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Effect of exercise-based cardiac rehabilitation on anxiety and depression in patients with myocardial infarction: A systematic review and meta-analysis

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ABSTRACT

Background: Cardiac rehabilitation (CR) has been shown to provide the best social, psychological and physical conditions for patient recovery after myocardial infarction (MI).
Objectives: The aim of present study was to quantify the efficacy of exercise-based CR treatments in terms of relief from symptoms of anxiety and depression symptoms among patients with MI.
Methods: Literature published up to August 2017 was reviewed systematically using relevant keywords, MeSH terms, and Emtree headings to search PubMed, Embase, CINAHL (Ebsco), Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science. The results of included studies were compared meta-analytically.
Results: We found that exercise-based CR had a significant effect on decreasing anxiety and depression scores. Furthermore, exercise-based CR may alleviate anxiety and depressive symptoms at different time periods.
Conclusions: For patients with MI, exercise-based CR has been demonstrated to alleviate anxiety and depressive symptoms. These findings highlight CR as essential and beneficial for minimizing MI patient anxiety and depression during recovery.

Introduction

Acute myocardial infarction (AMI) is a serious cardiovascular event that has an effect on the health-related quality of life (HRQoL) of both patients and their families due to intense cardiac disease progression and repeated readmissions to healthcare facilities.[1,2] Notably, psychological symptoms, such as anxiety, depression, hostility and so on, appear to negatively affect cardiac outcomes after AMI.[3,4] Akhtar et al. has shown that up to 50% patients with AMI have been found to suffer from symptoms of anxiety and/or depression one week after AMI.[5] Another prospective study revealed that the 12 month prevalence rates among 288 MI patients were 37.2% for depressive symptoms, 41.0% for anxious symptoms and 51% of patients had both anxiety and depression.[6] Anxiety also had a negative correlation with prognosis in post-MI patients.[7] Patients with depressive symptoms after AMI have been found to have relatively lower levels of full time work and working hours.[8] Moreover, psychological risk factors such as hostility,[9] anger,[10,11] anxiety,[12] depression,[13] have been shown to be a trigger for AMI and MI. Many studies have shown that post-MI patients with anxiety have higher rates of hospitalization[14] and recurrent cardiac events after acute hospitalization.[15] Large studies identified that post-MI depression, even minimal symptoms of depression,[16] were significant risk factors for reinfarction and death.[17,18] Finally, a meta-analysis has proposed that the odds ratio of post-MI with depression leading to mortality was 2- to 2.5-fold greater than without depression.[19]

The significance of curing anxiety and depression in patients with MI should not be understated. Fortunately, reducing psychological discomfort also has the potential benefit on long-term mental health status and outcomes for post-MI patients.[20] Many randomized and

Abbreviations: AMI, acute myocardial infarction; CR, cardiac rehabilitation; HRQoL, health-related quality of life; PTCA, coronary angioplasty; CHD, coronary heart disease; PCI, percutaneouscoronary intervention; CABG, coronary by-pass surgery; MI, myocardial infarction; SAQ, Speilberger Anxiety Questionnaire; SRQ-D, the self-rating questionnaire for depression; HADS, Hospital Anxiety and Depression Scale; BDI, Beck Depression Inventory; UC, usual care; PGWBI, The Psychological General Well-Bening Inventory; SDS, Self-rating Depression Scale; CSPFQ, Cattell Sixteen Personality Factor Questionnaire; CBT, cognitive behavioral therapy; iCBT, internet-based cognitive behavioral therapy.

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non-randomized controlled trials have addressed the positive effects of exercise-based cardiac rehabilitation (CR) on anxiety and depression with AMI patients.[20–39]

CR includes exercise training, vocational counseling, psychological and emergency support, medical surveillance as well as risk factor modification (cessation of smoking, control of hypertension and diabetes, reducing LDL cholesterol, etc.). The aim of CR is to ensure the best possible social, psychological and physical conditions for patients living with cardiac disease.[40,41] A previous meta-analysis found that exercise-based CR could reduce depressive symptoms in patients with coronary artery disease (CAD).[42] However, the effects of exercise-based CR on anxiety and depression among post-MI patients remains unclear.

