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A Pilot study Examining the Safety and Effectiveness of 8-weeks of early cardiac rehabilitation on physical function and psychological well-being in patients following aortic root replacement

Abstract.

Aim. To determine the effects of a structured, moderate-intensity, early cardiac rehabilitation (CR) program on physical function and psychological wellbeing in patients following aortic root replacement. **Materials and methods***:* Patients were randomly assigned to either an 8-week (24 sessions) cardiac rehabilitation (CR) program, 4 to 6 weeks after aortic root replacement using the Bentall procedure, or to an age- and sex-matched control group undertaking no structured exercise. Physical function (via exercise treadmill test (ETT)) and psychological wellbeing (assessed via DASS-21 and SF36) were assessed before and following 8-weeks of CR. **Results:** 30 patients (15 in the control (mean age: 37±10 years) and 15 in the intervention group (mean age: 38±11 years)) completed the 8-week CR programme and no adverse events were reported over the intervention period. In the CR group, all sub-components of the SF-36 and DASS-21 increased (all $P<0.05$), showing an overall improvement in psychological function, anxiety, and depression following the intervention. Distance walked on the ETT (improved significantly following 8-weeks of CR (490 ± 167 m v 659 ± 141m; ʌ improvement = 169 m; $P<0.05$). There were no changes in physical function and psychological wellbeing in the controls ($P>0.05$). A significant group-by-time interaction effect was evident for physical function and all sub-components of the SF-36 and DASS-21 (all $P<0.05$) highlighting significant improvements in outcomes in the CR group compared to controls. **Conclusions:** This small sample, aerobic-based, moderate-intensity CR is safe and effective, and can be tolerated only 4-6 weeks after complex aortic root replacement surgery.

Keywords: cardiac rehabilitation, Bentall procedure, depression, anxiety

1. Introduction

For individuals requiring aortic root replacement, the Bentall technique is considered the "gold standard" procedure [1]. This technique is commonly performed on the bicuspid aortic valve due to a congenital abnormality of the aortic root affecting 0.5 to 2% of the general population [1]. The vast majority of procedures undertaken involves the replacement of the aortic root with a mechanical valved conduit [2,3]. The mechanical valve is rarely used in patients over 70 years of age; in older populations, the biological valve has been shown to be more effective [1]. A limitation of the mechanical valve is that whilst it provides a robust solution it requires life-long anti-coagulation therapy associated with increased bleeding risk. A recent meta-analysis indicates that rates of aortic root re-operation have decreased in recent years as techniques have been refined. However, rates of late mortality, thromboembolic complications, and incidents of major bleeding still exist highlighting the risks associated with the procedure even in the light of modern surgical procedures [4].

Cardiac rehabilitation (CR) is a multi-dimensional strategy combining structured exercise training, education, and psychological and nutritional interventions to improve physical function and mental wellbeing in patients with a history of cardiac disease [5,6]. Previous work has shown how CR can help improve physical function, health-related quality of life (HRQoL) and reduce stress, anxiety, and depression [7]. Following cardiac intervention, post-surgical complications are most likley to affect the pulmonary system (33%), cardiac system (30%), and negatively affect psychological wellbeing (26%) [8]. Such complications will often lead to increased length of hospital stay, increased bed rest, and may exacerbate symptoms of stress, depression and anxiety resulting in decreased functional capacity, muscle wasting, joint stiffness and a decrease in HRQoL [8].

The evidence-base strongly indicates that structured comprehensive CR helps to improve physical function, recovery from surgery and psychological wellbeing due to the work of an effective multi-disciplinary team including dieticians, counsellors, smoking cessation practitioners, and exercise specialists [9,10]. From a surgical perspective, there may be some anxiety associated with the impact of prolonged exercise on a recently fitted valve replacement, at least in the short term. Resistance (strength) training is known to significantly increase diastolic and systolic blood pressure and would appear to be contraindicated, at least in the short term, for patients recently undergoing aortic root replacement [3]. However, the role of CR on patient outcomes following aortic root replacement compared to usual care has received little attention. Most CR studies which have followed surgical intervention have focused on outcomes following coronary artery bypass graft or angioplasty. To our knowledge, little is known about the impact of CR following aortic root replacement using the Bentall procedure as it is rarely performed [1]. Therefore, this pilot study aimed to investigate the safety and efficacy of an 8-week CR program on physical function and psychological wellbeing in patients following aortic root replacement surgery using the Bentall procedure compared to patients receiving usual care.

