

Quality of life and arterial stiffness indices in patients with chronic limb-threatening ischemia

Qualidade de vida e índices de rigidez arterial em pacientes com isquemia crônica ameaçadora ao membro

Claudineia de Oliveira Otoni¹; Ana Flávia Couret¹; Joana Storino¹; Daniel Mendes-Pinto²; Maria da Glória Rodrigues-Machado¹

ABSTRACT

Introduction: The factors associated with impaired quality of life in patients with chronic limb-threatening ischemia are not well established. **Objective:** Check whether there is an association between quality of life and arterial stiffness indices, pulse wave velocity (PWV) and augmentation index corrected to 75 beats per minute heart rate (AIx@75). **Methods:** This is a cross-sectional, observational study, with the participation of 17 patients (65.65 ± 11.79 years) with chronic limb-threatening ischemia defined by the Rutherford classification 4, 5 and 6, and with the ankle-arm index (ABI) < 0.80. The evaluation of vascular parameters and arterial stiffness indices was performed with the Mobil-O-Graph[®] device that generates the aortic pulse wave from the brachial artery oscillometry. Quality of life was assessed using the questionnaire Vascular quality of life questionnaire (VascuQoL-6), short version, developed specifically to evaluate patients with circulatory, arterial or venous involvement. **Results:** The values of the ITB and the quality of life score were 0.48 ± 0.14 and 15.88 ± 1.03; respectively. Of the 17 patients, 12 had systolic arterial hypertension and sixteen had PWV greater than 10 m / s. No correlations were observed between the quality of life score with AIx@75 (p = 0.54 and r = 0.16), PWV (p = 0.332 and r = 0.248) and ABI (p = 0.707 and r = 0.098). **Conclusion:** The present study demonstrated that patients with chronic limb-threatening ischemia present significant impairment of quality of life without association with arterial stiffness and ABI.

Keywords: pulse wave velocity, arterial stiffness, peripheral arterial disease, aortic pulse wave.

RESUMO

Introdução: Os fatores associados ao comprometimento da qualidade de vida em pacientes com isquemia crônica ameaçadora ao membro não estão bem estabelecidos. **Objetivo:** Verificar se existe associação entre a qualidade de vida e os índices de rigidez arterial, velocidade de onda de pulso (VOP) e o índice de aumento normalizado para a frequência cardíaca de 75 bpm (AIx@75). **Métodos:** Trata-se de um estudo transversal, observacional, com a participação de 17 pacientes (65,65 ± 11,79 anos) com isquemia crônica ameaçadora ao membro definida pela classificação de Rutherford 4, 5 e 6, e com o índice tornozelo-braço (ITB) < 0,80. A avaliação dos parâmetros vasculares e os índices de rigidez arterial foram realizadas com o aparelho Mobil-O-Graph[®] que gera a onda de pulso aórtica a partir da oscilometria da artéria braquial. A qualidade de vida foi avaliada pelo questionário Vascular quality of life questionnaire (VascuQoL-6), versão curta, desenvolvido especificamente para avaliar pacientes com comprometimento circulatório, arterial ou venoso. **Resultados:** Os valores do ITB e do escore de qualidade de vida foram 0,48 ± 0,14 e 15,88 ± 1,03; respectivamente. Dos 17 pacientes, 12 apresentavam hipertensão arterial sistólica e dezesseis apresentaram a VOP maior que 10 m/s. Não foram observadas correlações entre o escore de qualidade de vida com o AIx@75 (p=0,54 e r=0,16), a VOP (p=0,332 e r=0,248) e o ITB (p=0,707 e r=0,098). **Conclusão:** O presente estudo demonstrou que pacientes com isquemia crônica ameaçadora ao membro apresentam comprometimento importante da qualidade de vida sem associação com os índices de rigidez arterial e ITB.

Palavras-chave: Velocidade de onda de pulso. Rigidez arterial. Doença arterial periférica.

