Role of structured and supervised exercise programmes in peripheral artery disease patients with and without claudication — A Systematic Review and Meta-analysis

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Abstract

Objectives: This review aimed to determine the impact of exercise protocol among peripheral artery disease patients. Literature search was done from 2005 to 2018.

Methods: Databases such as Google Scholar, Medline and PubMed was reconnoitred for the purpose of research articles by using key words like exercise training, peripheral artery disease, ankle brachial index, haemodynamic and atherosclerosis. Studies fulfilling the inclusion criteria were retrieved and encompassed in the present study.

Results: The heterogeneity of the studies included in the analysis and the impact of exercise programmes on outcome measures were assessed by using hedge g statistical model.Of the54 studies found, 9(16.6%) were analysed that suggest supervised and structured exercises programmes significantly improved ($p<0.05$) outcome variables.

Conclusion: Future randomized controlled trials related to the duration of exercises regimes are required in order to tailor the training programmes according to the need of individuals.

Keywords: Exercise training, Peripheral artery disease, Ankle Brachial Index, Haemodynamic, Atherosclerosis.

Introduction

Multiple healthcare guidelines have been established during the last two decades by various international organisations like the American College of Sports Medicine (ACSM), American Heart Association (AHA), American Association of Cardiovascular and Pulmonary Rehabilitation (AACPR_ and others which have incorporated exercises programme as an integral part of interventional strategies for the management of peripheral artery disease (PAD).[1] They have recommended exercises as a first-line therapy for the management of claudication among PAD patients and even in those patients who do not exhibit claudication.[2]

Atherosclerotic plaque in the tunica intima of peripheral arteries leads to the development of PAD (Table-1).[3] It is the third leading cause of morbidity due to atherosclerosis after coronary heart disease (CHD) and stroke.[4] Prevalence of the disease increases with growing age, presently affecting 202 million people globally of whom approximately 54.8 million are southeast Asians with an increase of 28.7% within the last decade alone.[5] The risk factors of PAD are similar to that of cardiovascular diseases; since PAD is an atherosclerotic disease, analogous factors like smoking, diabetes, hypertension, dyslipidaemia, obesity and physical inactivity raise the prospects of occurrence of disease.[6]

A number of researches have provided evidence of the presence of coronary artery and cerebrovascular disease in one-third to one-half of PAD patients.[7] PAD symptomatically presents itself as an intermittent claudication that is a tight cramp like pain in the region of calf, thigh and buttock induced during exercise and usually relieves within 10 minutes of rest (Table-2).[8] Other symptoms may include atypical leg pain which is prevalent in almost 50% cases, whereas in some cases there are no symptoms and asymptomatic atherosclerotic obstruction at the level of peripheral arteries is present.[9]

Table-1: Effects of exercises in peripheral artery disease.

Pathophysiology	Fictional Impairment	Effect of Exercise
Arterial obstruction due to atherosclerosis plaque	Reduce blood flow	Angiogenesis
Endothelial Dysfunction	Decreased vasodilator function	Improved Nitric Oxide dependent vasodilatation
Mitochondrial Dysfunction	Impaired Energy Production	Improved mitochondrial energetic

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Table-2: ACSM recommended exercises protocol.[17]

Frequency	Intensity	Time	Type
3-5 days/week	40-60% of Heart rate reserve	30-50 mints	Aerobic Training
2-3 days/week	1RM	2-3 sets	Anaerobic Training

1RM : Repeated Maximum

Symptoms characterising PAD directly impact the functional capacity which leads to clinical impact, including progression of disease and increase in cardiovascular risk.[10] Significant evidences are also available which show that risk of cardiovascular disease increases four times in patients with diagnosed PAD.[11]

To rule out PAD from the differential diagnosis of conditions like spinal stenosis, Raynaud's phenomena, popliteal artery entrapment etc., the Ankle Brachial Pressure Index (ABPI) is used that indicates the presence, or otherwise, of PAD.[12]

Insufficient blood supply to the legs affects the daily activity in the same way as atherosclerotic plaque in the coronary artery causes angina.[13]

ABPI is a standard diagnostic tool for patients with PAD[14] and it provides an indication of disease severity; a value <0.9 indicates the presence of disease and a value <0.4 indicates severity which may be characterised by serious reduction in circulation, ischaemic rest pain and tissue loss due to ulceration and gangrene.[15,16] There are potential benefits of exercise on PAD (Table-3).[17]

Table-3: ACSM exercise protocol for resisted exercises.[17]

Frequency	Intensity	Time	Type
3-5 days/week	Ischaemic leg pain score of mild to moderate (8 bouts of Exercises)	50min/day	Resisted Exercises

Hence, it is important to investigate the effects of different exercise protocols on PAD patients with or without claudication and to investigate the impact of resistive type of exercises on improving the symptoms of peripheral artery disease. The current study was planned to review literature on the impact of exercise protocol in PAD patients.

