuvant cardiotoxic chemotherapy to one of two groups for 12 months. The IG will receive supervised combined HIIT and HIRT in addition to their breast cancer treatment for 6 months. The control group (CG) will follow general exercise recommendations per WHO guidelines during breast cancer treatment (figures 1 and 2). Eligible participants must have histologically confirmed breast cancer and must not have received any neoadjuvant or adjuvant treatment before inclusion in the CHiB study. Upon confirmation of eligibility (t_0), all participants will undergo a baseline examination before initiation of breast cancer therapy (t_1), which includes echocardiography, CMR, blood tests, questionnaires, a physical examination with anthropometric measurements and cardiopulmonary exercise testing (CPET). Randomisation into the IG or CG will be conducted using a predefined randomisation list. The examination series, encompassing all components, will be repeated at 6 months (t_2) and 12 months (t_3) following the intervention (figure 1).

Objectives and hypotheses

The primary objective of the study is to determine whether a structured programme of HIIT and HIRT can mitigate symptomatic or asymptomatic CTRCD in patients with breast cancer undergoing cardiotoxic cancer therapies and to assess whether HIIT and HIRT have no adverse effects on inflammation as detected by CMR. Secondary objectives include investigating

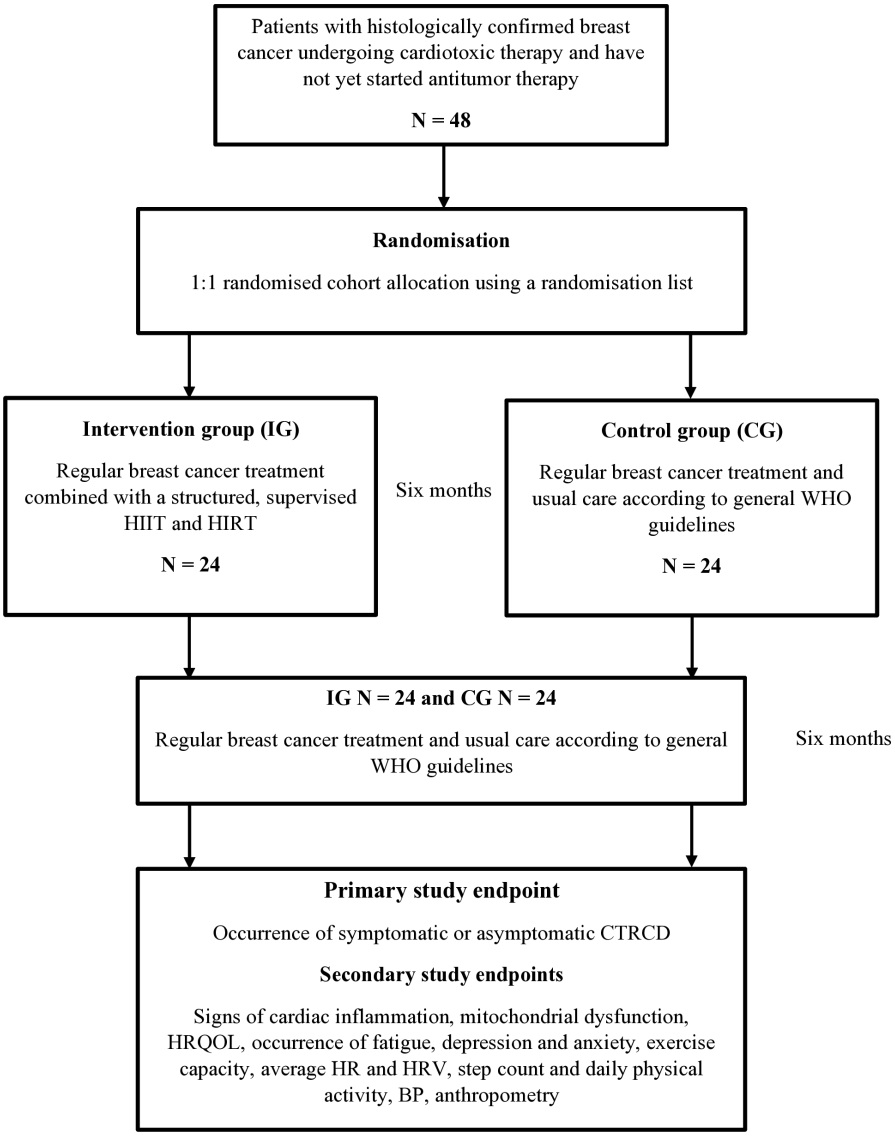

Figure 2 Flowchart of the study design of the Cardiac Health in Breast Cancer study. BP, blood pressure; CTRCD, cancer-therapy-related cardiac dysfunction; HIIT, high-intensity interval training; HIRT, high-intensity resistance training; HRQOL, health-related quality of life; HR, heart rate; HRV, heart rate variability.

mitochondrial dysfunction and mental health outcomes, specifically depression, fatigue and anxiety. Additionally, the study will evaluate health-related quality of life and vital parameters such as average heart rate and heart rate variability (HRV). We hypothesise that a structured exercise programme incorporating HIIT and HIRT will prevent or minimise the incidence of CTRCD without increasing cardiac inflammation. Furthermore, we anticipate that HIIT and HIRT will improve mitochondrial function, reduce average heart rate and enhance HRV. We also hypothesise that these exercise interventions will positively impact mental health by decreasing levels of depression, fatigue and anxiety.

Primary and secondary endpoints