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Editor Associado Responsável:

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Conflito de Interesse:

Não há.

Recebido em: 07/08/2020.

Aprovado em: 27/10/2021.

Data de Publicação: 28/01/2022.

DOI: 10.5935/2238-3182.2021e31119

INTRODUCTION

Peripheral arterial disease (PAD) is classified as an atherosclerotic disease caused by narrowing or blocking of the arteries of the lower limbs¹. PAD is highly prevalent worldwide, being a common, serious condition with a high risk of cardiovascular events². The main prognostic factor for PAD is the ankle brachial index (ABI), considered a marker of cardiovascular mortality³. ABI assessment is a simple, low-cost and non-invasive technique. It is measured by the ratio between the systolic blood pressure (SBP) of the posterior tibial and dorsalis pedis arteries with the highest SBP of the brachial artery. ABI values less than 0.9 increase from 2.5 to 5.0 times the mortality from any cause⁴. In addition to general cardiovascular risk, the ABI measurement can identify the patient's risk for lower limb events, requiring a lot of attention and education for wound prevention (*European Society for Vascular Surgery*, 2017).

A recent study⁶ showed that there is an inverse relationship between the degree of limb ischemia, measured by the ABI, and arterial stiffness measured by the rate of increase (Alx@75, *augmentation index*), as well as advanced stages of WIfI (*Wound, Ischemia and Foot Infection*) were predictors of increased pulse wave velocity (VOP) and Alx@75⁷. PWV is the main indicator of arterial stiffness and Alx@75 provides indirect parameters of arterial stiffness and is considered an independent predictor of cardiovascular risk in patients with advanced atherosclerosis⁶.

In this study, the quality of life of patients with chronic limb-threatening ischemia was evaluated using the VasuQoL-6 questionnaire, specific for patients with arterial or venous circulatory impairment in the short version⁷ translated and adapted for the Brazilian population⁸. The aim of this study was to verify whether there is an association between quality of life and arterial stiffness indices in patients with chronic limb-threatening ischemia.

METHODS

This is an observational cross-sectional study, with a convenience sample. Patients were evaluated at the Angiology and Vascular Surgery Unit of a tertiary level hospital. Data collection from the quality of life questionnaire was carried out from October to December 2019. Patients aged between 50 and 90, with ABI <0.80 and who presented with chronic threatening limb ischemia defined by the Rutherford classification 4, 5 and 6, characterized by ischemic ulcer or pain at rest, were included. Patients with stabilized arterial disease, classified as asymptomatic or claudicating (Rutherford classes 0 to 3) and patients with ABI > 1.30 were excluded. Patients with any type of lower limb amputation and cognitive impairment were also excluded.

Comorbidities were considered for analysis. Smokers were considered to be patients who smoked at the time of the interview or who had stopped smoking in the last six months. Diabetes was defined by fasting blood glucose \geq 126 mg / dL or use of insulin or oral hypoglycemic agents. Hypertension was defined as systolic pressure \geq 140 mmHg or diastolic pressure \geq 90 mmHg during the interview or by the use of antihypertensive drugs. Dyslipidemia was defined as total serum cholesterol above 200 mg / dL or use of statins. Past history of coronary interventions or acute myocardial infarction (coronary heart disease), stroke or

transient ischemic stroke and congestive heart failure were considered for analysis.

ANKLE/ARM INDEX MEASUREMENT

This index is defined by the relationship between systolic blood pressure in the ankle and the arm. Foot pressure is measured with a portable continuous Doppler device and aneroid sphygmomanometer. The ABI of each leg is calculated by dividing the highest pressure measured in the posterior tibial and dorsalis pedis arteries (also called the dorsal artery of the foot) by the highest pressure measured in the right or left brachial artery. The limit for the diagnosis of PAD, described in reference publications, is ABI \leq 0,90¹⁰. The examination was performed with the patient in the supine position. The determination of the flow in the tibial arteries was established by means of continuous wave Doppler with a variable probe between 7 and 10 MHz. In this case, the cuff is inflated until the flow is interrupted and then deflated until the auscultation of the arterial sound, at the level of the corresponding systolic pressure.