This systematic review and meta-analysis aims to statistically analyze the effects of exercise-based CR on the anxiety and depressive of MI patients. In this study, the exercise intervention was based on national guidelines and informed phase I and/or a phase II CR program. The level of physical exercise was individualized, in order to maintain 60% to 80% of a target heart rate among other measures. Exercises included a series of aerobic exercises, resistance training, and flexibility training, which performed for 30 min–50 min a day or longer time for 3–5 days per week. Moreover, due to differences in years when the studies were conducted, there are slight differences between standard procedures in each CR programs. Finally, all included study participants were assessed using the Hospital Anxiety and Depression Scale (HADS), Speilberger Anxiety Questionnaire (SAQ), Beck Depression Inventory (BDI), Self-Rating Questionnaire for Depression (SRQ-D), General Well-Being Inventory (PGWBI), Self-rating Depression Scale (SDS), and the Cattell Sixteen Personality Factor Questionnaire (CSPFQ). The results of our meta-analysis suggest that the reduction of anxiety and depression plays a important role in enhancing HRQoL, as well as reducing morbidity and mortality for patients with MI.

Methods

The literature was searched for eligible articles using keywords, such as cardiac rehabilitation, myocardial Infarction, anxiety and/or depression, MeSH terms, and Emtree headings on databases such as PubMed, Embase, CINAHL (Ebsco), Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science (Supplementary materials) for studies published up to August 2017.

Articles from the search results were included if the following conditions were met: (1) study design consisted of an intervention study (RCT or non-RCT); (2) the outcomes included anxiety and/or depression; (3) all participants experienced AMI, including percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG); (4) the trial intervention was exercise-based cardiac rehabilitation. We excluded articles that were not written in English. Moreover, this meta-analysis and systematic reviews was conducted and reported in accordance with Meta-Analysis of Observational Studies in Epidemiology (MOOSE) statements and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). This study was registered at International Prospective Register of Systematic Reviews (NO. CRD42018084418).

We processed data following the Cochrane handbook for Systematic Reviews of Interventions. The information extracted from eligible study articles were the mean and standard deviation of anxiety and/or depression scores, which were continuous variables. Each outcome of each study was analyzed by mean differences (MD) with 95% confidence intervals (CI). Then, analyses were repeated with a random effects model and checked for any possible differences. Overall heterogeneity was quantified with the I^2 statistic. We compared the characteristics of studies and performed subgroup analysis to assess the heterogeneity associated with unique study characteristics when high heterogeneity occurred ($I^2 \geq 50\%$). Studies were selected for data extraction and analysis by two authors (XZ and YZ) and any disagreements on inclusion were solved by a third author (JW). Furthermore, we estimated study risk of bias using the Cochrane Collaboration's recommended tool. Analyses were performed using RevMan v5.3.

Results

Search results

Our preliminary online search identified 948 studies, after reading the titles and abstracts, 905 were excluded because the articles did not meet our inclusion criteria. After reading full manuscripts, 20

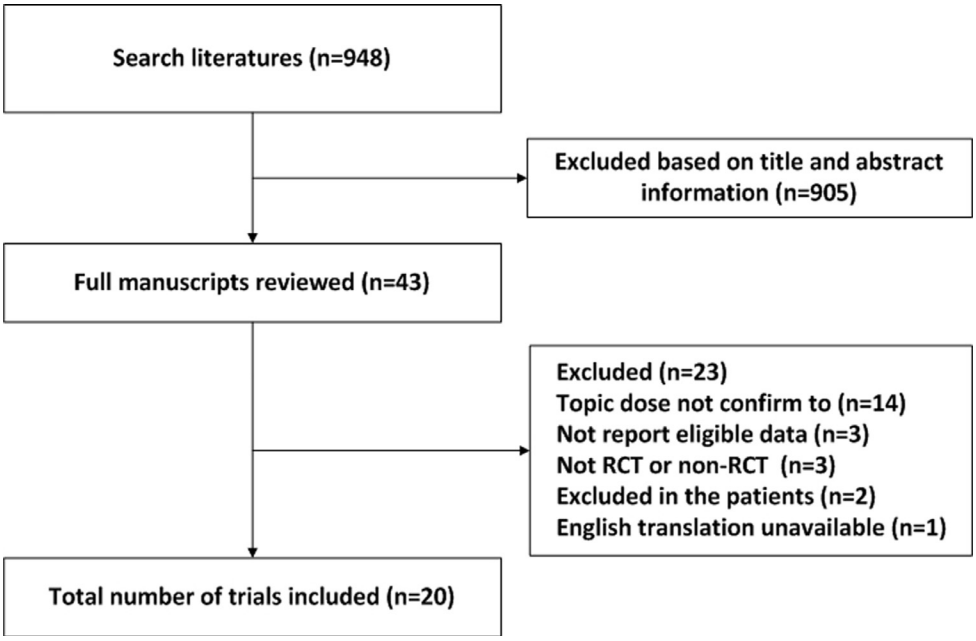

Fig. 1. Flow chart of the study extraction and selection process for meta-analysis.

