The Influence of Individual Factors on Adherence to Treatment in Patients With Peripheral Arterial Disease

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SUMMARY

The aim of this study was to examine the influence of individual factors on adherence to treatment in patients with peripheral arterial disease (PAD). The study included 82 patients diagnosed with PAD (Fontaine IIa, IIb) and treated at the Clinic for Vascular Surgery of the University Clinical Center Niš, during the period from January 1, 2020 to December 31, 2020.

We found a significant correlation between the degree of adherence to treatment and health-related quality of life in patients with PAD. Patients with a medium and high degree of adherence had a significantly higher quality of life compared to the respondents with a low degree of adherence.

The chi-square test of independence showed a significant correlation between obesity ($P = 0.007$) and the number of medications in therapy ($P < 0.001$) with adherence to therapy in patients with PAD.

Adherence was statistically significantly influenced by obesity and the number of medications in therapy, while sex, age, smoking, diabetes, dyslipidemia, the number of risk factors, and type of therapeutic modality did not show this association.

KEYWORDS

Individual factors; *Adherence*; *Peripheral arterial disease*

Introduction

Previous research indicates that patients with peripheral arterial disease (PAD) had a reduced quality of life before the initiation of pharmacotherapy. A study that used the SF-36 Health Survey to measure the subjects' quality of life (QOL) demonstrated that QOL improved after the initiation of pharmacotherapy. It also showed a significant correlation between the degree of adherence to treatment and health-related QOL in patients with PAD; patients with a medium and high degree of adherence to treatment had significantly higher scores in all investigated domains of health-related QOL compared to the group of respondents with a low degree of adherence to treatment[1]. It is of note that applied therapeutic modalities are significantly influenced by risk factors such as the female sex, dyslipidemia, hypertension, and smoking, while age, obesity, and the male sex are risk factors where such a correlation is not present[2,3].

Therefore, the aim of this study was to examine the influence of individual factors on adherence to treatment in patients with PAD.

Patients and research methods

The examined group of patients

This prospective clinical trial included patients with PAD treated on an outpatient basis at the Clinic for Vascular Surgery of Clinical Center Niš, during the period from January 1, 2020 to December 31, 2020. The research included respondents diagnosed with PAD for the first time. The diagnosis was determined on the basis of anamnesis, a clinical examination, Doppler echosonography, and/or MSCT angiography of the main arteries of the lower extremities. The inclusion criteria were patients with stage IIa and IIb PAD of the lower extremities verified by Doppler sonography or MSCT angiography[4]. The classification of the respondents' disease stage was determined according to Fontaine: stage I (asymptomatic); stage IIa (moderate claudication distance (CD) > 200 m); stage IIb (moderate to severe CD < 200 m); stage III (ischemic pain at rest, CD up to 50 m), and stage IV (presence of ulceration and gangrene). The patients with Fontaine stage IIa and IIb were included in the study.

The exclusion criteria were patients with PAD stage I, III, and IV according to Fontaine, amputation of the lower extremities, ejection fraction ≤ 40%, chronic peritoneal dialysis and hemodialysis, malignancies, and associated diseases that lead to an impaired general and physical condition.

Methodology

The research protocol was approved by the Ethics Committee of the Faculty of Medicine in Niš (12-15637-2/5 dated 12/24/2019). The research was fully adapted to the Declaration of Helsinki on ethical behavior and conducted according to the principles of Good Clinical Practice (GCP). All patients were informed about the purpose of the study and voluntarily signed the consent form. The research was designed as a prospective cross-sectional study comprising a survey. The survey included questions with closed answers and different variants from dichotomous to combined ones, as well as with additional open-ended questions.

In order to adequately analyze the data, the subjects were divided into groups according to: sex, age (< 65 years and ≥ 65 years), applied pharmacotherapy (pentoxifylline 1200 mg/day + acetyl-salicylic acid (ASA) 100 mg/day or cilostazol 200 mg/day + ASA 100 mg/day); the presence of

risk factors (smoking, obesity, diabetes, dyslipidemia, and hypertension), the number of risk factors (≤ 3 and > 3), and the number of drugs used (≤ 4 and ≥ 5).