Materials and Methods

The review study was conducted at Ziauddin College of Rehabilitation Sciences and comprised literature searches from 2005 to 2018 that were conducted on virtual databases, such as Google Scholar, Medline and PubMed, by using key words like exercise training, peripheral artery disease, ankle brachial index, haemodynamic and atherosclerosis. The heterogeneity of the studies included in the analysis and the impact of exercises programme on outcome measures were assessed by using hedge g statistical model.

The searches were carried out and categorised (Figure-1) based on the guidelines of Preferred Reporting Items for

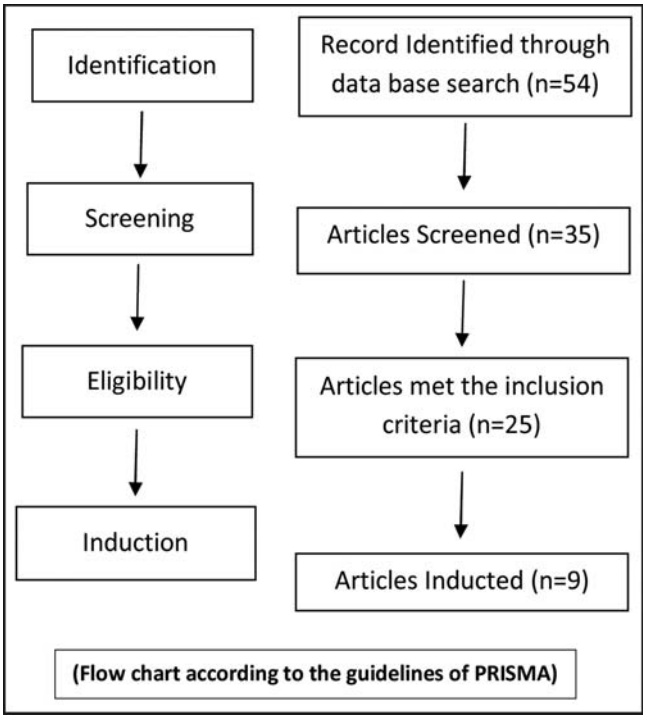

Figure-1: Flow chart.

Systemic Review and Meta Analyses[18] (PRISMA).

Randomised clinical trials (RCTs) conducted to determine the effects of structured and supervised exercises on PAD patients with or without claudication were included, while those which involved the use of surgical interventions, medication, or was conducted before 2005, were excluded.

Risk of bias of RCTs was assessed on the basis of Cochrane Collaboration tools for assessing such risks[19] (Figure-2 and 3).

Four studies define adequate sequence generation for randomization.[20,22,24,28] One study described allocation concealment by means of computer randomisation.[22] Allocation concealment was not defined in other studies.[20,21,24,25-27] Only one study achieved the criteria of blinding of participants.[22] Blinding of outcome was achieved in seven studies.[20-22,24,26-28] However blinding of outcome was not achieved in only one study be as it used

Domains	Iurciuc S et al 2016[20]	Januszek R et al 2014[21]	Mc Dermot MM et al 2009 and 2014[22,23]	Fakhry F et al 2011[24]	Treat-Jacobson et al 2009[25]	Garg PK et al 2009[26]	Crowther RG et al 2008[27]	Okamoto T et al 2006[28]
Random Sequence Generation	✓	×	✓	✓	?	×	×	✓
Allocation Concealment	×	?	✓	×	?	×	×	?
Blinding of Participants and Personnel	×	×	✓	×	×	×	×	×
Blinding of Outcome assessment	✓	✓	✓	✓	×	✓	✓	✓
Incomplete outcome data	✓	✓	?	✓	✓	✓	✓	✓
Selective reporting	✓	✓	✓	✓	✓	✓	✓	✓
Other bias	×	×	?	✓	✓	✓	?	?

