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BENEFITS OF PHYSICAL ACTIVITY ON DIABETIC AND NON-DIABETIC PATIENTS IN FONTAINE'S STAGE IIA OF PERIPHERAL ARTERY DISEASE IN BOSNIA AND HERZEGOVINA

SID SOLAKOVIĆ[1], MENSUR VRCIĆ[2], RATKO PAVLOVIĆ[3]
[1]*Clinic for Vascular Surgery, Clinical Center of University of Sarajevo, BOSNIA AND HERZEGOVINA.*
[2]*Faculty of Sport and Physical Education, University of Sarajevo, BOSNIA AND HERZEGOVINA*
[3]*Faculty Physical Education and Sport, University of East Sarajevo, BOSNIA AND HERZEGOVINA.*
Email: *sid.solakovic@gmail.com*

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ABSTRACT

The aim of this study was to estimate the increasing level of claudication distance through exercise effect in diabetic and non-diabetic patients in Fontaine's stage IIa of peripheral artery disease. This study was conducted from beginning of May 2014 till end of May, 2015 at the Clinic for Vascular Surgery, Centre of Sarajevo University, included 60 patients, male and female with diabetes mellitus and without diabetes mellitus who suffer from mild claudication symptoms with verified micro & macro angiopathie in Fontaine's stage IIa of peripheral artery disease. In all studied patients we investigated the claudication distance, benefits of or irregular physical activity in diabetic and nondiabetic patients with influence on claudication distance after one-year study. The frequency of every second day physical activity levels were higher measured 36.7% (11 patients) compared with diabetic patients 16.7% (5 patients) and was significantly proved ($p>0.05$). $\chi 2=18.489$; $p=0.002$. The most frequent claudication distance in was recorded in 8 non-diabetic patients 28.6 % at 800-900m versus over 1400 in diabetic patients. In this study we have concluded that physical activity significantly has a positive influence by improving significant the claudication distance over 2000m in Fontaine's stage IIa of peripheral artery disease after one-year study in 22 non-diabetic patients or 74.1% versus 16 diabetic patients or 55.2% ($p<0.05$).

Keywords: *Physical activity, claudication, collateral circulations, Fontaine's stage IIa of peripheral artery disease, diabetes mellitus.*

Correspondence: Ratko Pavlović (Ph.D.), Associate Professor, Faculty of Physical Education and Sport, University of East Sarajevo, BOSNIA AND HERZEGOVINA, Tel: 0038765934131, Email: pavlovicratko@yahoo.com

1. INTRODUCTION

The most important role of regular physical activity benefits is slowing down the progression of claudication distance in diabetic and non-diabetic patients with mild and moderate claudication symptoms (Colleran, Li, Yang, Laughlin, & Terjung, 2010). The regular physical activity, regarding low fat and low carb diet, and regular anticoagulant medical treatment has positive influence on peripheral artery disease involvement. Controlling the effects of diabetes mellitus on arteries, the early exercising program with life style modification, can slow down the accelerations rate of peripheral artery disease progression in diabetic and non-diabetic patients. Manifestation of a symptoms in the form of peripheral artery disease, cramping, burning, limping and feeling tired legs even when walking a short distance is well known as intermittent claudication symptomatology. The Intermittent claudication is common symptom of circulatory problem in which narrowed arteries reduce blood flow (Gardner, & Poehlman, 1995; de Liefde, van Domburg, Bax, Klein, Verhagen, & Poldermans, 2010). Claudication symptoms combine with diabetic disease affects rapid progression of micro and macro circulation causing tissue damage referring to leg discomfort causing the limbs pain. The leg pain provoked by insufficient blood flow in the legs, especially during walking caused by arteries stenosis is a component of systemic atherosclerosis also confers a markedly heightened risk of cardiovascular morbidity and mortality in one of 20 people over age 50. This gravely condition may reduce blood flow throughout the legs. The risk factors that increase atherosclerosis progression with developing the risk of peripheral artery disease include: smoking, diabetes mellitus, high blood pressure (140/90 millimeters of mercury or higher), obesity (a body mass index over 30), high cholesterol (total blood cholesterol level over 240 milligrams per deciliter, or 6.2 m mol per liter), stroke (male under 55 years female under 45 years) or heart disease and positive family history of peripheral artery disease (Hankey, Norman, & Eikelboom, 2006; Lewington, Clarke, Qizilbash, Peto, & Collins, 2002). Vasan, Beiser, Seshadri, Larson, Kannel, D'Agostino, & Levy, (2002) confirms in study that exercise therapy combined with constant low carb diet, antiplatelet medications, and regular medical treatment has the potential to benefit patients with claudication symptoms by preserving or improving functional capacity and reducing cardiovascular events (Vasan, Larson, Leip, Evans, O'Donnell, Kannel, & Levy, 2001; Stewart, Hiatt, Regensteiner, & Hirsch, 2002). People who have mild claudication symptoms in Stage IIa usually have physical activity recommendations (walking or very middle intensity fast walking are the most effective exercises for long distance claudication symptoms). Semenza, (2007) in his study also confirms that exercise training can increase and improve a walking distance ability in patients with claudication symptoms by flow-inducing

