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Exercise-based cardiac rehabilitation effects on severity of angina, HRQoL and exercise capacity in patients with microvascular angina: systematic review and meta-analysis

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Background: Microvascular angina (MVA) is a clinical syndrome caused by coronary microvascular dysfunction in patients with angina symptoms and no flow limiting blockages in their main coronary arteries. Patients experience recurrent angina, low health related quality of life (HRQoL) and limited exercise tolerance, making them more likely to repeatedly present to healthcare services.

Aim: To establish the effects of exercise-based cardiac rehabilitation (CR) on the severity of angina, HRQoL and exercise capacity among adults with a diagnosis of MVA compared to a no-exercise group.

Methods: Searches were performed in 14 online databases. We included randomised controlled trials (RCTs) that assessed the independent effect of CR versus a no-exercise group in adults with a probable or definite diagnosis of MVA according to the COVADIS criteria. Risk of bias was assessed via the Cochrane RoB2 tool at outcome level and the quality of the evidence using the Grading of Recommendations, Assessment, Development and Evaluations framework. Meta-analysis using random effects models were used to estimate mean difference (MD) or standardised mean difference (SMD) with 95% confidence intervals (CI).

Results: Of the 15,873 reports identified, five studies (n=222) were included. Reasons for RoB judgements varied between studies and outcomes, however all were scored at either 'high risk' or 'some concerns'. Participants were mostly female (97%), average ages ranged from 51 to 64 years. The CR programmes utilised aerobic exercise and resistance training. Meta-analysis of the effect of CR on severity of angina (2 RCTs; n=85) was not possible due to the limited data presented in one of the reports. The narrative synthesis concluded that there is no evidence of an effect of CR on severity of angina symptoms. Meta-analysis of the effects of CR versus no-exercise on HRQoL were conducted at domain level of the Short Form-36 (SF-36) questionnaire (2 RCTs; n=75), and exercise capacity as measured by peak VO₂ (3 RCTs; n=101). The evidence of the effect of CR versus no-exercise intervention of the SF-36 domains from the meta-analyses was classified as 'very low certainty', meaning we have very little confidence in the effect estimates calculated. CR versus no-exercise intervention was estimated to result in a SMD of 1.06 (95% CI -0.7 to 2.19, low certainty of evidence) for measurements of peak VO₂ in favour of CR. A SMD of 1.06 is estimated to be equivalent to a 4.42 ml/kg/min change in peak VO₂, which is believed to represent a clinically meaningful difference.

Conclusions: CR may improve exercise capacity outcomes in patients with MVA compared to controls, however our confidence in the effect estimate is limited. We remain uncertain as to

the effect of CR on the severity of angina symptoms and HRQoL. High-quality, well-reported RCTs are needed to more rigorously assess the benefits and harms of exercise-based CR for adults with MVA.