REVIEW ARTICLE

Effects of Cardiac Rehabilitation on Health-Related Quality of Life in patients with Cardiovascular Disease: A Systematic Review

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ABSTRACT

The effective cardiac rehabilitation (CR) in patients with cardiovascular disease (CVD) remains controversial. We performed a meta-analysis to examine the effects of CR on health-related quality of life (HRQOL) in patients with CVD. We searched MEDLINE, PubMed, The Scientific Electronic Library Online, Google Scholar (from the earliest date available to September 2016) for randomized controlled trials (RCTs) examining the effects of CR versus control on quality-of-life (HRQOL) in CVD. Mean differences (MDs) and 95% confidence intervals (CIs) were calculated, and heterogeneity was assessed using the I² test. Six studies met the selection criteria (total 482: 261 CR and 221 control patients). The results suggested that CR compared with control had a positive impact on HRQOL. Global HRQOL Physical Component Summary (SF-PCS) standardized mean differences (4.77, 95%CI 2.32 to 7.22, p=0.0001) and Mental Component Summary (SF-MCS) score 2.65 (95%CI -3.96 to 9.27, n=294, p=0.43) improved in the CR group compared to the control group. Our results suggest that CR compared with control had a positive impact on HRQOL. CR enhances HRQOL in patients with CVD. Larger RCTs are required to further investigate the effects of CR in patients with CVD.

<Key-words>
cardiac rehabilitation, mental health, health-related quality of life, cardiovascular disease

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I. Background

Cardiovascular disease (CVD) still remains the most prevalent chronic disease in individuals, and the debilitating effects of the disease are evident by the high rate of hospitalization among patients (Mendis, Puska & Norrving; WHO, 2011). Patients with CVD have a high mortality risk and a serious impairment in all generic and disease-specific domains of health-related quality of life (HRQoL) (Piepoli, Conraads, Corrâ, et al., 2001; Chen & Li, 2013; Flynn KE, Pina & Whellan et al. 2009; Issa, Hoeks, & Scholte op Reimer, et al., 2010; Edelmann, Gelbrich & Düngen, et al., 2011). Patient with CVD performed aerobic exercise training, typically included in cardiac rehabilitation (CR) program, improved lower the risk of myocardial reinfarction, lower mortality rates, and improve cardiac function (Shephard & Balady, 1999).

Cardiac rehabilitation (CR) is suggested to improve exercise capacity, prognosis, health-related quality of life (HRQoL) and functional modifications of the heart in patients with cardiovascular disease (CVD) (Iqbal J, Francis L, Reid J, Murray, et al. 2010; Issa, Hoeks & Scholte op Reimer, et al., 2010; Schopfer DW, Forman DE., 2016; Davies EJ, Moxham T, Rees K, et al., 2010). According to Japanese Circulation Society (2014), studies of cardiac rehabilitation in patients with CVD have been conducted mainly performing programs combining several exercise trainings. Exercise training is also strongly recommended to improve the QOL in patients with CVD (Piepoli, Conraads & Corrâ, et al., 2001; van Tol, Huijsmans & Kroon, et al., 2006; Schopfer & Forman 2016). Several reviews that focused on patient with CVD showed that exercise training can increase HRQoL (van Tol, Huijsmans & Kroon, 2006; Chen & Li., 2013; Parmenter, Dieberg & Phipps, etal., 2015; Davies, Moxham & Rees, et al., 2010). However, these review studies focused on HRQoL patient with each disease separately, such as Chronic Heart Failure, Heart Failure, and Peripheral Artery Disease. There is still no systematic review about effects of CR in patients with a wide range of CVD.

Therefore, we therefore sought to conduct an updated systematic review, while also undertaking appropriate meta-analysis, with a particular focus on quality of life outcomes. The aim of present study was to systematically review the effects of CR on HRQoL in patients with CVD.

II. Methods

1. Search strategy

Studies on the effects of cardiac rehabilitation in patients with cardiovascular disease published between January 2012 and September 2016 were independently identified by two researchers, using the following electronic database MEDLINE, PubMed, The Scientific Electronic Library Online and Google Scholar. The search strategy, formulated in MEDLINE, was adapted for another electronic database. The keywords and Medical
Sub Headings were as follows: Cardiac rehabilitation, cardiovascular disease (CVD), exercise, Health-related Quality of Life (HRQoL), Depression, Anxiety, Randomized, clinical Trial. Two reviewers independently scanned all the titles, abstracts and full-texts.