2. Material and methods

2.1.Participants

The pilot study received full ethical approval from the local medical ethics board (approval code: IR.TUMS.NI.REC.1399.046), and all patients provided full written informed consent before participation in the study. Patients who underwent aortic root replacement surgery using the Bentall procedure in Shariati Hospital (Tehran University of Medical Sciences, Iran) between the years 2016-2019 were referred to a CR center 4 to 6 weeks following surgery.

Prior to enrolment in CR, patients underwent echocardiography, completed a symptom-limited exercise test with treadmill (modified Bruce protocol), and medication was reviewed by a cardiologist. Patients assigned to the CR group were subsequently referred to the Department of Cardiac Rehabilitation, where they underwent a supervised 8-week exercise training program including three sessions per week (24 sessions in total). Controls did not engage in any structured exercise rather they were advised to undertake physical activity by walking daily and to stop smoking as per usual care.

The inclusion criteria were: clinically stable and deemed suitable for engaging in regular exercise sessions, optimal medical treatment for cardiac and other underlying diseases, left ventricular ejection fraction (LVEF) >40%, able to follow study instructions, able to complete study questionnaires. Exclusion criteria: unstable cardiac conditions including uncontrolled arrhythmias, uncontrolled cardiac risk factors including hypertension or diabetes mellitus, co-existing respiratory disease, orthopaedic limitations, and post-surgical complications resulting in the inability to participate in structured exercise sessions.

2.2.CR program

Patients were enrolled onto the local 8-week CR program, 4 to 6 weeks after receiving aortic root replacement surgery. The program consisted of 24 structured exercise training sessions, plus an education session focused on cardiovascular risk factors, lifestyle modification after surgery, stress management, quit smoking, and warfarin therapy.

At baseline, clinical history, risk factors, and medication usage were logged [11]. Bodyweight and height were recorded, and subsequently, body mass index (BMI) was calculated. The exercise program was performed according to the American Association of Cardiac Rehabilitation

(AACVPR) guidelines. The patients were divided into 3 groups of low, moderate, and high risk based on cardiac risk stratification. An individualized aerobic exercise training program consisting of treadmill walking, cycling, and arm ergometer exercise was provided. Exercise training sessions were completed 3 times per week for 8 weeks (24 exercise training sessions). Patients trained between 40-60% of their percentage heart rate reserve (%HRR), with a rating of perceived exertion (RPE) between 11-14 on the Borg scale [12,13]. Each training session lasted 30-60 minutes which also included a 15-minute warm-up and 10-minute cool-down. At the beginning and end of each training session, blood pressure was measured and heart rate was monitored with heart rate and blood pressure monitors. The INR levels were monitored regularly throughout the intervention, if the INR was ≥ 4.5 the training session would be postponed until it dropped within a normal range [14]. In addition, patients received weekly counselling sessions which were themed around dealing with anxiety and depression, managing risk factors, smoking cessation, and making positive lifestyle changes. On completion of the 8-week CR program, patients were re-referred to a cardiologist and underwent an echocardiographic investigation, treadmill-based exercise tolerance test, and medication review.

2.3.SF-36 and DASS-21

Patients completed two psychological outcome measures on two occasions, before and following their engagement in the 8-week CR program, and at the same time-points for controls. These included including quality of life assessment (SF-36), and the depression, anxiety, and stress scale (DASS-21). The SF-36 questionnaire consists of 36 questions with eight health-related concepts: physical functioning; role limitations due to physical problems; bodily pain; general health

perceptions; vitality; social functioning; role limitation due to emotional problems; and mental health. A higher quality of life is associated with a higher score. The reliability and validity of the SF-36 questionnaire have been previously established in the Persian language [15]. The DASS-21 is a 21-item self-reported measure of psychological distress. This questionnaire consists of three subscales, which evaluate depression (7 items), anxiety (7 items), and stress (7 items). The reliability and validity of the DASS-21 questionnaire have been previously established in the Persian language [16]. Each questionnaire was completed at baseline and within one week of completing the CR program.

