Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 18 July 2026
Revised 25 Aug 2026
Accepted 10 Sep 2026

Natural Resources for Human Health 2026, Vol. 6 (22s): 299–309

KEYWORDS:
pulmonary hypertension; congenital heart disease; exercise training; cardiac rehabilitation; right ventricular function; speckle-tracking echocardiography.

Six-week Exercise Training and Right Ventricular Free-Wall Longitudinal Strain in Congenital Heart Disease-Associated Pulmonary Hypertension

Erni Herawati A[1*], Yulius Patimang[1], Aussie Fitriani Ghaznawie[1], Zaenab Djafar[1], Melda Warliani[2], Andi Alfian Zainuddin[3]

[1]Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Hasanuddin – Integrated Heart Centre, Dr. Wahidin Sudirohusodo General Hospital, Makassar 90245, Indonesia
[2]Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Universitas Hasanuddin – Dr. Wahidin Sudirohusodo General Hospital, Makassar 90245, Indonesia
[3]Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Hasanuddin, Makassar 90245, Indonesia
[*]Corresponding author: Erni Herawati A, Department of Cardiology and Vascular Medicine, Faculty of Medicine, Universitas Hasanuddin, Makassar 90245, Indonesia.
E-mail: erniherawatia658@gmail.com
ORCID iDs: EHA 0009-0005-8191-8212; YP 0009-0006-9661-1632; AFG 0009-0002-4478-1665; ZD 0000-0003-4566-7004; MW 0000-0002-6653-4895; AAZ 0000-0003-4590-6407

ABSTRACT: Pulmonary hypertension (PH) complicating adult congenital heart disease (CHD) imposes chronic right ventricular (RV) pressure overload, and RV free-wall longitudinal strain (RVFWLS) detects subclinical RV systolic dysfunction earlier than conventional indices; whether short-term exercise training modifies RVFWLS in CHD-associated PH is unknown. This single-arm, pre–post pilot study evaluated the effect of a six-week exercise programme on RVFWLS in clinically stable adults aged 18–50 years with CHD-associated PH (World Health Organization functional class I–III, targeted therapy unchanged for at least three months) at a tertiary referral hospital in Makassar, Indonesia. Participants completed six weeks of supervised moderate-intensity aerobic training (40–60% of heart-rate reserve, 30 min, twice weekly) plus home breathing exercises three times daily, and RVFWLS measured by speckle-tracking echocardiography before and after training was compared using a paired t-test. Thirteen participants (mean age 31.76 ± 8.49 years; 11 women; atrial septal defect in 10) completed the programme. Mean RVFWLS was −15.76 ± 6.03% at baseline and −15.03 ± 3.25% after training (mean difference 0.73 percentage points; 95% confidence interval −4.22 to 2.76; P = 0.657). Individually, five participants (38.5%) shifted towards more negative (improved) strain, seven (53.8%) towards less negative strain and one (7.7%) was unchanged, while Doppler-estimated pulmonary pressures declined descriptively in all CHD subgroups. A six-week, twice-weekly moderate-intensity exercise programme was feasible but did not significantly change RVFWLS in adults with CHD-associated PH, although inter-individual variability was marked; larger controlled trials with longer, higher-dose programmes are warranted.

Natural Resources for Human Health
eISSN: 2583-1194

1. INTRODUCTION

Congenital heart disease (CHD) is the most common congenital anomaly worldwide, with a birth prevalence of approximately 8–9.5 per 1,000 live births (Hasan et al., 2023; Meng et al., 2024). In Indonesia, the incidence is estimated at 9 per 1,000 live births annually, and a large proportion of septal and ductal lesions remain unrepaired into adulthood (Marwali et al., 2021). Because more than 90% of children with CHD now survive to adulthood, adults with CHD constitute a steadily growing population (Mulder, 2012). Uncorrected left-to-right shunts expose the pulmonary circulation to chronic volume and pressure loading, driving progressive pulmonary vascular remodelling and, ultimately, pulmonary hypertension (PH) and Eisenmenger physiology (Salehian et al., 2005; Bartelds et al., 2014). In Asian registries, PH affects 4–5% of adults with CHD and more than doubles all-cause mortality compared with CHD without PH (Chiu et al., 2022). The Indonesian COngenital HeARt Disease in adult and Pulmonary Hypertension (COHARD-PH) registry reported that most affected patients are young women with unrepaired secundum atrial septal defect (ASD) diagnosed in the third decade of life, frequently already with established pulmonary arterial hypertension (PAH) (Dinarti et al., 2020).

Right ventricular (RV) systolic function is the principal determinant of symptoms and survival in PH of any aetiology (Voelkel et al., 2006; Vonk Noordegraaf et al., 2019). Conventional echocardiographic indices such as tricuspid annular plane systolic excursion (TAPSE) and fractional area change are load-dependent and may remain within normal limits despite early myocardial impairment (Rudski et al., 2010). Two-dimensional speckle-tracking echocardiography (STE) quantifies myocardial deformation directly, and RV free-wall longitudinal strain (RVFWLS) has emerged as the most reproducible and prognostically robust STE parameter of RV function (Rudski et al., 2010; Tadic et al., 2021). RVFWLS identifies subclinical RV dysfunction in CHD-associated PAH (Pham and Nguyen, 2022), shows the highest diagnostic accuracy for reduced RV ejection fraction (Tadic et al., 2021; Mukherjee et al., 2025), and predicts all-cause mortality in a meta-analysis of 1,001 patients with PH, in whom impaired strain carried a 3.7-fold higher hazard of death (Fine et al., 2013; Shukla et al., 2018). Current guidelines therefore recommend RVFWLS as a complement to conventional right-heart assessment, with values less negative than approximately −20% considered abnormal (Badano et al., 2018; Mukherjee et al., 2025).