EVALUATION OF VASCULAR PARAMETERS AND ARTERIAL STIFFNESS INDICES USING BRACHIAL ARTERY OSCILLOMETRY

The evaluation of vascular parameters and arterial stiffness indices were performed with the Mobil-O-Graph device (IEM, Stolberg, Germany)⁴. It is a portable device that captures the variations of the pulse wave in the brachial artery with a cuff with a pressure transducer. The capture of pulse waves in the brachial artery occurs by means of a high-fidelity sensor incorporated in the cuff. After oscillometric measurements of blood pressure, the cuff re-inflates at the level of diastolic pressure for 10 seconds, and captures information from the pulse waves in the brachial artery. The aortic pulse wave is generated using a mathematical transfer function. The program separates the waves by decomposing the aortic pulse wave into ejected and reflected waves. Three consecutive measurements of the aortic pulse wave were performed and the mean between them was considered for final analysis. Arterial stiffness indexes - Alx@75 and PWV - and peripheral and central systolic and diastolic pressures, mean arterial pressure, central and peripheral pulse pressures (defined as the difference between systolic and diastolic pressures) were obtained.

QUALITY OF LIFE ASSESSMENT

Quality of life was assessed using the questionnaire *Vascular quality of life questionnaire* (VasuQoL-6), short version, developed specifically to evaluate patients with circulatory, arterial or venous involvement^{11,12}. This questionnaire consists of six questions, which cover different aspects of social activities and daily activities that are difficult to perform due to poor circulation in the legs¹³. The six items relate to limitation in activities (activity), tired legs (symptom), ability to walk (activity), concerns about poor circulation in the legs (emotional aspects), ability to participate in social activities (social aspects) and discomfort leg pain (pain). The scores for each item vary from one to four points (one, meaning more problems, up to four, meaning without problems). The total score ranges from 6 (worst quality of life) to 24 points (best quality of life).

This study was approved by the Research Ethics Committee of Hospital Felício Rocho (CAAE:

55440616.1.0000.5125). All participants read and signed the informed consent form, duly approved by the Ethics Committee.

STATISTICAL ANALYSIS

The variables were presented as mean \pm standard deviation. The normality of the data was verified by the Shapiro-Wilk test. Associations between quality of life and parameters of arterial stiffness, PWV, AIx@75 and ABI were assessed by linear regression models, using Pearson's or Spearman's coefficient, when indicated. All analyzes were performed using the GraphPad Prism software (version 5.0, GraphPad Software, Inc., La Jolla, California, USA).

RESULTS

86 patients of both sexes who presented with chronic limb-threatening ischemia were eligible for this study. Among those selected, five patients were excluded from the study for refusing to participate, five patients had lower limb amputations, forty-seven patients were not found, three patients were hospitalized, nine patients died. For the final analysis, 17 patients with several associated comorbidities were included.

Table 1 shows the patients' demographic data, comorbidities and medications. Table 2 shows the Rutherford classification with the description of the injuries. Figure 1 shows a representative image of level 5 in the Rutherford classification. With the exception of one patient who presented level 4, the others made up level 5 in the Rutherford classification.

Table 3 shows the central and peripheral vascular parameters, the arterial stiffness indices, ankle / arm index and the quality of life score. Of the 17 patients, 12 had systolic arterial hypertension and sixteen had PWV greater than 10 m / s. The ABI ranged from 0.31 to 0.80. The quality of life score ranged from 11 to 23 (15.88 ± 1.03). No

correlations were observed between the quality of life score and the AIx@75 ($p = 0.54$ e $r = 0.16$), the PWV ($p = 0.332$ e $r = 0.248$) and the ABI ($p = 0.707$ e $r = 0.098$). These results demonstrate that the quality of life, assessed by Vasc-6, did not significantly correlate with the arterial stiffness indexes. *Post-hoc* analysis of the sample size shows a statistical test power for correlations in 82%.