Body mass index (BMI) was determined based on the following formula: BMI = body weight (BW) ÷ body height (BH)^2. The patients were considered obese if their BMI was over 30 kg/m^2.

The presence of diabetes, dyslipidemia, and hypertension were established by adequate specialists and subspecialists.

Adherence assessment

Adherence to treatment was estimated using a validated scale for assessing adherence in patients with chronic diseases (The Adherence in Chronic Diseases Scale – ACDS). The ACDS is a survey designed to assess adherence to treatment in adults suffering from chronic diseases. It consists of 7 questions with predefined answers. The survey was designed to enable the assessment of adherence to treatment and the factors influencing it. The ACDS survey includes seven questions with five possible answers.

The first four questions refer to the regularity of taking medication in the prescribed doses, the fifth question to the acceptance of the prescribed therapy, and the last two questions to the cooperation between the doctor and the patient. The answers were scored according to the following principle: a = 4; b = 3; c = 2; d = 1; e = 0. We used the results of the ACDS survey to assess the patients' level of adherence to the treatment they were prescribed. The maximum number of obtainable points for all questions was eight. The degree of adherence resulting from the sum of the responses was assessed according to the predetermined scoring criteria: < 20 points marked a low level of adherence, 21–26 points a medium level of adherence, and 27 points a high level of adherence[5].

Statistical data processing

The statistical analysis was performed using the SPSS 16.0 software package for Windows. Descriptive and analytical statistics were used to analyze the data. The variables were described as proportions (percentages). The chi-square test was used to compare the categorical variable between the defined groups of patients in relation to their level of adherence to treatment with respect to the defined variables. The difference was marked as significant if $P < 0.05$.

Results

The study included 82 PAD patients treated at the Clinic for Vascular Surgery of University Clinical Center Niš, from January 1, 2020 to December 31, 2020. Table 1 presents the basic patient demographics, risk factors, and therapeutic modalities.

A total of 49 men (59.76%) and 33 women (40.24%) were included in the research. The average age of the respondents was 67.62 years (SD = 8.22). Smoking was the most prevalent risk factor (76.82%), while dyslipidemia was the least prevalent (63.71%). A total of 48.78% of the subjects were treated with pentoxifylline + ASA, and 51.22% were treated with cilostazol + ASA.

The influence of the respondents' individual factors on adherence to treatment is shown in Table 2.

An analysis of the obtained results revealed no statistical significance between sexes and the degree of adherence. In the group of male respondents, 24.49% had a low level of adherence; 44.90% a medium level of adherence, while a third of the respondents was highly adherent. Of the 33 women who participated in the research, 33.33% had a low level of adherence, 54.55% a medium level of adherence, and 12.12% a high level of adherence.

Table 1. Characteristics of the respondents

		N	%
Sex	Male	49	59.76
	Female	33	40.24
Age	< 65	29	35.37
	≥ 65	53	64.63
Factor	Obesity	59	71.95
	Smoking	63	76.82
	Diabetes	57	69.51
	Dyslipidemia	52	63.71
	Hypertension	62	75.60
Therapy	Pentoxifilline + ASA	40	48.78
	Cilostazol + ASA	42	51.22

The results show that low levels of adherence were more pronounced in respondents over the age of 65 (30.19% vs 24.14%), while high levels of adherence were recorded in respondents under the age of 65 (30.61% vs 12.12%). The influence of age on the subjects' adherence was not statistically significant.

The assessment of the influence of obesity on therapy adherence showed that obese patients achieved a low level of adherence, while patients with a BMI < 30 kg/m^2 showed a high level of adherence. The chi-square test of independence showed a significant correlation between obesity and adherence ($P = 0.007$), noting that patients with a lower BMI showed a higher level of adherence. Also, there was a significant correlation between the number of medications taken as part of the prescribed therapy and adherence. The respondents who took 4 or fewer types of medication showed a significantly higher level of adherence compared to those who took 5 or more types of medication ($P < 0.001$).