Supervised exercise training is now a Class I recommendation for patients with PAH who are clinically stable on optimised medical therapy (Humbert et al., 2022). Randomised trials and meta-analyses demonstrate consistent improvements in six-minute walk distance, peak oxygen uptake, quality of life and, in some studies, invasive haemodynamics (Mereles et al., 2006; Ehlken et al., 2016; Grünig et al., 2019). Physical activity interventions are likewise safe and beneficial in adults with CHD and are endorsed by current adult CHD guidelines (Williams et al., 2020; Baumgartner et al., 2021). Experimental data suggest that exercise may directly attenuate RV remodelling in PH through improved myocardial capillary density, endothelial nitric oxide bioavailability, calcium handling and neurohormonal regulation (Brown et al., 2017; Zhang and Xu, 2020). However, whether these mechanisms translate into measurable changes in RV myocardial deformation in humans, particularly within the short programmes that are feasible in resource-limited settings, remains uncertain, and data on RVFWLS as an outcome of exercise training in adults with CHD-associated PH are lacking.

We therefore conducted a pilot study to answer the following question: does a six-week structured, supervised exercise training programme change RVFWLS in clinically stable adults with CHD-associated PH receiving targeted therapy at a tertiary referral centre in eastern Indonesia?

2. MATERIALS AND METHODS

2.1 Study design, setting and ethics

This was a single-arm experimental study with a pre–post intervention design conducted at the outpatient cardiac rehabilitation unit of the Integrated Heart Centre, Dr. Wahidin Sudirohusodo General Hospital, the national referral hospital for eastern Indonesia, in Makassar, between November 2025 and January 2026. The study protocol was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia (approval No. 1050/UN4.6.4.5.31/PP36/2025, dated [DD Month 2025]), and the study was conducted in accordance with the Declaration of Helsinki and its later amendments. All participants provided written informed consent before enrolment. As a non-randomised single-arm pilot study, the study was not registered in a clinical trial registry.

2.2 Participants

Consecutive adults attending the adult CHD and PH clinic were screened. Inclusion criteria were: (i) age 18–50 years; (ii) PH associated with CHD diagnosed by transthoracic echocardiography and/or right heart catheterisation (mean pulmonary artery pressure [mPAP] >20 mmHg); (iii) World Health Organization (WHO) functional class I–III; (iv) pharmacological therapy unchanged for at least three months; and (v) willingness to attend the supervised programme. Exclusion criteria were WHO functional class IV, decompensated right heart failure, a history of exertional syncope, uncontrolled arrhythmia, pulmonary or musculoskeletal disease limiting exercise, resting peripheral oxygen saturation <80%, and any change in PAH-targeted therapy during the intervention period. Participants with adherence below 80% of scheduled sessions or who did not return for the six-week assessment were to be considered drop-outs.

2.3 Sample size

The sample size was calculated for the comparison of two dependent means ($\alpha = 0.05$, two-sided; power 80%) using published variability of RVFWLS change after exercise training, yielding a minimum of 12.2, rounded to 12 participants (Chow et al., 2017). Eligible patients were to be recruited by consecutive sampling until the minimum sample size was reached.

2.4 Intervention

All participants received standardised cardiac rehabilitation education covering medication adherence, stress management, risk-factor control and physical activity, together with a home exercise kit (1-kg dumbbells, incentive spirometer, digital sphygmomanometer, pulse oximeter, logbook and video material on exercise and education). The supervised component consisted of continuous aerobic exercise at moderate intensity (40–60% of heart-rate reserve, calculated by the Karvonen method from resting and age-predicted maximal heart rate (Karvonen et al., 1957)) for 30 min per session, twice weekly for six weeks (12 sessions), delivered under the supervision of the hospital cardiac rehabilitation team, with heart rate monitored to maintain the target intensity. PAH-targeted and other cardiovascular drugs (oral sildenafil, oral beraprost sodium, oral furosemide, renin–angiotensin–aldosterone system blockers and beta-blockers) were continued at the doses prescribed clinically and were not modified during the study. In addition, participants performed breathing exercises with the incentive spirometer three times daily at home. Attendance and home sessions were documented in the participant logbook, which was reviewed at each visit.

2.5 Echocardiography

Transthoracic echocardiography was performed at baseline and after completion of the six-week programme using a cardiovascular ultrasound system (Vivid E95; GE HealthCare, Horten, Norway) by a cardiologist experienced in strain imaging, following the American Society of Echocardiography recommendations for chamber quantification and right heart assessment (Rudski et al., 2010; Badano et al., 2018; Mukherjee et al., 2025). Left ventricular ejection fraction (LVEF) was measured by the biplane Simpson method. RV assessment included basal RV diameter, TAPSE, peak tricuspid regurgitation (TR) velocity and gradient, and pulmonary valve acceleration time. Pulmonary artery systolic pressure (PASP) was estimated from the TR gradient plus estimated right atrial pressure, and mPAP from PASP using standard formulae. RVFWLS was measured by two-dimensional STE from an RV-focused apical four-chamber view in accordance with the EACVI/ASE consensus on deformation imaging (Badano et al., 2018), with the septal segments excluded. RVFWLS was expressed as the mean peak systolic longitudinal strain of the basal, mid and apical free-wall segments (%), with values more negative than −20% considered normal (Evaldsson et al., 2020; Prieto et al., 2021; Mukherjee et al., 2025).