Structured physical exercise, including HIIT and HIRT, may reduce the primary endpoint, which is the occurrence of symptomatic or asymptomatic CTRCD in patients with breast cancer undergoing cardiotoxic cancer therapies. This potential occurrence is assessed at three distinct time points (figure 1), using transthoracic echocardiography and various CMR sequences and the measurement of cardiac biomarkers. CTRCD is defined, according to the current ESC guidelines, as a decrease in LVEF by more than 10% to below 50% or a drop greater than 15% in GLS from baseline, indicating subclinical LV dysfunction.[5] It may also include a new elevation in cardiac biomarkers such as troponin T above the 99th percentile or NT-proBNP ≥125 pg/mL.[5] The echocardiographic evaluation includes measurements of cardiac structure and function and markers for subclinical cardiac dysfunction, including longitudinal, radial and circumferential strain. Additionally, non-invasive-tissue characterisation parameters on CMR, such as native T1 time, T2 time, postcontrast T1 time for determining extracellular volume and late gadolinium enhancement (LGE), are assessed. The primary and secondary endpoints of the study are detailed in table 1.

Study population and eligibility criteria

Eligibility criteria include female patients aged ≥18 years with a histologically confirmed type of breast cancer independent of cancer stage who are planning to undergo cardiotoxic chemotherapy, either as neoadjuvant or adjuvant treatment. Exclusion criteria are current pregnancy, contraindications for MRI such as the presence of ferromagnetic implants or claustrophobia, or contraindications to gadolinium-contrast medium, a glomerular

Table 1 Primary and secondary endpoints of the Cardiac Health in Breast Cancer study

Endpoints	Description
Primary endpoint	
Occurrence of symptomatic/asymptomatic CTRCD	Assessment of cardiac structure and function using transthoracic echocardiography, CMR sequences, CPET and myocardial biomarkers (troponin T and N-terminal pro B-type natriuretic peptide)
Secondary endpoints	
Signs of cardiac inflammation	Detecting changes from baseline (t_1) to follow-up (t_2) and final examination (t_3) by CMR imaging
Mitochondrial dysfunction	Mitochondrial and molecular markers (galectin-3, klotho, kynurenine, cell-free mitochondrial DNA and nuclear DNA, musclin, nuclear respiratory factor 2, peroxisome proliferator-activated receptor-γ coactivator-1α, rhodanase)
Health-related quality of life	EuroQol-five dimension questionnaire
Fatigue	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-FA12 questionnaire
Depression	Patient Health Questionnaire-9
Anxiety	Generalised Anxiety Disorder-7 questionnaire
Average heart rate	Tracked by the fitness watch
Heart rate variability	Tracked by the fitness watch
Step count and daily physical activity	Tracked by the fitness watch
Blood pressure	Assessment at baseline (t_1), follow-up (t_2) and final examination (t_3)
Exercise capacity	CPET with an assessment of maximum oxygen uptake and maximum power
Strength capacity	Grip strength
Anthropometry	Body weight, body mass index, fat mass, free fat mass, waist-to-height-ratio