2. Inclusion and exclusion criteria

Inclusion criteria were as follows: 1) RCTs (randomized controlled trials), 2) included patients with CVD (diagnosis based on cardiac rehabilitation 2012 [Kwan & Balady, 2012]), 3) received an exercise program or cardiac rehabilitation, 4) evaluated outcome measure in HRQoL (the generic and disease-specific HRQoL questionnaires).

Exclusion criteria were as follows: 1) not RCTs 2) Animal studies and review paper, 3) Studies that did not have any of the desired outcome, 4) participants without diagnosed cardiovascular disease (based on cardiac rehabilitation 2012).

3. Risk of bias of included studies

The risk of bias of included RCT studies was assessed independently by two authors using the Cochrane Collaboration’s Risk of bias tool (Higgins & Green, 2011). The following criteria were assessed: sequence generation, Allocation concealment, blinding of participants, personnel and outcome assessors, incomplete outcome data, selective outcome reporting, other sources of bias.

4. Data statistical analysis

The outcome measures were changes in three items of the SF-12, 36 (Physical component Summary: PCS, Mental Component Summary: MCS, 8 subcomponents: Physical Function: PF, Role Physical: RP, General Health: GH, Body Pain: BP, Vitality: VT, Social Function: SF, Role Emotional: RE, Mental Health: MH) and Minnesota Living with Heart Failure: MLHFQ. The mean difference (MD) was calculated for the outcome measures by subtracting the baseline from post-intervention values.

Meta-analyses were completed for continuous data by using the change in mean (SD) of outcome. Change in post-intervention mean was calculated by subtracting the baseline from post-intervention. Results were required as 95% confidence intervals (CIs) for pre-post intervention change for each group. A fixed-effects meta-analysis was used except when statistical heterogeneity was identified when the more conservative random-effects model was used. All analysis was performed using Review Manager Software (version 5.0: Cochrane Collaboration, oxford, UK).
III. Results

1. Identification and selection of studies

Our initial search identified manuscripts: examination of the latest editions of relevant journals yielded a further Titles. After a review of the titles and abstracts of these, 55 papers were assessed. In total, 48 papers were excluded: 14 with not RCTs, 19 with did not measure QoL or depression, 11 with outcome measured but data not available, 4 with review article. Therefore, the total number of included trials was 7 (Figure 1). 7 trials were included that measured QoL or depression.

<Figure 1> Search and selection process for studies.

2. Trials included

Table 1 shows the characteristics of the seven included trial. All trials included a total 554 patients, 294 patients in the exercise group and 260 patients in the control group. Recruited subjects were patients with CVD, which were contributed by the Cardiac rehabilitation2012(Diabetes Mellitus, Heart Failure(HF), Heart Failure with Preserved Ejection Fraction(HF/pEF), Pulmonary Arterial Hypertension, Congenital Heart Disease(CHD), Peripheral Arterial Disease(PAD)) (Kwan & Balady, 2012).

In the seven trials, Three trials in patients with HF (Aksoy, Findikoglu & Ardic , et al.,2015: Borland, Rosenkvist & Cider.,2014: Chrysohoou, Angelis & Tsitsinakis,2015); Two trials in patients with HF/pEF (Fu, Yang & Wang, et al.,2016: Nolte,

In the seven trials, five trials used aerobic training (Aksoy, Findikoglu & Ardic, et al., 2015; Borland, Rosenkvist & Cider, 2014; Chrysohoou, Angelis & Tsitsinakis, 2015; Dulfer, Duppen & Kuipers, et al., 2014; Fu, Yang & Wang, et al., 2016), one trial used walking exercise (McDermott, Liu & Guralnik, et al., 2013) and one trials used endurance/resistance exercise (Nolte, Herrmann-Lingen & Wachter, et al., 2015). Exercise training ranged widely across the studies: duration, 20-60 min per session, frequency, two to five sessions per week, duration, 10 weeks to 24 weeks; intensity, heart rate 50-75% of peak oxygen uptake (VO2), 40-70% of maximal heart rate reserve or Borg scale of between 11 and 14.