Figure-2: Author judgement of risk of bias assessment.

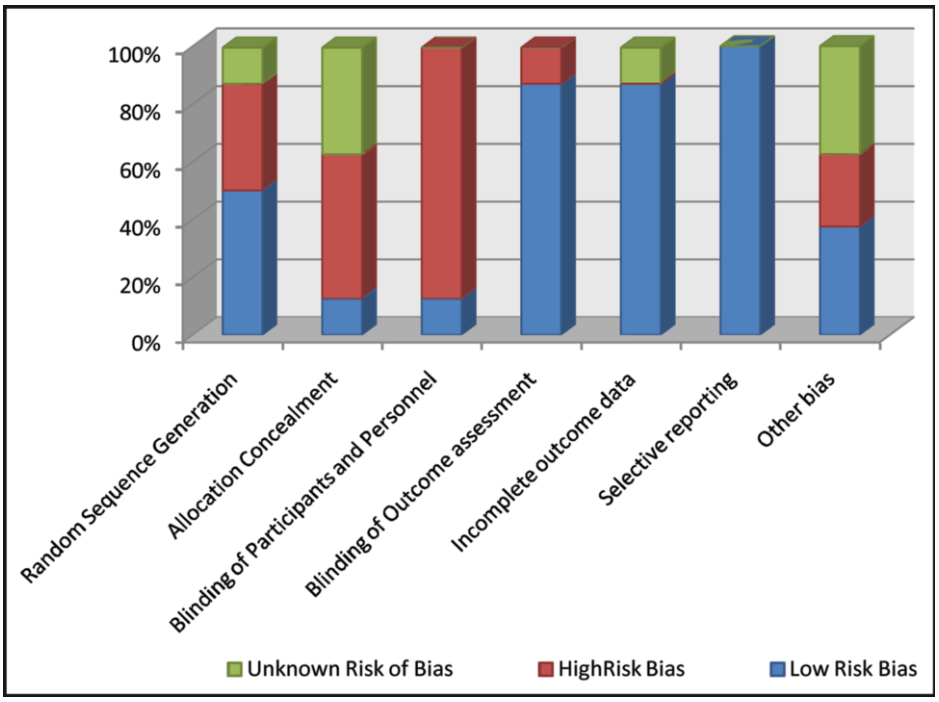

Figure-3: Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

walking distance as a primary outcome to determine the effects of training protocol on the participants, and, in such a condition, blinding of outcome is not possible.[25]

Reason for missing data was well described in all of the studies except one.[22] Besides that all studies described relevant outcome.

Other biases were assessed using a forest plot involving continuous measures variable[20,23,25,27-30] (Figure-4). The heterogeneity of the outcome measured I^2 (Table-4) and the total random and the fixed effects of exercises on the outcome variables were calculated by using hedges g statistics. Total fixed and random effects of the studies were also included (Table-5).

Table-4: Standardised mean difference showing random and fixed effect model.

Study	N1	N2	Total	SMD	SE	95% CI	t	P	Weight (%)	
									Fixed	Random
Mc Dermot MM, 2009[22]	103	53	156	-0.00510	0.168	-0.337 to 0.327			26.11	21.50
Jacobson, 2009[25]	12	8	20	1.657	0.510	0.586 to 2.727			2.85	8.07
Robert G. Crowther, 2008[27]	10	11	21	1.439	0.475	0.446 to 2.433			3.28	8.89
Andrew W. Gardner, 2014[30]	60	60	120	0.296	0.182	-0.0657 to 0.657			22.21	20.76
Mc Dermot MM, 2014[23]	81	87	168	0.362	0.155	0.0565 to 0.668			30.77	22.18
Andrew W. Gardner, 2011[29]	40	39	79	0.216	0.223	-0.229 to 0.661			14.79	18.60
Total (fixed effects)	306	258	564	0.302	0.0860	0.133 to 0.471	3.515	<0.001	100.00	100.00
Total (random effects)	306	258	564	0.443	0.173	0.103 to 0.782	2.560	0.011	100.00	100.00

SMD: Standaraised Mean Difference
SE: Standard Error
CI: Confidence interval.