vasodilatation of peripheral collateral arteries (Selvin, & Erlinger, 2004). The muscles need more oxygen during long distance walking. Regular exercise promotes development of collateral circulation with hemodynamic influence on pain intensity reduction and increasing of the claudication distance. If there are not supplied by enough blood, leg unpleasantness may appear such is pain and disappear a short time after rest. The Conductance of this circuit increases following occlusion of a primary hind limb artery. Interval training is the ultimate cardiovascular workout. Interval training makes it possible to improve systemic circulation status. Interval exercise training also improve blood flow through this collateral circuitry in animal models of occlusive artery disease (Tsai, Chan, Wang, Jeng, Hsieh, Kao, Chen, & Liu, 2002; McDermott, Greenland, Liu, Guralnik, Celic, Criqui, ……. & Clark, 2002). The stage benefit of alternative revascularization depends on improvements of collateral-blood flow to hind limb muscles that occur with exercise training accompanied with remodeling and enlargement of collateral vessels. The analysis has shown that the greatest improvements in walking occur when exercise sessions are of at least 30 min in length and when these sessions were done at least minimum of two times a week in patients with moderate and mild claudication symptoms Therapeutic strategies includes exercise training (Yang, Prior, Lloyd, Taylor, Li, Laughlin, & Terjung, 2008), attempting to increase pain-free walking distance returning symptomatic peripheral artery disease in asymptomatic stage without or mild claudication symptoms by increasing quality of life in these patients (McDermott, Ades, Dyer, Guralnik, Kibbe, Criqui, 2008). Physical activity in form of interval training is relatively inexpensive method witch has positive effects on hemodynamic development of collateral circulations. Physical activity process combined with life style modification can improve the quality of life diabetic and much more in non-diabetic patients with mild claudication symptoms by increasing the claudication distance and returning symptomatic stage of peripheral artery disease in asymptomatic stage of peripheral artery disease with reducing the cardiovascular events (Yang, Deschenes, Ogilvie, & Terjung, 1996; Eriksson, 1999; McDermott, *et al*., 2008). The aim of this study is to estimate the increasing level of claudication distance through exercise effect and antiplatelet therapy and life style modification in diabetic and non-diabetic patients in Fontaine's stage IIa of peripheral artery disease.

2. METHODS AND MATERIALS

2.1 Participants

This study was conducted at the Clinic for vascular surgery, Centre of Sarajevo University, included 60 patients, male and female with diabetes mellitus and

without diabetes mellitus who met the criteria for inclusion in the study. Patients were divided into two groups; the first group consisted of 30 diabetic patients insulin resist over 5 years with verified micro & macro angiopathie and (without diabetic neuropathy) and presentation of lower limb and foot sensibility in IIa stage of peripheral artery disease with mild claudication symptoms. Impellers group consists of 30 nondiabetic patients with verified micro & macro angiopathie (without diabetic neuropathy) and presentation of lower limb and foot sensibility in IIa stage of peripheral artery disease with mild claudication symptoms. The study was approved by an institutional review board and all patients gave their written informed consent.