The analysis of the influence of smoking habits, dyslipidemia, diabetes, hypertension, and therapeutic modalities on the degree of adherence to treatment did not show a statistical significance. However, the number of medications in the respondents' therapy had a statistically significant effect on the respondents' degree of adherence.

Discussion

PAD is a chronic disease that requires many years of pharmacotherapy. In this study, the largest number of respondents showed a medium level of adherence to therapy (48.78%), while a high level of adherence to therapy was recorded in 23.17% of the respondents, and a low level of adherence in almost one third of the respondents (28.05%). In their research, McConnen et al.[6] discovered that more than 60% of patients with chronic diseases

Table 2. The influence of the respondents' individual factors on adherence

Factor		Low level		Medium level		High level		Total	
		N	%	N	%	N	%	N	%
Sex	Male	12	24.49	22	44.90	15	30.61	49	100
	Female	11	33.33	18	54.55	4	12.12	33	100
Age	< 65 years	7	24.14	13	44.83	9	31.03	29	100
	≥ 65 years	16	30.19	27	50.94	10	18.87	53	100
Obesity	BMI < 30kg/m^2 †	**2**	**8.70**	**11**	**47.82**	**10**	**43.48**	**23**	100
	BMI ≥ 30kg/m^2	**21**	**35.59**	**29**	**49.16**	**9**	**15.25**	**59**	100
Smoking	No	4	21.05	9	47.37	6	31.58	19	100
	Yes	19	30.16	31	49.21	13	20.63	63	100
Diabetes	No	7	28.00	10	40.00	8	32.00	25	100
	Yes	16	28.07	30	52.63	11	19.30	57	100
Dyslipidemia	No	6	20.00	14	46.67	10	33.33	30	100
	Yes	17	32.69	26	50.00	9	17.31	52	100
Hypertension	No	6	30.00	8	40.00	6	30.00	20	100
	Yes	17	27.42	32	51.61	13	20.97	62	100
Number of risk factors	≤ 3	8	24.24	15	45.45	10	30.30	33	100
	> 3	15	30.61	25	51.02	9	18.37	49	100
Therapy	Pentoxifilline + ASA	15	37.50	16	40.00	9	22.50	40	100
	Cilostazol + ASA	8	19.05	24	57.14	10	23.81	42	100
Number of drugs	≤4	**5**	**16.67**	**11**	**36.67**	**14**	**46.67**	**30**	100
	≥5	**18**	**34.62**	**29**	**55.77**	**5**	**9.62**	**52**	100

†$P < 0.01$; ‡$P < 0.001$

were non-adherent, indicating the need for additional monitoring of this phenomenon. A study conducted by Hiatt et al. indicated a generally low degree of adherence in patients who used cilostazol in therapy. Namely, their results indicate that more than 60% of the respondents stopped using the prescribed medicine 36 months after therapy initiation, which can be significantly associated with difficulties in achieving long-term therapeutic goals[7].

The results of our research indicated that sex was not significantly associated with the degree of adherence. By analyzing the medium and high level of adherence together in relation to the low level of adherence, it was observed that the male sex is more adherent compared to the female sex (75.51% vs 66.67%). Similar results were obtained in a study conducted by Manteuffel et al., in which the influence of sex on the degree of adherence

during the use of medications in the therapy of cardiovascular diseases was examined[8]. The results of a study by Chen et al. showed a higher degree of adherence among male respondents[9].

A large number of factors can influence the achievement of a high level of adherence, including patient-related factors (sex, age, ethnicity), socio-economic characteristics (material status, education), therapy (the number of medications in therapy, therapy side effects and duration), health condition (the patient's subjective experience of the disease, comorbidities, acute/chronic condition), and the healthcare system (the availability of medications, doctor-patient relationship)[10].

Elderly adults are considered the most frequent medication consumers, mainly due to an increased amount of age-related chronic conditions[11]. In this regard, older age is quite frequently associated with a lower degree of adherence. The results of several studies indicate that the level of adherence among individuals with chronic diseases decreases after the age of 70, which is mainly explained by the deterioration of cognitive and physical functions with age[12,13]. In our study, low adherence was more pronounced in respondents over the age of 65 (30.19% vs 24.14%), while high adherence was recorded in respondents under the age of 65 (30.61% vs 12.12%), which is in accordance with previously conducted studies.