DISCUSSION

This study evaluated the association between quality of life and cardiovascular parameters in patients with chronic limb-threatening ischemia. Limb ischemia assessed by the ITB, the index for measuring the severity of PAD, ranged from 0.31 to 0.80 and the quality of life score ranged from 11 to 23. The quality of life score did not correlate with the AIx@75, VOP and ITB.

The patients in the present study had several risk factors for PAD, such as: diabetes, dyslipidemia and smoking. In addition to these factors, patients were also elderly, contributing to the onset of PAD and worsening quality of life.

This study used the VasuQoL-6 quality of life questionnaire, short version, consisting of six items, covering different aspects of social activities and difficulty in performing daily activities due to impaired circulation in the lower limbs. The results of the present study corroborate the findings of Correia et al (2018). These authors assessed the quality of life in the elderly (68.8 ± 10.6 years) with PAD and observed that the VasuQoL-6 score was 14.6 ± 3.5 . With the exception of obesity that was present in the study by Correia et al (2018), patients had risk factors for PAD similar to that observed in the present study. Corriere et al (2017) evaluated patients with chronic threatening limb ischemia to verify associations between the cumulative number of previous interventions in the treatment of DAP and quality of life adjusted for comorbidities and severity of the disease. The VasuQoL-6 score was 11.6 ± 4.2 and the

Table 1. Patients' demographic data, comorbidities and medications in use by 17 patients with CLTI, evaluated from October to December 2019, at Felício Rocho Hospital.

Variable	Study sample (n=17)
Age (years)	65.65 \pm 11.79
Height (m)	1.69 \pm 0.10
BMI (kg/m ²)	24.70 4.73
Smoking	3 (17.64)
Hypertension	13 (76.47)
Diabetes	11 (64.70)
Dyslipidemia	8 (47.06)
Coronary disease	7 (41.76)
Stroke	3 (17.64)
Antihypertensives	17 (100.0)
Oral hypoglycemic agents or insulin	12 (70.59)

Data are expressed as mean \pm SD (percentage)

CLTI: chronic limb-threatening ischemia. BMI: Body mass index.

Table 2. Distribution of cases according to sex, age, Rutherford classification, WIFI and description of injuries of 17 patients with CLTI, evaluated from October to December 2019, at Felício Rocho Hospital.

n	SEX	Age	Rutherford	Degree of wound ^a	Degree of ischemia ^a	Degree of infection ^a	WIFI Risk of amputation in 1 year	WIFI Benefit of revascularization	Description
1	m	57	5	1	1	0	1	1	Circumferential and superficial lesion in right leg
2	f	89	4	0	1	0	1	1	Rest pain
3	m	69	5	2	2	2	4	4	Lesion in left hallux and toes
4	f	68	5	2	2	1	4	4	Deep lateral injury in right foot
5	f	69	5	1	1	1	1	2	Medial right leg injury
6	m	74	5	2	1	1	3	4	Deep left forefoot injury
7	f	77	5	2	2	2	4	4	Right lateral foot necrosis
8	m	88	5	2	2	2	4	4	Left foot lateral injury
9	m	57	5	1	2	3	4	4	Right foot injury
10	f	79	5	2	1	1	3	4	Left Instep injury
11	f	88	5	2	2	1	4	4	Left Instep injury
12	f	66	5	1	3	1	4	4	Left toe injuries
13	f	74	5	2	3	1	4	4	Necrosis in left toes
14	m	82	5	2	2	2	4	4	Necrosis in two right toes and forefoot
15	f	63	5	0	1	1	2	2	Left lateral leg injury
16	f	83	5	1	0	0	1	1	Left lateral leg injury
17	f	82	5	1	2	1	3	4	2nd right pododactyl injury

M: Male; F: Female; WIFI: Wound, Ischemia and Foot Infection; a. The. Grade of wound, ischemia and infection correspond to the respective grades of the WIFI classification.