articles were eligible to be included in the meta-analysis and systematic review. In total, 1828 MI patients were included in this analysis, including 233 patients who underwent CABG, and the number of patients per studies ranged from 16 to 201. A flowchart representing study selection was shown in Fig. 1.

Description of included studies

These 20 articles included nine RCTs and two non-RCTs; five studies were based in Japan, two each in Canada, China, Italy, and US, and one in Taiwan (China), UK, Netherlands, Singapore, Iran, Scotland, and Poland, respectively. Follow-up time was different from hospital discharge to two years among studies. The mean age of participant ranged from 52 to 68.5 years. The percentage of women in the patient population was low except for the study by Mayou et al. The type of intervention studied in an overwhelming majority of cases was exercise-based CR and/or standard of care. Detailed information about each study is shown in Table 1. A summary of the effect seen in each study of exercise-based CR on anxiety and depression in MI patients are shown in Table 2. Fifteen of the included 20 trials indicated that exercise-based CR reduced anxiety symptoms, but the other five trials saw no difference between standard of care and exercise. Eleven of the seventeen trials supported exercise-based CR with a positive effect on depression. It is worth noting that one of the trials demonstrated exercise-only-based rehabilitation contributed considerably to a decrease in manifestations of depression and anxiety manifestations in post-MI women. Neither depression nor anxiety were changed significantly in men. On the other hand, exercise-based CR may allay anxiety and depressive symptoms at different time periods (Table 3).

Risk of bias in included studies

Several studies included within this analysis failed to provide enough detailed information to fully assess the potential risk of bias. Details about selection bias were poorly reported, such as random sequence generation and allocation concealment. Only six studies presented random sequence generation information and only three studies stated that they took the measures to address allocation concealment. All trials did not use a blinded approach for investigators and participants. Further, the majority of trials were unclear about selective reporting. Other biases were not described in each study. Assessment of included study biases are presented in Table 4.

Meta-analysis results about anxiety

Eight studies examining a total of 739 participants were evaluated for the effect of exercise-based CR on the anxiety. We found that exercise-based CR had a significant effect on decreasing anxiety among the entire dataset [95% CI: (−4.23, −0.95); P value 0.002; P value for heterogeneity = 0.0003; I^2: 75%] (Fig. 2(A)). Subgroup analysis was performed on all AMI and CABG patients. The results showed that exercise-based CR could decrease anxiety in AMI patients [95% CI: (−2.02, −0.15); P value 0.02; P value for heterogeneity = 0.24; I^2: 26%] (Fig. 2(B)) and CABG patients [95% CI: (−12.35, −1.02); P value 0.02; P value for heterogeneity = 0.02; I^2: 81%] (Fig. 2(C)).

Meta-analysis results about depression

Six studies, including 703 participants, were evaluated for their quantitative effect of exercise-based CR on depression. Using evaluation methods including BDI, HADS, SRQ-D, exercise-based CR resulted in a significant reduction in depression scores [95% CI: (−1.12, −0.09); P value 0.02; P value for heterogeneity = 0.47; I^2: 0%] (Fig. 3).

Discussion

To our knowledge, this study is the first to verify the effect of exercise-based CR on depression and anxiety symptoms in patients with MI. We demonstrated that exercise-based CR decreases anxiety and depression symptoms in this patient population. Further subgroup analysis of AMI and CABG patients also showed that exercise-based CR may relieve anxiety symptoms. Moreover, exercise-based CR may allay the symptoms of depression at different time periods.