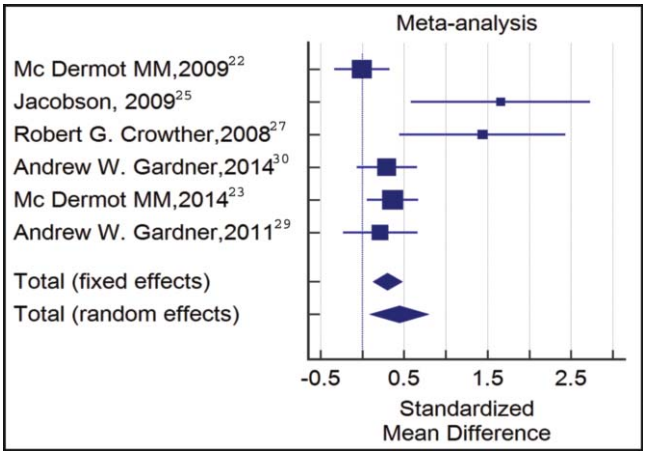

Figure-4: Forest plot depicting random and fixed effects.

Table-5: Test for heterogeneityl.[2]

Q	16.4448
DF	5
Significance level	P = 0.0057
I^2 (inconsistency)	69.60%
95% CI for I^2	28.63 to 87.05

Results

Of the 54 studies found, 9(16.6%) were analysed that supervised and structured exercise programmes ranging from 12 weeks to 12 months and significantly improved the outcomes measures ($p<0.05$).

The primary outcome measures analysed were haemodynamic variables, 6 minutes' walk test, maximal walking distance and the pain-free walking distance. It was observed that supervised and structured exercises programmes significantly improved outcome variables. It was observed that Physical Activity (PA) performed by an individual with PAD significantly reduced the chances of functional decline and showed significant improvement in the performance of their daily activity level during a four year follow-up study[26]. It was also analysed that 12 weeks of arms ergometer exercises with a duration of 3 hours per week significantly improved the pain-free walking distance and maximal walking distance. This was a novel approach of intervention where arm ergometers were used in patients with claudication and the result obtained interestingly increased the pain-free walking distance among the patients[25]. In another study it was observed that 12 months of supervised exercise training programme improved the conditions associated with PAD whereas 12 weeks of exercise programme significantly improved maximal walking time ($p<0.0001$) from the baseline among PAD patients who were given intervention via treadmill. However the impact of home-based exercise programme as observed in a study revealed that home-based exercise programme, improved the quality of life and functional capacity among the patients with PAD, and concluded that home-based exercise training programmes are feasible in the setups where supervised training programmes are not available[24].

Discussion

A review of different RCTs was performed to identify the impact of exercise regimes on the different outcome measures associated with PAD. It was observed that supervised exercise sessions of minimum 12 weeks,[25] and a maximum of 12 month, suggests significant improvement in the outcome measures.[27] An interesting findings of supervised exercise sessions revealed that 12 weeks of arm ergometer exercises was effective in improving the outcome measures in terms of pain-free walking distance and maximal walking distance and established that these exercises regimes were comparatively as effective as treadmill and other lower extremity exercise regimes and called this exercise regime a novel approach since involving a significant pain-free upper limb to induce a potential benefit in the affected lower limb was indeed a novel finding.[25] In another study it was observed that lifetime activities reduced chances of disability and functional loss among PAD patients.[26] It was also highlighted from the analysis of multiple studies that 12 weeks of supervised training session based on treadmill exercises sessions significantly impacted the outcome variables[21] among patients with stable intermittent claudication. Moreover it was also observed from the study that structured home-based exercise programmes showed a significant result on the outcome measures of patients with claudication. Among the 142 participants who were included in the analysis and completed 12 months of follow-up it was found that the quality of living and functional capacity were significantly improved from the baseline that produced a strong evidence in favour of structured home-based exercise regimes which were not only cost-effective but were as effective as supervised training sessions comparatively.[24]

Conclusion

Multiple RCTs suggested that supervised exercise regimes were beneficial in improving haemodynamic variables along with quality of life, and symptoms related to claudication. However, more RCTs are required to identify the dosage of different exercise regimes in terms of maximal benefit so that the training sessions could be tailored according to the need of the patients.

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