2.4.Exercise tolerance test

An exercise tolerance test was conducted before and immediately following the 8-week CR program. Patients performed a modified Bruce protocol (symptom-limited) on a treadmill. The modified Bruce protocol increased speed or gradient every 3 minutes; the first stage started at 2.7 km/h speed and 0% grade, and increased every 3 minutes thereafter until volitional exhaustion. Heart rate, blood pressure, and a 12-lead electrocardiogram were monitored throughout. The test was terminated when patients reached volitional exhaustion. Distance walked (m) on the treadmill (with BMS, Treadmill Track Master) was recorded. Before conducting the ETT, all patients were instructed to prepare for the test by (1) not eating, drinking alcohol or caffeine, or smoking in a 3 hour period before the test; (2) hydrating regularly in the 24 hours before the test; (3) not engaging in moderate to vigorous physical activity for at least 12 hours before the test; and (4) wearing appropriate footwear to perform the test. Heart rate and a 12-lead electrocardiogram were monitored throughout the test. blood pressure was recorded before the test and every 2 minutes

during the test. The test was terminated when patients reached maximum fatigue and were unable to continue based on self-reported symptoms [17].

2.5.Echocardiography

A cardiac echocardiographic assessment was performed before and immediately after the 8-week CR program using standard 2-D echocardiography (Medison EKO 7, Samsung, South Korea). The Simpson method using the apical four-chamber view was used to estimate LVEF [18,19].

2.6.Data analysis

Data were reported as mean ± standard deviation. Repeated measures analysis of variance (ANOVA) with a two-by-two design (two groups by two points) was used to compare the CR group and controls for physical function and psychological wellbeing parameters. An alpha level of $P<0.05$ was considered statistically significant. Data were analyzed using SPSS version 25 (IBM, NY, USA).

3. Results

Thirty patients were randomly assigned to the CR group (mean age 38 ± 11 years; 67% male) or usual care (mean age 37 ± 10 years; 73% male). We recruited 15 patients in the CR group (mean age 38 ± 11 years; 67% male), and 15 controls (mean age 37 ± 10 years; 73% male), who had all undergone aortic root replacement within the past 4-6 weeks. Baseline clinical characteristics are

168 presented in Table 1. There were no between-group differences in anthropometric variables,
169 physical function, or in sub-domains of the SF-36 and DASS-21 at baseline (all $P<0.05$).
170 All fifteen patients (CR group) completed the 8-week CR program and no adverse events were
171 reported over the intervention period. Table 2 shows that all sub-components of the SF-36 and
172 DASS-21 improved (all $P<0.05$), showing an overall improvement in QoL, stress, anxiety, and
173 depression following the intervention. Physical function based on mean distance walked following
174 an ETT improved significantly following 8-weeks of CR (490 ± 167 m v 659 ± 141m; ∧
175 improvement = 169 m; $P<0.05$). There were no changes in physical function and psychological
176 wellbeing in the controls ($P>0.05$). A significant group-by-time interaction effect was evident for
177 physical function and all sub-components of the SF-36 and DASS-21 (all $P<0.05$) highlighting
178 significant improvements in outcomes for the CR group compared to controls.
179
180 **TABLES 1-2 ABOUT HERE**
181
182 **4. Discussion**
183
184 Our pilot study showed that early CR is safe and effective in patients following aortic root
185 replacement using the Bentall technique. Patients who undertook early CR following aortic root
186 replacement surgery in the past 4-6 weeks showed significant improvements in physical function
187 and psychological wellbeing compared to age- and sex-matched controls. The CR program was
188 well tolerated with no adverse events being reported. Patients in the CR group improved
189 significantly in all components of the SF-36 and DASS-21, and in physical function (metres
190 walked on a treadmill) compared to controls.

A large body of evidence has shown that CR programs improve physical function in coronary heart disease and heart failure cohorts [20,21], as well as in those who have undergone coronary artery bypass grafting [22]. However, the evidence for the safety and efficacy of CR programs on patients following valvular surgery is far less established [23]. Recently, Tabet et al. [24] showed that mean peak oxygen consumption and first ventilatory threshold increased by 32% and 19%, respectively following 3-5 weeks of moderate-intensity CR. in 50 patients who had recently undergone aortic valve repair. This is in agreement with our findings as we found a ~26% increase in walking capacity following a symptom-limited exercise tolerance test.

A novelty of our study is the focus on psychological wellbeing which shows the benefits of CR in this population. Previous studies have shown the benefits of CR for cardiac patients following surgery [25], for improving depressive symptoms and quality of life [26], and stress and anxiety [27]. Psychological function and quality of life should continue to be assessed in the longer term following CR intervention. Longer-term interventions should focus on stress management, self-care coaching, and wellbeing counseling [28].

Cardiac rehabilitation has been well established for having beneficial effects on both physical function and mental wellbeing. Physical function is improved through increased maximal aerobic capacity due to improved endothelial function, increased muscle mass, and improvement in oxygen delivery and utilization [29]. Cardiovascular risk factors are positively modified, myocardial oxygen demand is reduced, autonomic tone is improved, and the likelihood of myocardial ischemia is reduced [30]. Epidemiological evidence indicates that CR can improve all-cause and cardiovascular mortality, reduce CVD events, reduce hospitalization rates, and enhance HRQoL in patients with coronary heart disease [29,30].