2.2 Procedure

The research was conducted as a case control study (retrospective study) from beginning of May 2014 till end of May, 2015, which included the period of validity of one year in which the group of diabetic patients with low and mild claudication symptoms, and a control group of non-diabetic patients with low and mild claudication symptoms should increase claudication distance during one-year period caused by aerobic exercise interval training. Interval training program was compose of: walking of 30-60 minutes with repetitions of 200-400m middle intensity fast walking with a recovery period following each repetition, also with self-control heart frequency 120-155 beats/min at max. intensity of 60 to 70% of heart rate for at least one year. The all patients were observed and clinically examined by vascular surgeon and by a medical team every three month, also to every patient was given detailed instructions about life style and foot modification, and also strict instructions how exercise by their own. During period of one-year research in nondiabetic and diabetic patient was not confirmed progress of underlying disease, diabetic neuropathy also the presence of absence of lower limb and foot sensibility during all period of study was not clinically confirmed. All patient who started this study with indicated exercise training, life style and food modification have successfully accomplished it. The antiplatelet therapy in patients (diabetic and nondiabetic) was also changed (150mg acetylsalicylic acid (ASA) per day/75mg every 12 hours over one year compare 100mg of acetylsalicylic acid (ASA) before of study every day. Before research beginning, all the patients were physical examined by a medical team, led by vascular surgeon and his medical team as well as at the end of the research.

3. RESULTS

Table 1: Gender representation and patients number with or without diabetes mellitus who finished study in of May 2014

		Group		Total
		Non diabetic patietns	Diabetic patients	
Male	N	8	10	18
	%	26.7	33.3	30.0
Female	N	22	20	42
	%	73.3	66.7	70.0
Total	N	30	30	60
	%	50.0	50.0	100.0

Table 2: Gender and representation and patients number with or without diabetes mellitus who finished study in May 2015

		Group		Total
		Non diabetic patietns	Diabetic patients	
Male	N	8	10	18
	%	26.7	33.3	30.0
Female	N	22	20	42
	%	73.3	66.7	70.0
Total	N	30	30	60
	%	50.0	50.0	100.0

Table 3: Claudication distance with verified micro and macroangiopathie (Fontain IIa) (without diabetic neuropathy) and confirmed presentation of lower limb and foot sensibility on beginning of May 2014

Claudication distance		Group		Total
		Non diabetic patients	Diabetic patients	
Over 1400m	N	1	9	10
	%	3.6	33.3	15.2
1200-1400m	N	3	5	8
	%	7.1	16.7	10.9
1000-1200m	N	3	7	10
	%	10.7	27.8	17.4
900-1000m	N	8	1	9
	%	25.0	5.6	17.4
800-900m	N	8	3	11
	%	28.6	11.1	21.7
600-800m	N	8	4	12
	%	25.0	5.6	17.4
Total	N	30	30	60
	%	50.0	50.0	100.0

Table 4: Walking 30-60min combine with 200-400m middle intensity fast walking per day with life style modification on regular (antiplatelet) medicament treatment

Lasting of Exercise		Group		Total
		Non diabetic patients	Diabetic patients	
Every week (one time the week)	N	0	**3**	**3**
	%	0.0	10.0	5.0
Every second day than every third day	N	**3**	**10**	**13**
	%	10.0	33.3	21.7
Every third day	N	**4**	**7**	**11**
	%	6.7	23.3	15.0
Every day than every second day	N	**8**	**5**	**13**
	%	26.7	16.7	21.7
Every second day	N	**11**	**5**	**16**
	%	36.7	16.7	26.7
Every day	N	**4**	0	**4**
	%	20.0	0.0	10.0
Total	N	30	30	60
	%	50.0	50.0	100.0

Table 5: Improving the caludication distance over 2000m one May 2015 (after year of study)

		Group		Total
		Non diabetic patients	Diabetic patients	
No	N	8	14	22
	%	25.9	44.8	35.7
Yes	N	22	16	38
	%	74.1	55.2	64.3
Total	N	30	30	60
	%	50.0	50.0	100.0