CMR, cardiac magnetic resonance; CPET, cardiopulmonary exercise testing; CTRCD, cancer-therapy-related cardiac dysfunction.

filtration rate of less than 30 mL/min and pre-existing cardiovascular diseases, including heart failure with reduced ejection fraction, cardiac arrhythmias, a history of coronary artery disease or previous pulmonary artery embolism. Further exclusion criteria include a history of cardiac surgery, congenital heart defects and orthopaedic or functional limitations that contraindicate physical exercise training. These criteria are designed to ensure the safety of participants undergoing the specified procedures and treatments in the CHiB study. Patients must provide written and oral informed consent using a standard information sheet and an informed consent form approved by the local ethical committee.

Training intervention

Patients with breast cancer will be randomised in a 1:1 ratio to either an intervention group (IG) or a control group (CG). The IG will participate in a supervised programme of HIIT and HIRT in addition to breast cancer treatment at the Department of Sports and Rehabilitation Medicine.[26] In contrast, CG will receive physical activity recommendations per WHO guidelines during the baseline examination. The IG will train twice weekly, each session lasting 45 min and consisting of HIIT and HIRT. HIIT will be conducted on a cycling ergometer, continuously monitoring intensity and heart rate (HR). The training loads for HIIT will be individually tailored using data obtained from the initial CPET. Supervised HIRT will be performed using six different strength training machines (Technogym, Cesena, Italy) targeting both upper and lower body muscle groups (see table 2). Exercises will be conducted at an intensity of 80% of the one-repetition maximum (1-RM), with eight to twelve repetitions per exercise and three sets per session. The 1-RM is the maximum weight a patient can lift with the correct form for a single repetition. Each training session will begin with a short warm-up period before commencing HIIT and HIRT exercises. The supervised training allows the exercise programme to be adapted to individual needs and illness-related conditions. After the 6-month follow-up (t_2), the supervised exercise programme in the IG will be discontinued, and participants in the IG will then receive physical activity recommendations according to WHO guidelines like the CG.

Exercise monitoring

Both groups will monitor daily physical activity using a fitness watch throughout the entire study period. All participants will be given a fitness watch (Garmin Forerunner165, Schaffhausen, Switzerland) and instructed to wear it consistently throughout the study period, emphasising its use during supervised training. In the IG, exercise intensity and HR will be continuously monitored during HIIT sessions on the bicycle ergometer. This real-time monitoring ensures that patients maintain their individualised training load, thereby ensuring the quality of the HIIT regimen. In addition to HR, HRV will be accurately tracked by the fitness watches. Data on step count and overall daily physical activity will also be collected. These metrics will facilitate the comparative analysis between the supervised IG and the CG and provide insights into individual progress and development trends over the study period.

Transthoracic echocardiography

According to current recommendations, transthoracic echocardiography will be performed with a study-specific protocol.[32 33] To assess cardiac structure and function, 2D and 3D echocardiographic imaging will be performed using an EPIQ seven ultrasound system equipped with a phased-array probe X5-1 (Philips GmbH, Hamburg, Germany). Captured data will include motion mode (M-mode), colour Doppler and tissue Doppler imaging. All recorded datasets will be exported and digitally stored on an EchoView 5.4 workstation (TomTec Imaging System GmbH, Unterschleissheim, Germany). A physician, who will be blinded to the patients' clinical and study-related information, will analyse the images using post-processing software (AutoStrain, Ultrasound Workspace, TomTec Imaging Systems, Unterschleissheim, Germany). Parameters assessed will include systolic and diastolic dimensions of the left ventricle, left and right atrial volumes and right ventricular (RV) size. LVEF will be determined using either 3DE or 2DE with Simpson biplane planimetry. RV function will be evaluated by measuring tricuspid annular plane systolic excursion and fractional area change. Additionally, diastolic function will be assessed, and speckle tracking analysis will be performed in all four cardiac chambers.