Anxiety is the earliest psychological response to an ischemic coronary event with the first symptoms of depression appearing between 48 and 72 h after MI.[43] Most patients, in this study, were found to be suffering from depression and/or anxiety symptoms one week after AMI. Previous study has found that the level of depression symptoms in patients with MI is closely related to survival at 1 year after admission.[44] Anxiety and depression symptoms were moderately associated with the risk of AMI[45] and directly related to poorer quality of life

Table 1
Summary of study characteristics

Study	Methods	Cardiac Population	Type of intervention	Number	Age(years)	Women (%)	Follow-up (weeks)
Dixhoorn et al. (1990)	RCT	MI	exercise plus relaxation and breathing therapy	156	55.7	25.0	6
Fallavollita et al. (2016)	Non-RCT	MI	5-week comprehensive cardiac rehabilitation program	37	66.0	16.2	5
Giallauria et al. (2006)	RCT	AMI	home-based CR or hospital-based CR	30	54.0	–	8
Korzeniowska-Kubacka (2017)	Non-RCT	MI	8-week training programme	62	58.1	48.4	8
Ku et al. (2002)	RCT	MI, CABG	Basic UC or phase I CR	60	68.5	13.3	Hospital discharge
Linden et al. (1995)	RCT	AMI	Basic UC or the Manual CR	34	61.5	32.4	1/3/6
Matsunaga et al. (2004)	Non-RCT	AMI	phase I rehabilitation program	42	62.0	–	Hospital discharge
Mayou et al. (2002)	RCT	AMI	Basic UC or Guideline-based early CR	114	52.9	88.0	4/12/48
Johnston et al. (1999	RCT	AMI	Basic UC or 6-week CR	100	56.1	35.0	8/24/48
Oldridge et al. (1991)	RCT	AMI	Basic UC or 8-week comprehensive CR	201	57.9	20.0	8/16/32/48
Oldridge et al. (1995)	RCT	AMI	Basic UC or 8-weeks CR	187	54.3	12.0	8/48
Pourafkari et al.,2016	Non-RCT	MI,CABG	8-week rehabilitation program	120	60.0	20.8	8
Sharif et al. (2012)	RCT	CABG	Basic UC or 4-week CR	80	–	32.5	8
Suzuki et al. (2005)	Non-RCT	MI, CABG,PCI	12-week CR with exercise training program	44	58.0	15.9	12
Schomer et al. (1983)	Non-RCT	MI	Basic UC or 6-week CR	16	–	–	24
Wang et al. (2012)	RCT	AMI	basic UC or home-based CR	160	57.3	14.7	6/12/24
Wang et al. (2016)	RCT	MI	Basic UC or 4-week home-based self-management CR	128	54.9	9.4	4/16
Yonezawa et al. (2009)	Non-RCT	MI, CABG,PCI	Basic UC or 20-week phase II CR	109	56.0	17.43	24
Yoshida et al. (1999)	Non-RCT	AMI	Basic UC or 4-week hospitalized phase II CR	63	57	7	4/24
Yoshida et al. (2001)	Non-RCT	AMI	Basic UC or 2-week hospitalized phase II CR	85	52	8	2/4

Table 2
Review of studies about the effect of exercise-based CR on anxiety state and depression in patients with MI

Study	Anxiety state scale	Difference between groups	Depression scale	Difference between groups	Country setting
Dixhoorn et al. (1990)	STAI	CR=Pre-CR	–	–	Netherlands, single hospital centre
Fallavollita et al. (2016)	PGWBI	CR>UC	PGWBI	CR>UC	Italy, single hospital centre
Giallauria et al. (2006)	STAI	CR=Pre-CR	BDI	CR=Pre-CR	Italy, single hospital centre
Korzeniowska-Kubacka (2017)	STAI	CR>Pre-CR (women) CR=Pre-CR (men)	BDI	CR>Pre-CR (women) CR=Pre-CR (men)	Poland, single hospital centre
Ku et al. (2002)	STAI	CR>UC	–	–	Taiwan(China), single hospital centre
Linden et al. (1995)	HADS	CR>UC	HADS	CR>UC	UK, single hospital centre
Matsunaga et al. (2004)	STAI	CR>UC	–	–	Japan, single hospital centre
Mayou et al. (2002)	STAI	CR>Pre-CR	BDI	CR=Pre-CR	Canada, six hospital centres
Oldridge et al. (1991)	HAD	CR>UC	HAD	CR>UC	UK, single hospital centre
Johnston et al. (1999)	HADS	CR>UC	HADS	CR>UC	Scotland, single hospital centre
Oldridge et al. (1995)	STAI	CR>UC	BDI	CR>UC	Canada, single hospital centre
Pourafkari et al. (2016)	BMS	CR>UC	BMS	CR>UC	US, single hospital centre
Sharif et al. (2012)	STAI	CR=UC	BDI	CR>UC	Iran, single hospital centre
Suzuki et al. (2005)	STAI	CR=UC	SDS	CR=UC	Japan, single hospital centre
Schomer et al. (1983)	CSPFQ	CR>UC	CSPFQ	CR>UC	US, single hospital centre
Wang et al. (2012)	HADS	CR>UC	HADS	CR=UC	China, tow hospital centres
Wang et al. (2016)	HADS	CR>UC	HADS	CR=UC	Singapore, single hospital centre
Yonezawa et al. (2009)	SF-36,HADS	CR>UC	SF-36,HADS	CR>UC	Japan, single hospital centre
Yoshida et al. (1999)	STAI	CR=UC	SRQ-D	CR>UC	Japan, single hospital centre
Yoshida et al. (2001)	STAI	CR>UC	SRQ-D	CR=UC	Japan, single hospital centre