In this short case study analysis including both groups (diabetic and non-diabetic patients) we used *p* value less than 0.05. Differences between the genders were more common in male population groups among respondents in non-diabetic population group (73.3%) than in patients with diabetes mellitus (66.7%) but no statistically significant differences between groups ($p<0.05$). $\chi 2=0.32$; $p=0.39$. Among nondiabetic patients the frequency of every second day physical activity levels was higher measured 36.7% (11 patients) compared with diabetic patients 16.7% (5 patients) and were significantly proved ($p>0.05$). $\chi 2=18.49$; $p=0.00$. 4 nondiabetic patient (20%) were practice every day active frequent walking program compare to no one from diabetic group with no statistically significant

differences in the groups ($p>0.05$). The claudication distance over 2000m in Fontaine's stage IIa of peripheral artery disease is improved after one-year study in 22 nondiabetic patients or 74.1% compared with 16 diabetic patients or 55.2% ($p<0.05$). In this study we have concluded that physical activity significantly affects improving the caludication distance in nondiabetic patients over 2000m after one-year study.

4. DISCUSSION

The purpose of this research was to monitor influence of complex training programme applied in diabetic and non-diabetic patients with claudication distance from 600 m to 1400 m with verified micro and macroangiopathie with II phase according to Fontain. Patients had a free choice of training program, continuous or individual applicable to the certain patient, with obligatory change of life-style and diet/minimal once a week, max daily, as noted: walking 30-60 min, combined with 200-400 m middle intensity fast walking per day with life style modification on regular medicament treatment; antiplatelet therapy 150 mg aspirin per day/75mg every 12 hours. Patients also were instructed to wear pulsometer during workout and heart frequency not to be under 120 or over 155 heartbeats when fast-walking 200-400 m and not under 120 during any workout program. All the patients stick to workout instructions, prescribed medicaments and diet and did not smoke. During the research, we found some fascinating facts and recorded certain unbelievable levels concerning diabetic and non-diabetic patients with claudication distance from 600 m to 1400 m. We also changed standard daily aspirin dose of 100 mg to 75 mg each 12 hours/total 150 mg in 24 hours, with improved results, compared with 100 mg a day without workout. U.S. Preventive Services Task Force reports on aspirin (ASA) in primary prevention, distinguishing average daily dose in <100 mg, 100mg, and >100mg. That an average daily dose of 100mg had the highest probability of reducing death, cancer death, and cancer incidence, whereas higher doses seemed superior for reducing cardiovascular events. Heartbeat frequency in diabetic and non-diabetic patients was 120-155. In the case of over frequency or other problems, high blood pressure, lack of motivation, etc. we suggested our patients to engage his/her vascular doctor to check on him; so from professional ethic point of view patient would not have any negative consequences or influences on his health condition. Taylor, Weston, and Batterham, (2015) in their work confirmed that the median proportion of exercise intervals meeting their high-intensity criterion of 90% of individual maximal heart rate was 58% (42% to 68%). We succeeded to reach satisfactory results of claudication distance over 2000 m in our study, with max. intensity of 60-70%. Galea, Bray, and Ginis, (2008) in their study put out that exercise programmes are not delivered as planned, with reasons why they might