Table 2 Strength training for the intervention group

	Strength training	1-RM (%)	Repetitions	Sets
First[t] block	Leg press and rowing machine	80	8–12	3
Second block	Knee extension with each leg individually	80	8–12	3
Third block	Knee flexors with each leg individually	80	8–12	3
Fourth block	Latissimus pulldown and chest press	80	8–12	3

Modified according to Schulz *et al*.[26]
RM, repetition maximum;

CMR imaging

CMR imaging will be conducted at three specific intervals: before the commencement of training (t_1), at 6 months (t_2) and 12 months (t_3). All study participants will undergo imaging using a 3.0 Tesla (T) scanner equipped with an 18-channel phased-array body coil (MAGNETOM Vida Fit, Siemens Healthineers, Erlangen, Germany). Images will be obtained with a balanced steady-state free precession cine sequence in three long-axis views (2-, 3- and 4-chamber) and contiguous short-axis views for comprehensive volumetric and functional assessment.[34] Strain parameters will be derived postprocessing using feature-tracking techniques. For parametric mapping, T1 maps will be acquired using a modified Look-Locker inversion recovery (MOLLI) sequence before and after gadobutrol administration (Gadovist, Bayer, Leverkusen, Germany). Extracellular volume (ECV) will be calculated using a standardised haematocrit value of 40%. T2 mapping will be performed with a T2-prepared True Fast Imaging with Steady-State Precession (TrueFISP) sequence, employing varying T2 preparation times (0, 25 and 55 ms). Both T1 and T2 mapping will be conducted in the mid-ventricular short-axis plane. Additionally, 10 min post-gadobutrol administration, an inversion-recovery gradient-echo sequence will be acquired, adjusted for individual inversion time using a Look-Locker sequence, to assess LGE in the same orientations as the cine sequences. All images will be interpreted by experienced examiners blinded to clinical data using established software (cvi42, Circle Cardiovascular Imaging, Calgary, Canada).

Cardiopulmonary exercise testing

CPET will be conducted according to the clinical recommendations for CPET. Data assessment in specific patient populations will be conducted during baseline (t_1), 6-month (t_2) and 12-month (t_3) follow-up examinations.[35] CPET will be performed on a cycle ergometer (Excalibur Sport, LODE B.V., Groningen, The Netherlands) using a breath-by-breath-gas analysis system (Quark CPET, COSMED, Srl, Rom, Italy). Each patient will undergo an incremental exercise test with a ramp protocol tailored to her age, weight and estimated fitness level. The protocol will be designed to reach volitional exhaustion within 8–12 min and to determine VO_2peak and maximum power. VO_2peak is defined as the average oxygen uptake measured during the final 30 s before the termination of the test. The data obtained from CPET at the baseline visit will be used to set the training loads for HIIT in the IG. During the CPET, a 12-lead ECG will be recorded using the Cardiopart 12 Blue/Blue-P system (AMEDTEC Medizintechnik Aue GmbH, Aue, Germany). CPET will be repeated during follow-up (t_2) and after the study (t_3) for both groups to evaluate changes in cardiopulmonary performance over time.

Blood samples

In addition to standard laboratory parameters, blood samples will be analysed for myocardial biomarkers (troponin T and NT-proBNP) and a panel of molecular and mitochondrial markers. These include galectin-3, klotho, kynurenine, the cell-free mitochondrial DNA and nuclear DNA in plasma, musclin, nuclear respiratory factor 2, peroxisome proliferator-activated receptor-γ coactivator-1α and rhodanese, measured at all three assessment time points. These biomarkers are implicated in key biological processes such as cellular growth and senescence, apoptosis, neurotoxicity, mitochondrial function, metabolic activity and oxidative stress. Comparative data from a healthy control cohort have been previously established at the Sports and Rehabilitation Medicine at the University Hospital of Ulm.

Questionnaires

Standardised questionnaires will be administered at baseline (t_1), follow-up (t_2) and final examination (t_3) to evaluate specific health-related outcomes. The assessment will focus on potential depression using the Patient Health Questionnaire-9,[36] fatigue using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-FA12 questionnaire[37] and anxiety using the Generalised Anxiety Disorder-7 questionnaire.[38] Additionally, overall health-related quality of life will be assessed using the EuroQol-five dimension questionnaire.[39] These instruments will facilitate the evaluation of any associations between therapy-related changes and the participants' mental health.