CR = UC: There is no difference between groups. ($p > 0.05$); CR > UC: There is difference between groups. ($p < 0.05$); CR: Cardiac Rehabilitation; Pre-CR: Before Cardiac Rehabilitation; UC: Usual Care; PGWBI: The General Well-Bening Inventory; SDS: Self-rating Depression Scale; BMS: Brief mood survey; CSPFQ: the Cattell Sixteen Personality Factor Questionnaire.

10 years after such an incident.[46] Another study found that the post-MI patients with over 6 months of depression had a worse prognosis compared to without depression. Thus, prevalence of these symptoms following the first AMI creates a demand for early evaluation and treatment, and early CR may play a key role in post-MI anxiety or depression. Additionally, this study indicates that CR may alleviate the symptoms of depression at different time periods during treatment. CR has been shown not only to be able to improve anxiety and depression among patients with MI, but also have a better HRQoL and survival.[41]

Anxiety symptoms had no association with a patient's infarct severity, sex, education, or history of previous AMI, but risk factors associated with coronary heart disease, such as smoking, hyperlipidemia, hypertension and physical inactivity aimed at coping with anxiety.[47] For this reason, anxiety is more likely to be related to current marked reminders of ill-health or risk to future health.[46] There are many sources of depression, such as direct reactions to the shock of the MI as well as feelings of ineffective coping with the ensuing stress.[48] Patients with anxiety are more likely to develop depression later on compared to patients without anxiety, and there is a significant association between anxiety/depression and MI, but the underlying pathophysiological mechanisms are not yet deeply understood. Possibly, the main mechanisms by which anxiety/depression has an affect on MI disturbances is in the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system which can raise catecholamine secretion and sympathetic nerve activity, causing platelet activation and inflammation.[49] Other possibilities include behavioral mechanisms such as delays in seeking medical help, unhealthy lifestyle, and failure in risk factor modification.[50,51] Unfortunately, anxiety and depression are frequently underestimated among patients with MI.[52,53] Therefore, the major issue is to enhance awareness among clinical workers about this comorbidity. Promisingly, one study shown that anxious patients are more likely to participate in CR,[45] which can lead to a better prognosis and optimal recovery.

Besides exercise training, purely psychological treatment, such as cognitive behavioral therapy (CBT), problem-solving therapy (PST), interpersonal psychotherapy (IPT), and possibly psychodynamic psychotherapy, as well as pharmacotherapies are also effective for treating depression and anxiety in patients with MI.[38,54] These interventions are all part of CR. In addition, the latest research shows internet-based CBT (iCBT) may improve patient access to acceptable, effective, and cost-effective psychological treatment,[55] and has been found to reduce symptoms of depression and anxiety among patients with MI.[56] On the other hand, there are cultural differences in how patients address anxiety and depression, such as the forest therapy used among Koreans and Japanese, Taijiquan and Baduanjin exercises for Chinese, and religious beliefs of American and Indian, among others.[57]

The limitations of this meta-analysis and our systematic review should be considered. First, a poor level of reporting within the available studies made it difficult to evaluate study quality and to judge the risk of bias in the included RCTs and non-RCTs. Secondly, our study incorporated nine non-RCTs, which may have increased the publication bias present in this study (Fig. A and B). Finally, heterogeneity was identified in the subgroup analysis of anxiety.