In the seven trials, seven trials measured HRQoL using SF-12, 36 or MLHFQ (Aksoy, Findikoglu & Ardic, et al., 2015; Borland, Rosenkvist & Cider, 2014; Chrysohoou, Angelis & Tsitsinakis, 2015; Dulfer, Duppen & Kuipers, et al., 2014; Fu, Yang & Wang, et al., 2016; McDermott, Liu & Guralnik, et al., 2013; Nolte, Herrmann-Lingen & Wachter, et al., 2015). Two trials measured depression using ZDRS or PHQ-9 (Chrysohoou, Angelis & Tsitsinakis, 2015; Nolte, Herrmann-Lingen & Wachter, et al., 2015).

Table 1: Summary of trial characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Characteristics of patients</th>
<th>Training features</th>
<th>Outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aksoy et al (2015)</td>
<td>Sample size: 30 (EG:15, CG:15) Age: 63.7 (8.8) Male: 13/13 CVD: HF</td>
<td>Modality: 35 min, 3 times a week, aerobic exercise Intensity: heart rate 50-75% of peak oxygen uptake (VO2) Follow-up: 10 weeks</td>
<td>SF-36 (8 items) LVD-36</td>
<td>SF-36: VT, MH ↑</td>
</tr>
</tbody>
</table>
3. Risk of bias

Table 2 shows the risk of bias assessment. In the sequence generation, 5 studies included the use of randomization such as computer of randomly permuted block method. In the allocation concealment, 5 studies adequately concealed allocation. In the blinding of participants, personnel and outcome assessor, 3 studies published descriptions of concealment procedures judged to be adequate. In the incomplete outcome data, 5 studies adequately addressed missing outcome data. In the selective outcome reporting, 5 studies were free of suggestion of selective outcome reporting. Finally, in the other sources of bias, 5 studies were apparently free of other bias.
<Table 2> The risk of bias assessment

<table>
<thead>
<tr>
<th>Sequence generation</th>
<th>Allocation concealment</th>
<th>Blinding of participants, personnel and outcome assessors</th>
<th>Incomplete outcome data</th>
<th>Selective outcome reporting</th>
<th>Other sources of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borland et al (2014)</td>
<td>Unclear</td>
<td>High</td>
<td>Unclear</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Dulfer et al (2014)</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Fu et al (2015)</td>
<td>Unclear</td>
<td>High</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>McDermott et al (2016)</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Nolte et al (2014)</td>
<td>Low</td>
<td>High</td>
<td>Unclear</td>
<td>High</td>
<td>Unclear</td>
</tr>
</tbody>
</table>

Abbreviations: Low=low risk of bias; High=high risk of bias; Unclear=uncertain risk of bias

4. Meta-analysis results

1) Health Related Quality of Life (HRQoL)-PCS

SF-PCS data were available four studies (Figure 2). Overall, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 4.77 (95%CI 2.32 to 7.22, n=341, p=0.0001). We detected significant heterogeneity within this group (I²=89%, p<0.00001).

2) Health Related Quality of Life (HRQoL)-MCS

SF-MCS data were available three studies (Figure 3). Overall, a no significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 2.65 (95%CI -3.96 to 9.27, n=294, p=0.43). We detected significant heterogeneity within this group (I²=97%, p<0.00001).
3) Health Related Quality of Life (HRQoL) - PCS sub component

SF-PF, RP, GH, BP data were available three studies (Figure 4). Overall of PF, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 13.43 (95%CI 0.73 to 26.12, n=121, p=0.04, I²=97%, Figure 4A). Overall of RP, no significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 8.35 (95%CI -2.20 to 18.90, n=87, p=0.12, I²=49%, Figure 4B). Overall of GH, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 5.19 (95%CI 1.17 to 9.22, n=91, p=0.01, I²=58%, Figure 4C). Overall of BP, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 7.13 (95%CI 3.38 to 10.88, n=122, p=0.0002, I²=58%, Figure 4D).

<Figure 4> Mean difference in PF (A), RP (B), GH (C), BP (D) scores: exercise versus control.