Non-adherence is immensely pronounced in patients suffering from several diseases at the same time, as a result of polypharmacy (consumption of more than 5 medications) and comorbidities[14,15]. In our study, 59.76% of the respondents had more than 3 risk factors in addition to PAB, including smoking, obesity, dyslipidemia, diabetes, and/or hypertension. Our examination of the influence of obesity on adherence to therapy showed that obese patients had a low level of adherence, while patients with a BMI of $< 30\,kg/m^2$ showed a high level of adherence ($P = 0.007$). Obesity is associated with an increased risk for various chronic diseases often associated with the development of depression, which can ultimately accelerate the progression of an already existing chronic disease, due to reduced adherence to recommendations given by health professionals[16].

Our analysis of the influence of smoking habits, dyslipidemia, diabetes, hypertension, and therapeutic modalities on the degree of adherence did not show statistical significance. However, the number of medications in the respondents' therapy had a statistically significant effect on their degree of adherence. Our results indicated a significant correlation between the number of medications applied in therapy and adherence. Due to basic and associated diseases, 63.41% of our respondents took 5 or more medications per day. The respondents who took 4 or fewer medications per day showed a significantly higher level of adherence compared to those who took 5 or more medications per day ($P < 0.001$). Other research has also shown that an increase in the number of medications taken per day correlates with a decrease in adherence[17]. This can be explained by the fact that levels of adherence are significantly influenced by the complexity of therapeutic modalities, including the number of medications taken, the dosing interval, and the duration of therapy[18]. Our results are in accordance with already existing literature data, which indicate that the degree of adherence is higher in patients whose therapy includes fewer medications, and that adherence decreases significantly in therapeutic protocols including 5 or more medications[12,19]. In this regard, it is necessary for doctors to apply a strategic approach in order to improve the degree of adherence to therapy in patients with PAB and associated diseases, considering the comorbidities and the impact of polypharmacy on the final outcome of therapy.

Conclusion

In our study, a low degree of adherence was observed in 28.05% of the respondents. Out of the respondents' individual factors, adherence was statistically significantly influenced by obesity and the number of medications in the therapy, while sex, age, smoking, diabetes, dyslipidemia, the number of risk factors, and type of therapeutic modality did not show this association. ■

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SAŽETAK

Utjecaj individualnih čimbenika na pridržavanje terapije kod bolesnika s perifernom arterijskom bolešću

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Cilj ovog istraživanja bio je ispitati utjecaj individualnih čimbenika na pridržavanje terapije u bolesnika s perifernom arterijskom bolešću (PAD). U istraživanje su bila uključena 82 bolesnika s dijagnozom PAD-a (Fontaine IIa, IIb) koji su liječeni u Klinici za vaskularnu kirurgiju Univerzitetskog kliničkog centra Niš u razdoblju od 1. siječnja do 31. prosinca 2020. godine.

Utvrđena je značajna povezanost između stupnja pridržavanja terapije i zdravstveno povezane kvalitete života u bolesnika s PAD-om. Bolesnici s umjerenim i visokim stupnjem pridržavanja imali su značajno višu kvalitetu života u usporedbi s ispitanicima s niskim stupnjem pridržavanja.

Hi-kvadrat test neovisnosti pokazao je značajnu povezanost između pretilosti ($P = 0,007$) i broja lijekova u terapiji ($P < 0,001$) s pridržavanjem terapije u bolesnika s PAD-om.

Na pridržavanje terapije statistički su značajno utjecali pretilost i broj lijekova u terapiji, dok spol, dob, pušenje, dijabetes, dislipidemija, broj čimbenika rizika i vrsta terapijskog modaliteta nisu pokazali takvu povezanost.

KLJUČNE RIJEČI

Individualni čimbenici; Adherencija; Periferna arterijska bolest