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Research Column

Review of article: Jansen, S.C.P., Hoorweg, B.B.N., Hoeks, S.E., van den Houten, M.M.L., Scheltinga, M.R.M., Teijink, J.A.W, Rouwet, E.V. A systematic review and meta-analysis of the effects of supervised exercise therapy on modifiable cardiovascular risk factors in intermittent claudication. *Journal of Vascular Surgery* 2019;69(4), 1293-1308

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Lower extremity peripheral artery disease (PAD) is a prevalent and disabling atherosclerotic condition affecting an estimated 10%–15% of Americans over age 65.[1] PAD imposes a significant risk of morbidity and mortality, with a 5-year mortality rate of approximately 20%; 70% of these deaths are caused by fatal cardiovascular events.[2] Management of cardiovascular risk, the primary focus of optimal medical management, is essential in the treatment of PAD.[3] Supervised exercise therapy (SET) is the primary guideline-recommended therapy to improve walking ability and quality of life in individuals with symptomatic PAD,[3] yet little is known about the effects of SET on modifiable cardiovascular risk factors such as blood pressure, lipids, glycemic status, and body mass index in this population. The purpose of the systematic review and meta-analysis published by Jansen et al[2] was to determine the effects of SET on modifiable cardiovascular risk factors among individuals with symptomatic PAD.

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METHODS

The authors conducted searches of MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, CINAHL, EBSCOhost, and Google Scholar to identify relevant articles. Articles were eligible for inclusion if they reported the results of a randomized controlled trial (RCT), prospective cohort study, or case-control study testing the effects of SET as an intervention in individuals with symptomatic PAD. Articles were also required to include information on baseline and follow-up assessments of at least one of the following modifiable cardiovascular risk factors: resting blood pressure (systolic or diastolic), resting heart rate, weight, body mass index (BMI), lipid profile (low-density lipoprotein [LDL], high-density lipoprotein [HDL], total cholesterol, or triglycerides), glycemic status (glycated hemoglobin or blood glucose), or smoking status. SET was defined as walking exercise (either treadmill or over-ground) with at least one supervised session per week for at least 6 weeks. Articles published in a language other than English or reporting the results of interventions that were not predominately walking were excluded. Pooled mean differences between baseline and follow-up were compared using random effects models to account for between-study variance. Since length of the interventions and follow-up periods varied, studies were groups so that the effects of SET on each risk factor were examined separately for short-term (between 6 weeks and 12 weeks) and midterm (between 6 months and 12 months) follow-up periods.

RESULTS

After screening approximately 3,000 articles, a total of 28 publications based on 27 studies (15 RCTs) were eligible for inclusion. Results of 808 patients, 42%–100% male, mean age 57–74 years, who received SET were included in the review. Interventions differed in duration, ranging from 6 weeks to 12 months, and included samples ranging in size from 8 to 73 participants. SET interventions consisted of primarily treadmill-based walking exercise to onset of pain or moderate pain.

The authors found evidence of a significant reduction in resting systolic blood pressure of 4 mmHg (95% confidence interval [*CI*] −6.40 to −1.76) in short-term but not midterm follow-up (−1 mmHg, 95% *CI* −6.20 to 3.73). Subsequent meta-analysis of the 5 RCTs that compared exercise to usual care indicated a significant improvement of 8 mmHg in favor of exercise (95% *CI* −10.84 to −4.73). Similarly, a significant improvement in diastolic blood pressure was seen at short-term follow-up (2 mmHg, 95% *CI* −3.64 to −0.22) in the 8 studies that included diastolic blood pressure as an outcome, but not at midterm follow-up (2 studies, −0.6 mmHg, 95% *CI* −2.40 to 1.23).

Significant improvements were also noted in LDL at midterm follow-up (4 studies, −0.2 mmol/L, 95% *CI* −0.30 to −0.12), but not at short-term follow-up (7 studies, −0.2 mmol/L, 95% *CI* −0.41 to 0.10). Similarly, improvements were found in total cholesterol at midterm follow-up (4 studies, −0.2 mmol/L, 95% *CI* −0.38 to −0.10) but not at short-term follow-up (7 studies, −0.1 mmol/L, 95% *CI* −0.40 to 0.20). No significant improvements were noted in resting heart rate, body weight, BMI, HDL, triglycerides, glycated hemoglobin, blood glucose, or smoking at either short-term or midterm follow-up.

LIMITATIONS

Limitations identified by the authors include the substantial heterogeneity in the studies included in the review (eg, outcomes, SET characteristics, duration of follow-up) and a significant risk for publication bias as the outcomes of interest for the review were primarily secondary outcomes. Additionally, the inclusion of many nonrandomized studies and incomplete information on participant medication use made it difficult to discern how much of the observed effects were related to SET versus medical management.

CONCLUSIONS

The authors concluded that significant reductions of blood pressure and cholesterol levels were observed in patients completing SET for symptomatic PAD and that these findings support prescribing SET to not only improve walking and quality of life, but also to manage cardiovascular risk.

IMPLICATIONS FOR PRACTICE AND RESEARCH

This article provides insight into the effects of SET on modifiable cardiovascular risk factors in individuals with symptomatic PAD. Although the conclusions that can be drawn from the study are limited due to the heterogeneity of the included studies and lack of RCTs to enable meta-analyses with each outcome, the results are meaningful. The reduction noted in systolic blood pressure is clinically relevant, as a reduction of 4 mmHg has been linked to an 8% reduction in cardiovascular risk and a 5% reduction in all-cause mortality.[2,4] Therefore, the potential role of SET in the management of cardiovascular risk in patients with PAD should be examined, particularly since many of the risk factor improvements that occur in cardiac rehabilitation can be mediated through exercise.[5] Additionally, as SET is an established recommendation for treatment of symptomatic PAD, future work should focus on efforts to incorporate greater discussion of lifestyle modification and risk factor management in SET. Inclusion of educational content has been shown to promote greater increases in physical activity, healthier dietary habits, and smoking cessation in cardiac rehabilitation,[6] and development of a similar multi-dimensional programming could help support the effects of SET on walking outcomes, quality of life, and markers of cardiovascular risk.

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