Table 3
Summary of effects of cardiac rehabilitation at different time periods

Outcome or subgroup	No of studies	No of participants		Effect estimate (95% CI)	Heterogeneity			
		CR	UC		Tau^2	df	*P* value	I^2(%)
anxiety								
At 1–8 week follow-up	4	231	229	−3.07 (−5.70 to −0.44)	5.50	3	0.0006	83
At 2–12 month follow-up	4	230	233	−1.48 (−3.26 to 0.30)	1.89	3	0.03	65
Depression								
At 1–8 week follow-up	4	230	233	−1.45 (−2.22 to −0.68)	0.00	3	0.71	0
At 2–12 month follow-up	3	201	200	−1.66 (−4.03 to 0.70)	3.71	2	0.003	88

Table 4
Summary of risk of bias assessment

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Other bias
Dixhoorn et al. (1990)	Unclear	Unclear	High	Unclear	Low	Unclear
Fallavollita et al. (2016)	High	High	High	Unclear	Low	Unclear
Giallauria et al. (2006)	Unclear	High	High	Unclear	Unclear	High
Korzeniowska-Kubacka (2017)	High	High	High	Unclear	Unclear	Unclear
Ku et al. (2002)	Unclear	Unclear	High	Unclear	Low	Unclear
Linden et al. (1995)	Low	Low	Unclear	Low	Low	Unclear
Matsunaga et al. (2004)	High	High	High	Unclear	Unclear	Unclear
Mayou et al. (2002)	Low	Unclear	Unclear	Unclear	Unclear	Unclear
Johnston et al. (1999)	Low	Low	Unclear	Low	Low	Unclear
Oldridge et al. (1991)	Unclear	Unclear	Unclear	Low	Low	Unclear
Oldridge et al. (1995)	Unclear	Unclear	Unclear	Low	Low	Unclear
Pourafkari et al. (2016)	High	High	High	Unclear	Unclear	High
Sharif et al. (2012)	Low	Unclear	Unclear	Unclear	Low	Unclear
Suzuki et al. (2005)	High	High	High	Unclear	Unclear	Unclear
Schomer et al. (1983)	High	High	High	Unclear	Unclear	Unclear
Wang et al. (2012)	Low	Unclear	High	Unclear	High	Unclear
Wang et al. (2016)	Low	Low	Unclear	Unclear	Low	Unclear
Yonezawa et al. (2009)	High	High	High	Low	Low	Unclear
Yoshida et al. (1999)	High	High	High	Unclear	Low	Unclear
Yoshida et al. (2001)	High	High	High	Unclear	Unclear	Unclear