<Figure 3> Mean difference in SF-MCS scores: exercise versus control.
4) Health Related Quality of Life (HRQoL)- MCS sub component

SF-VT, SF, RE, MH data was available from three studies (Figure 5). Overall of VT, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 7.00 (95%CI 1.03 to 12.98, n=121, p=0.02, I²=97%, Figure 5A). Overall of SF, no significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 3.91 (95%CI -19.65 to 27.47, n=122, p=0.75, I²=98%, Figure 5B). Overall of RE, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 4.46 (95%CI 2.44 to 6.47, n=87, p<0.0001, I²=0%, Figure 5C). Overall of MH, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) 2.87 (95%CI 1.53 to 4.21, n=120, p<0.0001, I²=0%, Figure 5D).

5) Health Related Quality of Life (HRQoL)- MLHFQ total score.

Three studies assessed MLHFQ total score. Overall, a significant improvement was observed in exercise participants versus controls: Mean Difference (MD) -15.33 (95%CI -19.50 to -11.18, n=192, p<0.00001). We detected significant heterogeneity within this group (I²=98%, p<0.00001).
6) Heterogeneity

The Cochrane I2 scores from analyses in Figures 5C and 5D showed zero heterogeneity. Analysis in Figures 2-4, 5A, 5B and 6 exhibited low to high evidence of between-study heterogeneity, ranging from 49% to 98%.

IV. Discussion

In the present systematic review, a meta-analysis of six studies demonstrated augmentations in HRQOL in Patients with CVD after CR when compared to controls. Our results suggest that CR compared with control had a positive impact on HRQOL. This review is important because it analyzes HRQoL as a potential modality in CR.

The SF-36 is commonly used in the assessment of the HRQoL in patients with cardiovascular disease. The PCS and MCS were used to assess global components of HRQoL [Ware, Kosinski & Keller.1996]. 4 of 6 studies were reported the effect of CR on SF-PCS, MCS score in CVD. Our meta-analysis showed 11.0% improvement in SF-PCS in the CR group. The mean SF-PCS in the four studies analyzed was 41.47 at baseline and 46.12 at the end of the intervention. SF-MCS is not improvement in CR group. According to JCS, successful results of the improvement in MCS performed CR for at least 16weeks [Japanese Circulation Society; JCS,2014]. However, our results in CR intervention of five studies were reported the 10-12 weeks. 3 of 6 studies were reported the effect of CR on SF-8 subcomponent. SF-MCS is not significant, but CT, RE, MH of SF-MCS sub component is significant. We meta-analysis showed 5.0 % of SF-GH (64.31 and 67.51), 4.8% of SF-BP (80.89 and 84.73), 4.85% of SF-VT (66.33 and 69.55), 8.0% of SF-RE (80.73 and 87.20), 6.1% of SF-MH (74.64 and 79.02) improvements in the CR group. The magnitude of change is similar to a previous meta-analysis that evaluated the effect of different modalities of exercise in patients with CVD [Parmenter, Dieberg & Phipps, et al. 2015; Gomes-Neto, Rodrigues-Jr, & Silva-Jr, et al., 2014].

3 of 6 studies showed the effect of CR on MLHFQ total score. In those using the MLHFQ total score, exercise groups were on average 10 points higher than control groups. These results are similar to recent meta-analysis [Davies, Moxham & Rees, et al,2010].

Analyses in Figures 5C and 5D showed zero heterogeneity, suggesting the analyses of SF-RE and MH were appropriate. Analyses in Figures 2-4, 5A, 5B and 6 exhibited
moderate to high evidence of between-study heterogeneity, suggesting results of data pooling of, SF Physical and Mental Components and MLHFQ must be interpreted with caution.

Our review is limited, our search strategy only found six RCTs with small samples and short period of intervention. However, HRQoL appears to be an interesting assessment of CR and deserves further investigation with better-controlled RCTs. Future CR trials should include more severe CVD patients, and need larger and long enough periods to assess clinical HRQoL outcomes for generalizability.

In conclusion, our meta-analysis demonstrated improvement on HRQOL in patients with CVD by performing CR. Our results suggest that SF-PCS had a positive impact compared with control group. The effects of CR on HRQoL in patient with CVD still needed to be determined.

References