Limitations: Our pilot study was small with only 30 patients included so we must recognize this as a potential confounder. We recommend larger-scale studies be developed to confirm our tentative findings. Our study was focused on aerobic-based, moderate-intensity training and it would be interesting for other studies to focus on the viability of conducting higher intensity training with a resistance training component for the patient undergoing complex aortic root surgery. This may need to be conducted under close clinical supervision in a hospital setting to maximize safety considerations.

5. Conclusion

We found significant improvements in physical function and psychological wellbeing after an 8-week, aerobic-based, moderate-intensity CR program compared to age- and sex-matched controls who had all received aortic root replacement surgery using the Bentall technique in the past 4–6 weeks.

Conflict of interest

None to report.

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Table1. Baseline clinical characteristics of people in the CR group and controls (n=30)

Variables	CR group (Mean ± SD)	Controls (Mean ± SD)	*P*-value
Age (years)	38±11	37±10	0.12
Stature (cm)	169±10	168±11	0.45
Body mass (kg)	77.7±12.3	76.5±11.4	0.32
Sex (male/female)	(10/5)	(11/4)	0.22
SF36			
Physical functioning	71±17.2	73±16.2	0.23
Physical limitations	41.3±11.8	40.3±10	0.76
General health	57.6±8	56.6±6	0.10
Vitality	28±7	29±6	0.54
Social function	14.6±4	12.8±3	0.63
Pain	27±15.5	26±14	0.55
Emotional limitations	28.6±9.9	27±10	0.16
Mental health	36±9.1	35±9.4	0.32
DASS 21			
Stress	14.6±5.7	13.2±4.6	0.66
Depression	12.1±4.5	13.1±3.5	0.82
Anxiety	10.9±4.2	11.5±3.2	0.43
Distance walked during ETT (m)	489.9±166.6	460.9±154.2	0.12

DASS-21: The Depression, Anxiety, and Stress Scale; SF36: Quality of life assessment; ETT: exercise tolerate test.

Table 2: Comparative changes in physical function and psychological wellbeing between the CR group and controls (N=30)

	CR group Mean +SD		***P*-value (change within group)**	**Controls Mean +SD**		***P*-value (change within group)**	***P*-value (interaction effect)**
SF36	Pre	Post		Pre	Post		
Physical function	71 ± 17.2	86.3 ± 12.02*	0.02	70 ± 16	71 ± 14.2	0.09	0.02
Physical limitations	41.3 ± 11.8	28 ± 12.07	0.001	42 ± 12	41 ± 11	0.12	0.01
General health	57.6 ± 8.7	61.6 ± 8.9	0.04	58 ± 9.1	57 ± 10.2	0.23	0.01
Vitality	28 ± 7.7	32.3 ± 7.7	0.04	26 ± 7.2	25 ± 6.2	0.53	0.04
Social functioning	14.6 ± 4.4	17.3 ± 4.08	0.06	15.1 ± 4.1	14.8 ± 3.2	0.27	0.01
Body pain	27 ± 15.5	15.6 ± 8.5	0.01	25.2 ± 14	26.1 ± 8.1	0.76	0.01
Emotional limitations	28.6 ± 9.9	19.3 ± 8.8	0.02	29.6 ± 8.2	30 ± 6.4	0.16	0.02
Mental health	36 ± 9.1	43 ± 7.9	0.04	34 ± 7.2	35 ± 7..5	0.54	0.04
DASS16							
Stress	10.9 ± 4.2	11 ± 4.4*	0.01	12.3 ± 3.6	12.2 ± 3.3	0.88	0.01
Depression	12.13 ± 4.5	9.06 ± 2.8*	0.03	11.8 ± 3.6	11.5 ± 3.3	0.21	0.01

Anxiety	14.6 ± 5.7	8.4 ± 2.8*	0.02	13.9 ± 5.2	13.2 ± 6.3	0.92	0.01
Distance walked following an ETT (m)	489.9 ± 166.6	658.8±140.6*	0.01	482 ± 162.3	485±164.6	0.51	0.01

351 DASS 21: The Depression, Anxiety, and Stress Scale; SF36: Quality of life assessment; ETT:
352 exercise tolerance test; * indicates a significant difference, CR: cardiac rehabilitation; $P< 0.05$.
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