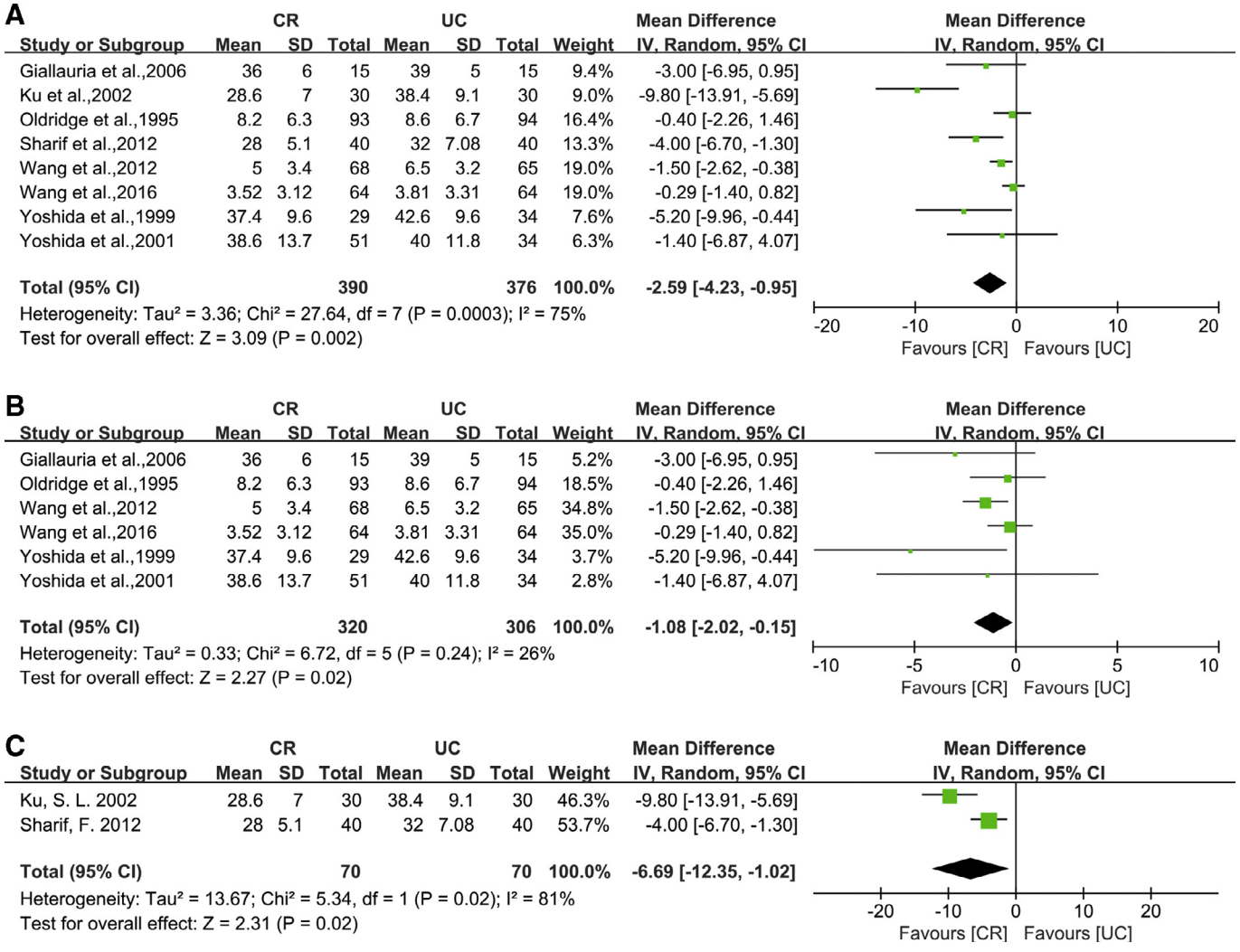

Fig. 2. (A) Forest plot of exercise-based CR effect on anxiety state; (B) Forest plot of subgroup analysis of AMI; (C) Forest plot of subgroup analysis of CABG.

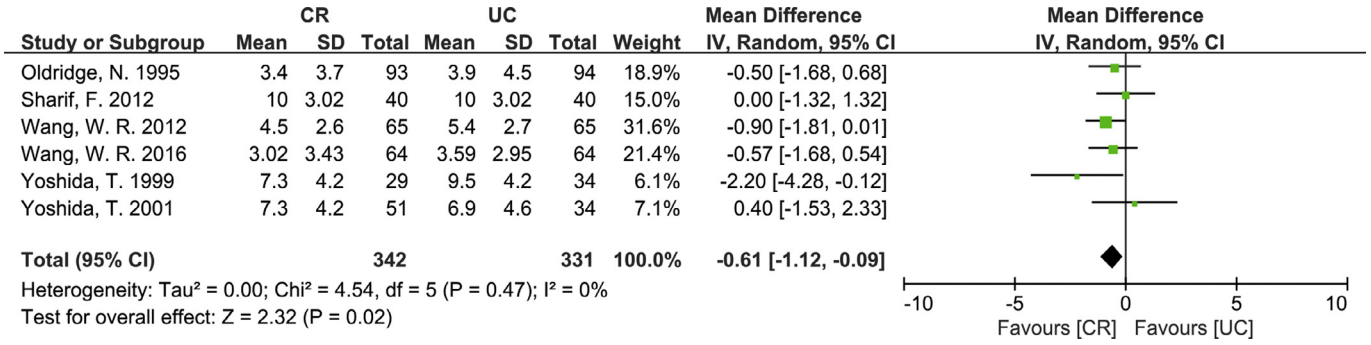

Fig. 3. Forest plot of exercise-based CR effect on depression.

Conclusion

In conclusion, exercise-based CR should be considered to be an effective treatment tool for symptoms of anxiety and depression in post-MI patients. Furthermore, early CR of these patients with anxiety or depression is essential in order to reduce negative effects on quality of life as well as morbidity and mortality. Future studies are required to explore the effect of CR in anxiety and depression at different times during overall recovery prognosis, which may be used to further guide clinical rehabilitation.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2018.09.011.

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