2.6 Right heart catheterisation

Diagnostic right heart catheterisation had been performed as part of routine work-up, with oximetry in the venae cavae, right atrium, RV, pulmonary artery and descending aorta, and pressure measurements in the right atrium, RV, pulmonary artery, left atrium (through the defect where accessible) and aorta. Pulmonary-to-systemic flow ratio (Qp/Qs), pulmonary arteriolar resistance (PAR, Wood units) and the PAR-to-systemic vascular resistance (SVR) ratio were derived by the Fick method.

2.7 Outcomes and statistical analysis

The pre-specified primary outcome was the change in RVFWLS from baseline to six weeks. Secondary echocardiographic parameters were summarised descriptively by CHD subtype. Data were analysed using statistical software (IBM SPSS Statistics

version 21; IBM Corp., Armonk, NY, USA) by a co-author with formal training in biostatistics and public health. Continuous variables are presented as mean (standard deviation [SD]) and categorical variables as absolute numbers with percentages. The distribution of RVFWLS and its change was assessed with the Shapiro–Wilk test; the paired t-test was planned for normally distributed data and the Wilcoxon signed-rank test otherwise, with the mean difference and its 95% confidence interval (CI) reported. Individual responses were categorised as a shift towards more negative strain (improvement), a shift towards less negative strain, or no change. Exact two-sided P values are reported, and $P < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Baseline characteristics

Thirteen consecutive eligible patients were enrolled between November 2025 and January 2026; all 13 completed the six-week programme and the follow-up echocardiography, and none met the drop-out criteria. Baseline characteristics are shown in **Table 1**. Mean age was 31.76 (SD 8.49) years, 11 of 13 participants (84.6%) were women, and mean body mass index was 19.59 (SD 3.03) kg/m². Six participants (46.2%) had completed senior high school and five (38.5%) university; five (38.5%) were students and five (38.5%) homemakers. The underlying lesion was ASD in 10 participants (76.9%), ventricular septal defect (VSD) in two (15.4%) and patent ductus arteriosus (PDA) in one (7.7%). All participants were receiving sildenafil, nine (69.2%) beraprost, 11 (84.6%) furosemide, four (30.8%) a renin–angiotensin–aldosterone system blocker and three (23.1%) a beta-blocker; none received calcium-channel blockers.

Table 1. Baseline characteristics of the study participants (n = 13)

Characteristic	Value
Age (years)[a]	31.76 (8.49)
Female sex	11 (84.6)
Body mass index (kg/m²)[a]	19.59 (3.03)
Educational attainment	
Primary school	1 (7.7)
Junior high school	1 (7.7)
Senior high school	6 (46.2)
University	5 (38.5)
Occupation	
Student	5 (38.5)
Homemaker	5 (38.5)
Employee	2 (15.4)
Self-employed	1 (7.7)
Congenital lesion	
Atrial septal defect	10 (76.9)
Ventricular septal defect	2 (15.4)
Patent ductus arteriosus	1 (7.7)
Medication	
Sildenafil	13 (100)
Beraprost	9 (69.2)
Furosemide	11 (84.6)
Renin–angiotensin–aldosterone system blocker	4 (30.8)
Beta-blocker	3 (23.1)
Calcium-channel blocker	0 (0)

Note: Values are n (%) unless otherwise indicated; [a]mean (SD). SD, standard deviation.

3.2 Invasive haemodynamics

Right heart catheterisation confirmed severe pulmonary hypertension in the cohort (**Table 2**): mean pulmonary artery pressure was 61.00 (SD 22.51) mmHg and PAR 24.34 (SD 23.09) Wood units. The wide ranges of Qp/Qs (0.30–22.00) and of the

PAR/SVR ratio (0.11–2.70) indicate that disease severity extended from predominantly left-to-right shunting to Eisenmenger physiology.

Table 2. Baseline right heart catheterisation findings (n = 13)

Variable	Mean (SD)	Range
Right atrial pressure, mean (mmHg)	8.23 (4.21)	3–16
RV systolic pressure (mmHg)	88.67 (39.30)	19–150
RV end-diastolic pressure (mmHg)	10.33 (14.08)	1–40
Pulmonary artery systolic pressure (mmHg)	96.42 (35.10)	31–146
Pulmonary artery diastolic pressure (mmHg)	38.08 (19.46)	1–71
Pulmonary artery mean pressure (mmHg)	61.00 (22.51)	12–96
Left atrial mean pressure (mmHg)	10.82 (3.95)	6–17
Aortic mean pressure (mmHg)	79.42 (16.59)	50–109
Superior vena cava saturation (%)	62.08 (12.13)	42–79
Pulmonary artery saturation (%)	73.31 (12.30)	49–95
Aortic saturation (%)	88.17 (7.90)	72–98
Qp/Qs	2.81 (6.10)	0.30–22.00
Pulmonary arteriolar resistance (WU)	24.34 (23.09)	0.14–72.20
PAR/SVR ratio	1.19 (0.92)	0.11–2.70

Note: SD, standard deviation; RV, right ventricular; Qp/Qs, pulmonary-to-systemic flow ratio; PAR, pulmonary arteriolar resistance; SVR, systemic vascular resistance; WU, Wood units.