Adverse events (AEs)

Any unfavourable or unintended signs, symptoms, or outcomes that occur during or after participation in the exercise intervention will be reported as AEs. In this breast cancer study, serious AEs may include death, life-threatening conditions, cardiovascular events or inpatient hospitalisation. Additionally, minor AEs may encompass musculoskeletal injuries, respiratory issues, pre-existing conditions, exacerbation and fatigue or overexertion symptoms. All such events will be carefully monitored for both groups at each study visit and for the IG at each exercise session. Comprehensive documentation will be maintained to ensure participants' safety and the study's integrity.

Blinding

The CHiB study is an open-label study in which neither the participants nor researchers and staff are blinded to the group assignments. During the entire intervention period and related procedures, blinding is not implemented for the researchers and staff. However, blinding will be applied to evaluating echocardiographic images, MRI data and laboratory analyses.

Data management

Data will be stored within our department following established local protocols. Data entry will be conducted by local study personnel and recorded in a password-protected document. Upon completion of the study, the data will be checked for plausibility before being

anonymised. Due to the small sample size and the non-commercial nature of this study, it has been determined that a data monitoring committee and formal interim analysis are not required. Statisticians and all involved researchers will be blinded to group assignments for statistical analysis.

Statistical considerations

The statistical analysis will be conducted longitudinally across time points using 2×3 analysis of variance (ANOVA), with post hoc tests (p-value adjustment using Bonferroni-Holm) applied where necessary. Additionally, ANOVAs based on robust linear regression models with heteroskedasticity robust SEs will be used when assumptions for repeated measures ANOVA are not fulfilled. Categorical variables will be compared using χ^2 tests. The effect of the intervention on the risk of developing CTRCD (at least mild CTRCD) will be assessed using logistic regression analysis with a random intercept and group, timepoint and their interaction (group×timepoint) as fixed predictors. Data will be presented as mean±SD. All analyses will be conducted using R V.4.4.1 (RRID:SCR_001905). The required sample size was calculated using G*Power V.3.1.9.7. The effect of the intervention (HIIT and HIRT) on cardiac parameters (primary endpoint: occurrence of symptomatic or asymptomatic CTRCD) will be analysed using a 2×3 ANOVA. With an effect size of f=0.2, a power of 0.8 and α=0.05, a total sample size of 48 participants (24 per group) is required. The calculation is based on the primary endpoint, and due to the expected group homogeneity, this sample size is sufficient to address the primary research question.

TRIAL STATUS

The study has received approval from the local ethics committee of Ulm University (427/23) and is registered at DRKS00034962.

CLINICAL IMPLICATIONS

With advancements in therapeutic approaches, patients with breast cancer are surviving for longer and increasingly experiencing the long-term effects of their cancer treatments. Current research focuses on understanding how these treatments specifically impact cardiac health and exploring potential strategies for primary prevention of CTRCD. In addition to medical heart failure therapy, structured exercise programmes, such as HIIT and HIRT, could play a crucial role in mitigating the cardiotoxic effects of breast cancer treatment, particularly given the evidence-based feasibility for this patient population. Given the limited research on the effects of exercise on cardiac function in patients with breast cancer, the clinical findings of this study could be pivotal for CTRCD research, potentially leading to the development of targeted exercise prescription guidelines during cardiotoxic cancer treatment.

CONCLUSION

The CHiB randomised controlled trial is the first to evaluate the long-term impact of HIIT and HIRT on the occurrence of symptomatic and asymptomatic CTRCD and cardiac inflammation in patients with breast cancer, hypothesising that structured exercise alongside anti-tumor therapy can prevent or reduce CTRCD without exacerbating cardiac inflammation. We also anticipate that HIIT and HIRT will improve mitochondrial function, reduce average heart rate and enhance HRV while positively affecting mental health by decreasing levels of depression, fatigue and anxiety.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by local ethics committee of Ulm University (427/23). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement Data are available upon reasonable request. The data will be shared on reasonable request to the corresponding author.

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