not be, including patient-related factors such as lack of motivation, claudication pain or other co-morbidities limiting the amount of exercise that can be performed. We can significantly confirm that diabetes is one of most important risk factors with strong influence on non-increasing claudication distance over 2000 m, especially in insulin resistant patients with insulin treatment lasting over 5 years. The incidence diabetes in patients increases with increasing age, partly because of the decline in muscle mass associated with aging. This corresponds with a decline in metabolic function, supporting the usefulness of resistance training (Eriksson, 1999). Based on the published studies reviewed an optimal exercise program for individuals with type 2 diabetes mellitus, involving aerobic endurance exercise for improving cardiorespiratory fitness, muscular strength and health in general (Gorely, Crank, Humphreys, Nawaz, & Tew, 2015). Walton, Finlin, Mula, Long, Zhu, Fry, ……, and Peterson, (2015) discovered that exercise training protocol, consisted of stationary cycle ergometer, gave normal angiogenic response to aerobic exercise training in skeletal muscle, but not in adipose tissue because reduced vessel density (Gorely, *et al.*, 2015). But lack of studies left a question opened which workout type for diabetic patients is better: stationary cycle or walking treadmill in therapy management of peripheral artery disease in Fontaine's Stage IIa. Lane, Ellis, Watson, & Leng, (2014) in their study "Exercise for intermittent claudication" points out that exercise significantly improved maximal walking time were compared with usual care or placebo with an overall improvement in walking ability of approximately 50% to 200%. Walking distances were also significantly improved: pain-free walking distance 82.29 metres and maximum walking distance to 179.78 metres. After two years of preforming a study increasing walking treadmill distances and walking times were at least twice a week (Lane, *et al.*, 2014). We were not able to prove benefits of the therapy in diabetic and non-diabetic patients with micro and macro angiopathie, without signs of trofic ulcerations before, during and after executing research for claudication distance from 600 m to 1400 m, in spite the fact that all the patients were applying workout program twice or thrice a week. This situation could be caused by a few different reasons: vascular complications on arteries because of the initial disease, diabetes mellitus, life-style, diet including too much saturated animal fat, smoking habits, usual in BiH. It is necessary to complete additional research regarding therapy possibilities of asymptomathical and symptomatical IIa stage according to Fontain, in order to improve therapy benefit effects, because phase of the disease is not in attractive domain for vascular reconstruction or hospital conservative angiologic therapy, also in order to decrease progression of aterosclerotic disease resulting in better life quality of a patient and avoid future surgical intervention. Surprising fact is that, in spite of lower number of repeating, 16 diabetic patients had benefits of this program. No one in both groups of patients (diabetic and non-diabetic) patients had any clinical

sign of deterioration of claudication distance during research period, meaning that negative influence was not statistically proved. Non-diabetic patients had significant improvement of claudication distance over 2000 m during one year, with workout intensity thrice in a week, more frequent than diabetic group. We could reach very satisfactory results in patients with claudication distance IIa according to Fontain, using adequate workout program every second day, supported by anticoagulation therapy (150 mg daily) change of diet and life-style. Regular short distance very low intensity running combined with walking substantially improves walking performances with influence on claudications distance in nondiabetic patients. Therapeutic exercise recommendations for claudication generally consist of 30-60 minutes or more, (Vasan, *et al.*, 2002; Semenza, 2007) or more times per week, for at least one year, ideally under medical supervision. The aim is to increase the amount of time that you can walk without reproducing mild pain in your legs. However, the important connection is risk factor such as diabetes mellitus with its consequences who significantly limit access to exercise rehabilitation programs for most patients suffering of peripheral artery disease (Fontaine's stage IIa). Diabetes mellitus should not be neglected as risk factor; from this analysis we can conclude that regular cycle of exercise make progress and ability to walk for longer distance without unpleasantness or pain disappearing. This study suggests that therapeutic strategies should include regular exercise frequent training, attempting to increase pain-free walking distance and returning. During our research on diabetic patients, we discovered that these patients should be drawn to more attention with consideration on etiology of the underlying disease. Nevertheless, the reductions of Physical Activity frequency in diabetic patients, according to this study, caused continuing of claudication symptoms; while non-diabetic patients derive additional favorable effects of this program in increasing the claudication distance from physical activity, developing new collateral vessels which directly improve pain tolerance and claudication distance.

5. CONCLUSIONS

The findings of this study will help us to slow the progression through therapeutic and interval training strategies of peripheral artery disease in Fontaine's Stage IIa, trying not to ignore devastating potential of underlying disease. Interval training should be incorporated into current guidelines for the management of peripheral artery disease in Fontaine's Stage IIa. It is clear that further investigations are necessary, in order to improve exercise program for diabetic patients, stationary cycle or walking (treadmill walking) because of significantly limited exercise program effects. Implementation of secondary prevention in peripheral artery disease is vital to mitigate high cardiovascular risk for diabetic and non-diabetic

population, in order to avoid certain invasive surgical interventions like revascularization and amputation treatment.

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