3.3 Primary outcome: right ventricular free-wall longitudinal strain

RVFWLS values were normally distributed (Shapiro–Wilk test), and the paired t-test was therefore applied. Mean RVFWLS was −15.76% (SD 6.03%) at baseline and −15.03% (SD 3.25%) after six weeks of training (**Table 3**). The mean change of 0.73 percentage points towards less negative values was not statistically significant (95% CI −4.22 to 2.76; P = 0.657). Both pre- and post-intervention means remained below the normal reference range, indicating persistent RV systolic impairment. The dispersion of RVFWLS narrowed after the intervention (SD 6.03% versus 3.25%), and the box plot (**Figure 1**) showed a more homogeneous distribution without extreme outliers. Individual trajectories were heterogeneous: five of 13 participants (38.5%) shifted towards more negative (improved) strain, seven (53.8%) towards less negative strain, and one (7.7%) showed no change. The largest individual change was 8.30 percentage points.

Table 3. Right ventricular free-wall longitudinal strain before and after six weeks of exercise training (n = 13)

Variable	Pre-training	Post-training	Mean difference (95% CI)	P value[a]
RVFWLS (%), mean (SD)	−15.76 (6.03)	−15.03 (3.25)	0.73 (−4.22, 2.76)	0.657
Individual response, n (%)				
More negative strain (improved)			5 (38.5)	
Less negative strain			7 (53.8)	
No change			1 (7.7)	
Largest individual change (percentage points)			8.30	

Note: [a]Paired t-test; data normally distributed (Shapiro–Wilk test). RVFWLS, right ventricular free-wall longitudinal strain; SD, standard deviation; CI, confidence interval. More negative values denote better systolic function; normal reference more negative than −20%.

Natural Resources for Human Health
eISSN: 2583-1194

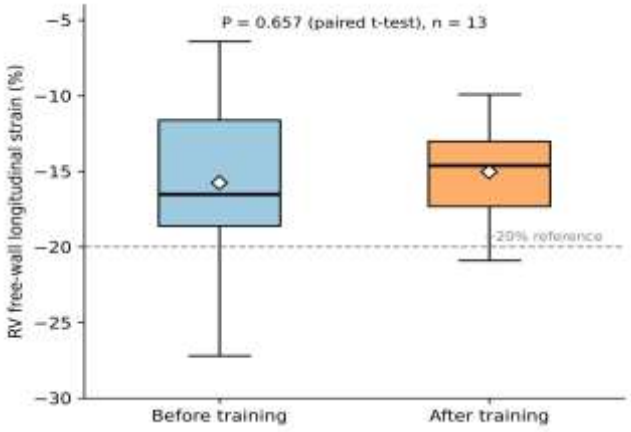

Figure 1. Box plot of right ventricular free-wall longitudinal strain (RVFWLS, %) before and after the six-week exercise training programme (n = 13). Boxes represent the interquartile range with the median (thick horizontal line); diamonds indicate the mean (−15.76% before and −15.03% after training); whiskers extend to the minimum and maximum values; no extreme outliers were identified. The dashed line marks the −20% normal reference threshold; more negative values denote better right ventricular systolic function. P = 0.657, paired t-test.

3.4 Secondary echocardiographic parameters

Descriptive changes in conventional echocardiographic parameters by CHD subtype are presented in **Table 4**; no inferential testing was performed for these exploratory outcomes. Doppler-estimated pulmonary pressures were lower after training in all three lesion subgroups: in the 10 participants with ASD, estimated PASP fell from 81.35 (SD 31.21) to 70.16 (SD 22.89) mmHg and estimated mPAP from 51.60 (SD 19.04) to 44.79 (SD 13.99) mmHg, with corresponding reductions in the two participants with VSD and in the single participant with PDA. In the ASD subgroup, peak TR velocity decreased, pulmonary valve acceleration time lengthened and basal RV diameter decreased, whereas TAPSE was unchanged. LVEF and defect size did not change in any subgroup.

Table 4. Echocardiographic parameters before and after training by congenital lesion (descriptive)

Parameter	ASD pre (n = 10)	ASD post (n = 10)	VSD pre (n = 2)	VSD post (n = 2)	PDA pre (n = 1)	PDA post (n = 1)
Defect size (mm)	3.07 (1.36)	3.07 (1.36)	1.30 (0.42)	1.30 (0.42)	7.00	7.00
LA major axis (cm)	5.30 (0.97)	5.06 (1.06)	6.30 (0.70)	6.00 (1.97)	4.60	4.60
RA major axis (cm)	5.96 (1.28)	5.69 (1.17)	5.95 (2.61)	5.70 (2.26)	5.00	5.00
RV basal diameter (cm)	5.34 (0.77)	4.80 (0.81)	5.10 (1.83)	5.15 (2.47)	3.60	3.60
LVEF (%)	65.63 (5.95)	66.00 (4.26)	49.00 (28.28)	49.00 (28.28)	75.00	75.00
TAPSE (cm)	1.90 (0.40)	1.89 (0.50)	1.95 (0.21)	2.20 (0.14)	1.90	1.90
Peak TR velocity (m/s)	4.16 (0.95)	3.88 (0.71)	4.00 (1.57)	3.15 (1.90)	5.26	4.00
TR gradient (mmHg)	71.80 (31.75)	62.04 (23.59)	67.51 (52.77)	47.83 (49.30)	110.63	64.10
PV acceleration time (ms)	101.20 (31.60)	123.70 (37.91)	106.80 (31.39)	115.50 (4.94)	119.00	119.00
Estimated PASP (mmHg)	81.35 (31.21)	70.16 (22.89)	80.63 (55.47)	58.48 (53.06)	118.67	72.00
Estimated mPAP (mmHg)	51.60 (19.04)	44.79 (13.99)	51.18 (33.83)	37.67 (32.36)	74.38	45.92
RVFWLS (%)	−15.98 (6.60)	−15.36 (3.53)	−14.70 (6.50)	−13.60 (3.04)	−15.80	−14.60