Figure 1. Representative image of level 5 in the Rutherford classification. Dry gangrene of the fifth toe of the left foot. Author file.

Table 3. Vascular parameters, arterial stiffness indices, ankle / arm index and the quality of life score, evaluated from October to December 2019, at Felício Rocho Hospital.

Variable	Mean	SD
Blood pressure (BP)		
Peripheral systolic BP (mmHg)	150.2	20.72
Peripheral diastolic BP (mmHg)	80.98	9.43
Peripheral mean arterial BP (mmHg)	112.6	14.00
Peripheral pulse pressure (mmHg)	69.14	14.11
Central systolic BP (mmHg)	132.5	17.35
Central diastolic BP (mmHg)	81.86	9.85
Central pulse pressure (mmHg)	50.22	10.52
Arterial Stiffness		
Augmentation pressure (mmHg)	16.55	7.57
Reflection coefficient (%)	66.02	6.76
Augmentation Index, AIx@75 (%)	34.27	11.10
Pulse wave velocity, PWV (m/s)	13.03	1.93
Ankle / arm index	0.48	0.14
Quality of life	15.88	1.03

CLTI: chronic limb-threatening ischemia.

multiple regression model showed that the largest number of previous interventions had a negative impact and the ABI positively impacted quality of life. Unlike expected, comorbidities were not associated with a worse quality of life. These results suggest that symptoms are the most important factors in determining quality of life.

In the present study, central and peripheral vascular parameters and arterial stiffness indices were evaluated in patients with chronic threatening limb ischemia. Of the 17 patients, 12 had systolic arterial hypertension and 16 had PWV greater than 10 m / s, considered the cutoff point for increased cardiovascular complications¹⁴. The prevalence of hypertension increases with age, reaching 60% over the age of 60 and 75% over the age of 75. Arterial stiffness, which results from arteriosclerosis and loss of elasticity in the large arteries, is the major cause of systolic arterial hypertension in the elderly¹⁵.

In this study, all patients used antihypertensive drugs and still had systolic arterial hypertension and arterial stiffness. Arterial stiffness contributes to the early return of the reflection wave, resulting in high central systolic blood pressure. The increase in the reflection wave increases the augmentation pressure and consequently the AIx@75.

In the present study, the mean PWV was 13,03 ± 1,93 m/s. These results are in agreement with a previous study (Mendes-Pinto et al, 2019) which showed that patients with chronic ischemia threatening the limb had PWV and AIx@75 significantly higher than the control group, matched for age, sex and weight. A negative correlation was also observed between the ABI and the AIx@75, that is, the lower the ABI, the greater the magnitude of the reflection wave and, consequently, the AIx@75. In a recent study (Mendes-Pinto et al, 2020) these findings were confirmed, improving the knowledge in this area and showing that the

advanced stages of WIFI are predictors of arterial stiffness, PWV and AIx@75.

A limitation of this study was the small sample size, which may have limited the power to detect some associations. Prospective studies with a larger sample will be needed to detect whether there is an association between quality of life and arterial stiffness. In addition, the patients came from a single center, making it impossible to extrapolate the results to the general population.

In conclusion, it was observed in the present study that there was no association between arterial stiffness indices and quality of life in patients with limb-threatening chronic ischemia. However, these present an important compromise in the quality of life.

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AUTHORS' CONTRIBUTION

We describe contributions to the papers using the taxonomy (CRediT) provide above: Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing: Mendes-Pinto D., Oliveira - Otoni C., Rodrigues-Machado MG, Storino J. Project administration, Supervision & Writing – original draft: Mendes-Pinto D., Rodrigues-Machado MG. Storino J. Data curation & Formal Analysis: Couret AF, Mendes-Pinto D., Oliveira - Otoni C., Rodrigues-Machado MG..

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