Note: Values are mean (SD); single values for PDA. No inferential testing was performed for these exploratory outcomes. ASD, atrial septal defect; VSD, ventricular septal defect; PDA, patent ductus arteriosus; LA, left atrium; RA, right atrium; RV, right ventricle; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; PV, pulmonary valve; PASP, pulmonary artery systolic pressure; mPAP, mean pulmonary artery pressure; RVFWLS, right ventricular free-wall longitudinal strain; SD, standard deviation.

3.5 Comparison with previous studies

In this pilot study, a six-week supervised, twice-weekly, moderate-intensity aerobic training programme supplemented by daily breathing exercises did not produce a statistically significant change in RVFWLS in adults with CHD-associated PH. The point estimate shifted marginally towards less negative strain, the confidence interval was wide and encompassed both clinically meaningful improvement and deterioration, and individual responses diverged markedly. These findings should be interpreted in the light of the small sample, the absence of a control arm and the modest exercise dose, but they provide STE-based data on RV myocardial deformation in response to exercise in this population and inform the design of future trials.

Our results are consistent with a comparable six-week STE study: in a comparison of hospital-based and remotely supervised cardiac rehabilitation in patients with heart failure with reduced ejection fraction, Antonius et al. (2025) observed a non-significant trend in RVFWLS, which the authors attributed to the small sample, lack of randomisation and self-reported adherence. By contrast, the landmark trials that established exercise training in PH used considerably higher doses: Mereles et al. (2006) delivered 15 weeks of training beginning with a three-week in-hospital phase of daily sessions and demonstrated improvements in six-minute walk distance, peak oxygen uptake and quality of life, and Ehlken et al. (2016) showed, in a randomised trial with the same 15-week protocol, significant reductions in invasive pulmonary vascular resistance and increases in cardiac index alongside functional gains. The European Respiratory Society statement recommends supervised programmes of at least 10–15 weeks with five to seven sessions per week, tailored to disease severity (Grünig et al., 2019). Our programme, designed for feasibility in an outpatient setting serving a large and geographically dispersed catchment, delivered approximately one-quarter of that supervised volume, which likely explains the absence of a group-level myocardial response.

3.6 Interpretation of the right ventricular strain response

Baseline RVFWLS in our cohort (−15.76%) was substantially impaired and close to the pooled free-wall strain of −16.2% reported in a meta-analysis of 1,001 patients with PH, a level associated with increased mortality (Fine et al., 2013; Shukla et al., 2018). Invasive haemodynamics confirmed severe disease, with a mean PAP of 61 mmHg and PAR/SVR approaching unity, and nine of 13 participants (69.2%) required dual therapy with sildenafil and beraprost. Sustained pressure overload of this magnitude induces RV hypertrophy, interstitial fibrosis, capillary rarefaction and metabolic remodelling that are unlikely to reverse within six weeks (Voelkel et al., 2006; Vonk Noordegraaf et al., 2019; Zhang and Xu, 2020). Experimental work suggests that the RV can adapt structurally to exercise, with increased capillary density, normalised glycogen synthase kinase-3 signalling and reduced fibrosis, but these effects were most evident with high-intensity interval protocols, whereas continuous moderate-intensity training failed to reverse RV hypertrophy in a rat model of PH (Brown et al., 2017; Zhang and Xu, 2020). The dose–response relationship observed in animals is therefore concordant with our clinical observation.

Two secondary observations merit comment. First, the variance of RVFWLS decreased after training, with the post-intervention distribution more tightly clustered around −15%. Because strain is load-dependent, this may partly reflect the concurrent descriptive reductions in estimated PASP and mPAP and the lengthening of pulmonary valve acceleration time, which suggest a modest reduction in RV afterload after training. The reduction in estimated pulmonary pressure was observed in all three lesion subgroups and is biologically plausible, given the documented effects of exercise on pulmonary endothelial nitric oxide synthase expression and neurohormonal activation (Zhang and Xu, 2020), and the complementary vasodilator effect of phosphodiesterase-5 inhibition received by every participant (Malenfant et al., 2021). However, these estimates are Doppler-derived, were not tested statistically, and are susceptible to regression to the mean and to day-to-day variability in TR jet alignment; they should be regarded as hypothesis-generating. Second, the heterogeneity of individual strain trajectories, with five participants improving and seven worsening slightly, highlights that group means may obscure clinically relevant responder and non-responder phenotypes. Identifying predictors of response, such as baseline haemodynamic severity, shunt direction, RV–pulmonary arterial coupling or training adherence, will require larger studies.

3.7 Cohort characteristics in context

The demographic profile of our participants closely mirrors the Indonesian COHARD-PH registry, in which 78.5% of adults with shunt lesions were women, secundum ASD accounted for 73% of lesions overall and 89% of those with PAH, and the mean age at diagnosis was 34.7 years (Dinarti et al., 2020). Similar female predominance and lesion distribution were reported in the Taiwanese national cohort (Chiu et al., 2022) and in the COMPERA-CHD registry (Kaemmerer et al., 2020). The low mean body mass index (19.6 kg/m²) is likewise typical of chronic PH in CHD, reflecting increased metabolic demand, chronic hypoxaemia and reduced activity tolerance (Amelia et al., 2023). The predominance of young, unrepaired ASD in this and other series reflects late diagnosis of a lesion that is often asymptomatic until the third decade, by which time pulmonary vascular disease may be irreversible (Dinarti et al., 2020; Nikolić et al., 2025). Our cohort is therefore representative of the adult CHD–PH population encountered in Indonesian referral centres, and the intervention tested reflects what can realistically be delivered within existing cardiac rehabilitation services.

3.8 Clinical implications

Despite the neutral primary result, several features are clinically relevant. All 13 participants, including those with Eisenmenger-range haemodynamics, completed the supervised programme without meeting drop-out criteria, adding to the evidence that carefully screened and monitored exercise training is feasible in CHD-associated PH (Grünig et al., 2019; Williams et al., 2020; Humbert et al., 2022). International guidelines already recommend exercise training for stable PAH on the basis of functional and quality-of-life benefits (Humbert et al., 2022), and these benefits do not depend on demonstrable changes in RV strain. RVFWLS nevertheless remains an attractive mechanistic endpoint: it is reproducible, sensitive to subclinical change and prognostically validated (Fine et al., 2013; Shukla et al., 2018; Tadic et al., 2021; Mukherjee et al., 2025), and its routine incorporation into rehabilitation follow-up would allow future programmes to be titrated to RV response. The present data indicate that, for a myocardial effect to be detectable, programmes will probably need to be longer (≥12–15 weeks), more frequent (≥3 sessions per week) and possibly include interval training, resistance and inspiratory muscle components, as recommended in the European Respiratory Society statement (Grünig et al., 2019).

3.9 Limitations

This study has important limitations. The sample size, although consistent with the a priori calculation, was small, and the study was powered only to detect a large effect on RVFWLS; subgroup comparisons by lesion type were descriptive. The single-arm design without a concurrent control group means that natural history, regression to the mean and the effects of concomitant therapy cannot be separated from the effect of exercise. The exercise dose was low relative to established protocols, and exercise capacity was not quantified by six-minute walk test or cardiopulmonary exercise testing, precluding assessment of functional response. Adherence was documented by participant logbooks rather than objective monitoring, and home-based breathing exercises were unsupervised. Echocardiographic pulmonary pressures were estimated non-invasively and were not tested statistically; catheterisation was not repeated after training. Interobserver and test–retest variability of RVFWLS was not formally assessed, although measurements were performed by a single experienced operator on the same platform. Finally, the cohort was heterogeneous with respect to lesion type and haemodynamic severity, and the follow-up was limited to the immediate post-training period, so delayed adaptation cannot be excluded.

4. CONCLUSION

A six-week, twice-weekly, moderate-intensity supervised aerobic exercise programme combined with home breathing exercises did not significantly alter RV free-wall longitudinal strain in clinically stable adults with CHD-associated pulmonary hypertension, although inter-individual responses varied widely and non-invasive estimates of pulmonary pressure declined descriptively across lesion types. Structured, supervised exercise training was feasible in this severely affected population. Adequately powered randomised controlled trials employing longer and more intensive programmes, objective adherence monitoring, functional capacity testing and repeated strain imaging are needed to determine whether exercise can modify RV myocardial function in adults with CHD-associated PH.

Acknowledgements

The authors thank the cardiac rehabilitation team and the echocardiography laboratory staff of the Integrated Heart Centre, Dr. Wahidin Sudirohusodo General Hospital, Makassar, for their technical and logistic support. This work was derived from the first author's specialist training thesis in Cardiology and Vascular Medicine at the Faculty of Medicine, Universitas Hasanuddin. Claude (Anthropic, San Francisco, CA, USA) was used exclusively for English language editing and formatting of

the manuscript; it was not used to generate scientific content, perform analyses or interpret data, and the authors take full responsibility for the accuracy, integrity and originality of the work.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Author Contributions

Erni Herawati A: Conceptualization, Methodology, Investigation, Data Curation, Writing—Original Draft, Writing—Review & Editing.

Yulius Patimang: Conceptualization, Methodology, Supervision, Writing—Review & Editing.

Aussie Fitriani Ghaznawie: Conceptualization, Methodology, Formal Analysis (echocardiographic strain analysis and interpretation), Writing—Review & Editing.

Zaenab Djafar: Resources (cardiac rehabilitation protocol, provision of patients and study materials), Writing—Review & Editing.

Melda Warliani: Resources (design and supervision of the exercise training programme), Writing—Review & Editing.

Andi Alfian Zainuddin: Formal Analysis (statistical analysis), Validation, Writing—Review & Editing.

All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that there is no conflict of interest. Completed ICMJE uniform disclosure forms for all authors accompany this submission.

Ethics Statement

The study protocol was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia (approval No. 1050/UN4.6.4.5.31/PP36/2025, dated [DD Month 2025]). The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants before enrolment. No identifiable patient data or images are reported.

Data Availability Statement

The de-identified individual participant data supporting the findings of this study are available from the corresponding author upon reasonable request and can be provided to the journal as supplementary material if required.

REFERENCES

[1] Amelia, P., Yosephine, A.G., Tobing, T.C., Savira, M., Viandy, V., Inglin, M, 2023. Association between type of congenital heart disease with child growth and development status: a cross-sectional study in Medan, Indonesia. *Narra J* 3(3), e414. https://doi.org/10.52225/narra.v3i3.414

[2] Antonius, R., Djafar, Z., Ghaznawie, A.F., Warliani, M, 2025. Hospital vs. remotely supervised cardiac rehabilitation: a 6-week comparison of right ventricular function in HFrEF patients. *Romanian Medical Journal* 72(4), 471. https://doi.org/10.37897/RMJ.2025.4.1

[3] Badano, L.P., Kolias, T.J., Muraru, D., Abraham, T.P., Aurigemma, G., Edvardsen, T., et al, 2018. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *European Heart Journal – Cardiovascular Imaging* 19(6), 591–600. https://doi.org/10.1093/ehjci/jey042

[4] Bartelds, B., Borgdorff, M.A., Berger, R.M, 2014. Right ventricular adaptation in congenital heart diseases. *Journal of Cardiovascular Development and Disease* 1(1), 83–97. https://doi.org/10.3390/jcdd1010083

[5] Baumgartner, H., De Backer, J., Babu-Narayan, S.V., Budts, W., Chessa, M., Diller, G.P., et al, 2021. 2020 ESC Guidelines for the management of adult congenital heart disease. *European Heart Journal* 42(6), 563–645. https://doi.org/10.1093/eurheartj/ehaa554

[6] Brown, M.B., Neves, E., Long, G., Graber, J., Gladish, B., Wiseman, A., et al, 2017. High-intensity interval training, but not continuous training, reverses right ventricular hypertrophy and dysfunction in a rat model of pulmonary hypertension. *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology* 312(2), R197–R210. https://doi.org/10.1152/ajpregu.00358.2016

[7] Chiu, S.N., Lu, C.W., Lin, M.T., Chen, C.A., Wu, M.H., Wang, J.K, 2022. Pulmonary hypertension in adult congenital heart disease in Asia: a distinctive feature of complex congenital heart disease. *Journal of the American Heart Association* 11(7), e022596. https://doi.org/10.1161/JAHA.121.022596

[8] Chow, S.C., Shao, J., Wang, H., Lokhnygina, Y, 2017. *Sample Size Calculations in Clinical Research*. 3rd ed. Chapman & Hall/CRC, Boca Raton, FL, USA.

[9] Dinarti, L.K., Hartopo, A.B., Kusuma, A.D., Satwiko, M.G., Hadwiono, M.R., Pradana, A.D., et al, 2020. The COngenital HeARt Disease in adult and Pulmonary Hypertension (COHARD-PH) registry: a descriptive study from single-center hospital registry of adult congenital heart disease and pulmonary hypertension in Indonesia. *BMC Cardiovascular Disorders* 20(1), 163. https://doi.org/10.1186/s12872-020-01434-z

[10] Ehlken, N., Lichtblau, M., Klose, H., Weidenhammer, J., Fischer, C., Nechwatal, R., et al, 2016. Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. *European Heart Journal* 37(1), 35–44. https://doi.org/10.1093/eurheartj/ehv337

[11] Evaldsson, A.W., Lindholm, A., Jumatate, R., Ingvarsson, A., Smith, G.J., Waktare, J., et al, 2020. Right ventricular function parameters in pulmonary hypertension: echocardiography vs. cardiac magnetic resonance. *BMC Cardiovascular Disorders* 20(1), 259. https://doi.org/10.1186/s12872-020-01548-4

[12] Fine, N.M., Chen, L., Bastiansen, P.M., Frantz, R.P., Pellikka, P.A., Oh, J.K., et al, 2013. Outcome prediction by quantitative right ventricular function assessment in 575 subjects evaluated for pulmonary hypertension. *Circulation: Cardiovascular Imaging* 6(5), 711–721. https://doi.org/10.1161/CIRCIMAGING.113.000640

[13] Grünig, E., Eichstaedt, C., Barberà, J.A., Benjamin, N., Blanco, I., Bossone, E., et al, 2019. ERS statement on exercise training and rehabilitation in patients with severe chronic pulmonary hypertension. *European Respiratory Journal* 53(2), 1800332. https://doi.org/10.1183/13993003.00332-2018

[14] Hasan, A.A., Abu Lehyah, N.A.A., Al Tarawneh, M.K., Abbad, M.Y., Fraijat, A.G., Al-Jammal, R.A., et al, 2023. Incidence and types of congenital heart disease at a referral hospital in Jordan: retrospective study from a tertiary center. *Frontiers in Pediatrics* 11, 1261130. https://doi.org/10.3389/fped.2023.1261130

[15] Humbert, M., Kovacs, G., Hoeper, M.M., Badagliacca, R., Berger, R.M.F., Brida, M., et al, 2022. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *European Heart Journal* 43(38), 3618–3731. https://doi.org/10.1093/eurheartj/ehac237

[16] Kaemmerer, H., Gorenflo, M., Huscher, D., Pittrow, D., Apitz, C., Baumgartner, H., et al, 2020. Pulmonary hypertension in adults with congenital heart disease: real-world data from the international COMPERA-CHD registry. *Journal of Clinical Medicine* 9(5), 1456. https://doi.org/10.3390/jcm9051456

[17] Karvonen, M.J., Kentala, E., Mustala, O, 1957. The effects of training on heart rate; a longitudinal study. *Annales Medicinae Experimentalis et Biologiae Fenniae* 35(3), 307–315. PMID: 13470504.

[18] Malenfant, S., Lebret, M., Breton-Gagnon, É., Potus, F., Paulin, R., Bonnet, S., et al, 2021. Exercise intolerance in pulmonary arterial hypertension: insight into central and peripheral pathophysiological mechanisms. *European Respiratory Review* 30(160), 200284. https://doi.org/10.1183/16000617.0284-2020

[19] Marwali, E.M., Purnama, Y., Roebiono, P.S, 2021. Modalitas deteksi dini penyakit jantung bawaan di pelayanan kesehatan primer [Early detection modalities for congenital heart disease in primary health care]. *Journal of the Indonesian Medical Association* 71(2), 100–109. (in Indonesian) https://doi.org/10.47830/jinma-vol.71.2-2021-241

[20] Meng, X., Song, M., Zhang, K., Lu, W., Li, Y., Zhang, C., et al, 2024. Congenital heart disease: types, pathophysiology, diagnosis, and treatment options. *MedComm* 5(7), e631. https://doi.org/10.1002/mco2.631

[21] Mereles, D., Ehlken, N., Kreuscher, S., Ghofrani, S., Hoeper, M.M., Halank, M., et al, 2006. Exercise and respiratory training improve exercise capacity and quality of life in patients with severe chronic pulmonary hypertension. *Circulation* 114(14), 1482–1489. https://doi.org/10.1161/CIRCULATIONAHA.106.618397

[22] Mukherjee, M., Rudski, L.G., Addetia, K., Afilalo, J., D'Alto, M., Freed, B.H., et al, 2025. Guidelines for the echocardiographic assessment of the right heart in adults and special considerations in pulmonary hypertension:

recommendations from the American Society of Echocardiography. *Journal of the American Society of Echocardiography* 38(3), 141–186. https://doi.org/10.1016/j.echo.2025.01.006

[23] Mulder, B.J, 2012. Epidemiology of adult congenital heart disease: demographic variations worldwide. *Netherlands Heart Journal* 20(12), 505–508. https://doi.org/10.1007/s12471-012-0335-1

[24] Nikolić, A., Veljković, S., Lakčević, J., Peruničić, A., Šljivo, A., Babić, M., et al, 2025. Adult congenital heart disease in Serbia: insights from a single-center registry. *Diagnostics* 15(4), 498. https://doi.org/10.3390/diagnostics15040498

[25] Pham, T.T., Nguyen, H.T.T, 2022. Global and regional right ventricular function investigation by 2D speckle tracking echocardiography in congenital heart disease patients with pulmonary arterial hypertension. *Cardiovascular Imaging Asia* 6(2), 41–49. https://doi.org/10.22468/cvia.2021.00332

[26] Prieto, O., Cianciulli, T.F., Stewart-Harris, A., Rodriguez, A., Saccheri, M.C., Lax, J.A., et al, 2021. Speckle tracking imaging in patients with pulmonary hypertension. *Journal of Cardiovascular Imaging* 29(3), 236–251. https://doi.org/10.4250/jcvi.2020.0192

[27] Rudski, L.G., Lai, W.W., Afilalo, J., Hua, L., Handschumacher, M.D., Chandrasekaran, K., et al, 2010. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography. *Journal of the American Society of Echocardiography* 23(7), 685–713. https://doi.org/10.1016/j.echo.2010.05.010

[28] Salehian, O., Horlick, E., Schwerzmann, M., Haberer, K., McLaughlin, P., Siu, S.C., et al, 2005. Improvements in cardiac form and function after transcatheter closure of secundum atrial septal defects. *Journal of the American College of Cardiology* 45(4), 499–504. https://doi.org/10.1016/j.jacc.2004.10.052

[29] Shukla, M., Park, J.H., Thomas, J.D., Delgado, V., Bax, J.J., Kane, G.C., et al, 2018. Prognostic value of right ventricular strain using speckle-tracking echocardiography in pulmonary hypertension: a systematic review and meta-analysis. *Canadian Journal of Cardiology* 34(8), 1069–1078. https://doi.org/10.1016/j.cjca.2018.04.016

[30] Tadic, M., Nita, N., Schneider, L., Kersten, J., Buckert, D., Gonska, B., et al, 2021. The predictive value of right ventricular longitudinal strain in pulmonary hypertension, heart failure, and valvular diseases. *Frontiers in Cardiovascular Medicine* 8, 698158. https://doi.org/10.3389/fcvm.2021.698158

[31] Voelkel, N.F., Quaife, R.A., Leinwand, L.A., Barst, R.J., McGoon, M.D., Meldrum, D.R., et al, 2006. Right ventricular function and failure: report of a National Heart, Lung, and Blood Institute working group on cellular and molecular mechanisms of right heart failure. *Circulation* 114(17), 1883–1891. https://doi.org/10.1161/CIRCULATIONAHA.106.632208

[32] Vonk Noordegraaf, A., Chin, K.M., Haddad, F., Hassoun, P.M., Hemnes, A.R., Hopkins, S.R., et al, 2019. Pathophysiology of the right ventricle and of the pulmonary circulation in pulmonary hypertension: an update. *European Respiratory Journal* 53(1), 1801900. https://doi.org/10.1183/13993003.01900-2018

[33] Williams, C.A., Wadey, C., Pieles, G., Stuart, G., Taylor, R.S., Long, L, 2020. Physical activity interventions for people with congenital heart disease. *Cochrane Database of Systematic Reviews* 10(10), CD013400. https://doi.org/10.1002/14651858.CD013400.pub2

[34] Zhang, X., Xu, D, 2020. Effects of exercise rehabilitation training on patients with pulmonary hypertension. *Pulmonary Circulation* 10(3), 2045894020937129. https://doi.org/10.1177/2045894020937129